XXIInd Canadian Congress of Neurological Sciences

Vancouver, British Columbia
June 24-27th, 1987

MONDAY, JUNE 22, 1987

PRELIMINARY SCIENTIFIC PROGRAMME

CONGRESS SATELLITE SYMPOSIUM #1 (0830-1700)

MYELINATION AND DEMYELINATION: IMPLICATIONS FOR MULTIPLE SCLEROSIS

This symposium is supported in part by the MS Society of Canada and the Medical Research Council of Canada.

BASIC SCIENCE:

SAM LUDWIN	Mechanism of the CNS remyelination
JOHN KAMHOLTZ	Isolation of cDNA for human myelin basic protein
DAVID PLEASURE	Lipid and protein metabolism in oligodendrocytes
SEUNG KIM	Biology of oligodendrocytes in culture

IMMUNOLOGY:

JOHN SCHRADER	Cytokines in immune regulation
JACK ANTEL	Immune regulation in multiple sclerosis
JOEL OGER	Immunoglobulin secretion in multiple sclerosis
DALE McFARLIN	Immune regulation in experimental allergic encephalomyelitis

VIROLOGY:

PETER DOHERTY	Immune mechanism in the pathogenesis of CNS viral infections
GEORGE RICE	The role of retrovirus in the etiology of demyelinating diseases
LORNE KASTRUKOFF	Mechanism mediating HSV1 induced multiple CNS demyelination
ROBERT FUJINAMI	Molecular mimicry: mechanism of virus induced autoimmunity

CLINICAL ADVANCES IN MS:

CEDRIC RAINE	Pathogenesis of multiple sclerosis: ultrastructural studies
ELLSWORTH ALVORD	EAE as a model of multiple sclerosis
KEN WARREN	Myelin basic protein antibody in multiple sclerosis
DONALD PATY	MRI in multiple sclerosis

TUESDAY, JUNE 23, 1987

CANADIAN ASSOCIATION OF CHILD NEUROLOGY ANNUAL MEETING

FACULTY CLUB, UNIVERSITY OF BRITISH COLUMBIA

ADVERSE EFFECTS OF ANTIEPILEPTIC DRUGS:

S.P. SPIELBERG	Mechanisms underlying idiosyncratic drugs reactions
K. FARRELL	Pharmacological aspects of valproic acid toxicity
EVA ANDERMANN	Teratogenic effects of antiepileptic drugs
P. CAMFIELD	Recommendations for laboratory monitoring for side-effects of antiepileptic drugs

RECENT ADVANCES IN THE STUDY OF PERINATAL BRAIN INJURY:

A. HILL	Hypoxic ischemic brain injury in the term newborn
E.H. ROLAND	Hypoxic ischemic and hemorrhagic brain injury in the premature newborn
O. FLODMARK	Neuroradiological aspects of perinatal brain injury

ASSESSMENT OF VISION IN CHILDREN:

J.E. JAN	Clinical assessment of vision in children
P.K. WONG	Neurophysiological assessment of vision

TUESDAY, JUNE 23, 1987

CONGRESS SATELLITE SYMPOSIUM #2 (1800-2000)

HEADACHE

This symposium and meeting sponsored by SANDOZ CANADA INC.

ROBERT NELSON	Introductory address
E.L.H. SPIERINGS	Recent advances in the understanding of headache
PANEL DISCUSSION	The management of headaches (to be announced)
BUSINESS MEETING	
DINNER	

For registration (free) please contact Dr. M. Gawel (416) 480-4468, (416) 281-3323.

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WEDNESDAY, JUNE 24, 1987

CONGRESS COURSES

COURSE #1 PAIN (Half Day)

CHAIRMAN: Dr. F. LeBlanc

G. VANDERLINDEN	Spinal stimulation for chronic pain
I. TURNBULL	Spinothalamic cordotomy for chronic pain
B. NASHOLD	DREZ surgery for chronic pain
R. TASKER	CNS stimulation for chronic pain

COURSE #2 EVOKED POTENTIALS (Full Day)

CHAIRMAN: Dr. T. Picton

JOHN MURPHY	Physiological principles
TERENCE PICTON	Recording techniques
ARNOLD STARR	Auditory evoked potentials
ANDREW EISEN	Somatosensory evoked potentials
IVAN BODIS-WALLNER	Visual evoked potentials
MICHAEL AMINOFF	Evoked potentials in demyelinating disorders
MARGOT TAYLOR	Pediatric applications
PETER RAUDZENS	Intraoperative monitoring
HELEN NEVILLE	Cognitive evoked potentials
HAROLD WEINBERG	Event-related magnetic fields

COURSE #3 NEURO-GENETICS (Full Day)

CHAIRPERSONS: Dr. M. Hayden, Dr. D. Sadovnick

MICHAEL SMITH	The structure of the gene DNA Polymorphisms
JUDITH HALL	Principles of genetic counselling
BARBARA McGILLIVRAY	X-linked mental retardation (clinical presentation)
COLLIN HAY	X-linked mental retardation (molecular genetic presentation)
MICHAEL HAYDEN	Huntington's Disease
RONALD G. WORTON	Duchene Muscular Dystrophy
ROGER ROSENBERG	Cerebellar ataxia
OKSANA SUCHOWERSKY DONALD CALNE	Genetics of movement disorders, including dystonia, and Parkinson's Disease
EVA ANDERMANN	Genetics of epilepsy
DESSA SADOVNICK	Multiple Sclerosis
PATRICIA BAIRD	Genetics of other common neurological disorders, including migraine, amyotrophic lateral sclerosis, mental retardation and neural tube defects

THURSDAY, JUNE 25, 1987

MORNING

WELCOME	Dr. William A. Webber, Dean Faculty of Medicine, University of British Columbia
PETER SELAND FRANK LEBLANC	PRESIDENTIAL ADDRESS

PLENARY SESSION #1 GUESTS OF THE CONGRESS

CHAIRMAN: Dr. A. Eisen

ALBERT AGUAYO	Guest of the Canadian Neurological Society McGill University, MONTREAL, QUEBEC A spectrum of responses to neural injury in mammalian CNS
ROGER ROSENBERG	Royal College Lecturer University of Texas, DALLAS, TEXAS Molecular genetics and neurological disease: recent advances
BLAINE NASHOLD	Penfield Lecturer Duke University, DURHAM, NORTH CAROLINA Deafferentation pain and the dorsal horn of the spinal cord
ARNOLD STARR	Canadian Society of Clinical Neurophysiology University of California, IRVINE, CALIFORNIA Long latency evoked potentials and cognition
JULIUS METRAKOS KATHERINE METRAKOS	Awardees of the Canadian League Against Epilepsy McGill University, MONTREAL, QUEBEC
PETER CAMFIELD CAROL CAMFIELD	Do all Convulsive disorders need anticonvulsant therapy?

AFTERNOON

FREE COMMUNICATIONS

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FRIDAY, JUNE 26, 1987

PLENARY SESSION #2 AMYOTROPHIC LATERAL SCLEROSIS

CHAIRMAN: Dr. A. Hudson and Dr. A. Eisen

ARTHUR HUDSON	Introduction: Clinical evidence for pathogenetically distinct forms of ALS
SEUNG U. KIM	Tissue culture studies on spinal motor neurons
GLYN DAWSON	The role of gangliosides and hexosaminidase in ALS
JACK ANTEL	Tropic and immunochemical factors in ALS
CARLETON GAJDUSEK	Physiological changes inducing motor neuron disease; common and distinguishing features
ASAO HIRANO	Pathological variations and extent of the disease process in ALS
PETER SPENCER	Environmental factors and diseases of the motor neurons
JOHN STEELE	Geophysical and nutritional factors in Guamanian ALS
ANDREW EISEN DONALD CALNE	Latent Neuro-abiotrophies: A clue to ALS

AFTERNOON

FREE COMMUNICATIONS

SATURDAY, JUNE 27, 1987

PLENARY SESSION #3 REGENERATIVE AND RESTORATIVE NEUROLOGY NEURAL GROWTH AND REPAIR

CHAIRMAN: Dr. A. Aguayo

FRED GAGE	Factors involved in the Transplantation of Functional Grafts to the Brain
TOM REESE	Relationships of Fast Axonal Transport to Growth Cone Extension
RICHARD STEIN	Replacement Function after Nerve Lesions in Man

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XXIInd Canadian Congress of Neurological Sciences

Abstracts of the Scientific Program

Cerebrovascular Diseases I (Platform)

THURSDAY, JUNE 25TH 1330-1700

Co-Chairmen: DR. J.W. NORRIS (Toronto)
DR. B. WEIR (Edmonton)

1.

The Value of Carotid Doppler Ultrasound in Asymptomatic Extracranial Artery Disease

N.M. BORNSTEIN (Toronto, Ontario)

The Francis McNaughton Memorial Prize

Recently a variety of non-invasive tests have been developed to evaluate the extracranial arteries, and data from our carotid Doppler Laboratory has shed light on several controversial aspects of neurovascular disease.

In patients with newly discovered neck bruits the Doppler ultrasound can differentiate between an internal carotid artery lesion and a benign bruit (eg. subclavian artery, external carotid artery or superior thyroid artery). This reassures the patient and the physician and no further investigation is needed. Neurological outcome of patients with asymptomatic carotid bruits is highly correlated with the severity, and subsequent progression of carotid stenosis, two factors which can be accurately detected, determined and evaluated by Doppler ultrasound. Additional B-mode imaging provides the ability to identify different plaque composition and perhaps even to identify unstable plaques.

Carotid artery occlusion is detected with high accuracy by carotid Doppler and our data indicates that the outcome of these patients is relatively benign. Subclavian steal phenomenon is easily detected by continuous wave Doppler and may represent only a harmless hemodynamic phenomenon.

Carotid Doppler ultrasound is a clinically useful device that provides anatomic information using simple hemodynamic principles that produce valuable and accurate information about the extracranial arteries.

2.

Predictors of Survival After Stroke

B.L. SHURVELL, J.W. NORRIS, V. HACHINSKI, J. MUKHERJEE and P. FLANAGAN (Toronto, Ontario)

Seven hundred and nine consecutive patients with cerebral infarction and hemorrhage, admitted to an intensive care stroke unit from a well defined urban catchment area, were followed for at least five years to determine predictors of post stroke survival.

The Cox proportional hazards model was used to identify predictor variables for two clinically defined phases after stroke. The acute phase (first 30 days post stroke) included the following predictor variables: 1) degree of impairment of consciousness (drowsy, stuporous, coma); 2) stroke type (infarction or hemorrhage); 3) total paralysis of the arm, and 4) age. After 30 days (chronic phase) the predictive value for drowsiness, stupor and total arm paralysis remained the same, while the presence of coma became less important and age became more important. The stroke type no longer affected the length of survival.

A prognostic index that reflects the presence of the predictor variables for each patient is provided by the model. For each phase the population was divided into quartiles based on this index. The 30 day survivorship was 96% for the lowest risk quartile and 89, 86 and 51% respectively for the other quartiles. In the chronic phase the corresponding quartiles for 5 year survival were 79, 54, 35 and 23%.

The use of these predicted survival times may have clinical importance for an individual patient. The information may be more relevant to groups of stroke patients where it could prove useful in planning health care resources or measuring the impact of stroke in subjects in therapeutic trials.

3.

Stroke Outcome and The Unstable Carotid Plaque

N.M. BORNSTEIN, A. KRAJEWSKI and J.W. NORRIS (Toronto, Ontario)

In the Toronto asymptomatic cervical bruit study, we have followed 500 patients for a mean of 4.5 years to evaluate the effect of local (arterial) and systemic (metabolic) factors on neurological outcome. In addition, plaques removed from 40 consecutive symptomatic patients were pathologically evaluated and compared with Doppler, angiography and surgical appearances.

In 248 patients (496 arteries), followed clinically and by carotid Doppler for two years, mean stenosis increased from $23 \pm 31\%$ to $32 \pm 34\%$ ($p<0.0001$). Carotid stenosis remained unchanged in 68%, progressed in 28%, and regressed in 4%, ($p<0.0001$). Progression and severity of stenosis were significantly related to occurrence of ischemic neurological events ($p<0.0001$). Putative risk factors for stroke did not play a significant role in progression.

Neurological outcome in patients with carotid stenosis correlates with acute local changes in severely stenosed (>75%) plaques. Progression and regression reflect plaque instability and relate closely to outcome.

4.

Post-operative Patency After Carotid Endarterectomy

W.S. TUCKER, V. CHAUDHRY, E. KLODAS and E. COLAPINTO (Toronto, Ontario)

Between June 1982 and July 1986, 212 consecutive carotid endarterectomies (CE) were performed by the senior author on 193 patients.

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One hundred and twenty-three of the cases were males with an average age of 64 years, while 70 cases were female with an average age of 63 years. Data was collected prospectively for risk factors and the presenting cerebral symptoms.

One hundred and ninety-five operations were performed on a symptomatic stenosed artery. Three operations were performed on a symptomatic occluded artery. Four operations were conducted on the artery opposite to the symptomatic occluded artery. Ten arteries were prophylactically repaired.

Primary closure was performed in 210 procedures and 2 were repaired by saphenous vein grafts. Seventy-seven percent of patients remained on platelet inhibitor therapy at the time of follow-up. Post-operative patency was evaluated by continuous wave doppler scan in 203 vessels and venous DSA or transfemoral arteriography in 4 vessels. The average time interval between the operation and the patency assessment was 225 days with a range of 1 day to 1411 days. Two hundred and four of the 207 vessels assessed were patent (98.6%).

Late follow-up was obtained in 169 of the 193 patients. Six patients died a stroke-death, 4 of whom had the stroke ipsilateral to the operated artery. Two of these 4 cases had occlusion of the repaired vessel at the time of the fatal stroke. One had the stroke contralateral to the operated artery and 1 had a probable vertebrobasilar stroke. Twenty-one patients out of 169 experienced focal cerebral symptoms post-CE. One of these 21 patients had occlusion of the repaired artery at the time of the cerebral symptoms. One hundred and twenty-nine (76.3%) patients were asymptomatic with respect to their repaired carotid vessels.

Current CE technique permits a high post-operative patency rate. Post-operative occlusion is associated with a very high morbidity/mortality.

5.

Borderzone Ischemia

R. LEBLANC, L.Y. YAMAMOTO, J.L. TYLER and A. HAKIM (Montreal, Quebec)

We have studied 7 patients with severe carotid stenosis using positron emission tomography (PET). The six males and one female aged 51 to 68 years (mean: 59.4 years) presented with transient cerebral and/or retinal ischemia (5 cases) or progressive stenosis (2 cases). Three patients had 80% and 4 had 95% or greater atherosclerotic narrowing of the origin of the internal carotid artery. Three patients also had ipsilateral hypoplasia or aplasia of the first segment of the ipsilateral anterior cerebral artery. Cerebral blood flow (CBF), cerebral blood volume (CBV) and oxygen utilization ($CMRO_2$) were measured, and the CBF/CBV ratio and the fractional extraction of oxygen by the brain (OEF) were calculated. These parameters were studied in the anterior and middle cerebral artery distributions and in the borderzone regions between these two arteries (the anterior borderzone) and in the borderzone region between the middle and posterior cerebral arteries (the posterior borderzone). Results obtained in patients were compared, using Student's t test, to those obtained in 6 elderly control subjects of the same age group. The CBF and CBF/CBV ratio were diminished ($p<.05$ and $p<.025$ respectively), indicating hypoperfusion and diminished hemodynamic reserve capacity, in the anterior borderzone region ipsilateral to the carotid stenosis but not in other vascular compartments. There was a tendency towards diminished oxygen utilization but this did not achieve statistical significance perhaps because of the small number of cases.

These data indicate that 1) the borderzone region between the anterior and middle cerebral arteries is especially susceptible to hypoperfusion and 2) transiently symptomatic or progressive carotid stenosis produces hypoperfusion and diminished hemodynamic reserve capacity in this region.

6.

The Effect of Mannitol, Nimodipine and Indomethacin Singly or in Combination on Cerebral Ischemia

G.R. SUTHERLAND, H. LESIUK, A. SIMA and R. BOSE (Winnipeg, Manitoba)

The effect of Mannitol, Nimodipine, and Indomethacin on ischemic neuronal injury was examined in 45 rats subjected to 10 mins of forebrain ischemia (bilateral carotid occlusion and hypotension of 50 Torr). Seven days post-ischemia, the brains were perfusion fixed, sectioned coronally into 2.8 mm slices and stained with H & E. Quantification of dying neurons was performed by direct counting of standardized levels chosen from the serial sections. Results from the CA_3 portion of the hippocampus are presented below:

Group (n = 5)	Ischemic/Ischemic + Normal Neurons	Significance — ANOVA	
1. Control	.80±.07		
2. Normal Saline	.59±.13		
3. Mannitol	.28±.17	<0.05	Compared to Group 1
4. Nimodipine	.35±.21	<0.05	
5. Indomethacin	.44±.12	NS	
6. Mannitol + Indomethacin	.19±.09	<0.05	
7. Mannitol + Nimodipine	.32±.20	<0.05	
8. Nimodipine + Indomethacin	.31±.16	<0.05	
9. Mannitol + Nimodipine + Indomethacin	.04±.04	<0.01 <0.05	Compared to Group 2

A similar distribution was seen within the hippocampal CA_1/CA_2 region, inner dentate blade and frontal cortex. A trend towards increased beneficial effect with triple therapy was found in all regions examined. We conclude that the use of multiple agents in cerebral ischemia is the most effective way of inhibiting irreversible neuronal injury.

(Supported by grants from the Canadian Heart Foundation and Manitoba Health Research Council)

7.

Intrathecal Nimodipine Therapy in a Primate Model of Chronic Cerebral Vasospasm

P.J. LEWIS, B.K.A. WIER, Y. HANDA, M.G. NOSKO and M.G. GRACE (Edmonton, Alberta)

The safety, prevention, and treatment of chronic vasospasm by repeated administration of intrathecally applied nimodipine is being evaluated in a primate model of chronic cerebral vasospasm. Twenty-four female cynomolgus monkeys were randomized into 3 groups of 8: 1) sham control 2) clot-nontreatment control and 3) clot + intrathecal nimodipine. All animals underwent bilateral frontotemporal craniectomy and arachnoid dissection, following baseline angiography. An average of 8 ml of autologous blood clot was placed bilaterally over the major cerebral arteries, in the clot group animals. Nimodipine was administered postoperatively by subcutaneous injection of 1 ml-0.2 mg tid for 6 days, through an Ommaya reservoir with the catheter placed in the subarachnoid basal cisterns. The safety of nimodipine applied in this way and its effect on prevention of delayed ischemic neurological deficits and angiographic vasospasm was evaluated by neurological assessment, repeat angiography at day 7 post-SAH induction, and brain pathological examination. The effect of intrathecally applied nimodipine on dilatation of normal and vasospastic vessels in vivo, was assessed by serial angiography following an injection of 1 ml (0.2 mg) of

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nimodipine into the Ommaya reservoir at day 7 in all animals. Horseradish peroxidase was given intrathecally before sacrifice to study its penetration of normal and vasospastic cerebral vessels from the adventitial surface. The vessels were then studied by scanning and transmission electron microscopy. The results will be reported.

8.

Hemodynamic and Metabolic Effects of Cerebral Arteriovenous Malformations Studied by Positron Emission Tomography

R. LEBLANC, J.L. TYLER, L.Y. YAMAMOTO and A. HAKIM (Montreal, Quebec)

Eighteen patients with an intracranial arteriovenous malformation (AVM) were studied with positron emission tomography. Cerebral blood flow (CBF), cerebral blood volume (CBV), the CBF/CBV ratio, the fractional extraction of oxygen by the brain (OEF), and glucose and oxygen metabolism ($CMRG_1$ and $CMRO_2$) were evaluated in the anterior, middle and posterior cerebral artery distributions in both hemispheres. Results obtained in patients were compared, using Student's t test, to those obtained in healthy young volunteers.

In the ipsilateral hemisphere but in areas remote from the malformation the CBF was significantly decreased in 44% of patients and the CBV increased in 79% of patients. The CBF/CBV ratio, an index of hemodynamic reserve capacity, was most severely decreased with lesions greater than 6 cm. Hemodynamic changes were associated with impaired glucose and oxygen metabolism in 54% and 36% of cases respectively. Hemodynamic and metabolic abnormalities were more frequent and more severe with larger AVMs and were present, to a lesser degree, contralaterally.

These data indicate that 1) shunting of blood through arteriovenous fistulae is detrimental to the ipsilateral brain remote from the lesion as well as to the contralateral hemisphere; and 2) that deleterious hemodynamic and metabolic effects are related to the size of the AVM. The CBF/CBV ratio, an index of cerebral hemodynamic reserve, correlates with increasing size of the AVM and impairment of oxygen metabolism. It can therefore serve as an index of the hemodynamic and metabolic compromise produced by cerebral AVMs.

9.

Nimodipine Administration in Poor Grade Patients Following Subarachnoid Hemorrhage: Results of a Multi-centre, Double-blind, Controlled Trial

L.B. DISNEY (Edmonton, Alberta)

A multi-center trial was carried out to evaluate the safety and efficacy of oral nimodipine in poor grade aneurysm patients following subarachnoid hemorrhage (SAH). Seventeen centers across Canada recruited 188 patients between January 1984 and November 1986. Patients were randomized to receive either nimodipine 90 mg or placebo, every four hours, orally, for 21 days.

Functional outcome in both groups was assessed at 3 weeks and 3 months post SAH. Angiography was carried out on admission and at 8 days post hemorrhage to observe differences in the occurrence and severity of angiographic vasospasm. Survivors to 3 months underwent repeat CT scanning to determine the extent of low density areas.

The incidence of delayed ischemic deficits from vasospasm and subsequent outcome is compared in the placebo and nimodipine groups. All determinations were made in a double-blind fashion by the University of Alberta review committee.

10.

Prognostic Factors For Outcome in Poor Grade Patients Following Subarachnoid Hemorrhage

B. WEIR (Edmonton, Alberta)

Radiographic and clinical data was collected prospectively on 188 poor grade aneurysm patients enrolled in the Canadian Nimodipine Trial. Patients underwent computerized tomography (CT) and cerebral angiography within 96 hours of the ictus. Repeat angiography was carried out at 8 days post hemorrhage and repeat CT was carried out at 3 months post SAH in survivors. Vital signs were measured as soon as possible after the SAH and then every four hours after entry into the nimodipine trial. Patients neurological status was graded daily and noted to be improving, stable, or deteriorating.

Admission and followup CT scans were assessed by a blinded review committee and a determination made as to amount of subarachnoid blood, degree of intraventricular hemorrhage, size of intracerebral clot, degree of ventricular dilatation, degree of periventricular lucency, size of midline shift and size of low density areas.

Angiograms were reviewed and aneurysm size, location and presence or absence of a loculus or daughter aneurysm was noted. Vasospasm extent and severity was graded. The relation of these clinical and radiographic factors to the development of delayed ischemic deficits from vasospasm or rebleeding and to functional outcome at 21 days and 3 months post hemorrhage was determined.

11.

Diagnosis of Post-SAH Vasospasm by Means of Intracranial Pulse-Wave Analysis

E.R. CARDOSO, K. REDDY and D. BOSE (Winnipeg, Manitoba)

Post-subarachnoid hemorrhage (SAH) vasospasm cannot be monitored continuously. However, cases of severe SAH usually undergo intracranial pressure monitoring, thus allowing continuous observation of the intracranial pulse wave (ICPW). Because the amplitude of ICPW may depend upon the caliber of pulsatile intracranial vessels, the effects of post-SAH vasospasm on the amplitude of the ICPW have been investigated.

Continuous pressure recordings from the descending aorta, 3rd cerebral ventricle and cisterna magna were obtained from 30 anesthetized cats. The data was digitized for computerized analysis of the configuration, amplitude and area of ventricular and aortic pulse waves. The cisternal cannula was used for injection of artificial CSF, blood or 5-hydroxytriptamine (5-HT).

Eleven control cats underwent 21 cisternal injections of 2 ml of artificial CSF. There was no significant alteration of wave amplitude and area for systemic arterial pressure and 3rd ventricular pulses. Twelve other animals that underwent cisternal injection of 2 ml of autologous blood showed narrowing of amplitude and area of the 3rd ventricular pulse-wave, with no change in blood pressure wave. Five of these animals which underwent control injections of artificial CSF did not exhibit any changes in the measured parameters. Seven other animals were subjected to cisternal injection of 2 ml of 10^{-4}M solutions of 5-HT, similar to the ones produced by SAH.

Cerebral vasospasm produced by SAH and 5-HT was observed angiographically and compared with measurable changes in the ventricular pulse wave in 8 cats. Angiograms were also performed in 6 control animals showing no vasospasm. The results demonstrate the post-SAH vasospasm in cats can be monitored by analysis of the ICPW. This method may allow early diagnosis and continuous monitoring of cerebral vasospasm in humans.

12.

Early Surgery and Induced Hypervolemic/Hypertensive Therapy in the Treatment of Ruptured Intracranial Aneurysms

J.L. CARON, S.J. PEERLESS, C.C. DRAKE and G.G. FERGUSON (Montreal, Quebec and London, Ontario)

Seventy-eight patients submitted to surgery within 96 hours of their last subarachnoid hemorrhage (SAH) were analysed following hypervolemic - hypertensive therapy in the postoperative period. There were 30 males and 48 females. After clipping of the aneurysm(s), treatment consisted of maintaining normal intravascular volume with blood pressure kept at/or 10 to 20 mm Hg above baseline systolic pressures. If delayed ischemic neurologic deficits occurred, aggressive intervention to maintain a systolic blood pressure of 180 to 200 mm Hg and a central venous presure of 15 cm to H_2O was initiated with intravenous infusions of crystalloid and/or albumin, and dopaminergic vasopressor agents. At the time of discharge, 67 of the 78 patients (86%) obtained an excellent or good result; 58 of the 64 grade I and II patients (91%) achieving a similar outcome. The size and site of the aneurysm had no influence on the final outcome. Out of 17 patients with delayed ischemic neurological deficits (22%), presumably from vasospasm, three had severe permanent residual deficits (4%), and one died of the effects of vasospasm (1.3%). These results are compared to similar reports using the calcium channel blocking agent, Nimodipine, and showed no significant difference in the final outcome. This study supports the hypothesis that acute surgical treatment in combination with improved blood rheology and increased cerebral perfusion obtained with the hypervolemic - hypertensive therapy is beneficial in good grade patients harboring uncomplicated ruptured intracranial aneurysms.

Cerebrovascular Diseases II (Poster)

THURSDAY, JUNE 25TH, 1987 P.M.

13.

Gauze Reinforcement of Aneurysms: Hazards of "Gauzoma"

I.P. CHAMBI, R.R. TASKER, F. GENTILI, W.M. LOUGHEED, J. MARSHALL, H.D. STEELE and S.K. LUDWIN (Toronto, Ontario)

It is a common practice to wrap berry aneurysms with chopped muslin gauze, either to reinforce a technically inadequate clipping, or to provide added insurance after apparently adequate clipping.

We report 4 patients in which various problems - cranial nerve deficits, headache, epilepsy and death followed 2-16 months after surgery for ruptured aneurysms in which the aneurysm was clipped and the clipping reinforced with chopped muslin gauze. One patient went on to develop extensive fibrosis due to foreign body type granulomatous inflammation and to die four years after the gauze application. This shocking experience led to a careful literature search. Based on the experience of these four patients, we can state that:

1. The application of gauze around an aneurysm at various sites in the anterior circulation produces a gauzoma which may represent as an enhancing mass on C.T.
2. The gauzoma may be associated with an inflammatory reaction producing localized headache, csf pleocytosis, evidence of bacterial infection.
3. The gauzoma mass may lead to focal epilepsy, or cranial nerve palsies; thus the seriousness of gauzoma adjacent to the optic and oculomotor nerves.
4. The clinical course suggests ischemic events affecting smaller arteries. Angiography never demonstrated vessel occlusion.
5. All our patients were females. However, no other risk factors emerge.

We make the plea that gauze wrapping of aneurysms be discontinued, especially in the vicinity of the optic nerves, especially if there is no concern about the adequacy of clippings of the aneurysm.

14.

Ictal Anosognosia

F. GRAND'MAISON, J. REIHER, M.L. LEBEL and J. RIVEST (Sherbrooke, Quebec)

Lasting anosognosia is a well-known manifestation of non-dominant parietal lobe lesions. That anosognosia may also occur as a sudden, brief and transient phenomenon, as in five of our patients, is less well-known and deserves wider recognition.

In four (4) patients, transient anosognosia for equally short-lived left-sided hemiparesis was a manifestation of transient ischemic attacks (TIAs). In one patient, diagnosis was delayed; untreated, he suffered a completed stroke with lasting anosognosia and hemiparesis. In three (3) patients, early diagnosis led to prompt and successful treatment.

The remaining fifth patient, anticoagulated for vertebro-basilar TIAs, was initially referred because of a left hemiparesis and non-fleeting anosognosia; anticoagulants were discontinued, and an intracerebral right parietal hematoma evacuated. Two years later, while under treatment for recurrent left sided motor seizures, two episodes of transient anosognosia and left hemiparesis of ten and twenty-five minute duration were witnessed. Since their very onset was not ever observed, possible considerations included manifestations of Todd's phenomenon and TIAs.

Ictal anosognosia can be a manifestation of widely diverse pathophysiologic mechanisms. Early recognition, despite potentially misleading patient denial, is mandatory for proper diagnosis and for prompt initiation of specific therapy.

15.

Late Treatment Failure in Giant Cell Arteritis: The Role of Atherosclerosis

J. GORDON, Y. ROBITAILLE and D. MELANSON (Montreal, Quebec)

A 62-year-old man with multiple atherosclerotic risk factors presented to our hospital with transient cerebral ischemia and a six week history of systemic symptoms characteristic of giant cell arteritis. After initial diagnostic uncertainty, treatment was initiated and progressed from standard therapy with steroids and anticoagulants to empirical trials of angioplasty and intensive immunosuppression. Temporal artery biopsy and cerebral angiography were non-diagnostic. Despite treatment, his condition deteriorated relentlessly over six months, culminating in death from cerebral ischemia. Autopsy confirmed the presence of both giant cell arteritis and severe atherosclerosis.

Existing literature suggests that early giant cell arteritis is responsive to treatment with steroids. Treatment failure late in the disease is not generally discussed, and is never explained. We propose that treatment failed in our patient because of coexisting giant cell arteritis and severe atherosclerosis, the combination of which produced refractory disease. We suggest that late treatment failure in giant cell arteritis might, in other cases, be similarly explained.

16.

Microanatomy of Heubner's Recurrent Artery

G. MOHR and W. GORCZYCA (Montreal, Quebec)

The microvascular anatomy of Heubner's recurrent artery (RAH) was studied in 50 human brains (100 hemispheres) using acrylic paint under the operative microscope. In 30 cases, the vessels were opacified

using lead-oxyde for radiological examination and in 4 cases, india-ink was used to visualize the capillary bed on coronal slices.

The recurrent artery of Heubner was constantly found in this study: a single vessel was found in 28 cases (28%) and multiple vessels were observed in 72%, double vessel in 48%, triple in 23% and quadriple in 1%. Altogether 197 RAH were found in 100 hemispheres averaging 1.97 arteries per hemisphere. In 44 instances, the RAH originated from the proximal part of the A_1-segment of the anterior cerebral artery (ACA) and in 153 instances, it originated from the proximal part of the A_2-segment of the ACA or at the junction of the ACA and the anterior communicating artery (ACoA). The diameters of the RAH ranged from 0.4 mm to 1.5 mm. Their vascular territory was variable including the anterior part of basal ganglia - head of caudate nucleus, lenticular nucleus-, the anterior limb of internal capsule - in few cases also the genu-, the frontal cortex and the anterior hypothalamus.

Four groups of distributing branches were found in the RAH: frontal and hypothalamic, olfactory, perforating and sylvian-fissure branches. Only the perforating branches were found in all cases, most often passing through the lateral part of the anterior perforating substance. The olfactory branch was observed in 85 cases whereas the frontal, hypothalamic and sylvian branches were small and inconsistant. In one case, the RAH vascularized a large section of the left frontal lobe. Perforating branches of the RAH vascularized the head of the caudate nucleus, the anterior part of the lenticular nucleus and the anterior portion of the internal capsule.

In 12 hemispheres, anastomoses were found between the perforating branches of the RAH and the middle cerebral artery. In 5 cases (5%) anastomoses were present between the perforating branches of the MCA and the olfactory branch of the RAH. In one case (1%) an anastomosis was found between 2 RAH.

17.

Rupture of Middle Cerebral Artery Aneurysm in a Newborn: Value of Early Diagnosis and Treatment. Case Report and Review of Literature

F.B. MAROUN, G. RONAN, W. ANDREWS, B. CRAMER, W. HENEGHAN and J.C. JACOB (St. John's, Newfoundland)

Rupture of cerebral aneurysm in the newborn is extremely rare. A 3-day-old newborn presented with focal seizures involving the face and arm immediately after birth. Cranial ultrasound followed by CT and angiography revealed a large M.C.A. aneurysm with massive intracerebral hematoma and cerebral spasm leading to infarction of the majority of the hemisphere. Successful surgical treatment was achieved.

The importance of early diagnosis and treatment is emphasized. Review of the literature of ruptured M.C.A. Aneurysm in the neonate will be presented.

18.

Pediatric Moyamoya Disease: Surgical Options and Results

R. GRIEBEL, H.J. HOFFMAN and H. SCHUTZ (Saskatoon, Saskatchewan)

Moyamoya is a progressive disease of childhood that can cause permanent disability. The search for effective treatment has been largely unsuccessful in the past, but recent efforts of surgical intervention have shown promising results.

Twenty-three children with radiologically confirmed moyamoya disease have been seen at the Hospital for Sick Children in Toronto from 1971-1985. The clinical features of these patients, as well as their treatment and outcome, are reviewed. Eight of the children were not treated surgically and of these 2 have died and all but 1 of the remainder are severely disabled, either mentally or physically. Fifteen of the children were treated with surgical procedures, including superficial temporal artery to middle cerebral artery bypass and/or encephalo-duro-arteriosynangiosis (EDAS). Three of the 5 patients who underwent an STA-MCA anastomosis, have had excellent results and the results have been good in 2. Seven of the 13 patients who underwent an EDAS procedure have had an excellent result, while neurological status of the 6 others has either improved or stabilized. These findings would seem to support that early aggressive management is indicated in all cases of confirmed moyamoya disease.

19.

Lidocaine Partially Protects Against Ischemic Cell Injury in Rats

G.R. SUTHERLAND, B. ONG and A. SIMA (Winnipeg, Manitoba)

The effect of Lidocaine on ischemic neuronal injury was examined in 18 rats (one control group, one group received normal saline (1.5 cc) and a third group Lidocaine (5 mgm/Kg) diluted in normal saline to 1.5 cc) subjected to 10 minutes of forebrain ischemia (bilateral carotid occlusion and hypotension of 50 Torr). Seven days post-ischemia, the brains were perfusion fixed, sectioned coronally into 2.8 mm slices and stained with hematoxylin and eosin. Quantification of dying neurons was performed by direct counting of standardized !evels chosen from the serial sections and expressed as ischemic neurons/ischemic + normal neurons. Comparisons were made by an analysis of variance followed by Tukey HSD procedure.

In the hippocampal CA_1/CA_2 region, Lidocaine treated animal showed less ischemic injury ($.34 \pm .14$) compared to the other two groups (control: $.64 \pm .09$ and normal saline: $.70 \pm .10$) $P<0.08$. The comparison between the Lidocaine ($.31 \pm .14$) and the control group ($.80 \pm .05$) reached greater significance in the CA_3 region $P<0.05$. However, in this region, ischemic injury in the normal saline group ($.59 \pm .13$) was not significantly greater than the Lidocaine group nor significantly less than the control group.

Other regions examined, i.e. hippocampal CA_4 region, dentate gyrus, medial frontal, and lateral inferior frontal cortex showed no difference in ischemic neuronal injury between groups. We conclude that Lidocaine has a mild beneficial effect on forebrain ischemia in the rat seen only in the pyramidal layer of the hippocampus.

(Supported by grants from the Canadian Heart Foundation and the Manitoba Health Research Council)

20.

Staged Territorial Surgery for Giant Arteriovenous Malformations

K.C. PETRUK (Edmonton, Alberta)

Four patients with giant arteriovenous malformations were managed with staged territorial excisional surgery in an attempt to reduce the incidence of intraoperative and postoperative normal perfusion pressure breakthrough. Complete excision of the AVM's previously considered inoperable, was achieved without incidence of significant permanent morbidity.

Surgical strategies based on comprehensive preoperative and intraoperative neuroangiographical techniques were utilized. A modified bipolar coagulating system was found to be superior to conventional bipolar coagulators in occluding small, thin-walled vessels at the periphery of the AVM's.

Complete angiography was performed preoperatively, after completion of the first stage of surgery and upon total removal of the AVM's. Each patient required two surgical procedures staged 1-4 weeks apart.

This surgical approach appears to minimize the risks of normal perfusion pressure breakthrough and provides an alternate method for transforming inoperable or marginally operable AVM's into totally excisable lesions. The rationale for utilizing the staged territorial surgical technique for giant AVM's will be discussed.

21.

Evidence for a Role of Epilepsy in the Development of Ischemic Brain Damage

C.L. VOLL and R.N. AUER (Calgary, Alberta)

Post-ischemic epilepsy is a subject often ignored in ischemia models because it is felt that epilepsy "contaminates" the interpretation of damage from the ischemic insult. In a rat model, we studied the clinical course, EEG activity, and histopathologic outcome of 10 minutes of transient forebrain ischemia. All rats were examined, and no rats were excluded because of epilepsy.

The rats were studied over the course of one week, with serial recording of clinical behaviour, blood glucose levels, EEG, and whole brain subserial sectioning and histologic examination.

Post-ischemic epilepsy was found to be a naturally occurring phenomenon, usually developing between 18 and 24 hours post-ischemia. Animals with violent epilepsy had a high mortality rate, but some recovered. Their brains tended to show greater histologic damage than animals without epilepsy.

Electroencephalographically, spike activity was seen. Spikes were also present in rats without overt clinical epilepsy, and slow waves were also present.

Pathologically, the thalamic reticular nucleus, a major inhibitory center known to consist solely of GABAergic neurons, was consistently destroyed. Focal pars reticulata infarcts were seen in the midbrain, akin to those described in "pure" epileptic insults. Damage was also seen in the neocortex, hippocampus, thalamus and caudate nucleus.

The findings suggest a role for post-ischemic epileptic activity in the development of ischemic brain damage.

22.

Calcium Antagonism in Experimental Middle Cerebral Artery Occlusion

R. LEBLANC and B. MAGWOOD (Montreal, Quebec)

We studied the effects of the calcium antagonist flunarazine on middle cerebral artery occlusion (MCA-0) in the cat using cerebral fluorescein angiography and krypton-85 (Kr-85) cortical blood flow analysis.

A hemispheric craniectomy was performed and the dura elevated, exposing the cortex and epicerebral circulation. Fluorescein angiography and Kr-85 blood flow studies were performed to obtain control values in the resting state (n = 9), and the MCA was the occluded by a transorbital approach. In the first series of experiments (n = 3), fluorescein angiography and Kr-85 flow studies, performed 30 minutes after MCA-0, documented severe ischemia in the MCA distribution and in the anterior and posterior watershed regions. Continuous intravenous infusion of flunarazine (1 mg/kg/hour) was instituted and fluorescein angiography and Kr-85 flow studies were repeated one and two hours later. The flow values in the MCA distribution became unobtainable, those in the anterior watershed region remained unchanged, and those in the posterior watershed region deteriorated. These results indicate that calcium antagonism following MCA-0 does not improve blood flow in the ischemic region. In the second series of experiments (n = 3) a continuous infusion of flunarazine (.05 mg/kg/hour) was instituted one hour before MCA-0. This resulted in a 40% decrease in cerebral blood flow in the MCA distribution at one hour following MCA-0 compared to unobtainable values in the placebo group (n = 3). A lesser degree of ischemia (20% and 11% respectively) was seen in the anterior and posterior watershed regions. These results indicate that pretreatment with flunarazine may mitigate the deleterious effects of MCA-0, probably by increasing blood flow across the watershed regions.

Pretreatment with calcium antagonists may be useful in cases where a cerebral artery is temporarily occluded during aneurysm surgery, or during carotid endarterectomy.

23.

Carbon Dioxide Laser Endarterectomy and Associated Prostaglandin Activity

F.W. GAMACHE, B.B. WEKSLER and D. ALONSO (New York, New York)

Laser irradiation of arterial endothelial surfaces has been used as a method for reducing arteriosclerotic plaque. Laser treatment has been associated with a reduction in prostacyclin (PGI_2) biosynthesis by arteriosclerotic vessels. To investigate the effects on the endothelial and muscular layers of the vessel both histologically and biochemically, the morphology and the formation of arachidonic acid products (thromboxane and PGI_2) were sampled in carotid arteries of normal dogs prior to, immediately following, and 3 hours following laser endarterectomy. Eight dogs weighing approximately 10 kg each underwent this procedure. A standard Sharplan carbon dioxide laser was employed for the endarterectomies. Vessels were obtained and immediately fixed for standard light and scanning electron microscopy. Segments immediately adjacent to the fixed segments were removed to iced medium for analysis of prostaglandin synthetic capacity by stimulation with arachidonic acid and subsequent RIA for 6-keto PGF_{1a} and thromboxane B_2, the stable hydrolysis products of PGI_2 and thromboxane A_2, respectively. An additional segment of artery from which the laser-induced coagulum had been removed prior to recirculation of blood through the endarterectomized vessel was also studied in each case. Laser angioplasty reduced 6-keto PGF_{1a} synthesis as well as thromboxane B_2 synthesis in carotid segments. The production of both substances was also reduced at the endothelial surface following laser endarterectomy. Despite these findings, areas of gross thrombus deposition were observed three hours following recirculation when the arteriotomy was reopened. Increased thromboxane was associated with these thrombi and the underlying vascular surface. These findings contrast with reports of angioplasty using other lasers. The implications of these vascular changes for surgical endarterectomy techniques require consideration.

24.

Non-Vascular Stroke: Mitochondrial Encephalomyopathies

A. PENN, V.P. SWEENEY, S.A. HASHIMOTO, J.L. LEE and L. HALL (Vancouver, British Columbia)

Stroke-like episodes are a feature of mitochondrial encephalomyopathies (ME). We have studied two families with this feature.

In one patient with parosysmal episodes of cortical blindness, myoclonus and stupor we observed two such attacks associated with heavy exercise sufficient to produce marked acidaemia. I.V. $NaHCO_3$ reversed the second attack rapidly and appeared to shorten further spontaneous attacks if given early. There was no change in the EEG during the ictus.

Dynamic P^{31} MRS of skeletal muscle confirmed a compromised bioenergetic economy with early and profound utilization of PCr at low mechanical work rates and inappropriately high lactate production. Muscle biopsy revealed ragged red fibers.

Conclusions:

1. Stroke-like episodes in ME may not represent the inability to deliver O_2 to brain but the inability to use it.
2. P^{31} MRS of skeletal muscle confirms a compromise of bioenergetic economy apparent under increased work load. If brain shares this compromise then threshold for decompensation metabolically may be reduced.
3. Systemic acidosis appeared to be sufficient to decompensate our patient. On a vascular basis, acidosis if anything, should augment cerebral blood flow.

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4. Acidosis may therefore be producing metabolic decompensation. Measures aimed at avoiding and treating acidosis in this patient appear to have helped her considerably.

25.

Cerebral Protection During Temporary Arterial Occlusion in Aneurysm Surgery

M.W. McDERMOTT, F.A. DURITY and M.A. MOUNTAIN (Vancouver, British Columbia)

Temporary arterial occlusion during aneurysm surgery aids in dissection of the aneurysm neck and provides protection from inadvertent aneurysm rupture. While short periods of occlusion seem to be tolerated, the resultant regional cerebral ischemia with prolonged occlusion carries an increased risk of stroke.

Barbiturates have been shown to protect the brain from focal ischemia/hypoxia by reducing the size of infarction that follows middle cerebral artery occlusion in animal models.

In a review of 171 cases of intracranial aneurysms treated by one surgeon between 1980-1986, 28 cases received intraoperative barbiturate protection during temporary arterial occlusion. Seven patients (25%) had unruptured aneurysms. Barbiturate doses of 10 mg/kg (21/28) and 15 mg/kg (7/28) were used. Occlusion times ranged from 3 minutes to 92 minutes 50 seconds, with an average of 12 minutes 42 seconds. Six of the twenty-eight patients had new neurological deficit immediately post-operative and in two these persisted. Twenty-one (75%) had a good clinical outcome and there was no operative mortality.

We believe that barbiturate protection during temporary arterial occlusion is a safe technique. In difficult cases it allows for complete dissection of the aneurysm neck, identification and preservation of the surrounding vascular anatomy, while reducing the risk of intraoperative aneurysm rupture and intra-/post-operative stroke.

Neurobiology I (Platform)

THURSDAY, JUNE 25TH, 1987 1330-1515

Co-Chairmen: DR. S.U. KIM (Vancouver)
DR. P. GIRVIN (London)

26.

Investigation into the Mechanism of Action of Somatostatin on Cortical Neurons

T.W.J. WATSON and Q.J. PITTMAN (Calgary, Alberta)

The Jasper Prize

Somatostatin (SS_{14}) is a putative central neurotransmitter found in high concentration within neurons in a number of areas of the mammalian CNS. In Alzheimer's Disease (A.D.) the level of SS_{14} is reduced in cerebral cortex to a degree similar to the reduction in levels of acetylcholine. Senile plaques in A.D. stain positive for SS_{14} immunoreactivity and somatostatinergic neurons contain neurofibrillary tangles. In Huntington's Disease the levels of SS_{14} are markedly elevated in the basal ganglia. Thus the neurochemical evidence suggests that SS_{14} may play a role in the pathophysiology of these disease processes, however, the actions and physiological roles of SS_{14} are poorly understood. The purpose of these experiments was to investigate the electrophysiological effects of SS_{14} and the underlying mechanism.

350 μm thick transverse rat hippocampal slices were submerged in the recording well of a standard slice chamber, maintained at 32-34°C and continuously perfused with oxygenated artificial CSF. Intracellular records were obtained from CA1 pyramidal neurons using high resistance glass capillary microelectrodes and conventional recording techniques. Known concentrations of SS_{14} were applied via the bath.

SS_{14} caused a hyperpolarization and inhibition of firing associated with an increase in membrane conductance. This persisted in TTX and in low Ca/high Mg containing perfusate where synaptic transmission was blocked. The effect of SS_{14} could be blocked by membrane hyperpolarization. The hyperpolarization was not altered by recording with 2M KCl filled electrodes and does not involve an increase in Cl^- conductance. 10 μm TEA and partial Cs loading with a 2 M Cs-acetate filled microelectrode failed to block the response. The response was also blocked by 1 mM Ba in the perfusate. These results indicate that SS_{14} exerts a direct inhibitory effect on CA1 pyramidal neurons by activation on a membrane K^+ conductance possibly involving m channels.

27.

A New Polymorphic DNA Marker (D4S62) which Maps Close to the Gene for Huntington Disease

M.R. HAYDEN, J. HEWITT, J. HAINES, P. MacLEOD, J.J. WASMUTH, S. LANGLOIS and J. KASTELEIN (Vancouver, British Columbia)

The finding of a closely linked polymorphic marker (D4S10) to the gene for Huntington disease has allowed development of a programme in Canada for preclinical and prenatal detection of this disorder. We report the results of genetic linkage studies in Canadian families with HD using a new polymorphic DNA probe (D4S62). Maximal lod scores obtained for a linkage between D4S10 and D4S62 are 4.85 at a $0 = 0.03$. Southern blot analysis to a human-hamster hybrid panel containing chromosome 4 and derivatives of the short arm of 4 maps the newly described marker to 4p is − 4pter. Once this DNA fragment (D4S62) is more precisely mapped, it will be able to be used for preclinical and prenatal diagnosis of HD in conjunction with D4S10.

28.

Adult Human Neurons Cultured in Vitro

S.U. KIM (Vancouver, British Columbia)

Survival of neurons in tissue culture has traditionally depended on the use of fetal or neonatal animals as a source of tissue. Attempts to maintain adult mammalian neural tissue in culture have met with variable success. Although several groups have previously cultured adult peripheral nervous system (PNS) neurons of mouse, guinea pig and rabbit, reports of successful culture of adult mammalian central nervous system (CNS) neurons have been much less convincing. In many cases, published photographs are of glial or fibroblastic cells.

We now report the unequivocal survival of neurons from the adult human CNS and PNS tissues in culture. Retinas from three adult humans (ages 29, 55 and 81) were obtained at autopsy, and maintained in vitro as small explants for as long as 152 days. Electron microscopy showed the preservation of normal neurons with intact synapses, photoreceptors and Müller cells. Trigeminal ganglion from two adult humans (ages 26 and 46) and sympathetic ganglion from one adult human (age 39) obtained at autopsy, were also prepared as dissociated single cell cultures and maintained for as long as 184 days. Electron microscopic examination of these neurons revealed all the ultrastructural features of healthy adult neurons. Of interest in these neurons is an accumulation of lipofuscin granules in the cytoplasm. The availability of adult human neurons maintained in culture should provide a model system for the investigation related to the nerve regeneration and neuronal aging.

29.

Phosphene Descriptions From Electrocortical Stimulation and Their Implications for an Artificial Prosthesis

J.P. GIRVIN (London, Ontario)

Over the last 18 years a number of studies have been done on sighted and unsighted individuals who have had their visual cortex stimulated under either local anesthesia for therapy, or chronically for experimental reasons. These studies were aimed at providing and collecting information which might be useful in the provision of artificial vision for the blind. Such a neuroprosthesis would consist of visual detection by a miniaturized camera, processing of this information and interfacing it with a stimulating electrode array over the visual cortex in such a way that the image from the periphery would be transferred into picture created by the multiple phosphenes as a result of multi-electrode stimulation.

Individual phosphenes, to be useful in such a prosthesis, should be small, homogeneous, densely packed, and of similar form. Unlike a reading prosthesis, a mobility prosthesis would require brightness modulation. Brightness modulation in turn would require the manipulation of the stimulus parameters.

From the literature available, the most potent stimulus parameter for varying brightness of individual phosphenes is that of current strength. The present report concerns the relationship between phosphene description and current strength. As the current strength is raised, there is a marked increase in a multiplicity of phosphenes. Such multiplicity comprises resolution and hence gives rise to concern about the usefulness of variation in current strength for achieving brightness modulation.

The results of stepwise increases in stimulus strength on phosphenes, the form and size of phosphenes, and the implications of multiplicity regarding visual cortical physiology will be discussed.

30.

Modulation of Laminin by Sensory Neurons *In Vitro*

R.J. RIOPELLE, S. MIRSKI and J.C. RODER (Kingston, Ontario)

Dissociated chick embryo sensory neurons adhere to and extend processes on laminin. In the presence of the monoclonal antibody HNK-1 (Leu 7) which recognizes a neuronal cell surface epitope, there was a time-dependent inhibition of process formation that was unrelated to influences on adhesion of viable neurons. Inhibition was not observed in the presence of two monoclonal antibodies to peptide domains of myelin-associated glycoprotein (MAG) which is expressed by sensory neurons and bears the carbohydrate epitope recognized by HNK-1 (Leu 7). When the laminin substrate was pre-treated with neuron-conditioned culture medium, maximal inhibition by HNK-1 (Leu 7) was observed from the earliest times. These data provide evidence for modulation of laminin by neuronal release of molecular species which interact with laminin and influence neurite outgrowth via a receptor at or in juxtaposition to the HNK-1 (Leu 7) epitope.

These observations provide a framework for approaching the molecular basis of pathway guidance and exquisite connectivity during growth and regeneration of axons.

Supported by MRC Canada and the M.S. Society of Canada.

31.

Cytoskeletal Elements in Motor Nerve Terminal Sprouting: An Immunocytochemical Study of Topographic Changes

W. YEE and A. PESTRONK (London, Ontario)

Evidence that axonal cytoskeletal elements play important roles in nerve sprouting and regeneration have come essentially from in vitro studies of neurite outgrowth from neuronal cells in culture. We studied the participation and axonal cytoskeletal elements in nerve outgrowth in an adult in vivo model. Immunocytochemical techniques were used to examine the sequential changes in topography of neurofilaments, microtubules and microfilaments in motor nerve terminal sprouting induced by botulinum toxin.

The soleus and rhomboid muscles of adult rats were directly injected with botulinum toxin to evoke nerve termnal sprouting. Thick longitudinal cryostat sections of muscles removed at 0, 5, 9 and 15 days, were first stained for cholinesterase to demonstrate the motor end plates. Neurofilament protein, both phosphorylated and non-phosphorylated, tubulin and its — and subunits, and cytoplasmic actin were demonstrated in the distal motor axons and terminals using a peroxidase anti-peroxidase technique, with monoclonal and polyclonal antibodies to these cytoskeletal elements as primary antibodies.

Nerve terminals and sprouts were strongly stained for neurofilament protein, with both phosphorylated and non-phosphorylated forms present. Staining for tubulin and actin was well demonstrated in the distal axons but staining in fine nerve terminals and sprouts was not clearly distinguished from background, a result we relate to relative smaller amounts of these elements. However, in the rhomboid muscle, which exhibited more profuse sprouting than the soleus, at individual endplates, tubulin staining of single large ultraterminal sprouts was demonstrated at day 15. This finding suggests a selective process of differentiation occurring among the many nerve sprouts.

Our results suggest that the topographic distribution of cytoskeletal elements in nerve terminal sprouting in vivo differs from that of neurite outgrowth in culture systems. Further studies using ultrastructural immunocytochemistry is in progress.

Neurobiology II (Poster)

THURSDAY, JUNE 25TH, 1987 P.M.

32.

Nuclear Magnetic Resonance Characterization of Astrocytoma Cells

J.F. MEGYESI, R.F. DEL MAESTRO and E. STROUDE (London, Ontario)

Since vasogenic brain edema is a major contributer to morbidity and mortality in patients with intracranial tumours its characterization is of importance. Nuclear magnetic resonance spectroscopy has proven to be a useful method of determining the properties and distribution of water molecules in tumours and the associated edematous tissue. The two parameters studied are the spin-lattice relaxation time (T1) and the spin-spin relaxation time (T2), both of which are elevated in edematous tissue. The C_6 astrocytoma line is a reproducible rat model with many of the characteristics found in malignant human glial tumours. It can be grown in monolayer and then into spheroids of progressively increasing diameter. An *in vitro* study was undertaken in order to determine the effect of spheroid size on the T1 and T2 relaxation times. The C_6 astrocytoma cells were grown in monolayer and then into spheroids of 350 microns, 550 microns, and 900 microns respectively. Results show that both T1 and T2 become progressively elevated from cells in monolayer through to the 550 micron size but then both decrease at the 900 micron size. These results suggest that T1 and T2 relaxation times are not a static feature of a tumour cell line but may reflect changing microenvironments. The distribution of bound and unbound water and other factors such as cell cycle may also contribute to the values measured. The T1 and T2 relaxation times which are seen in tumour tissue may be the result of a number of dynamic interrelating factors.

33.

Gamma-Aminobutyric Acid (GABA) and Sepsis-Related Encephalopathy

T. WINDER, G.Y. MINUK, L.E. NICOLLE, T.P. SELAND (Calgary, Alberta)

GABA, a potent inhibitory neurotransmitter, has recently been implicated in the pathogenesis of hepatic encephalopathy. In order to determine whether GABA might play a role in the pathogenesis of other disorders associated with altered levels of consciousness, serum and CSF GABA levels were measured by ion-exchange fluorometry in 11 adult patients with bacterial or viral sepsis and depressed levels of consciousness. The results were then compared to 16 age and sex matched control patients with predominantly disc disease and without evidence of sepsis or alterations in consciousness. Septic patients had significantly elevated serum GABA levels (0.40 ± 0.11 μM, mean ± SD) compared to controls (0.26 ± 0.16 μM, $p<0.05$). CSF GABA levels, however, were similar in the two groups (0.85 ± 0.72 μM vs. 0.78 ± 0.52 μM respectively) ($p = 0.77$). In order to exclude the possibility that CSF GABA concentrations might not reflect brain tissue levels, GABA concentrations in six areas of the brain (cortex, diencephalon, striatum, hippocampus, midbrain, and pons-medulla) were measured in a rat model of sepsis (cecal ligation and perforation) ($N = 7$) and the results compared to those obtained from sham operated control animals ($N = 6$). All septic animals demonstrated signs of encephalopathy and had elevated serum GABA levels (0.92 ± 0.3 μM versus 0.48 ± 0.15 μM in controls, $p<0.01$). GABA content in the specific subcompartments of the brain, however, were similar in the two groups. These results indicate that, although serum GABA levels are elevated during sepsis, GABA is unlikely to play an important role in the pathogenesis of sepsis-related encephalopathy.

34.

Disturbances of Late Neuronal Migration in the Perinatal Period: A GFAP and Acridine Orange Study of Pathogenesis in 16 Human Fetuses and Neonates

H.B. SARNAT (Calgary, Alberta)

Abnormal neuronal migrations in the developing human brain are generally considered as early gestational events induced by genetic factors, teratogens, or infections. Though the major neuronal migrations forming the cortical plate occur by the 16th fetal week, late migrations into the cerebral cortex continue until a year of age. Brains of 9 normal fetuses and neonates of 16-44 weeks gestation and 7 infants dying with ischaemic/hypoxic encephalopathy, periventricular haemorrhage, ependymitis, or hydrocephalus were studied at autopsy using an immunoperoxidase method for glial fibrillary acidic protein (GFAP) and acridine orange (AO), a fluorochrome of nucleic acids. Intracerebral infarcts and haemorrhages, ependymitis, and anatomical distorsion of the brain by ventriculomegaly all resulted in interruption of the radial glial fibre system that guides neuroblasts during migration, or in retraction of these radial glial fibres from the pial surface. Subcortical heterotopia and imperfections in cortical lamination resulted, with neurons maturing in abnormal sites or with abnormal orientation. Subependymal gliosis develops within a few days in fetal brain and interferes with further neuronal migration from the germinal matrix. Cytoplasmic ribonucleic acid (RNA) proliferation, denoted by AO, coincides with beginning biosynthesis of neurotransmitters; this maturational feature follows the completion of neuronal migration in the cerebral cortex, but precedes the migration of cerebellar granule cells. RNA and transmitter production may proceed even if neurons do not complete their intended migration. The "minor" focal dysplasias resulting from disturbances of late neuronal migration may account for some chronic neurological handicaps and are potentially preventable by good perinatal care.

35.

A Theoretical Quantitative Structure-Activity Relationship Study of Hydantoin Anticonvulsants

D.F. WEAVER (Halifax, Nova Scotia)

The correlation of biological activity with molecular structure is central to modern medicinal chemistry, and enables an enhanced mechanistic understanding of drug action at the molecular level of reality. The antiepileptic activity of phenytoin is not understood at the molecular level, thus representing a major obstacle to the rational design of new anticonvulsants. To address this problem, a pattern recognition quantitative structure-activity relationship technique employing 55 theoretically calculated descriptors was devised and used to evaluate 80 hydantoin analogs of varying bioactivity. Geometric descriptors, reflecting molecular shape and size, were obtained from molecular mechanical calculations using a multidimensional potential energy function to describe the restoring forces acting on a hydantoin molecule when the geometry of minimal potential energy is perturbed. Electronic descriptors, describing electron distribution properties, were obtained from semi-empirical quantum mechanical calculations assuming the CNDO/2 approximation. Topological descriptors, encoding aspects of molecular composition and connectivity, were obtained from the topological indices of graph theory calculations. Physicochemical descriptors, describing molecular lipophilicity, were calculated using the technique of Klopman and by assuming that hydantoin solubility may be related to electrostatic forces involving charge densities. A classification algorithm was devised to identify the minimal number of descriptors capable of distinguishing active from inactive hydantoins. As a corollary, it was possible to identify the molecular fragment which constitutes the region of structural commonality among active hydantoins. Accordingly, the bioactive antiepileptic face of hydantoins consists of a 1.33 A long amide functionality (with an unsubstituted amide nitrogen capable of hydrogen bonding) bonded through a distance of 1.4-1.6 A via the carbonyl to a tetravalent atom which is substituted with bulky and preferably aromatic substituents.

36.

Interleukin-2 is not a Mitogen for Human Glial Cells in Culture

V.W. YONG, D.H. SHIN and S.U. KIM (Vancouver, British Columbia)

Interleukin-2 (IL-2) has been reported to be a mitogen for rat astrocytes and oligodendrocytes in culture, suggesting that it may have a role in the proliferation of glial cells during injury or disease. We have examined IL-2 and other agents for their capability to promote proliferation of human glial cells (astrocytes, oligodendrocytes, Schwann cells) in culture using immunolabelling by bromodeoxyuridine (BrdU) as an index of DNA replication. Astrocytes and oligodendrocytes were positively identified by antibodies directed against glial fibrillary acidic protein or galactocerebroside, cell-type specific markers for astrocytes and oligodendrocytes respectively.

Dissociated cells of brain or dorsal root ganglion from human fetus (8-10 weeks gestation) were established in culture to produce astrocytes and Schwann cells respectively. Oligodendrocytes were isolated from adult brain (corpus callosum) obtained at autopsy. Potential mitogens including IL-2, together with 10 μM BrdU, were added to the culture medium. The cells were immunostained and percent of Schwann cells, astrocytes or oligodendrocytes with BrdU-positive nucleus, relative to those of controls, was tabulated as proliferation index (PI). In all three types of human glial cells, IL-2 (50 or 500 U/ml) proved to be ineffective as a mitogen. In contrast, glial growth factor from bovine pituitary (1 μg/ml) produced proliferation of astrocytes ($PI = 4$) and Schwann cells ($PI = 2$). Platelet-derived growth factor (1 U/ml) was mitogenic for astrocytes ($PI = 2$) while nerve growth factor (100 ng/ml)

caused proliferation of Schwann cells (PI = 1.5). None of the agents tested was effective in promoting oligodendrocyte multiplication. We conclude that in contrast to previous reports, IL-2 is not a mitogen for human glial cells in culture.

37.

Transmitter Effects on Human Cultured Neurons

E. PUIL, I. SPIGELMAN, S.U. KIM (Vancouver, British Columbia)

The main characteristics of spikes and membrane responses to certain excitatory transmitters — aspartate and glutamate, in human cultured neurons have been previously found to be similar to those recorded in neurons of lower animals. In general, however, there is a paucity of knowledge about the sensitivities of human neurons to transmitter candidates. We have investigated the effects of compounds such as acetylcholine, γ-aminobutyrate (GABA) S-aspartate, S-glutamate, glycine and histamine on cultured neurons which have been obtained from different levels of the neuraxis, including the dorsal root ganglia (DRG), spinal cord and retina. These substances were applied and extracellularly by iontophoresis during intracellular recording. Aspartate and glutamate did not affect the membrane electrical properties of DRG neurons but depolarized certain neurons of the spinal cord and retina. Although the glutamate-depolarizations of retinal neurons were large compared to those obtained with similar applications made to the other types of neurons, there was no accompanying, significant change in membrane conductance. The responses of all DRG and retinal neurons to applications of GABA were in a depolarizing direction and accompanied by large increases in the input conductance of the membrane. In spinal neurons, similar reversible effects of GABA, including "desensitization", were observed except that the membrane potential responses were in a hyperpolarizing direction. The magnitude of the effects of GABA, glycine or histamine on such neurons was much greater than that observed in the responses of these neurons to the classical excitatory transmitters — acetylcholine, aspartate or glutamate. It is not clear if this is a consequence of age of culture, type of cell or of culture system employed. However, the responses of the DRG and spinal neurons to these transmitter compounds indicate an early development of functional receptor — ionophore complexes in human fetal neurons.

38.

Human Oligodenrocytes in Culture: Immunocytochemical Studies of Antigen Expression

S.U. KIM, V.W. YONG, K. WATABE, C.S. LEE, M.W. KIM, D.N. OSBORNE and D.H. SHIN (Vancouver, British Columbia)

Oligodendrocytes, as the cells which produce and maintain central nervous system myelin, serve as primary targets for possible immunopathological reactions in patients with multiple sclerosis (MS). To understand the pathogenesis of MS, investigation of human oligodendrocytes in isolation is desirable. We have succeeded in isolating and culturing adult human oligodendrocytes from brains obtained at autopsy. Cells were prepared by Percoll density gradient centrifugation, plated on coverslips, and cultured for the period of 1-12 months. These cells expressed cell type specific markers for oligodendrocytes such as galactocerebroside, myelin basic protein, myelin associated glycoprotein and cyclic nucleotide phosphodiesterase, and showed the ultra-structure of mature oligodendrocytes.

In addition, double immunolabelling experiments demonstrated that approximately 15-20% of galactocerebroside-positive oligodendrocytes expressed major histocompatibility complex (MHC) antigens HLA-DR, and 90-100% of oligodendrocytes contained HLA-A,B,C antigens. The presence of these MHC associated antigens in human oligodendrocytes may be important in the induction of an immune response to these cells and in the pathogenesis of MS.

Epilepsy I (Platform)

THURSDAY, JUNE 25TH, 1987 1530-1700

Co-Chairmen: DR. J. BRUNI (Toronto)
DR. A. SHERWIN (Montreal)

39.

Epilepsy Surgery in the Posterior Cortex

S. WHITING, W.T. BLUME and J.P. GIRVIN (London, Ontario)

We reviewed 13 patients with intractable seizures in whom surgery involved occipital and occasionally posterior temporal and parietal regions with at least 1 year follow-up.

Simple partial seizures were the most common (11 patients), all of whom had one or more visual components. Complex partial seizures occurred in 9 patients of whom 7 had preceding visual symptoms and in whom limbic-like phenomena occurred in 6 and automatisms in 5. Unilateral motor seizures appeared in 8 patients of whom 6 were contralateral to the seizure focus. Grand mal seizures occurred in 10.

Eleven patients had at least 2 seizures recorded from the occipital-posterior temporal-parietal region unilaterally, 11 by EEG and 2 by subdurally implanted leads. Interictal spikes appeared most commonly over the ictal region in all 11 patients with spikes. In addition, 9 patients had anterior temporal spikes and 5 had frontal spikes on at least 2 EEGs each.

Four patients had preoperative contralateral hemianopia and 4 had a quadranopia. Postoperatively, 2 of these became an hemianopia and 1 patient without preoperative deficit developed a permanent quandranopia.

Five patients are now seizure-free, while 3 have greater than 75% reduction. Factors mitigating surgical success included size of the epileptic zone posteriorly and the activity of distant epileptogenic zones.

40.

Pattern Recognition System for a Graded Context Based Analysis of Ambulatory Cassette EEGs

P. JAYAKAR, J. PATRICK, E. SHWEDYK and S.S. SESHIA (Winnipeg, Manitoba)

Ambulatory EEGs (AEEGs) are a useful cost-effective alternative or screen to intensive inpatient monitoring. Complete visual examination, the only reliable means to detect all abnormalities (Bridgers and Ebersole 1986), is very time consuming and strenuous. We, therefore, describe a pattern recognition system (PRS) to aid the electroencephalographer (EEGer) interpret 4-channel AEEGs.

The PRS developed on a PDP-11/73 microcomputer using Assembly and Fortran languages, identifies spikes/sharp waves (STs), spike-and-wave complexes (SSWs), artifacts and background activity.

Forty 30 second segments annotated by 2 EEGers and obtained from our database (Jayakar et al (in press); Electroenceph Clin Neurophysiol), were used to *train* the PRS. Training involved the following principles: 1) Both morphology as well as intra- and inter-channel context were considered, 2) Detections resembling STs/SSWs were graded from 10 to 1 based on their likelihood of being genuine or not and 3) Time domain/Mimetic methods were used.

The PRS was then *evaluated* using 60 *independent* AEEG segments. Its overall performance matched that of the 2 EEGers: 1) 39 out of 293 STs

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were missed. But only 126/293 had been identified by both EEGers, 2) none of the 16 SSWs were missed, 3) 96 artifacts resembling STs/SSWs were identified either correctly or as STs/SSWs with a low likelihood (Grade <5 out of 10) of being genuine, and 4) analysis of background was satisfactory.

The unique features of our PRS are: 1) Grading which avoids forced classification of every detection resembling ST/SSW, a possible limitation of existing automated systems and 2) Identification of all waveform types.

The PRS can be extended to analyze 8 or more channels of EEG recordings.

Funded by Health and Welfare, Canada and Children's Hospital of Winnipeg Research Foundation.

41.

Transient Postictal Downregulation of Alpha-1 Andrenoceptors in Rat Cortex: Similarity to Observations of Human Epileptic Foci

A.L. SHERWIN (Montreal, Quebec)

The number of alpha-1 adrenoceptors has been shown to be consistently decreased (mean, −31%) in surgically excised spiking human epileptic foci. These pathological specimens were by therapeutic necessity all obtained 30-60 min. after recording the electrographic seizure activity. To investigate these observations further, we determined the sequential changes in receptor density in a chronic rat model following serial (1/day x 15) electroconvulsive seizures (ECS). Animals were sacrificed at intervals before or after the last seizure and cortical membranes assayed using (^{3}H) prazosin as specific ligand. Maximal binding capacity (Bmax) and relative affinity (Kd) were calculated by Scatchard's Method. Comparative alpha-1 site numbers (Bmax) were as follows (mean±SEM): Sham ECS control (n = 8), 173.9±5.1 fmol/mg P; Immediately before last daily ECS (9), 220.2±4.4**, 15 min. following last ECS (6), 203.2±4.3*; 30 min. (7), 166.9±5.1; 90 min. (7), 169.1±6.3; 180 min. (4), 180.1±3.6; 240 min. (7), 231.8±11.7**. There were no associated changes in Kd. (Compared to sham ESC control *p<0.01, **p<0.001). The data reveals an approximately 180 min. postictal "window" of downregulation (or internalization) of cortical alpha-1 adrenoceptors, likely in response to the excessive release of noradrenaline, followed by a return to a state of relative upregulation. The duration of this event coincides with the previously well described postictal increase in seizure threshold following ECS in rats. Noradrenaline is an inhibitory neuromodulator which plays an important role in maintaining seizure threshold in man. Alpha-1 receptors are linked to secondary intracellular messengers responsible for calcium gating. Chronic seizure patients also likely undergo similar cyclic adrenoceptor changes which by "priming" catecholamine metabolism may contribute to the pathophysiology of epilepsy.

42.

Flunarazine, An Add-On Drug in the Treatment of Refractory Childhood Epilepsy

D. KEENE, S. WHITING, P. HUMPHREYS, H.P. FINDLAY and B. CUMMING (Ottawa, Ontario)

The calcium blocker, Flunarazine, has been reported in the literature to be an effective add-on drug in the treatment of refractory epilepsies.

Thirty-four patients (19 males, 15 females) followed at the Children's Hospital of Eastern Ontario Epilepsy Clinic were entered into a double blind cross-over study. Each child had at least 4 seizures per month and had had a good trial of standard anti-epileptic medications. Sixteen had partial seizures; 6 had partial seizures with secondary generalization; and 12 had generalized seizures only. In addition to their regular anti-epileptic medications, each patient received alternately both placebo or Flunarazine for 3 months.

Eight patients had a reduction of greater than 50% in their seizure frequency while taking Flunarazine; another 8 patients had a similar reduction while taking the placebo. The remainder had no significant changes in either phase of the study. No differences were found between responders and non-responders (i.e. seizure type, age of onset of seizures, etiology, sex, EEG, serum Flunarazine level). No major side-effects were detected while on the drug. No interaction with concomitant anticonvulsant medications were found.

Further evaluation of this drug is necessary before it can be recommended as an add-on treatment for refractory epilepsy in childhood.

43.

Clobazam for Refractory Childhood Seizure Disorders: A Valuable Add-On Drug

R. MUNN, C. CAMFIELD, P. CAMFIELD and J. DOOLEY (Halifax, Nova Scotia)

Clobazam is a new benzodiazepine not yet marketed in Canada. We report our experience with 27 children with severe epilepsy uncontrolled by other drugs. All had mixed seizure disorders (11 focal plus generalized, 16 mixed generalized) with at least daily seizures in 22. They had previously received an average of 6 other anticonvulsants indicating refractory epilepsy. Twenty-five were mentally retarded, 2 had learning disabilities. Thirteen of 27 of our cases had >75% and 2/27 had 50-75% reduction in seizure frequency. Four had no further seizures. Ten of 15 responders had reductions in comedication. Average length of treatment for responders was 26 weeks (range 6-60). Three were controlled with doses <0.75 mg/kg/day, 3 with 0.75 mg/kg/day and 9 with larger doses up to 17 mg/kg/day. In 10/15 responders dose increases have been needed to maintain efficacy. All but 1 patient responding in the first 2 weeks of treatment have continued on clobazam. All parents noted greater alertness in responders although the cause was not clear. One had bulbar side effects. No significant direct toxic effects of clobazam were seen; however, 7/12 nonresponders had a severe exacerbation of their seizures (in only 1/12 was there reduction of comedication at the same time). Drug interactions with clinical toxicity were noted once with phenytoin and once with nitrazepam.

We conclude that since clobazam shows sufficient promise in children with refractory seizures further trials are indicated in less abnormal children. The frequency of dramatic effects without serious sedation indicates that it should be tried when first line treatments have failed.

44.

Evidence of Augmented Serotonin and Dopamine Turnover in Epileptogenic Foci Resected from Human Brain

G.B. GLAVIN, K.M. KIERNAN and G.R. SUTHERLAND (Winnipeg, Manitoba)

Temporal lobe and hippocampal specimens were obtained from patients undergoing surgical resection of their epileptic foci. Samples were analyzed in triplicate by HPLC/ED and levels of noradrenaline (NA), dopamine (DA), and 5-hydroxytryptamine (5-HT) as well as their major CNS metabolites MHPG (3-methoxy-4-hydroxyphenylethyleneglycol sulfate); HVA and DOPAC (homovanillic acid and dihydroxyphenylacetic acid); and 5-HIAA (5-hydroxyindoleacetic acid), respectively, were obtained. Three out of 4 hippocampal specimens from actively spiking electrode sites showed huge (200-400%) increases in 5-HT turnover and smaller but reliable increases in DA turnover, compared to non-epileptic brain tissue. Analysis of actively spiking temporal cortical tissue revealed little evidence of exacerbated amine turnover, however, examination

of less electrically active temporal cortical specimens showed both exaggerated 5-HT and DA turnover. Since 5-HT is known to exert anti-seizure activity, we suggest that the rise in 5-HT turnover observed in these samples reflects recruitment of 5-HT for endogenous anti-epileptic activity. The significance of the enhanced DA turnover remains to be determined, however, we suggest that our method, sensitive to picomolar concentrations of monoamines and their metabolites, is a useful addition to the research armamentarium investigating the epileptogenic focus.

(Supported by the Health Sciences Centre, Winnipeg Research Foundation)

Epilepsy II (Poster)

THURSDAY, JUNE 25TH, 1987 P.M.

45.

Ambulatory Cassette EEGs in Children

P. JAYAKAR, J. PATRICK, E. SHWEDYK and S.S. SESHIA (Winnipeg, Manitoba)

We have reviewed 141 four channel ambulatory EEG tapes (AEEGs) recorded on 98 children and adolescents aged 3 weeks to 20 years. The objectives of recording were similar to those of Ives and Woods (1980). Period of recording ranged from 6 hours to 4 days.

The recordings were done using commercially available systems. The recording procedure was standardized (Jayakar et al 1985) to optimise quality. Montages were based on clinical information. All recordings were examined completely using a computer based display system (Brusse et al 1984).

AEEGs were considered to be useful if they provided information not obtained from conventional EEGs (CEEGs) done earlier.

Results: A. AEEGs were useful in: 1) 10 out of 22 patients evaluated for possible generalized seizures; 6 of these had events during the recordings, 2) 12 out of 24 patients evaluated for partial seizures of complex symptomatology (PCS); events were "captured" in 9, 3) 8 out of 15 patients with seizures in whom CEEGs were normal; events were captured in 3 and 4) 32 of 37 patients in whom frequency of electro-clinical events was being evaluated. These included 4 patients being monitored neurointensively.

B. Of the 141 AEEGs, 73 were of very good quality, 52 were satisfactory and 16 were poor or uninterpretable; 4 of the latter were due to tampering of the recorder by the children.

Our experience suggests that, as in adults, AEEGs can be useful not only in suspected generalized epilepsy but also in PCS in children, although precise localization is not possible in the latter.

Four channel AEEGs are an efficient and viable cost-effective alternative or screen to 8 channel AEEGs and intensive inpatient monitoring. They can have a positive impact on rising inpatient hospital costs in Canada.

Funded by Health and Welfare Canada and Children's Hospital of Winnipeg Research Foundation.

46.

Status Epilepticus in Children

J.Y. YAGER and S.S. SESHIA (Winnipeg, Manitoba)

We have prospectively reviewed 52 children (aged 2 months to 17 years with a median of 2 years) who presented with status epilepticus to the Children's Hospital, Winnipeg between May 1985 and December 1986. They represent 12.6% of 412 children seen with seizures (median age 25 months) in our Emergency Department during the same period. Status epilepticus was defined as a seizure or seizures lasting at least 30 minutes without consciousness being regained in between.

Thirty-four of the 52 children (65%) had not had seizures before. Nineteen of the 52 (36%) were neurodevelopmentally abnormal previously. The seizures were generalized in 30/52 (58%) and partial in 22/52 (42%). Children who were previously abnormal were more likely to present with partial seizures and seizures lasting longer than 60 minutes than those who were previously normal.

The etiologies of the status were as follows: (1) idiopathic — 17/52 (33%): 11 of the 17 had complex febrile seizures; (2) acute encephalopathic — 16/52 (31%): infectious — 7; metabolic — 6; vascular — 1; toxic — 2; and (3) chronic encephalopathic — 19/52 (36%): post-infectious — 3; perinatal insult — 5; post-natal hypoxic ischemic insult — 2; CNS malformation — 5; tumour — 2; degenerative CNS disease — 2.

Forty-nine of the 52 children have been followed for periods of 1 to 18 months. Three of the 19 previously abnormal children died and 4 showed neurodevelopmental worsening after the episode of status. Nine of 30 previously normal children had neurodevelopmental sequelae. However, only one child in the idiopathic group has sequela.

Status epilepticus remains a common and serious problem in pediatric practice. The median age of those who present in status epilepticus is no different from that of children presenting with seizures of shorter duration. The causes appear evenly distributed between idiopathic, acute encephalopathic and chronic encephalopathic groups. The outcome is favorable for those in the idiopathic category.

Supported by: Health & Welfare Canada.

47.

Sublingual Lorazepam in Childhood Serial Seizures

J.Y. YAGER and S.S. SESHIA (Winnipeg, Manitoba)

Lorazepam, administered intravenously, is effective in the treatment of status epilepticus. It is also effective rectally. A therapeutic range has not been established. We have used lorazepam sublingually in a dose of 0.05 mg to 0.1 mg/kg/dose to successfully abort serial seizures at home in six children. A representative example follows:

K.S. now 11 years old has had seizures since the age of 18 months. For the past 3 years, he has had bouts of seizures every 3 weeks. These are stereotyped: for a day or two before such episodes, he becomes hyperactive and sleeps poorly; seizures then start without warning either whilst awake or asleep. They occur serially for up to 3 hours if untreated with each seizure lasting 30 to 90 seconds at intervals of 1 to 5 minutes during which consciousness is regained. Clinical phenomena during a full seizure include screeching, unresponsiveness, chewing movements, blinking, facial flushing, pupillary dilatation, vocalizing, stiffening of all limbs and attempting to sit up. Sublingual lorazepam in a dose of 2 mg given at home after the first or second seizure aborts subsequent attacks. Twenty clinical-electrographic seizures (10 with pupillary dilatation alone and 10 full seizures as described) occurred during a 28 minute period of a video EEG recording. Lorazepam (2 mg) was given sublingually and the recording continued. He had one full seizure 1½ minutes later and only 9 brief clinical-electrographic seizures (with pupillary dilatation alone) over the subsequent 15 minutes of recording. He had no further seizures.

We suggest that sublingual lorazepam may be an effective alternative to rectal lorazepam in the home treatment of serial seizures in children provided the child regains consciousness between individual seizures.

Supported by: Health & Welfare Canada.

48.

Seizure Exacerbation Related to Antiepileptic Drug Treatment

J. BRUNI (Toronto, Ontario)

It is generally agreed that optimal seizure control if achieved with "adequate plasma concentrations" of the antiepileptic drugs. Drugs such as phenytoin may cause an aggravation of seizures at toxic plasma concentrations. It is less well appreciated that antiepileptic drugs may cause an aggravation of seizures at subtherapeutic and therapeutic plasma levels. This phenomenon of seizure exacerbation occurs more frequently in certain childhood seizure disorders.

Five patients are presented who developed an exacerbation of seizures when adjunctive therapy was added. Three patients developed an exacerbation of absence seizures when Carbamazepine therapy was added in an attempt to improve control of primary generalized tonic clonic seizures. Two patients developed an exacerbation of tonic clonic seizures when Valproic acid was added in an attempt to improve control of absence seizures. All five patients required discontinuation of the offending drug. The case histories of the five patients will be discussed and data will be presented from the literature that are useful in identifying patients at greatest risk.

49.

Clobazam in Refractory Seizure Disorders

J. BRUNI (Toronto, Ontario)

Twenty adult patients (11 males, 9 females) with seizures refractory to anti-epileptic drugs were treated with Clobazam a 1,5 benzodiazepine as adjunctive therapy. The patients experienced a variety of seizure types, primarily complex partial. Twelve patients were experiencing almost daily seizures prior to the addition of Clobazam in doses ranging from 10 mg to 40 mg daily. Follow up data are available up to 24 weeks. Twelve patients (60 percent) experienced a greater than 50 percent reduction in seizure frequency. Four patients remained seizure free. Two additional patients had only a temporary or transient beneficial effect. Side effects were minimal. Three patients developed mild drowsiness at initiation of treatment and one patient developed excessive salivation. No significant biochemical abnormalities were observed. One patient developed an increase in the plasma phenytoin concentration. No patient required discontinuation of treatment because of toxicity. Clobazam is an effective add-on drug for selected patients with partial seizures. The incidence of side effects is lower than reported with other benzodiazepines.

50.

Focal Delta Activity in Benign Rolandic Epilepsy of Childhood

D. GREGORY and P.K.H. WONG (Vancouver, British Columbia)

Normal background activity is one of the characteristic EEG findings in benign Rolandic epilepsy of childhood (B.R.E.C.). We report 3 patients (total of 8 EEG's during a 2½ year period) who had rhythmic 2 hertz delta activity in the centrotemporal region in ⅝ recordings.

This sinusoidal delta activity was 70- 100uV in amplitude and almost stereotypic in form and frequency. Of particular interest was the observation of a polarity reversal between the centrotemporal region and the frontal region. Eye opening, hyperventilation, and photic stimulation did not affect the delta. In two recordings the delta was persistent throughout the entire recording. It was always present in drowsiness and sleep. When the delta onset in sleep it persisted on arousal and in the waking record despite a reduction in the spike discharge rate. All patients had independant centrotemporal spike discharges of a dipole configuration.

The seizure free period at the time the delta was recorded ranged from 4 days to 14 months. The neurological exam was normal in all patients as was the CT scan obtained in one patient.

Possible mechanisms for this unusual delta activity include postictal slowing or a subclinical structural abnormality. A more likely hypothesis is that the delta originates from deep intracortical post-synaptic potential changes similar to the dipole spike activity from the same area.

The presence of rhythmic 2 hertz delta activity in the centrotemporal region with the above characteristics does not exclude a diagnosis of BREC.

51.

Childhood Epilepsy with Occipital Spikes

N. LOWRY and M.B.M. SUNDARAM (Saskatoon, Saskatchewan)

In 1982, Gastaut described a new epileptic syndrome in children with occipital spike waves ("Benign partial epilepsy of childhood"). We report our experience with 13 children with this disorder, studied prospectively (mean follow-up 18 months). Mean age at seizure onset was 5 years (range 3 to 10 years). Five presented with status epilepticus. Attacks were simple partial in 2, complex partial in 7 and generalized tonic clonic without focal clinical features in 4. Visual aura was obvious in only 2 and postical headache occurred in one patient. Neurological examination and CT scan were normal in all cases. Family history of epilepsy was positive in 8 patients. Ten of 13 cases remain seizure-free on anticonvulsants.

Our observations suggest that seizures in children with occipital spikes are varied and visual aura is uncommon. Majority of patients respond well to anticonvulsants. There also appears to be a strong familial tendency.

52.

Seizures Following Topical Lidocaine

M.B.M. SUNDARAM, H. DESAI and S. SUDHAKAR (Saskatoon, Saskatchewan)

Topical lidocaine is commonly used during bronchoscopy and for painful oropharyngeal-anorectal conditions. Intranasal lidocaine has recently been found effective in cluster headache (Kittrelle et al 1985). Adverse neurological reactions following topical use have been reported (mostly in children) and include dizziness, perioral numbness, diplopia, tremors, delirium and seizures (Fruncillo et al 1982, Rothstein et al 1982, Giard et al 1983, Mofenson et al 1983). We now report seizures following intraurethral lidocaine.

This 80 year old, previously seizure-free male presented with urethral stricuture and suffered mucosal trauma during catheterization. 20 ml of 2% lidocaine was instilled prior to cystoscopy. A few minutes later, he had a generalised convulsion. Next week, he had another tonic-clonic seizure minutes following 10 cc of intraurethral lidocaine, administered prior to cystoscopy to rule out nontraumatic causes for hematuria. Subsequent neurological examination, electrolytes, EEG and CAT scan of the brain were normal. Patient remains seizure-free without any anticonvulsants.

Previous mucosal trauma likely produced rapid "bolus" absorption of lidocaine, resulting in convulsion in our patient.

Lidocaine is rapidly absorbed from gastro-intestinal and tracheobronchial mucosa (Adriani et al 1964) but data for absorption from bladder and urethra in humans is not available. Both lidocaine and its metabolites are capable to causing adverse neurological reactions. Selective

blockage of inhibitory cortical synapses is thought responsible for CNS toxicity (Tanaka and Yamasaki 1966).

53.

Long-Term Anticonvulsant Efficacy of Acetazolamide

W.J. LOGAN, S.L. SPROUL and E.D. McLAUGHLIN (Toronto, Ontario)

Acetazolamide, a carbonic anhydrase inhibitor, has been shown to have anticonvulsant properties, both clinically and in experimental models of epilepsy. It is generally accepted that Acetazolamide loses its effectiveness after several months because of the development of tolerance and therefore is not a very useful anticonvulsant when given on a continuous long-term basis. In order to investigate the mechanisms underlying the development of tolerance, patients who were given this medication for seizure control were reviewed. This report describes a sub-group of these patients treated with Acetazolamide who have had a sustained response and have apparently not developed tolerance to it.

Nine patients have been identified who have shown improvement in seizure control for more than six months after Acetazolamide was instituted. Most of the patients have had seizures of unknown cause and most, but not all, have had complex partial seizures. Each case had been receiving other anticonvulsants and Acetazolamide had been added adjunctively. The dosage of this drug ranged from 250 mg to 1000 mg per day. None of these patients experienced significant side-effects attributed to the Acetazolamide.

It is concluded that Acetazolamide, in certain patients, is a well tolerated anticonvulsant which can have sustained efficacy when given adjunctively. Why some patients develop apparent tolerance to its effect is therefore a very important problem which still needs to be resolved.

54.

TIRDA or Temporal Interictal Rhythmic Delta Activity

M. BEAUDRY and J. REIHER (Sherbrooke, Quebec)

An interictal marker for complex partial seizures.

Among various epileptiform patterns such as wicket spikes, small sharp spikes and mid-temporal rhythmic theta activity, anterior temporal spikes or sharp waves (TS-SW) stand out as significant interictal abnormalities in most patients with complex partial seizures (CPS). That temporal interictal rhythmic delta activity (TIRDA) might represent yet another CPS marker, equivalent to TS-SW, deserves to be reported.

From charts review of 39 adult patients with TIRDA referred over the past 6 years, the following can be said:

- TIRDA consists of short bursts or prolonged runs of 50-100 μv rhythmic sinusoidal or saw-toothed 1-4Hz activity, distributed predominantly over inferior and anterior temporal areas, during wakefulness and sleep.
- TIRDA can occur either solely as an isolated abnormality, or concomitantly with TS-SW; either unilaterally with ipsilateral TS-SW, or bilaterally and asynchronously with equally bilateral independent TS-SW foci.
- TIRDA is found almost exclusively in patients referred for CPS; exceptionally — and then ipsilaterally — in patients with lesions known for their mere propensity to epilepsy.
- TIRDA may well be a more reliable indicator of imminent seizures than TS-SW.

In conclusion, TIRDA is a significant interictal CPS marker, equivalent to TS-SW and a potentially meaningful indicator of seizure activity.

55.

Epileptic Eye Deviation and Nystagmus with Metabolic Encephalopathy: Intensive Monitoring in 3 Patients

M.C. SKINNER, A. GUBERMAN and M. COUTURE (Ottawa, Ontario)

Three acute cases with partial status epilepticus or frequent epileptic seizures characterized by eye deviation and nystagmus were studied by EEG telemetry/video monitoring and electro-oculography. The EEG in all cases showed seizures limited to the occipital-parietal areas contralateral to the eye deviation. Two cases had cortical blindness which resolved in one when seizures were controlled. All three were elderly women with renal failure and other metabolic disorders (hyperosmolarity, hypercalcemia, sepsis). CT and autopsy (2 cases) revealed no lesions to account for the occipital seizures, which were presumably on a metabolic basis.

56.

Epileptic Munchausen's Syndrome: A Form of Pseudoseizures Distinct From Hysteria and Malingering

J. TEITELBAUM, F. ANDERMANN, G. SAVARD and H. LEHMANN (Montreal, Quebec)

A young female sought and obtained hospitalization in virtually every hospital in Québec, presenting with seizures and status epilepticus. Treatment led to intoxication with anticonvulsants, respiratory distress, aspiration pneumonia and multiple periods of anesthesia for up to seven days at a time in different institutions. A diagnosis of Munchausen's syndrome was made and reconfirmed during rehospitalization under a different name.

Review of the literature revealed no documented cases of epileptic chronic factitious disorder, although fits and seizures are always mentioned in the list of symptoms described in previous articles. Munchausen's syndrome is different from hysterical pseudoseizures where conversion mechanisms and unconscious motivations are involved. It differs from malingering where secondary gain is obvious, best described by Thomas Mann in "Felix Krull".

Chronic factitious disorders lack recognizable rational goals and are virtually always superimposed on a pre-existing personality disorder. From childhood, our patient was totally unable to accept responsibility. Her father was an alcoholic. She learned the phenomenology of seizures from her epileptic best friend. In repeated psychiatric interviews, the absence of emotional distress was always striking. Psychiatric treatment has unfortunately been unsuccessful so far.

57.

The Effectiveness of Clobazam in Adult Epileptics

S.J. PURVES and M.W. JONES (Vancouver, British Columbia)

Clobazam (supplied as FRESIUM by Hoescht under the Emergency Drug Release provisions of HPB) was introduced as an add-on drug to the anticonvulsant regime of 34 patients with poorly controlled seizures. Most (27/34) tolerated it well, but 6 found it too sedating, and in another it was stopped because of behavioral problems. Five other patients did not clearly benefit after a trial lasting up to 12 months, and thus the drug was discontinued.

The seizure patterns to benefit included generalized absences and tonic clonic seizures and atonic seizures (11 patients), and partial complex seizures of frontal or temporal origin (14 patients). Previous benefit from a benzodiazepine (nitrazepam or clonazepam) did predict

improvement with Clobazam, but some patients who had not tolerated these drugs also did well with Clobazam.

The drug was added on to one other drug in 8 patients, 2 other drugs in 20 patients, and substituted for another benzodiazepine or phenobarb in 3 patients already on 3 different anticonvulsants.

Laboratory results followed did not show any change in liver enzymes. Many patients showed T4 levels below the normal range before and after introduction of the drug but the TSH was normal, and they remained clinically euthyroid.

In all 25 patients remaining on the drug (4-22 month follow-up) there has continued to be a marked reduction in seizure frequency and severity. In many it was commented spontaneously by care givers that the patients were brighter and more alert, and often in those with frequent seizures the effect was immediate within 2 or 3 doses.

We conclude that this drug is clearly of value in improving seizure control in some difficult patients with epilepsy.

Spinal Cord Injury I (Platform)

THURSDAY, JUNE 25TH, 1987 1330-1515

58.

Functionally Significant Spinal Cord Regeneration Induced by an Applied Direct Current Field

M.G. FEHLINGS (Toronto, Ontario)

KG McKenzie Neurosurgical Award

Although central axons are capable of limited regrowth **functionally significant** regeneration of mammalian spinal axons has never been demonstrated. In the present experiment, the therapeutic value of an applied direct current (DC) field was studied in 40 rats with clip compression injuries of the cord at T1. The rats were randomly allocated to one of four groups (n = 10): two groups received a 17 g cord injury and two groups a 53 g injury. One group at each injury severity received a treatment DC stimulator (14 uA) and the other group a control stimulator 0 uA). Clinical neurological function was assessed weekly by the inclined plane technique. At 8 weeks after injury, motor and somatosensory evoked potentials (MEP and SSEP) were performed, and the axonal tracer horseradish peroxidase (HRP) was introduced into the cord at T6. The total number of HRP-labelled cells was counted in coronal sections through the brainstem and motor cortex. All outcome parameters were assessed blindly.

In the 17 g group, there were no significant differences in any outcome measure between treated and control rats. In contrast, in the 53 g group, the inclined plane scores ($p<0.001$), the amplitude of the MEPs ($p<0.05$) and the number of labelled cells in the red nucleus ($p<0.01$), raphe nuclei ($p<0.05$), and vestibular nuclei ($p<0.05$) were greater in treated than control rats. These data prove that an applied DC field can produce functionally significant regeneration of damaged spinal axons in the rat.

59.

The Effect of Localized Oriented Electric Field on Regenerative Changes in Double Hemisectioned Spinal Cord of Rats

M. KAHN, M. POLITIS and D. MUNOZ (Saskatoon, Saskatchewan)

A research project was conducted in an attempt to stimulate regrowth of axonal fibres across a double hemisection lesion of the rat spinal cord. The lesions were made at the mid-thoracic level on the right side, approximately 5 mm apart, using microsurgical techniques. It has been reported that axonal growth cones will grow towards a cathode (negative pole), and with this information, a device* which produces localized oriented electric fields was implanted in the epidural space at the proximal hemisection site of the spinal cord of experimental animals.

Thirty adult female Sprague-Dawley rats were used in this study. On 10 animals, the cathode was oriented just rostral to the proximal hemisection site, and reversed in another group of 10 rats. A group of 5 animals were used as controls (i.e. double hemisections without electrode implantation). A final group of 5 normal animals were used to monitor and compare normal functional status with experimental and the control groups using a tilted ramp. Animals were tested for functional deficit on a weekly basis for 8 weeks, following which they were sacrificed and perfused with a 10% formalin solution. The thoracic spinal cords were then removed and sectioned 1 mm above and 1 mm below the upper hemisection. Alternate sections were stained with Hematoxylin and Eosin for morphology and with immunoperoxidase stain for neurofilaments with the monoclonal antibody SM133. The results indicate significant functional improvement among animals subjected to electrical stimulation in comparison to the control group. However, no significant functional difference was noted between animals with anodal or cathodal current directed rostrally to the hemisections.

*We are legally obligated not to disclose details of the device at present.

(Electrode; Traxon, American Biointerface Corp.)

60.

Cervical Spinal Injury: X-ray Features Affecting Management and Outcome

B. SEARS and M. FAZL (Toronto, Ontario)

In a retrospective study of 140 patients with subaxial cervical spine injury, the plain x-rays, conventional and computed tomograms were studied and compared with anatomical outcome. The object was to determine which, if any, features of the injury at the time of presentation might be used to predict those patients who may be treated successfully by Halo traction and vest, and those patients who are likely to fail such conservative management and require surgery.

The patients were allocated to one of four outcome groups: Surgery for failure to achieve adequate closed reduction, (18); Surgery for failure to maintain reduction in Halo Vest (35) or after removal of the vest (5); "Good" anatomical result with Halo apparatus alone (58); "Poor" anatomical result with Halo apparatus alone (24).

Twelve of the 15 patients with wedge or burst fractures of the vertebral body without subluxation had "Good" anatomical results with Halo apparatus alone, while only 13 of the 65 patients with facet joint dislocations had similar "Good" results with conservative management.

Selected injury features (the degree of subluxation, angulation and interspinous space widening, the presence of facet joint dislocation, fracturing of vertebral body, pedicles, facets, laminae or spinous process and age) have been used to develop a model (using logistic regression) which allows the prediction of the probability $P = 0.0000$ $R = 0.401$ of success or failure with Halo apparatus.

61.

Results of 500 Cases of Lumbar Chemonucleolysis

R.R. HANSEBOUT and W.D. FRIEND (Hamilton, Ontario)

Chymopapain for injection of protruded lumbar discs has been available for many years. This technique has been used routinely in a few Canadian centres as an alternative to open surgery. Papers and presentations during the last few years have shown conflicting results as to the

efficacy of this method. In view of the continuing controversy we thought it appropriate to review the results of our combined series of over 500 cases.

The patients were unselected as to age, sex, compensation and litigation claims, or the number of disc levels involved. Discography was performed using fluoroscopy and contrast materials with the patient under local and neuroleptanalgesia. Discs found to be degenerated and/or reproducing the patient's usual pain were injected using Discase (Travenol). Follow-up in many cases was done by questionnaire.

Less than one half of cases had an excellent or good result. The rest had mediocre or no pain relief. Efficacy was substantially less in compensation or litigation cases. A few cases required open surgery as a sequel to injection, often with unimproved results.

The indications, technique and results will be presented.

62.

Cavernous Angiomas of the Spinal Cord

R. COSGROVE, G. BERTRAND, S. FONTAINE, Y. ROBITAILLE and D. MELANSON (Montreal, Quebec)

We report 5 cases of pathologically-proven cavernous angioma of the spinal cord. Acute lower extremity sensory disturbance was the initial symptom in 4 patients. One patient presented with weakness of the hand. Progressive neurological deficit occurred in all patients but the clinical course and outcome was extremely variable. Myelography revealed an intramedullary lesion in 2 cases but was completely normal in three. MRI was diagnostic in these patients. Subtotal removal was accomplished in two cases while myelotomy and biopsy was carried out in three. Four of the cavernous angiomas were located in the cervico-thoracic region while one was found in the thoraco-lumbar cord. All cases exhibited characteristic gross and microscopic features as well as hemosiderin-laden macrophages indicating remote hemorrhage. The diagnostic, therapeutic and prognostic implications of this rare condition are discussed.

63.

Cervical Spinal Deformity After Surgery for Posterior Fossa Tumors in Children

M.C. BOYD and P. STEINBOK (Vancouver, British Columbia)

Cervical spine instability after multilevel laminectomy for spinal cord lesions in children has been well documented. However, such a problem arising after multiple upper cervical laminectomies for posterior fossa tumor is not as well recognized. A severe bony deformity can develop which may require extensive spinal reconstruction. As a result of spinal cord compression a progressive neurological deficit can occur which may go unnoticed in the presence of previous neurological problems due to the primary tumor. In addition, postoperative radiation therapy for the tumor may further compromise the growing spine and delay healing of the supporting ligaments and musculature thus aggravating the instability.

Of 33 patients operated upon for posterior fossa tumors at B.C. Children's Hospital from 1982 to 1985, 5 have had more than one upper cervical lamina removed for surgical exposure. Three of these patients have survived more than one year after surgery and have developed significant spinal instability requiring fusion. Both of the remaining two died within a year of their surgery. Neither had developed significant deformity; although, one had developed a mild subluxation.

The 3 cases requiring fusion are reviewed in detail. The possible factors which may contribute to this serious complication and means by which they may be avoided are discussed.

Spinal Cord Injury II

THURSDAY, JUNE 25TH, 1987 0730-1700

64.

Posterior Clamping for Stability in Lesions Involving the C1/C2 Complex

G.P. MURRAY and R.O. HOLNESS (Halifax, Nova Scotia)

In earlier publications, we have described our experience with internal fixation of cervical injuries utilizing an interlaminar steel clamp designed in Halifax. This technique has been most successful, with a low complication rate, when used for C3-C7 fractures. Recently, we have expanded the use of this clamp for fractures/instability at the C1/C2 complex. This approach offers an alternative method of stabilization to traditional methods and affords immediate stability without the need for extensive external immobilization (e.g. the halo device). This is an advantage, particularly in patients with quadriparesis and/or chronic rheumatoid arthritis.

In this report, we present our experience with the first 11 patients we have treated with this method, seven of whom had C1-2 instability due to rheumatoid arthritis. In addition to application of the clamp, between the laminae of C1 and C2, 10 patients also had C1-2 bony fusion performed. However, in rheumatoid arthritis there is often difficulty in achieving solid bony fusion (up to 50% failure in some series) and the clamp offers extra "insurance" for stability.

Preoperative and postoperative radiological findings are presented, as well as a discussion of which lesions are most suitable for this method of stabilization and those which we would still prefer to manage by alternative methods.

65.

Real Time Intraoperative Ultrasound

B.G. BENOIT, N.A. RUSSELL and B. LEWANDOWSKI (Ottawa, Ontario)

Real time ultrasonic imaging provides valuable assistance to intraoperative decision making in a variety of cranial and spinal neurosurgical procedures. Subcortical and deep intracerebral lesions are readily displayed, allowing precise localization for biopsy, excision or drainage. The imaging is immediate, resulting in a more "dynamic" operative situation than is possible with prefixed stereotactic coordinates or a previous CT scan.

Intradural and intramedullary spinal cord elements, as well as the extradural space, CSF, and spinal pulsations may be viewed before and after surgical manipulation. A syrinx may be precisely measured and the most appropriate site for myelotomy chosen. We present our experience with intraoperative ultrasound in the surgery of a variety of cranial and spinal lesions. We used a high resolution real time duplex sector scan at variable frequencies (5.0 MHz - 10.0 MHz) with a doppler component (4.5 MHz). The technique and results will be illustrated by video tape.

66.

Pseudotumorous Cryptic Vascular Malformations of the Spinal Cord

F.A. DURITY (Vancouver, British Columbia)

Spinal cord vascular malformations are diagnosed by angiography and myelography. Cryptic vascular malformations of the spinal cord are not described in contemporary neurosurgical literature.

Two such patients are now described, both presenting with clinically painless progressive cervical myelopathy, with predominantly sensory dysesthethic symptoms and signs. Multiple sclerosis workup was negative. Radiological investigations including myelography, computerized tomography, and magnetic resonance imaging all suggested unusually focal, approximately 15 mm long, intrinsic cord tumors. Spinal cord angiography was negative.

At surgery totally intramedullary black, firm, tumor-like masses with tough "capsules" (fibrous tissue on rush diagnosis) poorly distinct at their borders from normal surrounding cord tissue were removed. Final histopathology confirmed the masses as vascular malformations.

In view of the significant surgical risks associated even with microsurgical total removal (both patients were somewhat worse postoperatively), this benign entity should be recognized and a less aggressive removal is advocated.

67.

Cranio-cervical Junction Osteomyelitis Following Neck Trauma and Unexplained Bacteremia

J.C.M. DELCAMPO and H. LESIUK (Winnipeg, Manitoba)

Cervical osteomyelitis has previously been reported in specific "at risk" groups (skin infections, urinary tract infection, bacterial endocarditis, intravenous narcotic addiction). High cervical involvement is rare in spite of the rich blood supply to the area.

We report the case of a 68 year old farmer whose initial presentation suggested neck sprain followed by unexplained S. aureus bacteremia. Antibiotics were given initially for only 10 days.

Neck discomfort continued but did not prevent farm work. A 12 kg weight loss was noted.

Three months after his initial presentation he suffered a sudden exacerbation of neck pain after bending forward, followed by dysarthria and dysphagia.

Neurological examination 2 weeks later revealed an emaciated afebrile man with nasal speech, a Lt. XII nerve palsy and a Rt. upgoing plantar response. Opening his jaw produced a shock-like feeling from the neck to the Rt. thumb.

Repeated needle aspiration and open biopsies failed to show neoplastic cells.

He was treated with external fixation and intravenous antibiotics.

Radiological features will be presented.

Chronic cervical osteomyelitis can be successfully treated with relatively non-invasive methods.

68.

Reduction of Acute Post Trauma Spinal Cord Edema by Omental Transposition: An Experimental Study in Rabbits

J. ABRAHAM, F.B. MAROUN, R. RANDELL, J.C. JACOB and E.S. WRIGHT (St. John's, Newfoundland)

Edema and ischemia are the two major pathologic changes occurring in acute spinal trauma. Edema is vasogenic, occurs immediately after injury, is maximal at 24-48 hours, and has been reported to persist for two weeks. We demonstrated a marked increase (115%) in water content of contused spinal cord 24 hours following injury compared with sham operated controls. This marked increase in water content within traumatized spinal cord, which is encased in an unyielding dural sheath, makes it a major factor in the chain of events leading to irreversible neural damage.

The absorptive property of greater omentum was utilized to reduce post traumatic spinal cord edema in rabbits by a pedicled omental transposition onto the injured site. This procedure resulted in a marked reduction ($P < .005$) in post trauma spinal cord edema.

Therapeutic implications of this experimental study will be discussed.

69.

An Adjacent Three Level Spinal Injury: A Case Report

F.B. MAROUN, P.G. PERKINS, D. MacMICHAEL and A.E. SHAPTER (St. John's, Newfoundland)

A case is presented of a three level adjacent injury occurring at the cervico-thoracic level in a young man. The mechanism of injury and features are discussed, and suggestions are made for treatment.

70.

Continuous Versus Intermittent Turning for Treatment of Acute Spinal Cord Injury

J.M. BUGAREST, C.H. TATOR, H.C. SANG, R. MAGGISANO and J.P. SZALAI (Toronto, Ontario)

Patients with acute spinal cord injury were entered in a randomized prospective trial to determine if automated, continuous, side-to-side turning would be more effective than manual intermittent turning for reduction of complications and length of stay in the acute hospital.

Patients admitted within 72 hours of acute spinal cord injury were eligible for inclusion in the study. Patients were stratified for the vertebral level of injury, the presence of multiple trauma, and randomly assigned to one of the treatment methods.

Fifty-two cases were entered in the study. The number of complications per patient were similar for the two groups, 2.0 ± 1.5 for continuous turning and 1.8 ± 1.3 for intermittent turning ($p > .05$). The required length of stay was 27.4 ± 11 days in patients complaint to continuous turning treatment and 32.6 ± 10 days in the intermittent turning group. With $\alpha = .05$, $\beta = .20$, and 25 subjects in each group, a seven day difference between the mean length of stay for each treatment group could be detected. Thus the observed difference of 5.2 days could not be reliably tested due to insufficient patient numbers.

In conclusion, the study failed to demonstrate statistically significant differences between the two treatment groups with respect to the end points measured. However, care of certain patients was facilitated by the continuous turning method. Continuous turning appeared helpful for the management of patients in traction and for patients at risk for respiratory complications.

71.

The Relationship Between Severity of Spinal Cord Injury, Motor and Somatosensory Evoked Potentials, and Spinal Cord Blood Flow

M.G. FEHLINGS, G.H. TATOR, R.D. LINDEN and I.R. PIPER (Toronto, Ontario)

Post-traumatic cord ischemia is important in the pathogenesis of spinal cord injury (SCI). We examined the relationship between severity of SCI, motor and somatosensory evoked potentials (MEP and SSEP), and spinal cord blood flow (SCBF). Fifteen rats received a 1.5 g ($n = 5$), 20.0 g ($n = 5$) or 56.0 g ($n = 5$) C8 clip compression injury. Mean arterial BP (maBP), pC02, pH, p02, and hematocrit were monitored. SCBF at the injury site was measured by the hydrogen clearance technique 30 minutes before and 30 minutes after SCI. Concomitantly MEPs from the cord (MEP-C) at T10 and from the sciatic nerve (MEP-N), and SSEPs were recorded.

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Although the maBP decreased after SCI (mean decrease 56.46 ± 16.43 mmHg), there were no differences among the 3 groups ($p > .05$). There were no changes in the pH, p02 or pC02. The SCBF decreased linearly with increasing SCI severity ($r = -.86$ $p < .0003$). The MEP was more sensitive to SCI than the SSEP. Indeed the SSEP was unchanged following the 1.5 g SCI, whereas there were significant abnormalities in the MEP-C and MEP-N. Following the 56.0 g SCI the SSEP was abolished in 3/5 animals and abnormal in 2/5, whereas the MEP-N and MEP-C were absent in 5/5 and 4/5 rats respectively.

This study demonstrates a strong relationship between the severity of SCI and the degree of post-traumatic cord ischemia. The MEP more accurately reflects the severity of SCI and the post-traumatic ischemia than the SSEP. These data indicate that the MEP may be more accurate in clinical monitoring of the spinal cord.

72.

MRI and the Central Cord Syndrome

D. FAIRHOLM (Vancouver, British Columbia)

Central cord syndromes are a common neurologic injury associated with hyperextension of the neck. They may occur in young people with congenitally narrowed spinal canals, or more commonly in elderly with canals narrowed by osteophytic degeneration. With hyperextension, the cord is pinched between the disc space and the bulging ligamentum flavum. This was presumed to cause central cord hemorrhage.

The development of MRI has allowed imaging of the spinal cord in selected cases of trauma. Two cases of central cord syndromes are presented in which central cord hematomas are clearly outlined by the MRI.

73.

A Classification of Intraspinal Cysts

N.A. RUSSELL, R.N. GOYAL, B.G. BENOIT and G. BELANGER (Ottawa, Ontario)

Advances in imaging technology have resulted in the identification of a variety of cystic lesions of spinal nerve roots. Failure to appreciate the different characteristics of these cysts has led to a confusion in terminology. Many are incorrectly called "perineural" or "Tarlov" cysts. Also, different terms are often used to describe the same lesion. In an attempt at clarification, the literature is reviewed and a simplified classification of spinal cysts is presented. Many synonyms are discarded, resulting in 4 broad headings, namely perineural cysts, root sleeve dilatation, arachnoid cysts and traumatic nerve root cysts. The distinguishing features of each of these lesions are discussed.

74.

Spinal Cord Compression by an Extradural Vertebral Osteochondroma

H.M.H. JABER and D. COCHRANE (Calgary, Alberta)

For an osteochondroma to arise from the vertebrae and grow in the intracanalicular space causing spinal cord compression is a rare reported incidence.

We present a case of a 20 year old man with C5/C6 osteochondroma causing antrolateral cord compression. The patient became symptomatic after a car accident and investigations revealed the occult neoplasm.

75.

Cauda Equina Compression by Extradural Vertebral Hydatid Cysts

H.M.H. JABER, M. LONG, I. JADUSINGH and L. NICOLE (Calgary, Alberta)

Hydatid cysts (Echinococcus Granulosa) are parasitic infections of the liver and lung and rarely of the C.N.S. (3%) or bone (5%) (with 50% in the vertebrae).

The vertebral infection is progressive, invasive, recurrent and may lead to complete paraplegia.

The disease is more common in S. America and the Oceanics, but is rare in Canada.

We present a case of vertebral hydatid cyst (L5/S1) leading to cauda equina compression in a 28 year old Canadian woman born and raised in Manitoba. In childhood, the patient was in contact with local sheep and dogs.

The management challenges — such cases evoke — are outlined as it is important to bear in mind the possibility of hydatid cysts when dealing with vertebral cystic masses to avoid further complications.

76.

Epidemiology of Spinal Cord Injuries in Saskatchewan

M. KHAN and C. EKONG (Saskatoon, Saskatchewan)

One hundred and seventy-five patients, ranging from 15 to 80 years, suffered from acute spinal cord injury in the province of Saskatchewan from Jan. 1980 to Jan. 1985, for an average of 35 cases per year. Eighty percent were males, but all patients suffering from cord injuries related to work were males. Motor vehicle accidents (MVA) accounted for 55% of all cord injuries, while work and sports related, falls at home and others were responsible for 22%, 10%, 8% and 5% respectively. About 90% of patients sustained their injuries between the months of April and November. Forty percent of work related injuries were due to farming accidents, 30% to construction and 10% industry. About 75% of patients were under 40 years of age for both MVA and work related accidents while 80% of patients injured from falls at home were over 70 years old. Diving accounted for most sports related cord injuries in the Northern half of the province while skidoo accidents were more common in the South. About 70% of all cord injuries from MVA involved the cervical cord, 20% thoracic and 10% thoraco-lumbar region. Seventy percent of these injuries were complete, in contrast to 60% of the work related and 80% of sport related injuries. However, only 50% of work related injuries involved the cervical cord.

Fifty percent of patients with work related cord injuries also sustained significant head injuries, and 10% had multiple injuries. Thirty-eight percent of patients with MVA related cord injuries suffered from head injuries and 30% had multiple injuries. Overall mortality during initial hospitalization was 15% but only 3% for work related injuries. Mortality was directly related to multiple injuries, upper cervical cord injuries and patients over 60 years old.

77.

Non-Contiguous Fractures of the Cervical Spine

P. SHEAR, H. HUGENHOLTZ, M.T. RICHARD, N.A. RUSSELL, E.W. PETERSON, B.G. BENOIT and V.F. DASILVA (Ottawa, Ontario)

Non-contiguous fractured/subluxations of the cervical spine are fractures and subluxations separated by at least one normal intervening cervical vertebra. Six such cases were identified among sixty-six consecutive cervical spine fractures treated by the Division of Neurosurgery at the University of Ottawa during twenty-six consecutive months.

Representative cases will be presented to demonstrate that such injuries involve the upper two cervical vertebrae in combination with fracture/subluxations of the lower cervical spine. When multiple unstable non-contiguous fracture/subluxations occur in the cervical spine, surgical stabilization of the lower injury is recommended followed by Halo vest immobilization of the upper injury in order to facilitate early ambulation.

Multiple non-contiguous fracture/subluxations of the cervical spine are a distinct entity that is not uncommon. Awareness of such injuries following violent trauma is essential and requires good quality radiographs of the entire cervical spine.

Movement Disorders I (Platform)

THURSDAY, JUNE 25TH, 1987 1530-1700

Co-Chairmen: DR. D.B. CALNE (Vancouver)
DR. D. GRIMES (Ottawa)

78.

A Follow-up Study of Surgical Treatment in Spasmodic Torticollis

R. BELL, O. SUCHOWERSKY and G. ROHS (Calgary, Alberta)

The managment of spasmodic torticollis by either medical or surgical means presents a major therapeutic challenge, frequently with less than gratifying results. In surgically treated patients, few follow-up studies have been conducted, and there has been little attempt to correlate subjective patient impression and objective results.

Sixteen patients were identified in Southern Alberta to have surgical treatment for spasmodic torticollis in the last 20 years. They were assessed by complete neurological evaluation to determine subjective response, degree of residual torticollis and complications of surgery. Ten patients had isolated spasmodic torticollis and 6 had additional writer's cramp or more widespread dystonia. Thirteen patients underwent anterior rhizotomy of upper ventral cervical roots and section of the spinal accessory nerve intradurally. Two patients underwent posterior rhizotomy and one bilateral peripheral extradural neurectomy of the spinal accessory nerve alone. Eleven patients had extradural accessory neurectomy and sternocleidomastoid myotomy prior to rhizotomy.

Results demonstrate 8 patients had good symptom relief which was maintained for the length of the follow-up (up to 10 years); these patients had minimal or no residual torticollis, and minimal complications (mild neck pain and restriction of movement). The remaining 8 patients had unsatisfactory results. This included significant residual torticollis, marked neck pain, decreased range of motion and/or cervical instability with myelopathy. In 6 of these 8 patients, dystonia recurred in other muscle groups following surgery, including laryngeal, buccolingual, and shoulder dystonia.

In conclusion, 50% of patients obtained a good result following surgical treatment. However, 50% of patients were left with residual torticollis, significant neck pain and instability, or experienced recurrence of dystonia in other contiguous muscle groups.

79.

Dopamine Agonists and Levodopa Should Be Initially Started Together in Younger De Novo Parkinson's Patients

J.D. GRIMES and M.N. HASSAN (Ottawa, Ontario)

Because of concern over late treatment complications, 25 de novo Parkinson's patients were treated with combination therapy. Initial treatment for 11 patients consisted of bromocriptine (maximum 30 mg daily) and 14 other patients received levodopa as first treatment (maximum 400 mg daily). The second drug was added as dictated by increasing Parkinsonian disability and the upper dosage limit for the first drug. The age at onset was a mean of 59 years, the time between starting the first and second drugs was a mean of 14 months. Initial average drug dosages were: Sinemet 355 mg, Bromocriptine 14 mg. In a mean follow-up of fifty-three months the drugs were slowly increased to Bromocriptine 25 mg and Sinemet 588 mg. Treatment complications (dyskinesias and fluctuations) were carefully watched for. These were classed as extreme if they were dose limiting or required drug timing adjustments.

During combination therapy, end of dose fluctuations occurred in seven patients (28 percent) and was extreme in four patients (16 percent). Three of these four patients had received Sinemet alone for one or more years. Five patients (20 percent) developed dyskinesias; of these only one was classed as extreme (four percent) and this patient received Sinemet first.

The incidence of late extreme complications in this group of patients is significantly less than expected with high dose levodopa monotherapy. It also suggests that a period of levodopa monotherapy is a major risk factor and supports the view that levodopa and Bromocriptine should be started together initially.

In the management of younger (less than 65 years) de novo patients there should now be serious consideration to beginning therapy initially with Sinemet, increasing the daily dose over four to six weeks to 200 mg to 300 mg and then adding Bromocriptine 7.5 to 15 mg daily.

80.

Dose Response of Unilateral Carotid MPTP injections in a Cynomolgus Monkey: Studies with Fluorodopa PET Scans

M. GUTTMAN, V.W. YONG, S.U. KIM, D.B. CALNE, S. BARWICK, E. WALSH, W.R.W. MARTIN, M.J. ADAM, T.J. RUTH and B.D. PATE (Vancouver, British Columbia)

The neurotoxin MPTP has been used to study parkinsonism in animal models. Cynomolgus monkeys develop irreversible chemical and pathological alterations that are similar to those found in Parkinson's disease. Unilateral internal carotid injections of MPTP have been shown to produce ipsilateral dopamine depletion while sparing the contralateral dopaminergic pathways. This is advantageous because there is an internal control to assess the neurochemical alterations and also because the animal can feed much more easily than after systemic administration and ambulate normally.

We have established a protocol for the use of 6-(^{18}F)-fluorodopa (6-FD) PET scans to study the striatal dopamine system in *Macaca fascicularis*. A male monkey had a 6-FD PET scan before MPTP administration. MPTP was then injected directly into the left internal carotid with a cut-down approach. Approximately two weeks after each injection, a PET scan was performed. Unilateral injections on the same side were repeated every 2-3 weeks. These studies enabled us to produce a dose response relationship between the amount of toxin given and the amount of 6-FD derived radioactivity. There was a progressive ipsilateral reduction in the striatal activity with each dose given. The PET studies were compared to the clinical features, if any, that were present. The initial studies showed a diminution of radioactivity in the posterior aspect of the striatum, similar to the change seen in patients with Parkinson's disease. This study demonstrates progressive, dose related, *in vivo* dysfunction of dopaminergic neurons secondary to MPTP and is further evidence of the usefulness of this toxin for studying Parkinson's disease.

81.

Botulinum Toxin For Hemifacial Spasm: Clinical Observations and Single Fibre EMG Studies

C.A. MELMED, J. WISE, D. GENDRON and S. BREM (Montreal, Quebec)

Local injection of botulinum A toxin (Botx) has been used to treat strabismus, blepharospasm, Meige syndrome, torticollis and hemifacial spasm (HFS).

Over the past 3 months, we have encountered 8 patients with "cryptogenic" HFS: 6 males, 2 females, ages 44-71 (mean 56). Mean duration of symptoms is 7.5 years. None had a previous history of Bell's palsy. All patients had otherwise normal neurologic examinations and investigations. One patient had unsuccessful microvascular decompression (MVD) in 1975 and one patient had 2 unsuccessful MVDs in 1984 and 1986. Six of the 8 patients had trials of various medications including carbamazepine, phenytoin, lioresal or combinations of these medications without effect. All patients have received at least one series of Botx treatment, 25 units, injected at 4 sites in the preseptal orbicularis oculi muscle avoiding the inferior punctum and mid-orbital position. Medial ectropion and upper eyelid ptosis from inadvertent levator palpebrae involvement did not occur. Two patients had injections into the zygomaticus major and minor, just lateral to the nasolabial fold. Mild clinical weakness developed and control of HFS occurred in 24-96 hours which lasted 2½-3 months. There were no local or systemic side effects such as limb muscle weakness or fatigability. HFS has been symptomatically much improved in all patients including mouth spasm following zygomatic injection.

Reports of single fibre EMG (SFEMG) measurements demonstrate jitter in remote muscles including extensor digitorum communis, suggesting a spread of Botx effect to remote muscles. SFEMG studies have been performed in facial and limb muscles. Additional patients will be entered into the study in a prospective manner; clinical and videotape results of injection in zygomaticus muscles in addition to orbicularis oculi will be discussed.

Botx treatment in HFS appears to be an effective, economical and safe alternative to MVD and pharmacological therapy. There is a very high degree of patient satisfaction. Injecting both orbicularis oculi and zygomaticus muscles provides even greater therapeutic benefit and has not been reported.

82.

Investigation of Cerebellar Limb Incoordination Using a Three Dimensional Movement Analysis System

R.G. LEE, W.J. BECKER, B.L. MORRICE and D.G. WHITE (Calgary, Alberta)

Although the descriptive terms dysmetria, incoordination, decomposition of movement, and intention tremor are used commonly in neurologic practice, it has been difficult, until recently, to analyse in detail the complex events which occur when a patient with cerebellar dysfunction is required to perform a target directed movement. We studied normal subjects and patients with upper limb incoordination due to cerebellar lesions using a three dimensional movement analysis system (WATSMART) interfaced to an IBM-AT computer. Infrared emitting diodes were attached to the tip of the index finger, the wrist, elbow and shoulder. Subjects were required to move the finger toward a target using a technique similar to that employed during the finger-nose test. Two infrared cameras recorded the position of each diode at rates up to 400/sec. and the results were converted into three dimensional coordinates which were used to generate plots of movement path and trajectory, velocity, and angles for the elbow and shoulder joints.

In normal subjects the limb followed a smooth trajectory and the path was similar for movements at a number of different velocities. Limb velocity plotted as a function of limb displacement resulted in smooth bell-shaped curves. In cerebellar patients trajectories were irregular and inconstant. The velocity profiles revealed numerous inappropriate accelerations and decelerations. In addition, the normally smooth relationship between shoulder angle and elbow angle was distorted in the cerebellar patients.

Our preliminary experience with the WATSMART system indicates that it will be a powerful tool to help understand abnormalities of motor function in neurologic patients.

83.

Spinal Myoclonus: Electrophysiological Observations and Response to Treatment

J.R. DONAT, M. SUNDARAM, A. RAJPUT (Saskatoon, Saskatchewan)

We report the findings in a 31-year-old woman with spinal myoclonus. Her illness began more than ten years before with pain in the legs followed by weakness, urinary retention, and rhythmic twitching. Examination showed weakness of the legs with a striking tremor involving most muscle groups. This was aggravated by stress and decreased during sleep. Extensive evaluation including myelogram and NMR did not reveal the etiology.

EMG showed synchronous and regular discharge of many muscles in the legs including agonists and antagonists at a rate of 7 to 8 per second. Myoclonic discharges in the gastrocnemius disappeared during the silent period elicited by stimulation of the posterior tibial nerve, but discharges in the anterior tibial did not show this silent period phenomenon. EEG performed with EMG monitoring showed that the twitching persisted during stages one and two of slow wave sleep, but disappeared during REM sleep. These electrophysiological observations permit differentiation from supraspinal involuntary movements such as extrapyramidal tremor and hysteria.

A videotape of the involuntary movements will be shown and the response to treatment with various medications will be reported.

Movement Disorders II (Poster)

THURSDAY, JUNE 25TH, 1987 0730-1700

84.

Can Antioxidant Therapy Slow the Progression of Parkinson's Disease?

J.D. GRIMES, M.N. HASSAN and J. THAKAR (Ottawa, Ontario)

Oxidative mechanisms in dopaminergic neurons may contribute to cell death and the progression of Parkinson's Disease. The free radical auto-toxicity concept has scientific observations both for and against it.

Manganese and 6-hydroxydopamine may cause neuronal damage via free radical producing mechanisms. Cellular enzymes which limit free radicals are deficient in Parkinson's Disease. There is however conflicting evidence whether free radicals are involved in the toxicity of MPTP. Attempts to prevent the toxicity of MPTP with antioxidants have had variable results and it has been shown that MPTP is a very poor generator of oxygen radicals and causes very little lipid peroxidation in subcellular fractions. Vitamin E deficiency does not cause Parkinsonism or basal ganglia pathology and no human studies have been reported documenting slowing of Parkinson's Disease with its use.

The oxidation of dopamine by monoamine oxidase produces toxic metabolites. Dopamine itself may have neurotoxic properties and con-

cern has been raised that exogenous levodopa may hasten the progression of Parkinson's Disease. Pathological studies of animals treated with longterm high dose levodopa have not supported these clinical concerns. MPTP studies have failed to prove either an increase in striatal dopamine or show evidence for autoxidation. Pretreatment with L-Dopa may actually reduce the dopamine depleting effect of MPTP. Monoamine oxidase B inhibition (Deprenyl) may prolong the course of human Parkinson's Disease, allow lower levodopa dosage, and in animal studies blocks MPTP neurotoxicity.

This scientific evidence is exciting but inconclusive. Nevertheless, there is significant hope of retarding progressive catecholaminergic neuron degenerative changes by augmenting the free radical scavenging system with Vitamin E and inhibiting catecholamine oxidation with Deprenyl and careful clinical trials are a necessity.

85.

Paroxysmal Dystonia From Hypoglycemia

S. SUDHAKAR, R.J. UITTI, E.M. ASHENHURST, D. MUNOZ-GARCIA and H.B. DESAI (Saskatoon, Saskatchewan)

Paroxysmal dystonic movements are unusual occurrences in hypoglycemia. We report a patient who, at the age of 49, developed episodes of involuntary movements along with unsteadiness, impairment of consciousness, and profound sweating. They lasted 5-10 minutes and occurred up to twice per week in the ensuing 10 years. Although previously suspected, hypoglycemia during an attack was confirmed only within the last year. He suffered from hypertension, but not diabetes mellitus; there was no family history of movement disorders. An insulin tolerance test was performed to induce hypoglycemia and this produced an identical reaction (videotaped). There was dystonic posturing of the extremities, trunk, neck, and facial grimacing. He was stuporous and his speech was slurred. There were clinically evident signs of hypoglycemia including rapid, bounding pulse, profuse sweating, and pupillary dilatation. His blood glucose level was low. There was prompt reversal of signs/symptoms with administration of intravenous glucose.

The patient died immediately following a massive basal ganglionic hemorrhage. At autopsy, examining the hemisphere spared from the hemorrhage, multiple sections throughout the basal ganglia and the upper brainstem showed partial neuronal loss and patchy areas of gliosis. The changes involved the ventral lateral nucleus of the thalamus, red nucleus, lateral and medial geniculate nuclei, pretectal area, and to a lesser extent, the subthalamic nucleus and mamillary body. The substantia nigra and pulvinar nucleus of the thalamus were spared. There were no chronic pathological changes in the hippocampus.

The multifocal gliosis in the basal ganglia was thought to be compatible with subinfarctive vascular insults in the territory of the posterior cerebral artery.

We conclude that hypoglycemia may cause dystonia in patients with otherwise asymptomatic lesions in the basal ganglia and should be considered as a possible cause in unexplained episodes of paroxysmal dystonia.

86.

A Clinicopathological Study of Neurofibrillary Tangles in Parkinsonism

S. SUDHAKAR, A.H. RAJPUT, B. ROZDILSKY and R.J. UITTI (Saskatoon, Saskatchewan)

The commonest pathological changes in Parkinsonism are those of substantia nigra atrophy and Lewy body inclusions. Neurofibrillary tangles may be seen in a variety of conditions in conjunction with clinical features of Parkinsonism. We are reporting 16 such cases seen over the last 25 (1963-86) years. They constituted 33% of Parkinsonian autopsies at University Hospital, Saskatoon. They were classified into five groups.

Group I — (4 cases) with prominent neurofibrillary tangles limited to substantia nigra (SN) and locus ceruleus (LC).

Group II — (2 cases) Alzheimer's pathology extending into SN and LC.

Group III — (4 cases) Alzheimer's disease and concurrent Lewy body Parkinson's Disease.

Group IV — (3 cases) SN pathology of Alzheimer's disease and Lewy body inclusions.

Group V — (3 cases) Widespread neurofibrillary tangles characteristic of progressive supranuclear palsy.

Group I patients were characterized by early onset (mean - 41 years) of Parkinsonism, prolonged course (mean - 34 years), absence of dementia and good response to medical therapy. There was no history of encephalitis in any of these cases. The significance of the isolated abundant neurofibrillary tangles and cell loss in SN and LC will be discussed. The clinical features and response to treatment of the different groups will be presented.

87.

The Combined Use of Positron Emission Tomography and DNA Polymorphism for Preclinical Detection of Huntington Disease

M.R. HAYDEN, J. HEWITT, A.J. STOESSL, C. CLARK, W. AMMANN and W.R.W. MARTIN (Vancouver, British Columbia)

Fifteen persons at risk for Huntington Disease (HD) have been studied using a polymorphic human DNA marker (D4S10) and positron emission tomography (PET). We determined the likelihood of inheritance of the gene for HD in 12 persons using DNA polymorphism studies. Of these, eight persons had a 95% probability of being asymptomatic heterozygotes for HD.

Four of these eight subjects had caudate glucose utilization detected by PET which was more than two standard deviations (SD) below the age-matched control mean. Measurement of caudate glucose utilization in the other 4 presumed asymptomatic heterozygotes, revealed results between one and two SD below the mean. Four persons who had a 5% likelihood of having inherited the abnormal gene for HD had normal rates of glucose utilization in the caudate nuclei. These studies suggest that the combined use of PET studies of caudate glucose utilization may help to confirm results of DNA studies in some persons.

88. WITHDRAWN

89.

Striopallidodentate Calcification

R. RANAWAYA, D.R. McLEAN and E.S. JOHNSON (Edmonton, Alberta)

Widespread intracerebral calcification affecting the basal ganglia, dentate nucleus, thalamus, depths of cortical sulci, cerebral and cerebellar white matter is commonly associated with deranged Ca-parathormone metabolism or familial occurrence with normal parathormone function and no dysmorphic skeletal changes of pseudohypoparathyroidism.

We report a 46-year-old lady who presented with dysarthria, ataxia and a progressively dementing illness starting at age 35 years. She has

normal parathyroid function and no dysmorphic skeletal changes. There are no similarly affected family members, all of whom have normal skull x-rays. Her CT scan shows widespread intracerebral calcification confirmed by brain biopsy. She also has a monoclonal gammopathy both in her serum and cerebrospinal fluid.

This case is reported to show that not all cases of Striopallidodentate calcification are associated with disorders of Ca-parathormone metabolism or are familial in nature. In clinical neurology many cases of "Multiple System Degeneration" are seen with no known etiology and non-specific pathological changes. At least in this condition the pathology is very striking.

90.

Glutamate Dehydrogenase Deficiency and Cerebellar Ataxia

G.B. YOUNG, B.A. GORDON, C.F. BOLTON and R.L. NICHOLSON (London, Ontario)

We wish to report 2 cases of progressive cerebellar ataxia with associated partial deficiency of glutamate dehydrogenase (GDH). These differ from previously-reported cases in that the disease was clinically restricted to the cerebellum and the onset was in early life. One patient, now aged 45, has been symptomatic since her early twenties. The other, a boy aged 15, first developed ataxia at age eleven years. Other causes of ataxia were excluded.

There was a profound depression in the thermo-labile GDH isoenzyme in leukocytes and fibroblasts in these patients. Results of magnetic resonance imaging and electrophysiological tests will be shown.

We suggest that patients with unexplained cerebellar ataxia be screened for GDH deficiency.

91.

Fluorodopa PET Scanning in Cynomologous Monkeys: A Model for the Study of the Dopamine System *In Vivo*

M. GUTTMAN, E. WALSH, W.R.W. MARTIN, T.J. RUTH, M.J. ADAM, B.D. PATE and D.B. CALNE (Vancouver, British Columbia)

Positron emission tomography enables the study of regional neurochemistry *in vivo*. Neurotransmitters such as dopamine can be assessed semiquantitatively with this technique. An animal model provides an opportunity to examine the dopaminergic pathways of the basal ganglia in normal and pathological states. The establishment of a reproducible protocol is necessary to evaluate this method for the study of cerebral disorders.

We performed 6-C(^{18}F)-fluorodopa (6-FD) PET scans with *Macaca fascicularis*. The UBC/TRIUMF PETT VI tomograph and a Picker 0.15 Tesla MRI machine are used. Male animals are first anesthetised and intubated. MRI images are performed to identify the exact location of the striatum. The head is fixed in position with a thermoplastic mask and skull x-rays are taken to establish the relationship of the cranial vault to the tray that carries the monkey. If PET scans are performed at a different time than MRI, the skull x-rays are used to reposition the monkey precisely. Positioning in the tomograph is achieved by applying the coordinates of the striatum from the MRI images. The monkey is then pretreated with carbidopa. After injection of 6-FD, blood samples are drawn from a femoral arterial line and analyzed for radioactivity and methoxy derivatives of the tracer. Sequential scans are performed in three positions that generate interleaving axial slices 4.8 mm apart. This technique has enabled us to perform reproducibly 6-FD scans in this species.

92.

Treatment of Dopamine Agonist Psychosis in Parkinson's Disease with Electroconvulsive Therapy

T.A. HURWITZ, D.B. CALNE and K WATERMAN (Vancouver, British Columbia)

Psychiatric disorders are among the most disabling complications of long term treatment of Parkinson's Disease with dopamine agonists. Management is difficult since lowering the dose of the dopamine agonists or administering neuroleptics ususally exacerbates the Parkinson's Disease. Two non-demented patients with chronic psychosis (unresponsive to manipulations of their dopamine agonists), each received a course of electroconvulsive therapy (ECT). Psychiatric symptoms, intellectual ability and Parkinson's signs were rated weekly. During ECT the dose of dopamine agonist medications were kept constant. Following ECT psychosis resolved in both patients. Subsequently the daily dose of dopamine agonists were raised to optimize control of their Parkinson's Disease without recurrence of psychosis. Both patients have remained free of psychosis, one for 3 months, the other for 5 months. Although our experience is limited to two subjects, we consider that ECT may be a useful treatment with sustained benefit in dopamine agonist psychosis and may be producing its beneficial effects by down regulating agonist induced super-sensitive dopamine receptors in the mesolimbic dopamine projection.

Muscle Diseases I (Platform)

THURSDAY, JUNE 25TH, 1987 1330-1700

Co-Chairmen: DR. C. BOLTON (London)
DR. J. OGER (Vancouver)

93.

Gucocorticoid Excess Induces Preferential Depletion of Myosin in Denervated Skeletal Muscle Fibers

G. ROULEAU (Boston Massachusetts)

André Barbeau Memorial Prize

The combined effects of dexamethasone treatment (1 mg/Kg/day) plus denervation (DEX-DEN), were studied at 7, 13 and 28 days by microscopic, biochemical and physiological techniques in plantaris and soleus muscles of adult rats. The results were compared to corresponding dexamethasone-treated (DEX) and denervated (DEN) muscles and appropriate controls. There was a significantly more marked atrophy of all fiber types in the DEX-DEN plantares at 7 and 13 days than in either DEX or DEN muscles. The degree of atrophy was greatest in type 2B fibers in DEX-DEN plantares. Electron microscopy revealed a severe preferential depletion of thick myofilaments in DEX-DEN plantares and solei but not in DEX or DEN muscles. The thick myofilament depletion in DEX-DEN muscles occurred in addition to a severe overall reduction of myofibrillar caliber. Gel electrophoresis showed a marked preferential decrease of myosin heavy chain in DEX-DEN plantares and solei, but not in either DEX or DEN muscles. Myosin light chains were also markedly reduced in DEX-DEN plantares and solei. In vitro physiological studies showed a marked reduction of the denervation-induced twitch potentiation in DEX-DEN solei. Maximal tetanic tension (20 Hz stimulation) per gm weight of muscle as well as the twitch-tetanus ratio was significantly reduced only in DEX-DEN solei in relation to controls. Myosin depletion in DEX-DEN muscles may be due to a severe preferential inhibition of its synthesis coupled with an accelerated catabolism.

94.

Motor Unit Numbers and Collateral Reinnervation in Polymyositis

W.F. BROWN and R. SNOW (London, Ontario)

A method has been developed using a combination of isometric contraction, discriminative intramuscular needle electrode recording and spike-triggered averaging for measuring the surface recorded 'macro' size of individual motor unit potentials, estimating the numbers of motor units present and assessing fiber densities and the incidence of linked potentials and blocking in the biceps-brachialis muscles in man.

Studies of patients with clinical muscle biopsy and EMG evidence of polymyositis show normal numbers of motor units. However, unlike the situation in normal subjects or neurogenic disorders, it was common in polymyositis for motor units clearly detectable in the intramuscular recordings to be undetectable at the surface. This finding strongly suggests that a substantial reduction in the overall sizes of motor units has taken place possibly through the loss of muscle fibers. As well the durations of motor unit potentials were often strikingly prolonged, these changes being accompanied by a greatly increased incidence of linked potentials. These findings strongly suggest the presence of substantial intramuscular collateral sprouting, and possibly wide differences in the conduction velocities of muscle fibers. Overall, the studies point to substantial losses of muscle fibers, widespread axonal sprouting and possibly wide differences in the diameters of muscle fibers.

95.

Dynamic P-31 MRS of Muscle and Mitochondrial Disease

A.W. PENN, J. LEE, T. PERRY and L. HALL (Vancouver, British Columbia)

Muscle is ideal for metabolic assay by P.31 magnetic resonance spectroscopy (MRS) in vivo, as it is accessible and can be driven over a wide range of measurable mechanical outputs. Our protocol is a modification of Chance's technique respecting the physiological peculiarities of muscle. The phosphate over phosphocreatine ratio from the MRS is related to parameters of the physical work done. The resultant relationship of biochemical and mechanical work is linear and represents biochemical economy. (BE)

We have plotted the biochemical economy in a number of mitochrondrial and "metabolic" myopathies and show them to be clearly separated from normals and other neurological controls. We have studied two families with a similar mitochondrial encephalopathy and have demonstrated abnormal BE in a completely asymptomatic member and in another with only deafness.

Conclusions

1. dynamic MRS appears both selective and sensitive, even to subclinical disease.
2. ME may be more widespread in probands than apparent clinically.
3. dynamic MRS may be useful in selecting cases for full biochemical analysis prior to biopsy and in assaying new therapies.

96.

A Comparison of Different Techniques in Recording Sound From Human Skeletal Muscle

C.F. BOLTON, A PARKES, M.R. CLARK and C.J. STERNE (London, Ontario)

Previous studies in our laboratory have shown that the single twitch method, because of its reproducibility, is an excellent means of comparing sound recording techniques. By this method it was demonstrated that muscle sound is composed mainly of frequencies below the human auditory range. However, the influence of the type of recording device and the method of coupling it to the overlying skin are still in doubt.

Therefore, three different types of recording devices were compared: a Hewlett-Packard microphone which has a direct skin contact device attached to a piezoelectric recording crystal; an electric microphone which has a 1 mm air interface between the skin and the condenser plates; and a 20 micron piezoelectric film which is applied directly to the skin but has multiple thin air spaces and direct contacts. All three were shown to give quite similar sound wave forms. With an air interface, the air must be completely "trapped." With direct contact the stability of the contact device with the skin is crucial. Of the three methods, the piezoelectric film was most easily applied over various muscles of the body, including muscles such as the diaphragm, whose mechanical properties have previously been difficult to study.

Thus, the observation that different recording techniques, providing certain technical rules are followed, give remarkably similar sound waveforms, supports the contention that this is a potentially reliable method of measuring mechanical energy generated by human muscle contraction.

97.

Muscle Sound Produced by Continuous Voluntary Contraction

C.F. BOLTON, A. PARKES, R.T. THOMPSON, M.R. CLARK and C.J. STERNE (London, Ontario)

Few studies of muscle sound have been reported. Most have been concerned with continuous voluntary contraction, but a variety of techniques were utilized. In particular, the lowest frequencies, below the human auditory range, were not recorded. We have shown, by the single twitch method, that such frequencies account for more than 90% of the total energy of the sound wave.

Therefore, we studied sound from thenar muscle during continuous voluntary contractions in 6 healthy subjects. Technical guidelines, previously established by the single twitch method, were carefully followed. The apparatus recorded frequencies between at least 0.07 and 1,000 Hz, the response being flat between 10 and 400 Hz. Fast Fourier frequency analysis was performed during a period of 0.5 sec. The waveform consisted of a variety of frequencies, the lowest frequencies, less than 15 Hz, being most prominent, faster frequencies being progressively less prominent, with those above 30 Hz being almost absent. Our results differ considerably from previous reports; in particular, no single frequency, such as 25 Hz, was more prominent than others.

We propose that our sound recordings of continuous contraction of human skeletal muscle give results which are consistent with known physiological and mechanical properties of muscle, and should serve as a basis for further research.

98.

Carnitine Palmityl Transferase Deficiency (CPTD) in a Female: Different Clinical Features than in the Male?

A. SHUAIB, C.T. MAN-SON-HING, D.L. SEVERSON and A.K.W. BROWNELL (Calgary, Alberta)

CPTD of skeletal muscle, first described in 1973, is now recognized to be the most commonly diagnosed metabolic muscle disease causing rhabdomyolysis and myoglobinuria. In total, 26 cases have been reported and myoglobinuria related to exercise has been the hallmark of every case, except for one. A definite male preponderance has been observed with only 15% of the reported cases having been observed in females. The single case report of CPTD without exercise induced myoglobinu-

ria was observed in a female. In this report we describe a second patient, also a female, with CPTD in whom there was no history of exercise induced myoglobinuria.

The patient was seen at age 33 because of a 7 month history of vague pains and cramps in her thigh and calf muscles that, at times, seemed to relate to exercise. She had never noted myoglobinuria. Her examination was normal. Although there was nothing convincing in her history to suggest that she had a metabolic myopathy, this was considered a definite possibility because her 36-year-old brother had experienced a well documented episode of rhabdomyolysis and myoglobinuria when he was 18. Biochemical studies on her skeletal muscle indicated that she had CPTD.

It has been suggested that females with CPTD may be less prone to develop rhabdomyolysis and byoglobinuria than males and therefore, may go undetected. Our experience supports this suggestion. If the clinical suspicion for making a diagnosis of CPTD in females is based solely on the symptoms and signs that have been described in male patients we believe that female cases may be overlooked. Until considerably more case reports of CPTD in females are documented in the literature, the full extent of its clinical manifestations will remain uncertain.

99.

The Usefulness of a Qualitative Assay for Acetylcholine Receptor Antibodies in the Diagnosis of Myasthenia Gravis

J. OGER (Vancouver, British Columbia)

We have modified the technique of Lindstrom and of Tindall to measure acetylcholine receptor antibodies (AchR Ab) to the human receptor in human serum.

We use AchR isolated from human muscle obtained at autopsy or from leg amputation following triton X extraction. Receptors are labelled with iodide 125, alpha bungarotoxin and 10 ul of serum are added. Complexes are precipitated with Staph A. Values of samples over 3 standard deviation above the mean of the controls are considered to be positive. Samples between 2 and 3 SD above the mean of the controls are considered to be borderline and the assays repeated.

We found positive results in 54 of 55 generalized active myasthenia gravis (98%), 8 of 21 (35%) MG in remission, 16 of 37 (57%) ocular myasthenia gravis and none of 55 healthy controls. 2 out of 38 non-MG samples were also positive. One had rheumatoid arthritis and was treated with pencillamine. The second was diagnosed as botulism even though the bio-assay for botulin toxin was found negative.

We conclude that this qualitative assay yields an excellent clinical-biological relation and is most useful for diagnostic purposes.

100.

Congenital Myasthenia Gravis (CMG): Diagnosis and Management

J.M. DOOLEY, H. WRITER and E. GIBSON (Halifax, Nova Scotia)

Congenital myasthenia gravis (CMG) accounts for approximately 1% of patients with MG. The characteristics are weakness in the first year of life, due to a defect neuromuscular transmission, and the absence of antibodies to acetylcholine receptors (AChR).

We present 6 children with CMG who have been followed for 3-14 years. The initial symptoms involved weakness of the muscles of the face and neck in all 6 patients, although ptosis was present in only 3 children. Whereas none of the families noted fatigability at the time of presentation it was eventually a prominant symptom in all. The progression of symptoms was very slow before the introduction of medication. Two patients are siblings; the other children have no family history of neuromuscular disease.

An improvement with IV edrophonium (Tensilon) was seen in only 3 of 5 patients. Repetitive nerve stimulation of some but not all nerves tested resulted in a decremental response in 6/6. One of the patients with a negative Tensilon test subsequently responded to Pyridostigmine (Mestinon). Five of the 6 patients responded to Mestinon. Two patients responded only after 3 days of therapy. A third developed toxic symptoms on a very low dose of Mestinon but responded to steroid therapy. Facial "tightness" was an early symptom of toxicity in 3.

Therefore CMG in our 6 patients presented with weakness but not apparent fatigability in the first year of life. Ptosis was eventually present in the 5 responders but not in the one non-responder to Mestinon. A Tensilon test may be negative and repetitive nerve stimulation should be carried out in more than 1 nerve in all patients suspected of having CMG.

101.

Acetylcholine Receptor Antibodies (ACHR AB) in MG: Lack of In Vitro Secretion in a Group of Seropositive Patients in Correlated with Low IGG Secretion

R.L. KAUFMAN and J. OGER (Vancouver, British Columbia)

We have measured IgG and AchR Ab secreted in vitro by peripheral blood lymphocytes (PBL) of 12 controls and 20 MG patients with antibodies in their serum.

Controls did not secrete AchR Ab. In controls the mean IgG secretion in response to pokeweed mitogen was 1305 ± 353 ng.

Among MG patients, only 11 secreted AchR Ab (0.1 to 16 fmoles/10^6/7 days) in the presence of PWM; 9 secreted AchR Ab even in the absence of PWM. In this group, IgG secretion was high (3556 ± 948). In contrast the 9 MG patients who did not secrete detectable amounts of AchR Ab had a low IgG secretion in response to PWM (351 ± 127). This was significantly different from controls ($p < 0.05$) and from in vitro AchR Ab secretors ($p < 0.01$). AchR Ab secretors also differed from non-secretors by a shorter disease duration: 10/11 secretors had a disease duration of less than 10 years versus 3/9 non-secretors ($p < 0.01$).

There was no correlation between the ability to secrete antibody in vitro and age, sex, type of MG or treatment.

We conclude that, in seropositive MG, ability of PBL to secrete IgG in response to PWM and to secrete AchR Ab are linked and decrease with time. This suggests that aspecific immune suppression is triggered as time passes.

102.

Ophthalmological Findings in the Fukuyama Type Congenital Muscular Dystrophy

M. OSAWA, N. OKADA, M. SUGAMA, H. SUZUKI et al (Hamilton, Ontario)

Because the cardinal lesions in Santavouri disease (MEB) and the Walker-Warburg syndrome (WWS) are commonly observed in muscle, eye and brain, a nosological relationship between these two conditions and the Fukuyama-type congenital muscular dystrophy (FCMD), where eye lesions have not, usually, been examined in detail, have been of interest to study. A detailed ophthalmological examination of patients with FCMD is reported here.

Thirty-eight patients with FCMD (Type I, 32 cases; Type III & IV, 6 cases), whose diagnosis was confirmed both clinically and histologically were examined by pediatric opthalmologists.

The overall incidence of opthalmological abnormalities in these patients were 55.3% (21/38). However, there were no patients with microphthalamos, glaucoma, corneal opacities, abnormalities of the iris or the

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anterior chamber or optic disc coloboma. In the patients with Type I FCMD the following opthalmological findings are reported: strabismus and abnormal eye movements (4/32), severe myopia (1/13), mild myopia (6/13), hyperopia (5/13), cataracts (2/13), pale optic disc (1/32), obscure optic disc margin (2/32), and "round lesion" at the periphery of the retina (5/32). Patients with type III & IV FCMD showed only strabismus (2/6), myopia (3/3) and cataracts (1/6).

The most striking finding was "round lesions" (15.6%; 5/32). In two patients where fluorescent angiography was done, the findings were negative. Although there appear to be a tendency of patients with "round lesions" to exhibit more severe clinical manifestations, there was not correlation between the clinical features of MEB such as glaucoma and those of the WWS, such as corneal opacities, abnormalities of the iris or the anterior chamber, and microphthalmos, were not found in the patients with FCMD we examined. In MEB and the WWS, the opthalmological abnormalities are detected in early infancy while the eye manifestations in FCMD are not and require a more thorough examination.

103.

Muscle Cramp and Pain

J.K. BARUAH, A.R. SULAIMAN and D. KINDER (Milwaukee, Wisconsin)

The extensive evaluation is often unrewarding in muscle cramp/pain syndrome. Ninety-eight patients with these symptoms studied extensively by EMG and muscle biopsy. Seventy-one patients had abnormalities in these studies and considered to have pathophysiologic role in the mechanism of cramp. Twenty-six patients had following electrophysiologic abnormalities (27&); continuous muscle fiber activity (4); impulse induced neurotonia (4); group discharges and myokymia (8); stiff-person syndrome (3); repetative motor unit discharges (2); benign fasciculation (3); and complex repetative discharges (2). The etiologic consideration of these electrophysiologic abnormalities in the genesis of cramp was established by their temporal relationship. The symptoms improved with the disappearance of these findings. Muscle histology-histochemistry and ultra-structural study revealed presence of glycogen storage disease (2); lipid storage muscle disorder (15); and mitochondrial abnormalities (3) and mild neurogenic pattern (25) or 26%. In spite of these studies 27 patients (28%) remain undiagnosed and in them electrophysiologic and muscle biopsy study failed to offer any clue to possible etiology. It is possible to establish an etiologic diagnosis in about two-thirds of patients (this series) with muscle cramps. Management of these patients may be rewarding either by treatment with membrane stabilizing drugs (cramps with definite electrophysiologic abnormalities) or by dietary regime (as in glyogen or lipid storage muscle disorder).

104.

Heterogenicity of Nemaline-Rod Myopathy

E. SHAHAR, R.C. TERVO, J.S. KOBAYASHI, L.E. BECKER and E.G. MURPHY (Toronto, Ontario)

Nemaline-rod myopathy (NRM) is a rare disorder characterized by abundant rods within the muscle fibers. A classification of NRM is proposed based on the clinical electrodiagnostic, and muscle biopsy data of a series of 13 patients diagnosed over the past 25 years. Three age-related groups of presentations have been identified: early infancy, childhood and adult. The progression and the outcome correlated with the age of onset. Three infants presented in the post-natal period with severe weakness and progressive respiratory failure leading to death. Seven young children at 1-7 years who presented with delayed motor milestones had mild proximal weakness which was non- or mildly progressive. These patients remain walking within a follow-up period as long as 25 years. We have identified a unique sub-group of young children who initially had mild weakness. However, during the second year of life, they abruptly developed severe limb and respiratory muscle weakness thus requiring prolonged artificial ventilation of 9-14 years duration. The adult patient presented at age 28 years with proximal weakness. No obvious correlation has been found between the severity of the disease and the laboratory, electrodiagnostic, and muscle biopsy data. However, quantitative morphometry on the nemaline rods has not been performed. Creatine kinase levels were normal. EMG studies (11 patients) were normal in 6 and myopathic in 5. Light microscopy showed nemaline rods within the muscle fibers. Electron microscopy was confirmatory showing nemaline rods with the pathognomonic, lattice-like appearance in continuity with the Z-bands. The present series substantiates previous observations of wide heterogenicity in NRM despite the common pathological denominator.

Muscle Diseases II (Poster)

THURSDAY, JUNE 25TH, 1987 P.M.

105.

Myopathy with Hypophosphatasia

G. DERBYSHIRE, J.C. HAWORTH, J. HOOGSTRATEN and S.S. SESHIA (Winnipeg, Manitoba)

Hypophosphatasia is an inherited disorder characterized by skeletal involvement. Serum and tissue alkaline phosphatase activites are low and levels of phosphorylethanolamine in the plasma and urine elevated. We present two unrelated children with hypophosphatasia. Both of them also have proximal muscle weakness, a finding not previously reported in the disorder.

C.H. was first seen at the age of 5 years because of difficulty in climbing stairs. A diagnosis of hypophosphatasia had been made previously on biochemical and radiological grounds. He did not walk until 18 months of age and his motor performance had always been inferior to his peers. He also experienced stiffness and pain in his muscles, particularly during winter and in the mornings. Physical examination revealed proximal muscle weakness (Grade 4/5) in all four limbs. He had a waddling gait, difficulty in climbing stairs and in getting up off the floor. The deep reflexes were present. Serum CPK levels were normal on several occasions. Motor and sensory conduction were normal. Electromyography of the right quadriceps and right tibialis anterior muscles suggested a "myopathy". Pathologic examination of a quadriceps muscle biopsy showed myofiber diameter to be in the range of 14 to 21 microns. There were no other abnormalities. C.H. is now 8 years old. There has been no deterioration in his neuromuscular status.

The second child, who was first seen at the age of 9 years, had similar clinical and laboratory findings. Muscle biopsy showed no abnormality. There has been no deterioration in the subsequent 7 years.

We suggest that a relatively non-progressive myopathy may be an important manifestation of hypophosphatasia. The biochemical basis for the myopathy is unknown but the clinical features resemble the myopathy seen with osteomalacia.

106.

Ulstrastructure of Motor Endplate in Centronuclear Myopathy

B. LACH, P. BOURQUE and D. PRESTON (Ottawa, Ontario)

Centronuclear myopathy (CNM) refers to the heterogeneous group of disorders that share the histological features of central nucleation,

nuclear halo and selective muscle fiber hypotrophy. We present clinical and morphological evidence linking motor endplate (ME) abnormalities to pathogenesis of sporadic forms of CNM.

This 24 year old man complained of life-long clumsiness, hypotonia and muscle weakness. He had striking pseudo-hypertrophy of deltoids and triceps surae, minimal bilateral ptosis, and no other neurological abnormalities. EMG showed increased insertional and spontaneous activity, high frequency discharges and positive sharp waves.

Muscle biopsy revealed central nucleation with Type I hypotrophy, expanded acetylocholine esterase activity around muscle fibers and sprouting of terminal axons. Ultrastructurally, the most striking finding was distortion of normal architecture of motor endplate. The synaptic clefts (SC) showed areas of disorganization and proliferation, alternating with a variable degree of atrophy. SC were often shallow and widened, contained an abundance of electron-dense granules and pleomorphic vesicular and membranous profiles. All ME showed severe collagenization and deposition of multiple layers of basement membranes. Terminal axons were occasionally withdrawn from the synaptic contacts and a few showed degeneration. There was also evidence of demyelination and remyelination of the most distal nerve fiber. Some terminal axons were separated from the underlying SC by processes of Schwann cells. All these changes were detectable in the ME of normal and atrophic muscle fibers.

Our findings indicate that some forms of sporadic CNM are related to severe, probably primary involvement of motor endplate and terminal axons.

107.

Myopathy in Primary Amyloidosis: Report of a Case and Review of the Literature

M. ROKE, W. BROWN, D. BOUGHNER and G.P.A. RICE (London, Ontario)

Involvement of the peripheral nervous system in amyloidosis is common. It is less well recognized that amyloid can directly infiltrate and weaken skeletal muscle. We report a case of a 73-year-old woman known to have cardiac amyloidosis who developed profound weakness secondary to amyloid myopathy. During a 2 week period in June 1986 she developed difficulty walking, climbing stairs, and raising her arms, with generalized myalgia. She was found to have profound muscle weakness in the pelvic and shoulder girdles. Wasting was present in the gluteal muscles but the calves were enlarged and doughy in texture. Tendon reflexes were normal. Electromyography revealed hypercomplex motor units, bizarre repetitive discharges, positive sharp waves and increased insertional activity. Nerve conduction studies were completely normal. Creatine phosphokinase measured 293 international units (normal 26-140) and was predominantly the MM fraction. LDH measured 563 units (203-378). Deltoid biopsy revealed some alteration in muscle fibre size, a tremendous increase in thickness of blood vessel walls and perimysial and endomysial connective tissue, and some Type 2 fibre atrophy. There was no muscle necrosis. Congo Red staining revealed prominent apple green birefringence in these tissues. Amyloidosis was confirmed by electron microscopy. Her weakness has progressed. Review of the 13 other cases in the literature revealed a fairly homogeneous clinical picture. Proximal weakness, muscle stiffness, pseudohypertrophy and myalgia appear to be the principal features. These clinical features usually develop in cases with well developed generalized amyloidosis. Although amyloid infiltration of skeletal muscle is recognized as a pathological phenomenon, muscle weakness secondary to this is rare. Direct infiltration of myofibrils does not occur, implicating changes in connective tissue elastance or physiological perturbations secondary to changes in blood vessel walls.

108.

The Scapulo-Peroneal Syndrome: Neurogenic or Myopathic?

C.A. SIMPSON (Victoria, British Columbia)

A mother and daughter with this rare syndrome are described. The important clinical features, nerve conduction studies and electromyography are described and discussed and it was difficult to decide if the changes found were neurogenic or myopathic. CT scan of limb muscles is shown. Muscle biopsy in these cases strongly suggests that this family has the myopathic rather than the neurogenic variety.

109.

Myasthenic Syndrome and Conjugate Gaze Paresis in Motor Neuron Disease

J.H. NOSEWORTHY, A. RAE-GRANT and W.F. BROWN (London, Ontario)

We report a clinicopathological study of a patient with motor neuron disease whose initial myasthenic presentation with gaze paresis, EMG studies and response to treatment suggested a diagnosis of myasthenia gravis.

A 60-year-old female presented with a 6 week history of progressive dysarthria, dysphagia for liquids and proximal weakness of upper extremities particularly late each day. Findings included severe dysarthria, bilateral ptosis, right lateral gaze paresis and weakness of facial, neck flexor and proximal limb muscles. EMG studies showed an abnormal decremental response to repetitive stimulation (3 Hz), post-tetanic exhaustion and post-tetanic facilitation. Respiratory failure requiring ventilation developed despite prednisone therapy. An initial apparent response to anticholinesterases and plasma exchange was not sustained. Progressive bulbar palsy, bilateral horizontal gaze palsies and quadriparesis with fasciculations of the tongue and extremity musculature ensued. Repeated EMG studies failed to reveal abnormal insertional or spontaneous activity in the sampled muscles.

In addition to findings characteristic of motor neuron disease (extensive neuronal degeneration in anterior horn cells and the cranial nerve nuclei of V (motor), VII, IX and XII with widespread neurogenic atrophy), postmortem examination revealed gliosis and neuronal degeneration in the nuclei of cranial nerves III, IV, and VI.

The electrophysiological and neuropathological findings of this informative case together with a review of the literature of the myasthenic syndrome and ophthalmoplegia in motor neuron disease will be presented in this poster.

110.

Progressive Neonatal Rigidity: Dudley Syndrome

J. TAPPER, G. DAVIDSON, W.G. SHERWOOD and E.G. MURPHY (Toronto, Ontario)

A five week old female infant, well during the first month of life, presented with respiratory distress and lethargy. On presentation rigidity of paraspinal muscles and recti abdominus was noted. Peripheral muscles were normal. Respiratory arrest necessitated ventilation. Weaning from the ventilator was unsuccessful due to splinting of the chest wall. Subsequently, increasingly high peak pressures were required for adequate ventilation. As well, progressive rigidity of peripheral muscles occurred. Muscles affected became rock hard with contractures, board-like rigidity of the trunk and a bullet-like tongue. Reintubation was difficult due to involvement of jaw muscles. The patient remained mentally alert and responsive.

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Serum CK was markedly elevated. EMG showed fibrillation potentials and polyphasia, most marked in the paraspinal muscles. Metacurine resulted in attenuation of the fibrillation. Clinically, there was no response to Citrate, Nifedipine, Dantrolene nor Valium. Muscle biopsy from seven different sites showed Z-band degeneration. Four cases previously described, as well as this case, were of native Indian and/or French Canadian extract. This myopathy appears to be of either familial or environmental origin, characterized by progressive muscle regidity involving respiratory muscles, resulting in a fatal outcome.

111.

Trans-cervical Thymectomy for Myasthenia Gravis

J.G. HUMPHREY, J.D. COOPER, A. JILAIHAWI and H.E. HUMPHREY (Toronto, Ontario)

In patients with myasthenia gravis (MG) without evident thymoma, we have employed the trans-cervical approach to perform complete thymectomy for management of this disease. We have reviewed 53 patients operated upon by the same surgeon and evaluated by the same neurologist between 1977 and 1984.

Patients were assessed using a modified Osserman classification (0 - asymptomatic; 1 - ocular signs and symptoms only; 2 - mild generalized weakness; 3 - moderate generalized weakness; 4 - severe generalized weakness and/or respiratory deficiency). The mean grade for all patients at the time of thymectomy was 2.7. Ninety-six per cent of patients had generalized weakness pre-operatively and 17% were on prednisone. No patient has been lost to follow-up. One patient died of viral pneumonia six years following thymectomy. At the most recent follow-up, the mean clinical grade was 0.5. Eighty-seven per cent of patients were free of weakness, 94% improved by at least one stage and 81% improved by two or more stages. Fifty-five per cent of patients are off all medication and in remission. No patient has shown deterioration.

The trans-cervical approach has been modified using a special sternal retractor which improves exposure and allows the entire retrosternal and mediastinal area to be directly visualized. This permits complete excision of the gland even when various described anatomic anomalies of the thymus gland are present. In the present group of patients, 94% had hyperplastic thymus glands and 5% were atrophic.

The trans-cervical approach allows complete thymectomy with minimum morbidity and facilitates the acceptance of early thymectomy for management of myasthenia gravis. The results are comparable to other groups of thymectomized MG patients.

112.

Treatment of Recessive Myotonia Congenita with Mexiletine

V. BAHN, T.J. BENSTEAD and L.P. HEFFERNAN (Halifax, Nova Scotia)

Disabling myotonia can occur in myotonia congenita and may by more severe in the recessive variety. We managed a 38-year-old man with clinical and electrophysiologic findings consistent with recessive myotonia congenita. His parents were unaffected. He had mild muscle weakness and hypertrophy of calf muscles. Myotonia severely impaired his mobility and was not relieved by acetazolamide, phenytoin or procainamide. Tocainide has been found effective in recessive myotonia congenita, however side effects may restrict its use. Mexiletine, a similar but possibly less hazardous drug, was given at a dose of 200 mgs q.i.d. greatly improving myotonic symptoms within a few hours. Symptoms returned to previous levels 24 hours after mexiletine was stopped. Electrophysiologic evaluation of mexiletine demonstrated a normal ulnar compound muscle action potential (CMAP) amplitude. On three trials, immediately after a 10 second exercise, the amplitude fell to 16-28% of baseline, returned to 70% of baseline by 60-120 seconds post-exercise and 90% by 120-180 seconds. On mexiletine the ulnar CMAP immediately after 10 seconds of exercise was 36-47% of baseline, 70% by 10-30 seconds post exercise and 90% by 60-120 seconds. With and without mexiletine 10 hertz repetitive stimulation produced a marked decrement. Mexiletine was well tolerated without evidence or major side effects nine months after introduction. We feel mexiletine can be an effective and safe medication for symptoms of recessive myotonia congenita. Clinical improvement is paralleled by less post exercise CMAP amplitude drop and faster recovery to baseline levels.

113.

Classical Friedreich's Ataxia and Mitochondrial Encephalomyopathy: A P-31 MRS Study

A.W. PENN, L. LEE and H. DUNN (Vancouver, British Columbia)

A metabolic defect, possibly in bioenergetic metabolism, has been variably implicated in Friedreich's Ataxia.

We have studied a 16-year-old patient who presented with classical features of Friedreich's Ataxia (FA), however, because of a past history of fatiguability and episodes of transient visual obscurations a diagnosis of mitochondrial encephalomyopathy (ME) was considered. Muscle biopsy showed only mild Type II fibre predominance with no ragged red fibres.

Dynamic P. 31 Magnetic Resonance Spectroscopy (dMRS) relating biochemical to mechanical work in active skeletal muscle, confirmed severely hampered bioenergetic economy as seen in the ME syndromes but absent in other neurological controls.

Another patient with Friedreich's Ataxia without fatiguability or visual loss had normal dMRS.

Conclusions

This patient may have a biopsy negative ME with the Friedreich's features of MERRF Syndrome. If so this closes the gap further between the ME's and classical FA, one distinction being in the spectrum of organ involvement.

Alkalinization with phosphocreative depletion similar to McArdles raises the possibility of a substrate level defect rather than one in the electron transport chain.

Epidemiology (Poster)

THURSDAY, JUNE 25TH, 1987 P.M.

114.

Neurological and Neurosurgical Procedures in Saskatchewan

A.H. RAJPUT and R.J. UITTI (Saskatoon, Saskatchewan)

Data concerning all procedures performed over the two most recent years by neurological specialists (neurologists, neurosurgeons, and pediatric neurologists) in Saskatchewan were obtained from provincial medical insurance records. All neurological specialists practicing in the province (with a population of approximately one million persons) are located either in Regina or Saskatoon, the province's two major cities. We report profiles for six groupings of procedures: electroencephalography (EEG), electromyography (EMG), lumbar puncture (LP), peripheral nerve decompression (PND), spinal surgery (SS), and cranial surgery (CS).

Summaries of the mean annual procedures revealed that just over ½% of the provincial population had an EEG performed (5253 persons) per year. 1598 patients had EMGs and 251 LPs performed annually.

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There were a total of 1057 surgical procedures performed annually, with PND patients, CS patients, and SS patients making up 41.4%, 38.5%, and 20.1% respectively of the total surgical patient load.

Details concerning the two neurological centers, one consisting mainly of academic specialists, the other solely private practitioners, and a regional profile of procedures will be presented.

115.

Neurological Disorders/Services in Saskatchewan Treaty Natives

R.J. UITTI, R. SEALEY, A.H. RAJPUT and A. SALEH (Saskatoon, Saskatchewan)

Several years of neurological practice at University Hospital, Saskatoon indicated that the native Indian population in Saskatchewan was being seen at a different frequency for various neurological conditions than the rest of the provincial population e.g. fewer cases of multiple sclerosis and a higher than expected number of tuberculosis-related neurological disease. We present a provincial profile of neurological disorders/services in Saskatchewan treaty natives based on medical care insurance commission records for 1983-84.

Our study was limited to registered natives (47,954 in the province). 474 natives or 1.0% of that population, were seen by neurospecialists (medical and surgical) during the year studied. In comparison, 1.6% of the total provincial population were seen in the same period. The median age of native beneficiaries was 26 years; for all provincial beneficiaries the median age was 45 years. There were an average of 1.5 services provided to each native beneficiary annually. 54% of native beneficiaries were male and males received 57% of services to natives.

21.2% of all neurospecialist contacts with natives were related to neurological injuries or poisonings. While intracranial injury was diagnosed in only 2.4% of contacts with the total provincial population, 8.4% of all contacts with natives concerned intracranial injury.

Our data correspond with mortality figures citing injury and poisoning as the number one cause of death in registered natives. As well, natives have a life expectancy ten years shorter than that of the general Saskatchewan population. In particular, our data shows a large disparity between intracranial injury in the native and general populations.

While our findings concern only a portion of the native population, i.e. the registered treaty, we believe that this data provides information that could be used to improve health care for all natives in Saskatchewan.

116.

Neuroepidemiology in Saskatchewan: Disorders and Services

A.H. RAJPUT, R.J. UITTI and T. WOLLIN (Saskatoon, Saskatchewan)

A record of every professional physician-patient contact in Saskatchewan is available through the medical care insurance commission provincial data-bank. We report a profile, based on records of the two most recent consecutive years, for all patients seen by neurological specialists (neurologists and neurosurgeons) in the province of Saskatchewan.

We found that only 1.6% of the provincial population was seen annually by a neurospecialist, a figure well below minimal U.S. estimates (2.5%). An average of 1.8 services was performed annually for each beneficiary. The median age of patients seen by neurospecialists was 45 years. 52% of services were provided to females and 48% to males. Most services were provided on an out-patient basis (62%); the balance of services (38%) were rendered in the emergency room or in the hospital. The median in-hospital stay was nine days in both Saskatoon (at an academic center) and Regina (under private practice neurospecialists).

The five most common diagnoses seen by neurospecialists are given below in order of frequency:

1. Headache
2. Neuropathies
3. Back & Spine disorders
4. Cerebrovascular disease
5. Insomnia/Dizziness

The overall pattern of diseases was similar to that reported in U.S. studies.

Service distribution over the province, by region, for both neurology and neurosurgery, will be presented, as well as discussion concerning apparent disparities between expected service utilization and actual provincial service utilization.

117.

Primary Intracranial Neoplasms in Manitoba, Canada 1980-1985

G.R. SUTHERLAND, R.C. FLORELL, A.A.F. SIMA and N. CHOI (Winnipeg, Manitoba)

The incidence of primary intracranial tumors in Manitoba, Canada, was reviewed from 1980 through 1985 (pop. = $(1043.3 \pm 7.3) \times 10^3$), with 657 tumors diagnosed (incidence = 10.5 ± 0.7/100,000 people/yr). The most common tumors were: astrocytoma 281 (43%), meningioma 145 (22%), and pituitary adenoma 111 (17%). Age specific annual incidence rates for all tumors showed two peaks; one in the 0-5 age group (3.9/100,000 people/yr), and one in the 60-69 age group (26.7/100,000 people/yr). After the 6th decade, the incidence declined. Among the malignant astrocytoma, the age specific annual incidence increased to the 6th decade (14.1/100,000 people/yr) after which it fell to 4/100,000 people/yr for the > 80 age group. The incidence of benign astrocytoma remained constant with age (1/100,000 people yr). Although meningioma initially increased in incidence, it plateaued in the 5th decade at 7/100,000 people/yr. Of 145 meningioma patients, 56 (39%) had meningotheliomatous histology, 48 (33%) transitional, 10 (7%) malignant, 7 (5%) fibroblastic, 6 (4%) psammomatous, 3 (2%) angioblastic, and 15 (10%) unspecified. Pituitary adenoma showed two peaks. One occurring in the 2nd decade (2.7/100,000 people/yr), and the other in the 5th decade (3.1/100,000 people yr). As the population within the Province of Manitoba has remained relatively constant during the period of study (with minimal emigration or immigration), we feel that the above figures reflect accurately the clinical occurrence of primary intracranial neoplasms.

Neuro-Oncology I (Platform)

FRIDAY, JUNE 26TH, 1987 1345-1700

Co-Chairmen: DR. G. BERTRAND (Montreal)
DR. D.R. McLEAN (Edmonton)

118.

Cerebral Metastasis from Malignant Melanoma

R.F. DELMAESTRO and I.M. MENDEZ (London, Ontario)

Six hundred and fifty-two patients with histologically proven primary malignant melanoma have been followed by the London Regional Cancer Centre from 1960 to 1985. Neurological signs and symptoms secondary to metastases to the brain developed in fifty-five patients (8.4%). The mean age was 49 years; 71% were male and 29% female. Multiple lesions were found in 61% and a single metastasis in 39%. The most common site for the primary lesion in females was the lower limb (37%) while for males was the trunk (44%).

Six month survival for patients with a single metastasis was 58% if wide surgical excision was possible and 25% of these patients survived greater than two years. In patients with multiple metastases that received

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radiotherapy, survival times of greater than 6 months were found in 12% of the patients.

Patients with a single metastasis appear to benefit by being managed by radical surgical removal of the lesion. Postoperative radiotherapy should be considered in cases of recurrence in the same site of the initial metastasis. In patients with multiple metastasis as the initial presentation, radiotherapy may have little impact on survival and its effectiveness should be carefully assessed as a palliative method of treatment.

119.

Surgical Strategies for Spinal Metastasis

R.G. PERRIN and R.J. McBROOM (Toronto, Ontario)

Controversy concerning the management of patients with symptomatic spinal metastasis has focussed firstly on the relative merits of radiation and surgery (alone or in combination) and secondly on the optimal approach (decompression from in front or from behind) in those patients selected for surgical treatment.

We have reviewed our experience with surgical management of patients with symptomatic spinal metastasis decompressed from behind (200 consecutive cases) and from in front (21 cases) to examine factors which determine the optimal surgical strategy.

The factors which must be considered in determining the most appropriate approach include 1. tumour location, 2. spinal level, 3. fixation factors, and 4. patient debility.

Successful surgical management of patients with symptomatic spinal metastasis requires not only decompression of the spinal cord and nerve roots, but also must provide for stability of the spinal column. Based on our experience with approaches from behind and from in front, a variety of factors determine the most appropriate surgical strategy. No single approach is always applicable and the treatment team must be prepared to execute the optimal approach.

120.

Preliminary Results of Treatment of Malignant Gliomas with a Protocol Incorporating ^{125}I Interstitial Irradiation

V.F. DaSILVA, L.J. EAPEN, B. LACH, D.J. STEWART, A.L. GIRARD, H. HUGENHOLTZ, N.A. RUSSELL and B.G. BENOIT (Ottawa, Ontario)

Starting in November 1985 a selected group of de novo malignant gliomas, was treated following craniotomy with 4,500 rad whole brain irradiation, 1,500 rad boost to tumor area, 6,000 rad to tumor periphery delivered by ^{125}I sources implanted stereotactically and intra-arterial BCNU, cis-Platinum and VM-26.

Patients were selected if their post-craniotomy Karnofsky score was => 70, if the tumors were located in the cerebrum but not in the thalamus, hypothalamus or corpus callosum, and if the pre-operative diameter of the tumor was less than 5 cm.

At time of writing only 6 patients were entered on protocol: 2 glioblastoma multiforme (GM), 2 anaplastic astrocytomas (AA) and 2 mixed malignant gliomas (MMG). The first 5 patients did not receive chemotherapy. Of these five, 2 developed steroid resistant brain swelling at the implant site and were reoperated. The first reoperated patient has died 13 months after implant and 15 months after diagnosis of a large GM; the second was successfully debulked and is tolerating steroid withdrawal. Despite the difference in outcome from an histological viewpoint the two cases are similar: compatible with radiation necrosis and residual/or recurrent tumor. The other four non-operated patients are steroid independent; all patients alive have Karnofsky rates above 70.

121.

Quality of Life Measurement in Patients with Brain Tumours

N. LAPERRIERE, T. PANZARELLA, E. ING and M. BERNSTEIN (Toronto, Ontario)

Although the need for a method of measuring the quality of life of patients harbouring brain tumours is clearly recognized, no adequately evaluated or feasible method has been established. We describe a method in which 29 items were assessed by patient self-report using linear analogue scales. This method is based on an instrument developed at the Princess Margaret Hospital for patients with breast cancer. The 16 items dealing with general health problems were retained. Thirteen items dealing with major problems associated with brain tumours were derived from clinical experience. This report deals with the results of a pilot study of this instrument on 40 patients with brain tumours. Each item of the measurement method will be discussed with regards to its feasibility, validity and reliability. Its ability to distinguish between clinically distinct groups of patients and its possible application to a research setting in evaluating newer and potentially more toxic therapies for brain tumours will be discussed.

122.

Phosphorus Magnetic Resonance Spectroscopy Reveals Major Metabolic Changes in Cerebral Glioma Within Hours of Treatment with BCNU

D.L. ARNOLD, E.A. SHOUBRIDGE, W. FEINDEL and J.G. VILLEMURE (Montreal, Quebec)

We have previously reported changes in the phosphorus magnetic resonance spectra of brain tumours in association with tumour therapy. The relationship of these changes to therapy as opposed to tumour growth as well as the timing of spectal changes with respect to changes visible on X-ray CT or MR images still needs to be clarified.

A 40 year old female with a recurrent mixed astrocytoma/oligodendroglioma was treated with intra-arterial BCNU at four week intervals. Phosphorus magnetic resonance spectroscopy was performed before, and on two occasions after her third treatment.

Before treatment, phosphodiesters were reduced by 25% and intracellular pH (pH_i) was increased to 7.14 (normal 6.97 ± 0.02). Eight hours following treatment phosphocreatine and phosphodiesters were reduced by 39% and 42% and pH_i further increased to 7.24. Thirty-two hours after treatment, phosphocreatine and phosphodiesters had reversed their decline but pH_i had increased to 7.35. MRI and x-ray CT scans did not show any change during this period.

This study demonstrates that chemical changes can be observed by magnetic resonance spectroscopy shortly after chemotherapy administration in a clinical setting and before changes are observable by imaging modalities. The mechanism of these changes is presently unclear. Alkalinization could result from a breakdown of cell membrane permeability characteristics or from an acceleration of acid extrusion from the cell. Deterioration in cellular energy state presumably reflects mitochondrial damage. Correlation with clinical response needs to be made.

123.

Methodology for Stereotactic Radiosurgery of the Brain with a Linear Accelerator

A. OLIVIER, E. PODGORSAK, J. HAZEL, M. PLA, A. DeLOTBINIERE, B. PIKE, T. PETERS and G. BERTRAND (Montreal, Quebec)

So far the main applications of external radiosurgery in neurosurgery have been in the treatment of AVMs, brain tumours and functional

disorders. The method has proven to be useful in the treatment of inoperable AVMs (Kjellberg, 1986). The principle goal of radiosurgery is to deliver a very high dose of high energy radiation to a predetermined target volume (AVM, brain tumour, fiber tract or nucleus) while delivering a minimal dose to normal structures. Until recently, external radiosurgery could only be done with the cross firing of cobalt collimated beams (Gamma unit, Leksell 1951) or heavy charged particle beams (proton beam, Kjellberg et al, 1968) and helium heavy ions (Lyman et al, 1977). More recently, some centers have utilized small photon beams (0.5 to 3 cm diameter) derived from the more accessible linear accelerator (Betti et al, 1983).

The McGill stereotactic system has the unique capability of integrating all imaging modalities, including subtraction digital angiography (SDA), CT, MRI, and Pet scanning. This advantage has been utilized to obtain optimal isodose planning for specific vascular malformation or tumour configuration.

The radiosurgical treatment proper is given according to two modes. One technique is based on a single plane rotation (Single Plane Radiosurgery). This procedure is used when a steep gradient is not necessary or desirable. The second technique is based on the simultaneous and continuous movement of both the gantry and of the treatment couch (Dynamic Radiosurgery). This procedure is preferable when a steep gradient (fall-off) is desired. Our early experience with six cases of AVMs and six cases of brain tumours is presented.

124.

Elective Occlusion of the Vein of Galen in Falcotentorial Meningioma

D. FAIRHOLM (Vancouver, British Columbia)

Slowly growing neoplasms such as meningiomas may occlude the straight sinus with the development of collateral venous drainage.

Large meningiomas arising at the falcotentorial junction may be one such cause. If careful angiographic studies reveal that good collateral has developed, then consideration can be given to elective division of the vein of Galen and permit complete removal of the tumour.

Six cases are presented in which large meningiomas of the falcotentorial region were removed by electively dividing the vein of Galen. Angiographic studies showed development of good collateral drainage. Gross total removal of the tumour was achieved in all patients. Four patients made an excellent recovery, one died, from a postoperative hemorrhage, and one developed recurrence of the tumour.

In selected cases, elective division of the vein of Galen may be safely carried out if collateral venous drainage has developed and will permit total removal of these tumours.

125.

Interstitial Radiation as "Up-Front" Therapy for Malignant Astrocytoma: A Prospective Study

M. BERNSTEIN, N. LAPERRIERE AND P. LEUNG (Toronto, Ontario)

Interstitial brachytherapy is a promising treatment for malignant brain tumours. It has been used extensively for over three decades in Europe but has experienced a growth in popularity in North America only within the last ten years. Definite efficacy has been demonstrated for patients with recurrent malignant astrocytomas but as yet a phase III study of interstitial brachytherapy for patients with newly diagnosed malignant tumours has not been done.

In order to define the clinical utility of interstitial brachytherapy as "up-front" therapy in patients with malignant astrocytomas (astrocytoma grade III and glioblastoma multiforme) we have designed a phase III randomized Toronto-wide study of interstitial brachytherapy with high-activity removable Iodine-125 sources. Following surgery, consenting adults between the ages of 18 and 70 years with supratentorial malignant astrocytoma and Karnofsky performance status $\geq$ 70 are randomized to a two-arm study. The standard arm consists of external radiation using regional fields to a dose of 5,000 cGy in 25 fractions. The experimental arm adds to external radiation, a stereotactic interstitial implant to give a peripheral tumour dose of an additional 6,000 cGy. Patients are followed closely in a neuro-oncology clinic with regular neurological assessment, CT scan, MRI scan, and a multifactorial quality of life analysis using a modified linear analogue scale self-assessment system. The trial has been underway since October 1986 and it is hoped that the 161 patients required for the two arms will be accrued within five years. The definitive end-point is survival at two years; the trial is designed to detect an improvement in survival of 15% at two years with a significance level of 0.05 and a power of 0.80.

It is hoped that this randomized, controlled, prospective study will help answer an important question in the modern treatment of patients with malignant gliomas.

126.

Superselective Intra-arterial BCNU Treatment of Malignant Gliomas: Survival Results

J.F. EMRICH, D. MELANSON, V. WALLE, S. FONTAINE and J.G. VILLEMURE (Montreal, Quebec)

The intra-arterial administration of BCNU results in an increased concentration of the drug within the tumor and has theoretical advantages over intra-venous chemotherapy. We have determined it to be efficacious in controlling or reducing tumor size in 75% of treatments. The procedure itself is safe and permanent complications related to the catheterization procedure are less than 3%.

28 patients with malignant gliomas have been treated with infusions of BCNU into the supraophthalmic internal carotid or middle cerebral artery, after surgical and radiation therapy. Mean survival was increased to 68 weeks as a result of increased delivery of drug to the tumor. This compares with survival rates of 46-51 weeks with intravenous chemotherapy.

Characteristics of the responders vs the non-responders will be discussed. We believe that survival can be increased further if patients likely to respond can be identified and when optimum dosage and timing of treatments are determined.

127.

Acridine Orange Histochemical Study of RNA in Human Pituitary Adenomas

H.B. SARNAT, J.H. GARCIA and B. CURRY (Calgary, Alberta)

Tricyclic aminoacridines, particularly acridine orange (AO), form bonds with nucleic acids; when excited by ultraviolet (UV) light, ribonucleic acid (RNA) emits a bright orange-red colour while deoxyribonuclei acid appears yellow-green. Various nervous system tumours differ in a predictable manner in the amount of cytoplasmic RNA demonstrated by this technique (Can J Neurol Sci 1986;13:31-41). Fresh-frozen and formalin-fixed, paraffin-embedded sections of 19 human pituitary adenomas and 6 normal pituitaries were incubated with AO and viewed in the UV microscope. Intensities of fluorescence were noted and photographed and correlations were made with histological, ultrastructural, and immunocytochemical findings demonstrating endocrine function. The secretory tumour cells exhibiting the strongest AO-RNA fluorescence were those producing prolactin (4 cases); strong but less intense fluorescence was seen in cells with immunoreactivity for adrenocorticotropic hormone (2 cases) and for growth hormone (3

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cases). Amongst 10 chromophobe adenomas showing no immunoperoxidase evidence of secretory activity, 7 displayed only minimal AO-RNA fluorescence, by contrast with the moderate intensity of normal adenohypophyseal cells; the other 3 inactive adenomas showed moderate AO-RNA fluorescence. The cells of most adenomas were uniform in their fluorescence, but one chromophobe adenoma had a few scattered cells with strong AO-RNA fluorescence and a similar number of cells immunoperoxidase-positive for prolactin. AO is a useful supplementary stain for demonstrating ribosomal content associated with secretory function. Our findings suggest that some "inactive" adenomas may retain a latent endocrine potential.

128.

Free Radical and Related Mechanisms in Primary Intracranial Neoplasms

G. SUTHERLAND, R. BOSE, A. SIMA and C. PINSKY (Winnipeg, Manitoba)

Tumor samples from different morphological regions were obtained from 20 patients undergoing resection of their primary intracranial neoplasm. Lipid peroxidation was measured by spectrophotometric assaying of thiobarbituric acid reactive substance and expressed as malondialdehyde generated (nM) per hour per gram of tissue. Both glutathione (GSH) and glutathione disulphide (GSSG) were assayed by measuring fluorescence of glutathione-OPT complex with the results expressed as total glutathione (nM/g) (GSH + 2 × GSSG). Part of the tumor samples are processed for ultrastructural quantification of peroxisomes-cytoplasmic organelles containing catalase and hydrogen peroxide-producing oxidase.

Lipid peroxidation was higher in benign astrocytoma (n = 6: 137.6 ± 41.8) than in other tumor types; (malignant astrocytoma n = 6: 61.5 ± 29.4; benign meningioma n = 6: 53.7 ± 18.4 and malignant meningioma n = 3: 11.5 ± 8.2). Similarly, total glutathione was much higher in benign astrocytoma (4416.8 ± 1967.3) than in the malignant histological type (1022.6 ± 125.1). The latter had approximately the same total glutathione as other malignant and benign cerebral neoplasms. We also found lipid peroxidation to be lower in the central portion of cerebral tumors compared to the surface. Quantification of peroxisome content showed an inverse relationship between the number of peroxisomes and the degree of malignancy of the cerebral tumor. The ultrastructural observations were, therefore, consonant with our biochemical data.

This data suggests variation in oxidative metabolism and free radical scavening activity within different intracranial tumors and within different regions of the same tumor. Inhibition of glutathione production could, in theory, induce free radical related injury in benign astrocytoma.

(Supported by a grant from the Cancer Research Society/Faculty of Medicine, The University of Manitoba)

129.

Photo-Dynamic Therapy of Malignant Primary Brain Tumours: Post-Operative ICP Brain

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

Photo-dynamic therapy [PDT] consists of the exposure of neoplastic tissue to visable light of an appropriate wave length in order to activate a photosensitizer, administered prior to the light application. An energy transfer occurs from the exited triplet state of the sensitizer to oxygen resulting in the generation of singlet oxygen which irreversibly oxidates essential components of the cell resulting in cell death. The use of PDT in the treatment of malignant brain tumours has been reported to cause an increase in cerebral edema.

We have measured post-operative ICP in the last 16 consecutive patients with malignant gliomas treated with intra-operative PDT at St. Michael's Hospital, Toronto; and, in 20 patients with similar pathology who did not undergo PDT, in order to determine whether there was a significant ICP difference in the first post-operative day.

In the control [no PDT] group there were 14 males and 6 females; the age range was 26-73 years [mean = 55 ± 13]; 12 patients had glioblastoma and 8 had malignant astrocytoma. All patients received dexamethasone [16 mg/day] a minimum of one day pre-operatively and during the ICP observation period. The total post-operative ICP observation time was 530 hours.

In the PDT group there were 11 males and 5 females; the age range of 17-73 [mean = 47 ± 15]; 8 patients had GBM, 7 had MA and one had a malignant ependymoma. All patients received dexamethasone [32 mg/day] a minimum of one day pre-operatively and during the ICP observation period. The total post-operative observation time was 502 hours.

The mean [±S.E.M.] post-operative ICP in the control and PDT groups were 7.7± −.246 and 13.4 ± 0.53, respectively [$p < 0.0001$]. The mean [±S.E.M.] of the 10 highest hourly ICP estimates in the control and PDT groups were 11.0 ± 0.40 and 20.0 ± 1.25, respectively [$p < 0.0001$].

Neuro-Oncology II (Posters)

FRIDAY, JUNE 26TH, 1987 0730-1700

130.

Lymphomatoid Granulomatosis Presenting as a Posterior Fossa Mass in a 3-Year-Old Child

R. APPLETON, A. OAKHILL and N. FOREMAN (Vancouver, British Columbia)

Lymphomatoid granulomatosis is a rare lymphoproliferative disorder which primarily involves the lungs, skin and nervous system. Presenting features include fever, respiratory distress, abnormal neurological signs and/or skin rash. The disease is often misdiagnosed initially as tuberculosis. Lymphomatoid granulomatosis must commonly affects adults and has been described previously in only two children, 8 and 10 years of age respectively. We describe a third child, the youngest yet reported.

This 3-year-old boy presented with a three week history of headache, vomiting, lethargy and ataxia. Initial examination demonstrated no respiratory or dermatological abnormalities. Computerised tomography of the head revealed an area of low attenuation within the vermis of the cerebellum which appeared to have some mass effect. He subsequently developed a swinging pyrexia and increasing respiratory distress. Chest radiography demonstrated soft nodular opacities throughout both lung fields. The tuberculin skin test was unreactive and the erythrocyte sedimentation rate was 2 mm in one hour. The cell count, protein and glucose levels in the cerebrospinal fluid were normal. Histological examination of biopsied lung tissue demonstrated characteristic features of lymphomatoid granulomatosis. The child made a rapid clinical and radiographic recovery following treatment with high-dose corticosteroids but he remains steroid-dependent. Twenty two months after diagnosis the neurological examination is normal.

This patient demonstrates that lymphomatoid granulomatosis is a treatable disease which should be considered in the differential diagnosis of a posterior fossa mass in children, even in the absence of a skin rash or respiratory symptoms.

131.

Target Tissue Hypofunction Presenting Clinically as a Pituitary Mass

J.P. KRCEK, B. BAYLIS, E. MacRAE and B. CORENBLUM (Calgary, Alberta)

Pituitary tumors comprise up to 15% of all intracranial neoplasms. Neurosurgical intervention is in many instances the treatment of choice. The presentation of these tumors results from local mass effects and manifestations of pituitary hyposecretion or pituitary hypersecretion. The etiology of most pituitary tumors is not known. Rarely, pituitary mass lesions may result from primary specific end-organ hypofunction. Such mass lesions may be the presenting feature. The recognition and precise diagnosis of these conditions may be difficult especially if the primary glandular disorder is subclinical. The importance of the correct diagnosis is that the pituitary mass lesions respond to end-organ hormonal replacement therapy and therefore may not require surgery. We describe a 35-year-old woman whose only presenting complaint was headache. She continued to have regular menses and was clinically euthyroid. Physical examination disclosed the presence of a small, firm thyroid gland, and galactorrhea. CT scan demonstrated a large sellar mass with suprasellar extension. The initial suspicion was that the patient had a non-secreting pituitary adenoma. Further laboratory investigation found a mildly elevated serum prolactin, borderline low serum thyroxin, a greatly elevated serum TSH (235 ug/L), and the presence of antithyroid antibodies. The diagnosis was made of primary thyroid disease due to Hashimoto's thyroiditis with secondary pituitary thyrotrope hyperplasia. The sellar mass presumably represented hyperplasia of the thyrotropes. She was treated with replacement oral thyroxin. This resulted in normalization of the serum thyroid indices, the serum TSH, and the serum prolactin. Repeat CT scan three months later demonstrated decrease in size of the sellar mass.

Conclusion: Important considerations in the management of a sellar mass include: 1) Clinical and biochemical assessment of target gland function. 2) Initial treatment with target gland hormone when end-organ hypofunction is accompanied by marked elevation of its pituitary tropic hormone.

132.

Neurophyschological Evaluation at Beginning and End of Multiple Daily Fractionated Radiotherapy for Supratentorial Malignant Astrocytomas

G.W. JASON, E.M. PAJURKOVA, B.D. BULTZ, P.A. TAENZER, K.H. SHIN and H.G. THOMAS (Calgary, Alberta)

Multiple Daily Fractionated (MDF) radiotherapy induces better local control for supratentorial malignant astrocytomas than conventional radiotherapy. In order to examine the effects of MDF radiotherapy on neuropsychological functions, a brief neuropsychological examination was given to 12 patients at the beginning and end of a six-week course of high-dose (8000 cGy) MDF radiotherapy. The examination included tests shown to be sensitive to atrophic focal cortical lesions, and provided measures of memory and language ability. Tests assessed verbal and visuospatial memory, constructional abilities, verbal and visual design fluency in controlled conditions, memory span, and language expression and reception. Ten of the 12 subjects showed improvement on some neuropsychological functions, even though in general these subjects were more easily fatigued at the end of radiotherapy. This improvement may be due to recovery from surgery, which preceded radiotherapy by two weeks, or it may represent a practice effect. In five subjects there was deterioration on some tests; in each case the deterioration was seen in functions related to the side and/or site of the primary tumour, where the most intensive radiation was directed. In four of the five cases, improvement was found in other functions not primarily related to the location of the tumour. Results suggest that exposure to high-dose MDF radiotherapy does not exacerbate functional deficits other than those which are already present and most closely related to the primary location of the tumour.

133.

Spontaneous Resolution of Hyperprolactinemia Resulting from Biopsy-Proven Selective Autoablation of a Prolactinoma

J.P. KRCEK, E. MacRAE and B. CORENBLUM (Calgary, Alberta)

The natural history of prolactin-secreting microadenomas is, as yet, not entirely clear. Spontaneous resolution of prolactinomas with normalization of pituitary hypersecretion has been reported. The majority of such cases have occurred during or after pregnancy or during therapy with bromocriptine. Rarely, it has occurred in the absence of these conditions. A plausible explanation is that vascular supply to the adenoma is compromised due to tissue hyperplasia, with resultant selective infarction of the adenoma. However, to date the evidence for this hypothesis has been indirect, based on clinical and biochemical parameters.

We describe a case of a previously healthy 22-year-old woman who presented with galactorrhea which developed while she was taking oral contraceptives. Following their discontinuation, the galactorrhea persisted and, in addition, she developed oligomenorrhea. Serum prolactin was four times normal. Remaining pituitary testing was within normal limits. CT scan demonstrated a pituitary mass. Bromocriptine therapy resulted in cessation of the galactorrhea and return of regular menses. However, due to intolerance of bromocriptine, neurosurgical intervention was considered most appropriate. Two weeks prior to surgery, she experienced a bitemporal headache. At the time of surgery, tissue resembling a hematoma was removed. Histopathological analysis identified it as a prolactinoma. It was later determined that the patient's galactorrhea had stopped shortly after her headache occurred. Serum prolactin drawn prior to surgery* revealed a normal level. Three year follow-up has been unremarkable with continuation of normal menses, and normal serum prolactin levels.

In summary, this case demonstrates spontaneous resolution of a proven prolactinoma, clearly due to selective autoablation of the hyperfunctioning tissue only, with complete resolution of its clinical manifestation.

*Result unavailable prior to surgery.

134.

Endothelium Isolated From Neoplastic and Non-Neoplastic Tissue: In Vitro Analysis

P. COSTELLO and R.F. DelMAESTRO (London, Ontario)

Endothelial cells from normal and tumour tissue microvessels are morphologically and functionally different. In our laboratory, endothelial cells have been isolated from tissue obtained at the time of surgical resection. Glial tumours were the source for neoplastic tissue while lobectomies performed for seizure disorder were the source of non-neoplastic samples. Microvessels were isolated using a homogenization method previously described (Debault and Coincilla, Av. Exp. Med. Biol. 131: 69, 1980) and incubated at 37° C in modified Lewis media with 15-20% fetal bovine serum. The collagenase treated microvessels give rise to plaques of endothelium identifiable by their cobblestone pattern of monolayer growth. Cell lines that stained positively for factor 8 antigen and negatively for GFAP antigen were designated as endothelium. The neoplastic (BRHTE) and non-neoplastic (BRHE) endothelial cell lines were maintained in vitro to examine the cell characteristics and angiogenesis at the cellular level.

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The BRHTE lines grow at a slower rate than the normal BRHE line and spontaneously form chromosomal aberrations at an early passage. The cobblestone appearance of the BRHE culture was maintained at all times while the BRHTE often varied in shape and response to various growth factors, such as platelet derived growth factor and endothelial cell growth factor. The influence of tumour cells on endothelial growth was tested using various tumour cell lines in a chemotactic experiment. The response varied with tumour type and endothelial cell origin. The cells were examined using electron microscopy and differences in intercellular junctions and intracellular organelles were noted.

135.

Cerebral Toxicity Associated with Radiotherapy and Intra-arterial Chemotherapy of Malignant Gliomas

J.F. EMRICH, J. TYLER and J.-G. VILLEMURE (Montreal, Quebec)

Unlike systemic chemotherapy for malignant gliomas, the dose-limiting factor of intra-cerebral administration of BCNU is cerebral toxicity. This is demonstrated clinically by progression of neurological deficit, on CT scan by hypodensity of the white matter and metabolically by decreased glucose utilization on PET scan.

We present the clinical, radiographic and pathological features of cerebral toxicity in patients having received intra-arterial BCNU for the treatment of malignant gliomas. After 56 treatments in 28 patients, 10% developed acute neurological deficits while 17% had evidence of delayed white matter changes on CT scan. In those patients who had concurrent radiotherapy, clinical and radiological changes of white matter toxicity were greatest.

Recommendations for BCNU dosage with intra-arterial administration and the timing of radiotherapy and chemotherapy will be discussed based on our findings.

136.

Pathological Type, Age and Sex Distribution in 1274 Brain Tumour Patients

P.J. MULLER, J. BILBAO, W. TUCKER and A. HUDSON (Toronto, Ontario)

In the 10 year interval from January 1977 to October 1986, 1274 patients with brain tumours came to surgical treatment at St. Michael's Hospital, Toronto. There were 17 patients with primary skull tumours, 160 with metastatic intracranial tumours and 1097 with primary brain tumours.

The pathological type, age and sex distribution, of those pathological groups with more than two cases, in order of frequency, are as follows:

Pathology		Number	Age±SD	M/F Ratio
Astro-Group		515	52±16	310/205
Pilocytic Astro	[1]	4	35±15	4/0
Astrocytoma	[2]	86	40±14	49/37
Malignant Astro	[3]	228	56±14	137/91
Glioblastoma	[4]	186	57±15	111/75
Gliosarcome		11	61±12	8/3
Meningioma		267	57±14	71/196
Metastatic		160	58±12	101/59
Pit-Adenoma		129	47±17	69/60
Acoustic		63	52±16	30/33
Lymphoma		22	59±16	9/13
Medulloblastoma		12	27±8	11/1
Hemangioblastoma		11	42±15	4/7
Ependymoma		7	58±29	5/2
Colloid Cyst		7	38±5	4/3
Pet		6	35±18	4/2
Epidermoid		6	53±19	2/4
Oligodendroglioma		5	38±15	2/3
Ganglioneuroma		3	37±13	2/1

8.6% of all tumours in this series occurred in the posterior fossa. 71% of ependymomas, 44% of metastatic tumours, 14% of lymphomas, 6% of meningiomas, and 4% of astrocytic tumours were in the posterior fossa.

137.

Primary Intracranial Hodgkin's Lymphoma

T.P.G. DOORLY, M.A. FARRELL and J.P. PHILLIPS (Toronto, Ontario)

Intracranial involvement by Hodgkin's lymphoma is rare with an incidence of 0.5% or less, and occurs almost exclusively in patients with relapsing disease elsewhere. Hodgkin's lymphoma arising primarily within the cranial cavity is exceedingly rare, the optimum treatment and prognosis of which have yet to be determined. We report the treatment of a patient with primary intracerebral Hodgkin's lymphoma who presented with a discrete intracerebellar tumour, and discuss the possible histogenesis of this unusual condition.

138.

Thermal Enhancement of Drug Cytotoxicity on U-87MG Malignant Glioma Line

V.F. DaSILVA, P. RAAPHORST, R. GOYAL and M. FEELEY (Ottawa, Ontario)

Chemotherapy of malignant gliomas ultimately fails because of microregional anatomical variation, resulting in areas of low drug concentration/time, and because of heterogeneity in the tumor cell populations.

To maximize chemotherapy we need a non toxic, repeatable, treatment, able to potentiate the drug cytotoxicity and to reverse or attenuate the cell resistance to drugs. These specifications may be met by hyperthermia.

To determine whether there is any benefit on increasing the temperature of drug treatments we have chosen a simple cell culture system. U-87MG cells, were treated as nearly confluent monolayers, with BCNU [1,3-Bis (2-chloroethyl)-1-nitrosourea], AZQ [Aziridinylbenzoquinone], Cis-Platinum [Cis-diaminodichloroplatinum(II)] and SHM [Spirohydantoin mustard] both at 37 and 42° C for one hour. Colony formation assay results indicate increased cell kill at 42 versus 37° C for all drugs except SHM. Thermal enhancement ratios (LD 90 at 37/LD 90 at 42° C) were as follows: BCNU = 1.6, AZQ = 2.8, cis-Platinum = 2.0 and SHM = 1.0.

These results show that the cell kill effects of BCNU, AZQ and cis-Platinum on human derived malignant glioma cells are, within our experimental conditions, potentiated by hyperthermia.

139.

Meningeal Melanocytoma of the Spinal Canal

B. LACH, N. RUSSELL and B. BENOIT (Ottawa, Ontario)

Primary melanocytic tumors of the nervous system are exceedingly rare. Melanocytoma of the leptomeninges and dura have been most commonly reported as pigmented or melanotic meningiomas.

We report the histological immunohistochemical and ultrastructural features of such a tumor involving the dura, spinal roots and leptomen-

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inges at the level of the cervical spinal canal, in a 21-year-old female. She did not have pigmented lesions anywhere else.

The light microscopic examination revealed a moderately cellular neoplasm displaying areas reminiscent of Schwannoma, cellular blue nevus, and nests of small epithelioid cells similar to that seen in the clear cell neuroblastic tumors. Marked focal accumulation of melanin was observed in the tumor cells and macrophages. Scattered neoplastic cells showed S-100 protein in the cystoplasm and/or nuclei. Occasional cells were also positive for neuron-specific enolase. Glial fibrillary acidic protein, epithelial membrane antigen, vimentin and 60 kD neurofilament protein were absent from the tumor cells. Electronmicroscopic examination revealed amelanotic cells without diagnostic features, and some with premelanosomes and melanosomes at various stage of formation. There was no ultrastructural evidence of arachnoidal or Schwannian differentiation.

Our ultrastructural and immunohistochemical studies support the concept of melanocytic and not arachnoidal origin of the tumor. Use of appropriate laboratory techniques and correct diagnosis and management of this benign lesion is stressed.

140.

Carcinoma Implantation in a Patient with Multiple Mixed Gliomas

D.E. STEINKE, D.R. McLEAN and E.S. JOHNSON (Edmonton, Alberta)

We report a patient who had a mixed glioma present for at least 15 years as evidenced by anatomically appropriate focal motor seizures. The tumor, located in the right parietal lobe was eventually diagnosed using modern imaging techniques in 1981 and treated by subtotal resection and radiotherapy. In 1984 he was discovered to have a poorly differentiated right parotid tumor which was incompletely resected. In 1985 he underwent radical neck dissection followed by radiation to the neck. In 1986 he presented with progressive left hemiplegia and at craniotomy a right frontal tumor proved to be a mixed glioma containing metastatic tumor from the right parotid gland. Both multiple glial tumors and metastases to cerebral tumors are exceedingly rare. The combination of both these events in this case makes it unique. The various CT scans and biopsy material will be presented, the pathophysiology discussed and the condition reviewed.

141.

Congenital Quadrantanopia with Occipital Lobe Ganglioglioma: Pathogenic Implications

W.A. FLETCHER, W.F. HOYT and M. NARAHARA (Calgary, Alberta)

Occipital hemianopia is distinguished as congenital by the ophthalmoscopic finding of trans-synaptic atrophy of retinal nerve fibres. Porencephaly, developmental anomalies of striate cortex and congenital vascular lesions account for most cases. We report a unique case of congenital quadrantanopia with occipital ganglioglioma.

A 24-year-old man had two nocturnal generalized seizures. Initial neurological examination was normal but Goldmann perimetry demonstrated an homonymous right upper quadrantic field defect. Corresponding atrophy of retinal nerve fibres nasal to the right optic disc was documented by ophthalmoscopy and fundus photography. CT and MRI showed a multi-loculated cystic lesion in the left anteromedial occipital lobe with no mass effect. MRI indicated CSF-like fluid in the loculated cysts, suggesting cavitation from old trauma or inflammation. However, angiography suggested a neoplastic process as it demonstrated an abnormal vein draining prematurely from the lesion. Biopsy and histopathological examination revealed a ganglioglioma with numerous thick-walled vessels.

The association of occipital ganglioglioma in adulthood with transsynaptic atrophy of retinal nerve fibres suggests that gangliogliomas may arise during fetal development and may be present for many years before onset of symptoms.

142.

Transdural Extension of Astrocytoma and Glioblastoma: A Case Report and Review of the Literature

J.B. SCHNITTKER, D.D. COCHRANE and B. CURRY (Calgary, Alberta)

A case is reported of a 21-year-old male who, seven years after the diagnosis of cerebeller juvenile pilocytic astrocytoma was made, presented with transdural extension of a posterior fossa malignant pleomorphic astrocytoma, at a site remote from the previous operative site. The literature contains ten other cases of astrocytoma or glioblastoma undergoing spontaneous direct transdural extension. The ages of the group ranged from 21 to 70 years. Primary tumour location was supratentorial in ten cases, infratentorial in only one. The middle cranial fossa was the transgression site in the majority. All tumours were classified as malignant; two cases consisted of a mixture of glioblastoma and fibrosarcoma. Where reported, survival was similar to that expected for the primary tumour except in the present case where unusually long survival was witnessed. Hypotheses to explain the mechanism of dural transgression in these cases are developed.

Nerve I (Platform)

FRIDAY, JUNE 26TH, 1987 1345-1700

Co-Chairmen: DR. A. WILBOURN (Cleveland)
DR. A.R. HUDSON (Toronto)

143.

Motor Neuron Disease/Parkinson's Disease-Presenile Dementia with Atrophy of the Amygdala

J. ROBERTS, B. LACH and J.D. GRIMES (Ottawa, Ontario)

The rare occurrence of a combination of motor neuron disease with Parkinson's disease and presenile dementia (MND/P-D) has been recently recognized outside of the endemic territories. This form of the disease lacks the usual hallmark of widespread neurofibrillary tangles (NFT) so characteristic of the Guamian-type of MND/P-D.

We examined a 58-year-old man who died 21 months after the onset of Parkinson's disease accompanied by dementia and rapidly progressing motor neuron disease. Histological analysis revealed severe loss of motor neurons throughout the spinal cord. There was only a single neuron containing a Bunina body. Marked neuronal loss, but no Lewy bodies was found in the substantia nigra (SN). The cerebral cortex showed very slight neuronal loss, accompanied by minimal secondary spongiosis. The lateral amygdaloid nucleus displayed shrinkage and marked gliosis. The nucleus of Maynert was normal. No single NFT or neuritic plaque was found in the CNS. Electronmicroscopic examination of the anterior horns of the spinal cord, and immunohistochemical studies for 68 kD and 200 kD neurofilaments, showed no evidence of "proximal axonopathy" in the motor neurons. There was no Influenza A or B viral antigens in the SN.

It is concluded that the non-Guamian complex of MND/P-D represents a unique clinico-pathological entity of a type already described,[1,2] and that the dementia in this disease may well be related to degeneration of the amygdaloid nucleus or its connections.

[1]Horoupian DS (1984) Ann Neurol 16:305.
[2]Mitsuyama Y (1984) J N Neuros Psych 47:953.

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144.

Familial Amyotrophic Lateral Sclerosis (ALS): Evidence for Distinct Populations of Phenotypic Expression

M.J. STRONG and A.J. HUDSON (London, Ontario)

Familial ALS accounts for less than 10% of all case reports of ALS and appears to follow an autosomal dominant pattern of inheritance. Compared to "classical" sporadic ALS, the mean age of onset of familial ALS is younger (circa 62 years and 48 years, respectively) with males and females being almost equally affected versus a slight male preponderance in sporadic ALS. The mean survival of sporadic and familial ALS has been viewed as comparable (approx. 2.5 years from date of diagnosis). However, familial ALS appears to be a heterogeneous disease with three subsets based on duration.

A short duration subset, which we term the "malignant" familial form, has a life expectancy of 12 months or less in all affected members. Four families with a total of 21 members who had rapidly progressing disease can be found in the literature. We describe here an additional family with three cases in three generations including the autopsy findings of one member. The duration of ALS was 9 to 12 months and the age of onset 41, 44 and 45 years. The second subset of familial cases is well detailed in the literature and closely parallels sporadic ALS in duration (2-5 years). The third subset of familial ALS is relatively benign and four families with a total of 37 cases have been reported. The average duration of life in these families was 15 years. However, the duration in the latter subset is quite variable. We report an additional family with these characteristics.

While the phenotypic expression of the majority of familial ALS patients parallels the classical disease, the subpopulations of short and long duration disease may, with careful correlation of clinical and pathologic studies, provide further clues to the mechanisms of motor neuron death in ALS.

145.

Prognostic Factors in the Management of the Guillain-Barre Syndrome with Plasmapheresis

J.G. HUMPHREY, T.E. FEASBY, J.D. STEWART, M. LEE, W. BECKER and the Guillain-Barre Syndrome Study Group (Toronto, Ontario)

The initial report of the multi-centre North American Study of plasmapheresis and the acute Guillain-Barre Syndrome (GBS) has confirmed the efficacy of plasmapheresis compared to conventional care in several pre-determined parameters — improvement at 4 weeks, time to improve 1 clinical grade, time to reach grade 2 (walking unassisted) and outcome at 6 months. These parameters were all statistically significantly better in pheresed patients compared to conventionally managed patients.

Further analysis of the data from the study has been made to identify predictive and prognostic factors that affect the course of GBS patients receiving plasmapheresis. The age of the patient, duration of illness prior to pheresis, and the severity of weakness at onset are all important factors. The distal amplitude of the evoked muscle action potential response on the initial EMG evaluation is the most sensitive indicator for the time to recovery (<20% of predicted normal indicates a much more prolonged course). An unexplained relationship has been noted between outcome and the technique and machine utilized for plasmapheresis — continuous flow plasmapheresis is clearly superior to intermittent flow.

Multi-variate analysis has been used to indicate the significantly related factors that provide probability values for various groups of patients e.g. at 1 month: if illness <7 days and distal amplitude <20%-18% of pheresed patients are improved, 11% of conventionally managed patients are improved; if distal amplitude >20% and illness under 7 days — 82% of pheresed patients are improved while 66% of conventionally managed patients are improved.

Six variables account for all the significant factors responsible for a reliable estimate of improvement in GBS patients. All other variables did not improve the reliability of this estimate.

146.

Purification of a Neuronal Growth Factor from Peripheral Nerves

P. RICHARDSON, R.J. RIOPELLE and M. ALTARES (Montreal, Quebec)

Mammalian peripheral nerves contain classical nerve growth factor plus at least one other neuronal growth factor, here designated ciliary factor. This latter molecule is assayed by its bioactivity on parasympathetic neurons from chick ciliary ganglia but also supports the survival of sensory and sympathetic neurons in tissue culture. Although present in many tissues, ciliary factor is relatively concentrated in nerve trunks: its cellular origin is unknown. Extracts of rabbit sciatic nerve, purified by two steps of reverse-phase liquid chromatography, yield a preparation that is half maximally active at less than 1 nanogram per molecule in bioassay with ciliary neurons. The protein, with apparent molecular weight of 10-20,000 daltons by gel filtration chromatography, appears biochemically distinct from other molecules with neuronotrophic activity that have been purified. Biochemical characterization of ciliary factor is being undertaken to permit future investigation of its function in normal and abnormal peripheral nerves.

147.

Guanethidine Sympathectomy in the Rat: An Animal Model of Selective Autonomic Neuropathy

D.W. ZOCHODNE, K.K. WARD and P.A. LOW (Rochester, Minnesota)

Chronic administration of intraperitoneal guanethidine to rats induces an immune mediated destruction of sympathetic neurons rendering a potential model of autonomic neuropathy. The selectivity and usefulness of this model was explored in young adult Sprague-Dawley rats given daily intraperitoneal guanethidine (48 mg/kg) over a 5 week period. Control rats received daily saline injections.

Before treatment the groups had similar weights and comparable sciatic-tibial motor, caudal motor and mixed caudal nerve conduction values. After 5 weeks the guanethidine animals had gained less weight and developed ptosis but somatic conduction values were well preserved. Intra-arterial recordings under pentobarbital anaesthesia disclosed a lower resting blood pressure, greater postural hypotension and a rebound supine increase of blood pressure in guanethidine rats. "C" potential amplitudes from unmyelinated fibers recorded in an *in vitro* chamber were reduced in the cervical sympathetic chain of guanethidine rats but preserved in the vagus compared to controls. The reduction in the SNS "C" amplitude correlated with norepinephrine depletion measured in the harvested contralateral (superior cervical) SNS chain and ganglion. Norepinephrine was also depleted in the harvested vagus, peroneal, sural and tibial nerves and in the nutrient artery wall of the sciatic-tibial nerve of guanethidine treated animals.

These findings further define the extent of the immune mediated sympathectomy induced by guanethidine and indicate that it is a useful model of a selective autonomic neuropathy.

148.

Diabetic Trunkal Neuropathy and the Anatomy of the Trunkal Nerves

J.D. STEWART (Montreal, Quebec)

The trunkal nerves (thoracic spinal nerves) innervate most of the skin and muscles of the thorax and abdomen. Each trunkal nerve divides into a dorsal and a ventral ramus. The dorsal ramus passes backwards through the paraspinal muscles (innervating these) and supplies the skin in the ipsilateral paravertebral area. The ventral ramus circles around the trunk, giving off a lateral cutaneous branch that supplies much of the skin of the lateral wall of the trunk, and ending in the medial cutaneous branch that supplies the skin of the anterior trunk.

Four patients with diabetic trunkal neuropathy (2 with recurrent episodes) are described. In each of these there was a highly variable degree of involvement of the different branches of the trunkal nerves. This variability can produce confusing symptoms and signs. These observations show that in this syndrome either individual branches of the trunkal nerves or the fascicles within the main trunkal nerve itself, can be variably affected.

149.

The Pronator Syndrome

E. SCHNEIDER, N.A. RUSSELL and B.G. BENOIT (Ottawa, Ontario)

The median nerve may be compressed in the region of the elbow, producing symptoms that may mimic those of carpal tunnel syndrome. Three sites of compression have been described i.e. beneath the lacertus fibrosus, between the two heads of pronator teres, and beneath the flexor digitorum superficialis arch. The symptoms include forearm pain, paresthesiae in the median nerve distribution and numbness of the hand. Unlike carpal tunnel syndrome, nocturnal symptoms are not prominent. An important physical sign is tenderness over the proximal forearm. A positive Tinel's sign may be elicited in the same area. Electrodiagnostic studies are usually normal, a puzzling finding, since most patients are suspected of having carpal tunnel syndrome. Diagnostic nerve block is useful and steroid injection about the nerve in the pronator area may bring about relief. Surgical decompression is reserved for those patients with disabling symptoms and no relief with conservative measures. We present our experience with 10 cases of pronator syndrome, 5 of which were treated by surgery. The differential diagnosis and management is discussed.

150.

Surgery for Post-Traumatic Radial Nerve Palsy

T.P.G. DOORLY, R.C. OSTRUP, M.W. ROSCOE, A.R. HUDSON, J.P. WADDELL and R.R. RICHARDS (Toronto, Ontario)

Several unique anatomical features make the radial nerve particularly susceptible to injury. We have reviewed 49 consecutive patients who underwent radial nerve exploration for isolated, complete, post-traumatic radial nerve palsy between 1975 and 1985.

The patient population consisted of 36 males and 13 females whose ages ranged from 15 to 60 years. Radial nerve injury was associated with fractures of the humerus in 66% of these patients: 46% occurred immediately post-trauma while 20% followed operative treatment of the fracture. Other causes of injury included stab wounds (14%), injection injury (8%), gunshot wounds (8%) and severe soft tissue injury (4%). All patients failed to show clinical or electrophysiological evidence of nerve regeneration 3 months or more following injury.

Following surgical exploration, interfasicular nerve grafting was performed in 30 patients, neurolysis in 10, direct end-to-end repair in 4, and 5 patients had lesions which were not amenable to any form of repair. All patients have been followed for at least 1 year postoperatively. Good to excellent results were achieved in 77% following interfasicular grafting, 90% following neurolysis, and 100% following direct end-to-end repair. Tendon transfers were subsequently performed in those with a poor result to try and salvage limb function.

Detailed analysis of the operative results has yielded guidelines for the optimum management of isolated, complete radial palsy following trauma. These will be presented.

151.

Lesions of the Lateral Cutaneous Nerve of the Forearm

J.D. STEWART and M. ABEBE (Montreal, Quebec)

The lateral cutaneous nerve of the forearm is the terminal sensory branch of the musculocutaneous nerve. Damage to this nerve is said to be rare, but we report six patients seen within a two year period.

Causes: Damage by venipuncture of the veins of the antecubital fossa (the nerve lies very close to the median cephalic vein) - 2; fracture and surgery to the elbow - 1; compression by a restraining band tied around the distal upper arm - 1; mononeuropathy multiplex - 2.

Damage to this nerve produces a characteristic area of sensory disturbance on the lateral aspect of the forearm. In two patients these paresthesias were painful. No muscle weakness was present as the nerve was damaged below the branches to the biceps muscle. In all but 1 patient the diagnosis was easily confirmed by nerve conduction studies,[1] combined with normal electromyographic studies of the biceps muscle.

[1]Spindler HA, Felsenthal G. Sensory conduction in the musculocutaneous nerve. Arch Phys Med Rehabil 59: 20-23, 1978.

152.

Inherited Predisposition to Pressure Palsies Presenting as Recurrent Brachial Plexus Neuropathies

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

Eleven members of three families demonstrated clinical and electrophysiologic features consistent with an inherited predisposition to pressure palsies. There were seven males and four females. Ages ranged from 12 to 54 (mean 35.4). Members from each family had relapsing-remitting neuropathies in nerves commonly subject to compression. All cases had electrophysiologic abnormalities in asymptomatic nerves. Only one had no clinical evidence of neuropathy. Electrophysiologic abnormalities were found in distal lower extremity nerves not subject to compression in 10 patients. Conduction block, sometimes asymptomatic, was found in six cases and significant conduction slowing across areas of compression in eight. Distal median neuropathies were present in eight. Conduction block persisted on repeat evaluations up to two years. Brachial plexus neuropathies occurred in seven patients and were bilateral in one, recurrent in two and in four was the presenting problem. In four cases no antecedent event could be determined. Only one was accompanied by pain. Features that distinguish this disorder from inherited brachial plexus neuropathy were the lack of pain in most cases, lack of minor dysmorphic features, episodes of compression in areas other than the brachial plexus and evidence of abnormalities in nerves not commonly subject to compression. Although the inherited predisposition to pressure palsies can present with brachial plexus neuropathy, there are factors that can distinguish the two disorders.

Nerve II (Poster)

FRIDAY, JUNE 26TH, 1987 0730-1700

153.

The Myth of Diabetic Femoral Neuropathy

A.J. WILBOURN and P. SWEENEY (Cleveland, Ohio)

The concept that isolated femoral mononeuropathies (IFMN) frequently occur in patients with diabetes mellitus, presumably on an ischemic basis, is entrenched in the medical literature. However, no well documented series of such "diabetic femoral neuropathies" has been reported, and review of our EMG laboratory experience over a recent five year period provides little support for this concept.

Of 11,500 patients studied, 864 known diabetics, 28 had EMG evidence of IFMN. Most were due to trauma (including iatrogenic) and hemorrhage; only one patient was diabetic. In contrast, 50 of the diabetic patients had lower extremity symptoms superficially suggestive of an IFMN, but EMG examinations demonstrated lesions were more proximally situated along the peripheral neuraxis, since denervation was present in both the anterior and medial (obturator nerve-innervated) thigh muscles; their ultimate clinical diagnosis was diabetic amyotrophy. These constituted almost half the L2-L4 radiculopathies/lumbar plexopathies seen during the assessed period.

Conclusions: Our results suggest that, literature claims notwithstanding, "diabetic femoral neuropathies" are extremely rare entities. Most diabetics with anterior thigh pain/weakness actually have more extensive neurogenic involvement — i.e., diabetic amyotrophy — and not an IFMN.

154.

Operative Management of Brachial Plexus Lesions

T.P.G. DOORLY, A.R. HUDSON and R.C. OSTRUP (Toronto, Ontario)

Lesions of the brachial plexus frequently result in permanent crippling of a young productive individual. Some disagreement persists concerning the value of operative intervention for such lesions. We have therefore critically analysed our operative experience with more than 300 consecutive patients with severe brachial plexus lesions who have been followed from 18 months to 13 years postoperatively.

All patients were managed according to a uniform protocol which included detailed clinical and electrophysiological assessment of each element of the brachial plexus to determine the degree of impairment and the extent of regeneration. These findings determined selection for and timing of surgery. Following operative exposure of the lesion sequential microsurgical dissection and nerve action potential recordings were employed to preserve functioning elements and to isolate injured elements for appropriate repair. Postoperatively the function of each element was graded according to the system proposed by Kline and Judice.

The results at follow-up were analysed with regard to multiple factors: age of patient, element injured, mode of injury, length of time from injury to surgery, microscopic and electrophysiological findings at operation, type of nerve repair including length of graft, subsequent reconstructive surgery.

We have been able to develop a rational protocol for the management of brachial plexus lesions and to determine that surgery is certainly worthwhile for selected lesions. This protocol and analysis of our operative results will be presented.

155.

Value of the EMG Examination with Long-Duration Footdrop

P. SWEENEY and A.J. WILBOURN (Cleveland, Ohio)

Electrodiagnosis is of unquestioned value for localization/prognosis with recent onset footdrop (FD). Less obvious benefits result from studying FD of many years' duration, particularly when prominent tibialis anterior (TA) atrophy indicates severe, chronic axon loss exists.

Reported are 3 patients with longstanding, unilateral FD whose EMG examinations materially aided in finally determining etiology and initiating appropriate therapy. 1.) Male, age 33, with FD for 7 years, following tibial fracture. EMG showed common peroneal mononeuropathy residuals but peroneal motor amplitude, recording TA, was normal — inconsistent with severe TA weakness. Clinical testing revealed impairment of passive as well as active foot dorsiflexion; thus, FD was of mechanical, not neurogenic, origin. Surgery revealed flexor tendon/muscle entrapment at fracture site. 2.) Male, age 45, with slowly progressive, painless FD for 20 years, culminating in flail foot. Sciatic nerve exploration at 13th year was negative. EMG showed multisegmental (L4-S2) intraspinal canal lesion (ISCL). Subsequent diagnostic studies/surgery revealed cauda equina lipoma. 3.) Male, age 24, with painless, static FD for 8 years, following subacute development. Peroneal nerve exploration at knee was negative at 1 year. EMG showed severe ISCL affecting L5 segment. Neuro-imaging techniques were unrevealing, suggesting focal motor neuron disease.

Conclusion: EMG examinations with even longstanding FD may help with clinical management.

156.

Sensory Neuron Degeneration in Motor Neuron Disease

T.R. WINDER and R.N. AUER (Calgary, Alberta)

A 53-year-old man developed motor neuron disease in childhood. In addition to motor abnormalities, sensory abnormalities were documented in his legs during life. There was a family history of a motor neuron disorder and this man's condition was felt to be a familial form of Wolfhart-Kugelberg-Welander type motor neuron disorder.

Autopsy revealed motor neuron loss in the spinal cord, with preservation of the phrenic nucleus. The lumbar dorsal ganglia showed active degeneration of sensory neurons. The fasciculus gracilis showed Wallerian degeneration.

The findings provide direct evidence that sensory neurons can degenerate in some forms of motor neuron disease.

157.

Sacral Neural Outflow Stimulation for the Neurogenic Bladder

A. TALALLA, K. MEULLER and J. BLOOM (Hamilton, Ontario)

Several electrical stimulation techniques have been considered for the treatment of the detrusor hyperreflexia and the detrusor/external urethral sphincter dyssynergia that can complicate spinal cord damage (1). Sacral anterior root stimulation has been useful for bladder evacuation and for diminishing incontinence in over 80% of 50 spinal cord damaged patients (2). We have achieved bladder evacuation with low residual volumes in a woman suffering from paraplegia due to a functionally complete cord transection at T6, by stimulation of the third

sacral nerve pair (3). In this presentation we will report our experiences with the extradural technique of sacral nerve stimulation as applied to this patient and to five other spinal cord injured patients. In comparing the extradural to the intrathecal technique of Brindley, we shall discuss outstanding issues in electrical stimulation of the lower urinary tract, including the invasiveness of the various surgical interventions, the necessity for sensory rhizotomy or efferent neurotomy, and the safe limits of electrical stimulation of peripheral nerve.

1) A. Tallalla. PACE 9:164-170, 1986.

2) G.S. Brindley et al. J. Neurol. Neurosurg. Psychiatr. 49:1104-1114, 1986.

3) A. Talalla et al. Neurosurg. 19:955-961, 1986.

158.

Ischiogluteal Bursitis: The Forgotten Differential Diagnosis of Sciatica

L. METZ, G.M. KLEIN and B.D. McLEOD (Calgary, Alberta)

We wish to present ten patients referred to us with "sciatica", who complained of back pain with pain radiating into one or both legs. Most had already seen a neurologist or a neurosurgeon. Four had had myelograms and two had had CT scans of the lumbosacral spine. All of these tests were unhelpful.

These patients complained of low back or buttock pain which was invariably worse with sitting down and generally relieved by lying down or standing. Pain radiating down the leg in the distribution of the sciatic nerve was present in all patients. They all had exquisite tenderness over one or both ischiogluteal bursae, and palpation in this region created pain going to the appropriate leg. All of these patients responded well to steroid injection into the bursa.

We feel that ischiogluteal bursitis is an important but often overlooked diagnostic consideration in sciatica. It should be considered in all patients with back and leg pain. It is a particularly important diagnosis to consider in patients who are tender over the low back or buttock and in those who have normal myelograms or CT scans.

159.

Two Syndromes Due to Compression of Lumbar-Sacral Plexus by Abdominal Aneurysms

J.-P. BERNIER, M. VIELLEUX, D. BONNEAU and L. BRAZEAU-LAMONTAGNE (Sherbrooke, Quebec)

A survey of the reported cases of abdominal aneurysms producing initial symptoms of leg pain leads to distinguish two syndromes according to localization of the vascular lesion and physiopathology of the compression of the nerve trunks derived from L2-L3-L4 roots (upper syndrome) by an aortic aneurysm complicated by a dissecting aneurysm into the iliopsoas muscle.

The second case is an instance of chronic compression of the proximal sciatic nerve (lower syndrome) by an expanding unruptured aneurysm of the hypogastric artery. To our knowledge, EMG findings have not been described previously. Both cases showed definite EMG evidence of denervation in the distribution of at least 2 lumbosacral segmental levels and of at least 2 different peripheral nerves. However, the lumbosacral paraspinal muscles were not involved in either case.

Prompt diagnosis and surgical treatment of ruptured aortic aneurysms mimicking "femoral neuropathy" can be lifesaving and the same early attention to the lower "sciatica" syndrome can alleviate a disabling pain and prevent progressive motor impairment in a lower extremity. When clinically suspected the diagnosis can be greatly faciliated by ultrasound studies and CT-Scan of the abdomen leading to angiogram as examplified in our patients.

160.

Single Fibre EMG in Diabetic Neuropathy

V. BRIL, M. WERB, D.A. GREENE, A.A.F. SIMA and J.L. TOKAR (Toronto, Ontario)

Single fibre electromyography (SFEMG), as described by Stalberg, provides a profile of regeneration and/or degeneration in neurogenic disorders. The combination of jitter and fibre density mirrors the tempo and severity of the process.

SFEMG done in the Tibialis Anterior muscles of 63 diabetics with clinical peripheral neuropathy showed the following: mean jitter — 73.5us (normal<60us), 44% of pairs abnormal (normal<10%), and mean fibre density — 2.90 (normal<2.00). The subjects were 50.2 years old, diabetic for 13 years, and neuropathic for 2.9 years. Routine nerve conduction studies showed a mean peroneal motor conduction velocity of 41.6m/s and a motor evoked potential amplitude of 5.0mV. All patients had some abnormalities of SFEMG, although conventional nerve conduction studies were not always abnormal. Median motor and sensory conduction velocities, but no other nerve conduction parameters correlated significantly with diabetic control as measured by glycosylated hemoglobin levels. The jitter increased as glycemic control worsened.

SFEMG is a sensitive technique for the detection of diabetic peripheral neuropathy, and may be a useful way to follow these patients and monitor results of therapy.

161.

Uncommon Electrophysiological Findings in Carpal-Tunnel Syndrome

J.K. BARUAH and G.R. BARUAH (Milwaukee, Wisconsin)

During electrophysiologic evaluation of carpal-tunnel syndrome in a series of 275 individuals following uncommon findings are noted in abductor pollicis brevis muscle (APB). These are (a) rhythmic involuntary motor unit potentials in 29/275 (10.5%); (b) impulse induced neurotonia in 8/275 (2.9%); (c) repetative group discharges and myokymia 25/275 (9.1%); (d) ischemia induced group discharges leading to electrical tetany 3/50 (6.0%); (e) decremental response to repetative stimulation 8/110 (7.2%); (f) repetative impulses to single nerve stimulus 2/275 (0.7%); (g) percussion myotonia 5/275 (1.8%). The local anesthetic infiltration at the carpal-tunnel abolishes the first four (a-d) discharges. The focal demyelination at the compression site may have led to ephaptic impulse origin from the denuded axonal membrane. The decremental response to repetative stimulation is only noted from APB muscle, as such responses are not noted following stimulation of ulnar or musculocutaneous nerves. This may be secondary to chronic denervation. The repetative impulse to single nerve stimulus is limited to involved thenar muscle and indicates an isolated local phenomenon. Recognition of these abnormal findings are important to prevent any extensive electrophysiologic evaluation in a given patient of carpal-tunnel syndrome with any of the above findings.

162.

A Freeze Fracture Study of Dorsal Sympathetic Chain in Streptozotocin Diabetic Rats

G. MONCKTON and H. MARUSYK (Edmonton, Alberta)

Freeze fracture replicas of dorsal sympathetic chain (D.S.C.) were obtained from 10 normal and 18 streptozotocin diabetic Wistar rats 14 days after induction of diabetes. 10 of these rats were given myoinositol adjuvant diet. Photographs at 60,000x and 90,000x were obtained of P

and E faces. Particle numbers were counted and sizes assessed by measuring particle shadows.

In the diabetic (D.S.C.) non myelinated fibres P faces there were fewer particles than normal ($P = 0.01$) but P faces of myoinositol treated rats (M.D.R.) were normal. Normal and diabetic E faces were similar. MDR had reduced E face counts ($P = 0.05$). On diabetic P & E faces there were reduced large particles. MDR had normal distribution of particle sizes. Analysis of axolemma juxta-axonal membranes had significantly fewer articles on P and E faces. MDR had improved P face and normal E face particle numbers. Analysis of axolemma P and E faces showed increased particle numbers on P face but normal E face numbers in non myelinated axons in MDR. The P face numbers were normal.

The apparent normalization of protein particle numbers and sizes in diabetic non myelinated juxta-axonal membranes by the addition of myoinositol to the diet is consistent with the findings of Fukuma et al (1978) in sciatic nerve in diabetic rats myelinated axon Schwann cell membranes, and supports the view that myoinositol is an important factor in maintaining normal neural and Schwann cell structure in diabetes.

Child Neurology I (Platform)

FRIDAY, JUNE 26TH, 1987 1345-1700

Co-Chairmen: DR. P. CAMFIELD (Halifax)
DR. H. DUNN (Vancouver)

163.

Hydrocephalus in Achondroplasia: Diagnosis and etiology

P. STEINBOK, O. FLOODMARK and J. HALL (Vancouver, British Columbia)

Increased head circumference and ventriculomegaly are common findings in children and young adults with achondroplasia. Many theories for the origin of the ventriculomegaly have been proposed, including obstructive hydrocephalus due to a small posterior fossa or narrow foramen magnum with compression of the basal cisterns, the outlets of the fourth ventricle or the tentorial incisura, and communicating hydrocephalus due to increased intracranial venous pressure and thus impaired reabsorption of CSF, caused by a stenosis of the jugular foramen.

We studied four achondroplastic children with ventriculomegaly in order to confirm the diagnosis and etiology of hydrocephalus. The intraventricular pressure was monitored over 24 hours followed by intraventricular injection of radionuclide alone or in combination with water-soluble contrast. The intraventricular pressure was elevated and the reabsorption of CSF into the sagittal sinus was slow in all cases but there was no obstruction to CSF flow. The spinal subarachnoid space was well seen in all patients. Jugular venograms with pressure monitoring was performed in three patients (bilaterally in one). These studies confirmed a narrow jugular foramen in all patients with recording of elevated venous pressure in the sigmoid sinus (mean 14.5 mmHg, range 9-25) and significant pressure-gradient (mean 5 mmHg, range 3-8) when pulling the catheter back through the foramen. A second gradient was found in the jugular vein in two patients at the level of the upper thoracic aperture. This gradient was 4 and 14 mmHg respectively. Identical venograms and monitoring of the venous pressure in a control group showed no pressure gradients.

We conclude from these studies that ventriculomegaly in achondroplastic children may represent hydrocephalus, which is likely secondary to raised intracranial venous pressure due to hemodynamically significant stenosis of the jugular foramen and in some cases the jugular vein in the thoracic aperture.

164.

Infantile Apnea or Seizures?

C. JOHNSON and H.Z. DARWISH (Calgary, Alberta)

Five patients are described whose underlying seizure disorder was unsuspected for many months due to atypical presentation and more likely alternative diagnosis. The patients presented early (age range 6 mths - 14 mths) with episodes of apnea and cyanosis initially. The physical exam and laboratory investigations revealed no etiology for the episode. On discharge, the diagnoses included obstructive apnea, cardiac dysrhythmia, syncope and breath-holding spells. In each case, it was not until subsequent admissions when the witnessed episodes revealed the appropriate diagnosis. In all, these episodes started with a 10 - 30 sec period of staring with facial flushing. The child subsequently would become flaccid, remain apneic and progressively more cyanotic. These episodes would last 30 sec - 3 min and four of the five patients required cardiopulmonary resusciation, prior to recovery. All five patients had tachycardia during the episodes and three of five had measured hypertension. All patients had a 15 - 30 min period of post-ictal drowsiness or irritability.

EEG recordings in the awake, drowsy and asleep states were entirely normal in three of five patients while awake recordings were normal in the remaining two. Prior to treatment the episodes were occurring on at least one or more days on a weekly basis with volleys of seizures on some days. These children have all remained seizure free on therapeutic levels of carbamazepine.

165.

Neurological Complications in the Hemolytic Uremic Syndrome (HUS)

P. NIEMAN and L. ROBSON (Calgary, Alberta)

The child with H.U.S. usually presents with an acute illness characterized by colitis, oliguria, thrombocytopenia, and seizures. The C.N.S. disturbance may be due either to cerebral microangiopathy, or to systemic metabolic derangements.

We reviewed 55 children managed for H.U.S. between 1978 and 1986. The mean age was 42.4 ± 38.3 months (range 1-166). 17 (31%) had neurologic complications. These included 15 with seizures (3 partial onset; 3 status) of whom 8 also had depression of conciousness (L.O.C.). 1 had only L.O.C. and another had the dysequilibrium syndrome. Among those with seizures 1 had transient blindness and another had hemiparesis. The group that demonstrated L.O.C. had a significantly higher serum creatinine (432 ± 88) at the time of the first seizure than the group that had seizures only (248 ± 35) ($p < 0.01$) In 8/15 the seizures were probably a result of hyponatremia. These usually occurred after the second day and recurrences were infrequent. In the group that survived after neurologic complications ($n = 14$) one was left with mild upper motor neuron signs and another experienced recurrences of seizure with fever.

Neurologic complications in H.U.S. are usually secondary to systemic factors such as azotemia and hyponatremia, (71%), and the outcome is excellent. In those in whom there was also evidence for direct cerebrovascular involvement, (24%), the outcome was quite poor and ¾ died.

166.

Childhood Stroke Associated with Deficiency of Proteins C and S

S.S. SESHIA and S. ISRAELS (Winnipeg, Manitoba)

Protein C and its co-factor, Protein S are naturally occurring anticoagulants that regulate the activity of the coagulation cascade by inhibiting

activated Factor V and VIII. We describe two children who developed hemiplegia acutely. One was deficient in Protein C and the other in Protein S.

Case 1: A 17 month old female presented with sudden onset of left hemiparesis during a febrile illness. CSF examination, C.T. scan of the brain and radionuclide brain scan were normal. Protein C antigen level was low at 40% (normal range 60% to 140%). Protein S antigen level was normal. Protein C levels were still low (44% and 40%) 6 and 12 months after the acute episode. The hemiparesis resolved almost completely within 3 months.

Case 2: A 13 month old male presented with a right hemiparesis which had its onset at the age of 4 months. C.T. scan of the brain revealed a left parietal porencephalic cyst consistent with an infarction in the middle cerebral artery territory. The protein C antigen level was 72%. Total Protein S antigen level was 110% (normal range 65 to 150%) with a free Protein S (representing the functional component) level of 38% (normal range 57 to 120%).

Cardiac evaluation, including echocardiography, metabolic screen specifically for homocystinuria, platelet aggregation, prothrombin time, partial thromboplastin time, fibrinogen and antithrobin III were normal in both children.

Deficiencies of proteins C & S have recently been associated with thrombosis but strokes in children have been not reported previously. The identification of such a deficiency is important, both in management of the affected child and in identifying other family members who may be at risk for thromboses since these conditions are usually autosomal dominant in inheritance. The role of aspirin or anticoagulant prophylaxis in this situation needs further study.

167.

Somatosensory Evoked Potentials in Children with Hydrocephalus

S.R. GEORGE and M.J. TAYLOR (Toronto, Ontario)

Somatosensory evoked potentials (SEPs) were recorded in 39 children (0-17y) with proven hydrocephalus.

Upper limb SEPs were recorded from C4′ and C3′ to median nerve stimulation in 25 infants (0-13m). Of 14 children from 0-3 months 5 showed clearly abnormal SEPs, 4 showed borderline normal results and 5 had unequivocally normal results. In the older age group (3-13m) 11 infants were tested: 7 infants revealed abnormal and 4 revealed normal SEP studies. Abnormalities in the SEPs consisted of prolonged latencies or complete loss of waveforms. In 11/25 infants interarm latency asymmetries were seen. In 19/25 children repeat studies (1-5 times) were performed after shunt insertion or shunt revision. Those with abnormal SEPs showed recovery of normal latencies and reproducible waveforms, except in two patients, who both developed shunt infections. Four older children (7-16y) with hydrocephalus also had upper limb SEPs tested, all of them showed normal results.

Lower limb SEPs were recorded from Cz to posterior tibial nerve stimulation in 10 children (7-17y). In 7/10 abnormal results were seen, which consisted of prolonged latencies from one or both legs. Six of these patients had repeat SEP studies after shunt insertion or revision. SEP latencies returned to normal in 5 patients and remained abnormal in one. Interleg SEP amplitude asymmetries greater than 50% were seen in 3/7 patients with abnormal SEPs. They were diminished but not resolved with second testing.

This study suggests that SEPs may be a valuable method to monitor hydrocephalic children pre and post shunting procedures.

168.

Cranial Magnetic Resonance Imaging in Sturge Weber Syndrome

M. BEAULIEU, G.V. WATTERS, R. ETHIER, A. O'GORMAN, K. METRAKOS, K. SILVER and B. ROSENBLATT (Montreal, Quebec)

The Sturge Weber Syndrome (S.W.S.) is a sporadic neurocutaneous syndrome characterized by a facial vascular malformation, the port-wine stain, leptomeningeal-angiomatosis and extra and intracranial complications. The major radiological characteristic is intracranial calcification seen in a "tram track" distribution on skull x-ray and computerized tomography (CT) scan. Magnetic resonance imaging (M.R.I.) scans were done in three children with S.W.S. It was found the M.R.I. scan was superior to the CT Scan in demonstrating atrophy, gyral anomalies in particular microgyri, and white matter changes. The classical calcified lesions well seen on CT-Scan were not well seen on the M.R.I. scan. These imaging modalities appear to be complementary in the investigation of this disorder.

169.

Transient Congenital Hypomyelination

H.G. DUNN, K. BERRY, A.K. JUNKER (Vancouver, British Columbia)

It is generally believed that congenital hypomyelination of peripheral nerves is either fatal in early infancy or may lead on to a chronic hypertrophic polyneuropathy with little myelin and with onion bulb formation. We have encountered a Chinese-Canadian infant in whom the condition was transient and may have been associated with maternal Epstein-Barr (E-B) virus infection. This female baby had shown weak fetal movements but was delivered spontaneously one week before term weighing 2353 g. After birth she cried and sucked weakly. On day 9 she was admitted to hospital with bronchopneumonia which required respirator care. In the third week she remained very weak and had poor muscle bulk, hypotonia and areflexia. Spinal fluid showed no white cells, protein 126, glucose 63 mg/dl. At 4 weeks conduction in motor and sensory fibres of right median, ulnar and peroneal nerves was severely impaired. Electromyography demonstrated partial denervation of right deltoid and extensor digitorum communis and subtotal denervation of right abductor pollicis brevis. Sural nerve biopsy on day 34 showed impaired myelination with both thinly and abnormally myelinated fibres, while the axons appeared normal in structure and number. The infant gradually became stronger. By day 33, spinal fluid protein level had fallen to 75 mg/dl. Repeat nerve conduction studies showed improvement on day 56 and normal findings after 1 year. The parents had normal nerve conduction. The baby's VCA IgG antibody titre against E-B virus was 320, EBNA antibody titre 100 on day 56, IgM antibody also present. The VCA IgG titre fell to 40, EBNA to <10, and IgM antibody was no longer demonstrable at 4 months. The mother had VCA IgG antibodies to a titre of 320 on day 51 and 160 at 4 months, with EBNA titre >100 and IgM antibodies demonstrable at both times, suggesting recent or reactivated infection with E-B virus. The baby started walking at 1 year and had normal tendon reflexes; at 2 years 7 months she was healthy and only mildly hypotonic.

170.

Syncope in Childhood: A Controlled Study of the Familial Tendency to Faint

P. CAMFIELD and C. CAMFIELD (Halifax, Nova Scotia)

Vasovagal and vasodepressor syncope (fainting) are common paroxysmal events in childhood. It is likely that sufficiently stressful

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circumstances could cause anyone to faint. This study examines the role of familial influences in syncope. We studied 30 consecutively referred children (22 girls, 8 boys), average age 10 years with clearcut histories of syncope (excluding pallid syncope and breath holding) without other neurological or cardiovascular disease.

The family history of each case was reviewed for syncope and for 24 cases was compared with the family history of the child's best friend. In all cases typical provoking factors for syncope were identified. None of the best friends had syncope. 27/30 cases and 8/24 best friends had at least one first degree relative (parent or sibling) with syncope (chi squared $p<0.01$). Of the 8 best friend controls with a parent or sibling with syncope in 7/8 the mother was affected and 4/7 of these mothers themselves had first degree relative(s) with syncope. In 11/26 patients both a sibling and parent had syncope compared with 1/24 of control families ($p<.01$).

We conclude that virtually all children who faint have a first degree relative who faints, a useful fact in differential diagnosis. The results suggest a strong inherited tendency for syncope, possibly autosomal dominant with variable penetrance, possibly multifactorial but still requiring pan environmental stimulus for expression.

171.

Autosomal Dominant Spinocerebellar Degeneration: A New Clinical Association

A.A. WILFONG, K.G. ROMANCHUK and N.J. LOWRY (Saskatoon, Saskatchewan)

We describe a large kindred involving seventeen affected individuals over five generations. The spinocerebellar degeneration involved is characterized by clinical onset in the person's late-twenties or early-thirties. Ataxia is the presenting sign and is typically progressive and severe. Over time, the patients loose ambulation and articulation. In contrast to Friedrick's ataxia, these individuals exhibit markedly exaggerated deep tendon reflexes. As the disease process advances, extrapyramidal involvement becomes apparent in the form of rigid tone and dystonic posturings. Features manifesting relatively late include horizontal nystagmus on lateral gaze and an upward gaze palsy. The mentation of all affected individuals has been preserved throughout.

Ophthalmologic examination reveals an interesting clinical association in these individuals. Use of the slit lamp has demonstrated three of the family members affected with spinocerebellar degeneration to have transillumination defects in the iris. The defects are present bilaterally in the mid-periphery and periphery of the iris. This is a rare finding in the general population. Other family members examined who do not have spinocerebellar degeneration, do not show the transillumination defect. Spinocerebellar degeneration has not been described in association with iris transillumination defects. This iris defect, present and identifiable from birth, may afford an early detection method for recognizing future family members who will go on to develop this spinocerebellar degeneration.

172.

The Role of Computed Tomography for the Diagnosis of Congenital Migrational Disorders of the Brain

A. HILL, E.H. ROLAND and O. FLODMARK (Vancouver, British Columbia)

Disorders of neuronal migration are an important cause of seizures, developmental delay, mental retardation, and focal neurological signs in children. They develop during the third and fifth months of gestation and result in major gyral abnormalities. Listed in order of decreasing severity, these congenital cerebral malformations include: schizencephaly (complete agenesis of part of the cerebral wall), lissencephaly (few or no gyri), pachygyria (decreased number of broad gyri) and neuronal heterotopias (collections of neurons in subcortical white matter). Although migrational disorders are well-defined neuropathological entities, diagnosis on the basis of clinical criteria alone is impossible. Although these abnormalities have been recognized with high resolution computed tomography (CT), the full potential of this technique for diagnosis has not been realized.

In this report we demonstrate the typical appearance on CT scan of each of the above migrational disorders. In addition, we delineate the optimal CT scanning parameters for their identification. In our experience, the recognition of migrational disorders on CT requires close attention to the following factors: (1) optimal CT technique (voltage and amperage) (2) careful elimination of motion artefact (3) use of thin slices (5mm) through the entire brain, particularly the top surface, in order to identify localized gyral abnormalities eg. pachygyria, heterotopic grey matter. In addition to these factors, the radiologist must be familiar with these disorders and maintain a high index of suspicion of the possible presence of a migrational abnormality. The optimal timing of CT scans appears to be beyond 6 months of age. Thus, in several cases, extensive gyral abnormalities eg. lissencephaly, could not be identified on scans performed during early infancy, but were easily recognizable on later scans. These data demonstrate that with careful attention to the factors outlined above, high resolution CT scanning has a major role in the diagnosis of congenital disorders of neuronal migration.

173.

Epilepsy Surgery In Children

E.C.G. VENTUREYRA, D. IZUKAWA, D. KEENE, P. HUMPHREYS and L.P. IVAN (Ottawa, Ontario)

From August 1981 to September 1986, Surgical intervention was performed in a carefully selected group of 17 boys and 11 girls with medically intractable focal epilepsy (23 cases) or non-atrophic structural lesion and associated seizure focus (5 cases). Mean age at surgery was 14.2 years with a mean interval of 6.5 years between onset of epilepsy and operation. All patients were evaluated preoperatively by; complete physical and neurological examination, interictal EEG's (nasopharyngeal/sphenoidal leads), ictal EEG's (seizure activation/telemetry/video-telemetry), CT Scan, visual field testing, neuropsychological testing and WADA test (intracarotid sodium amytal). All surgical procedures were performed under general anaesthesia with electrocorticographic control, (ECOG), with depth electrodes and cortical mapping. Surgical procedures consisted of osteoplastic craniotomy with; temporal lobectomy (15), excision of brain tumour and epileptogenic focus (5), frontal corticectomy (2), parietal corticectomy (3), frontal lobectomy (1), partial hemispherectomy (1), no resection (1).

Post-operative results were obtained for a mean follow-up period of 23 months. 18 patients had complete abolition of seizures while another two had only occasional auras (71% seizure free). Five patients (18%) showed a greater than 50% reduction in seizure frequency while only 3 (11%) obtained no benefit from surgery. There was no mortality or significant morbidity encountered in this series.

Surgery is a safe, effective and underutilized therapeutic alternative in the management of childhood epilepsy.

174.

An Unusual Benign Movement Disorder of Childhood

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

Unusual movement patterns in children are common and usually represent benign entities eg. simple motor tics. Nevertheless, they are

frequently a cause of worry to parents and occasionally to physicians. Thus, if the movements are frequent and bizarre, there may be concern that they represent epileptic phenomena or progressive neurological diseases.

We report 5 children (4 boys, 1 girl) with an unusual and characteristic pattern of movements which were associated principally with excitement. Onset was in early infancy (8-24 months). The movements consisted of a ritualistic twisting and writhing of the fingers and hands with intermittent clenching and rotation of fists in front of the face. The duration was approximately 30 seconds, during which time the child stared intently at the abnormal movements. There was no alteration of consciousness. Although the episodes occurred spontaneously, they were triggered by excitement or pleasure (sense of achievement) on most occasions. All children had a fascination or preoccupation with specific objects or situations eg. observation of straight lines, certain toys, TV programs (cartoons). Confrontation with these situations invariably triggered the abnormal movements. Although the ability to control these movements improved with increasing age, the typical pattern has persisted throughout the time of follow-up (3-10 years). Stress or anxiety did not appear to play a major role. A videotape will be provided to demonstrate the abnormal movements.

In each case, the birth history, past medical history, early development and neurological examination were normal. In one case, a paternal aunt had a similar movement pattern which persisted until adulthood. There was no other family history of movement disorder or other neurological disease.

The unusual movement patterns observed in these children were stereotyped, but differed in quality from typical motor tics of childhood. They may represent a form of "dystonic tic". In view of the clear association with excitement, these movements may represent an exaggerated "motor release phenomenon" of accumulated emotional tension which may be observed to a much lesser extent in normal individuals under conditions of extreme excitement.

Although the pathogenesis is not entirely certain, this abnormal movement pattern appears to be nonprogressive and unassociated with other neurological abnormalities. Thus, it should be added to the list of benign, nonepileptic spells which may be observed in children.

Child Neurology II

FRIDAY, JUNE 26TH, 1987 0730-1700

175.

Venous Infarction as a Cause of Intraventricular Hemorrhage in the Term Newborn

E.H. ROLAND, O. FLODMARK and A. HILL (Vancouver, British Columbia)

Intraventricular hemorrhage (IVH) occurs commonly in the premature infant (incidence 30-40%) and results from rupture of fragile vessels in the subependymal germinal matrix located at the head of the caudate nucleus. Because the germinal matrix resolves with increasing gestational age, hemorrhage from this location is uncommon in the term infant. Thus, when IVH does occur in the term newborn, the causes include hemorrhage from choroid plexus, arteriovenous malformation, tumour or occasionally from residual germinal matrix and/or coagulopathy.

We have reviewed the clinical and radiological features of 15 term newborns with IVH. Clinical signs suggestive of IVH eg. lethargy, irritability, seizures, and bulging fontanelle were evident on the first day of life in 5 infants. In the remaining 10 infants, the birth history was uneventful and clinical abnormalities did not occur until 8-16 days of age (mean: 11 days). Two infants did not receive Vitamin K at the time of delivery and developed a coagulopathy associated with IVH at 6 and 15 days of age. Computed tomography identified the following sites of origin of hemorrhage: thalamus (10/15 cases), residual germinal matrix (2/15 cases), and unknown origin (?choroid plexus) (3/15 cases). In one infant with thalamic hemorrhage, venous occlusion was demonstrated by cerebral angiography. In a second case, the CT scan demonstrated infarction in the thalamus and thrombosis in the straight sinus, suggestive of venous infarction with secondary hemorrhage. In two other infants, angiography was normal. One infant died, and 8/15 infants subsequently developed post-hemorrhagic hydrocephalus which required placement of a ventriculoperitoneal shunt.

The above data demonstrate a high incidence of thalamic hemorrhage as a cause of IVH in the term newborn. There was no clear association between birth asphyxia or trauma and subsequent IVH. Angiographic and CT scan evidence in two infants suggest venous thrombosis with subsequent hemorrhagic infarction as a possible cause of thalamic hemorrhage. The high incidence of progressive hydrocephalus compared to that observed in premature infants with IVH most probably reflects the decreased brain tissue compliance and decreased expandability of the skull in the term newborn.

176.

Early Diagnosis of Aicardi's Syndrome: New and Characteristic Features on Cranial Ultrasonography

E.H. ROLAND, A. HILL and O. FLODMARK (Vancouver, British Columbia)

Aicardi's syndrome occurs only in females and consists of agenesis of the corpus callosum, characteristic ocular lesions (chorioretinal lacunae) and infantile spasms. It carries a grave prognosis, resulting in profound mental retardation and death during childhood. Diagnosis may be difficult in early infancy, especially in the premature infant, in whom a cloudy cornea and/or pupillary membrane (normal at this age) may obscure the characteristic eye lesions. Furthermore, the findings of ventriculomegaly and absence of the corpus callosum on computed tomography (CT) are nonspecific.

We report a unique combination of cerebral abnormalities demonstrated by cranial ultrasonography (US) in two newborn infants in whom Aicardi's syndrome was diagnosed subsequently. The infants were born at 27 and 34 weeks of gestation respectively. Multiple nonspecific congenital anomalies were recognized at birth, including hypertelorism and microphthalmia. In each case, cranial US scans demonstrated the typical features of absence of the corpus callosum ie. widely separated frontal horns of lateral ventricles, elevation and irregular appearance of the third ventricle and radially-arranged pericallosal gyri. In addition, unusual and prominent cysts were observed within the choroid plexus. These particular lesions were not demonstrated by CT.

Aicardi's syndrome results from abnormal cerebral development prior to the third month of fetal life. Abnormalities of formation of the choroid plexus in combination with midline cerebral defects are consistent with this timing. In the past, the diagnosis of Aicardi's syndrome has depended on ophthalmoscopic findings of chorioretinal lacunae and the typical natural history of the syndrome. Furthermore, the abnormalities on CT scan are non-specific. The recognition on cranial US of this unique combination of cysts in the choroid plexus and absence of the corpus callosum may be pathognomonic of Aicardi's syndrome and may permit diagnosis in early infancy prior to the onset of seizures. Clearly, early diagnosis of Aicardi's syndrome in infants who have other serious medical problems, has important implications for management.

177.

Amaurosis Fugax in Adolescents

R. APPLETON, A. HILL and K. FARRELL (Vancouver, British Columbia)

Amaurosis fugax refers to transient monocular loss of vision usually lasting less than one hour. It occurs more commonly in older adults in whom it is associated frequently with atherosclerotic disease. Transient monocular blindness may also result from vascular spasm in migraine, cardiac emboli or abnormalities of hemostasis. In some patients no underlying etiology can be demonstrated.

We describe 5 patients who developed recurrent episodes of transient monocular blindness between 14 and 16 years of age. Four of the 5 described a characteristic "jigsaw" or "mosaic" pattern of visual loss. This started as isolated scotomata which gradually increased in size over 3 to 5 minutes until the individual scotomata became almost confluent. The duration of the maximal visual loss was between 4 and 5 minutes in 4 patients and between 20 and 30 minutes in the 5th patient. Although the episodes were not accompanied by headache, there was a history of migraine in 3 of the 5 patients. In one patient fundoscopy during an episode revealed pallor of the optic disc. Between attacks no patient had visual symptoms and cardiovascular, neurological and ophthalmological examinations were normal. The episodes occurred every 3 to 6 weeks. Treatment with propanolol and pizotyline in two patients was not effective.

Investigations did not demonstrate an underlying basis for the episodes. Thus carotid angiography was normal in 4 children in whom it was performed. In addition, the following investigations were normal in each patient: echocardiography, electrocardiography, computed tomography of the head, complete blood count, sedimentation rate, rheumatoid factor, antinuclear antibody and coagulation studies.

Consideration of the above suggests that transient monocular blindness in adolescents does not appear to be related to serious underlying disease. Thus, cerebral angiography is not warranted in most instances, particularly if there is a "jigsaw" or "mosaic" pattern of visual loss. The pattern and temporal profile of the visual loss is consistent with ischemia of the choroid secondary to vascular spasm and suggests that this disorder may be a variant of migraine.

178.

Congenital Abnormalities in Two Siblings Exposed to Valproic Acid in Utero

K. FARRELL, D. CHITAYAT, L. ANDERSON and J. HALL (Vancouver, British Columbia)

The incidence of birth defects in infants of epileptic women is approximately two to three times higher than in the general population. However, the relationship between such congenital abnormalities and exposure to specific antiepileptic drugs in less clear. Thus the teratogenic effects of valproic acid (VPA) are not understood fully. Growth retardation, neural tube defects and craniofacial abnormalities have been described in mouse embryo cultures exposed to VPA. In humans, neural tube defects, craniofacial, skeletal, cerebral, cardiovascular and urogenital abnormalities have been described in infants born to mothers receiving VAP during pregnancy.

We describe three siblings born to a mother with epilepsy. Only the two siblings exposed to VPA in utero had certain of the craniofacial features described in previous reports. The mother received VPA and carbamazepine during the two affected pregnancies and aspirin during one of them. She received carbamazepine and methsuximide during the pregnancy of the unaffected child. The mother had no seizures during the pregnancies and no other teratogenic factors were recognized. The abnormalities in the two affected infants included prominent forehead, small nose, anteverted nostrils, long upper lip, shallow philtrum, narrow upper vermilion, posterior angulated ears and hypoplastic nails. In addition, they both had lateral displacement of the medial border of the eyebrows, hypoplastic zygomatic arches and a carrying angle of 0 degrees.

Many of the dysmorphic features present in the two affected patients resemble those observed in rhesus monkeys exposed to VPA in utero. Thus, bulging forehead, retarded upper lip and nostril formation, maxillary hypoplasia, exophthalmos, low set and poorly defined ears, abnormal skeletal formation in the forelimbs and absent or shortened digits have all been described in this animal model. The similarity between the dysmorphic features in the two siblings exposed to VPA in utero and those in the Rhesus monkey model together with the absence of these features in the sibling who was not exposed to VPA suggest that they are a consequence of intrauterine exposure to VPA.

179.

Cerebral Arterial Ectasia and Recurrent Neurological Deficits in Children

R. APPLETON, O. FLODMARK and K. FARRELL (Vancouver, British Columbia)

Cerebral arterial ectasia is characterised by dilatation, elongation and tortuosity of the large intracranial arteries, particularly the internal carotid, vertebral and basilar. The underlying abnormality in the internal elastic lamina is most often associated with arteriosclerosis. In addition, it may be associated with trauma, infective emboli, connective tissue disorders, neurofibromatosis and generalised arteriectasis. Ectasia has been described almost exclusively in older adults and presents most commonly with cranial nerve palsies secondary to pressure, symptoms and signs of cerebral ischemia or with subarachnoid hemorrhage.

We describe two boys who developed recurrent neurological deficits associated with ectasia of the basilar and intracranial portions of the internal carotid arteries. In the first patient, five episodes occurred between 21 and 34 months of age. These included paraparesis, coma, bilateral 3rd nerve palsy and hemiparesis. The duration of the episodes ranged from 1 to 3 weeks and there was full recovery after each episode. The patient had transposition of the great arteries which was repaired by the Mustard procedure at 11 months of age. Echocardiography and cardiac angiography demonstrated no cause for emboli. He has a mild thrombocytosis (440-750 x 10^3/ul). No other underlying cause of stroke has been demonstrated. Following treatment with aspirin, he has had no further episodes over the past 5 months. The second patient had two episodes of hemiparesis associated with cranial nerve signs at 13 and 15 years of age. Both episodes were associated with severe headache and he subsequently developed classical migraine. The plasma factor XII level was 30% of the normal value. No other predisposing cause for stroke was demonstrated. Following the second episode he was treated with aspirin and dipyridamole and has had no further episodes over the past 2 years. In both children, cerebral angiography demonstrated ectasia of the basilar and the intracranial portions of the internal carotid arteries.

The similarity of clinical presentation, the absence of other causes for the neurological deficits and the response to treatment with acetylsalicylic acid suggest a causal relationship between the recurrent neurological deficits and the cerebral ectasia. The effect of aspirin may be mediated through its action on platelet aggregation and/or vasoconstriction.

180.

A Prospective Study of Computed Tomography in Acute Bacterial Meningitis

K. FARRELL, O. FLODMARK, D. CABRAL and D. SPEERT (Vancouver, British Columbia)

Bacterial meningitis may be complicated by cerebral infarction, subdural effusion, cerebral edema, hydrocephalus, subdural empyema and cerebral abscess. These abnormalities can be demonstrated by computed tomography (CT) of the head. Previous studies of the value of CT scans in bacterial meningitis have involved only patients selected on the basis of specific clinical complications. Thus the precise role of CT scan in the management of patients with acute bacterial meningitis is not known.

We studied prospectively 41 unselected children over two months of age with acute bacterial meningitis. Serial CT scans were performed without contrast at the time of admission, at discharge and 6 to 18 months after the illness. The CT scans were obtained using a GE 8800 scanner. Abnormalities on the CT scans performed at admission and discharge included subdural effusion (8 patients), focal infarction (5 patients) and pus in the basal cisterns (1 patient). Two of the 5 patients in whom there was an infarct on the second CT scan had a normal initial CT scan. All patients with focal infarction or cisternal pus had a hemiparesis. Two patients with hemiparesis had normal CT scans. Marked cerebral edema was seen in the two patients who died. Comparison of the scans performed on admission with those at discharge demonstrated enlargement of the ventricles and/or subarachnoid spaces on the second scan in 29 and 36 patients. The size of the ventricles and/or subarachnoid spaces was less on the third scan in 32 of 33 patients.

This study demonstrates that clinical examination is a sensitive method of detecting neurological complications in bacterial meningitis. Thus, no clinically significant CT abnormalities were demonstrated which were not suspected on clinical assessment. Cerebral infarction was observed on the CT scan only when focal neurological signs were present. Furthermore, the initial CT scan performed in the first week of the illness failed to demonstrate the infarction in 2 of 5 patients. Finally, mild ventricular dilatation was a common but transient abnormality, which did not require surgical treatment.

181.

Comparison of Computed Tomography, Ultrasonography and Magnetic Resonance Imaging for the Diagnosis of Periventricular Leukomalacia in Late Infancy

E.H. ROLAND, A. HILL, O. FLODMARK, M.F. WHITFIELD and B.A. LUPTON (Vancouver, British Columbia)

Periventricular leukomalacia (PVL) results from ischemic injury to periventricular white matter, a watershed zone of arterial supply in the premature brain. It is an important cause of motor handicap ie. spastic diplegia or quadriplegia in infants who were born prematurely.

This study compares the value of computed tomography (CT), ultrasonography (US) and magnetic resonance imaging (MRI) for the diagnoses of PVL during late infancy.

The study population comprised 15 children born prematurely and who had clinical evidence of PVL ie. spastic diplegia or quadriplegia. Cranial CT scans performed beyond 6 months of age demonstrated the following unique and characteristic abnormalities: 1) ventriculomegaly with irregular contour of ventricular walls, 2) prominent cortical sulci directly adjacent to the ventricles and 3) reduced quantity of periventricular white matter, particularly at the trigone of the lateral ventricles. Identification of these abnormalities was highly dependent on CT scanning technique. Thus, when CT was performed routinely with 10 mm slices, a decrease in the quantity of white matter was the only recognizable abnormality. However, when the scan was repeated with 5 mm slices at the level of the lateral ventricles, the characteristic features described above were observed. The location and extent of abnormalities on CT correlated well with the severity of neurological abnormalities observed at follow-up.

Conversely, US was less helpful for the diagnosis of PVL beyond four months of age. Thus, even in severe cases, nonspecific ventriculomegaly with irregular outline of ventricles was often the only demonstrable abnormality. Furthermore, in many instances, the small size of the anterior fontanelle at this age precluded US evaluation.

Preliminary observations with MRI suggest that this technique provides more detailed anatomic resolution of the pathognomonic features of PVL observed previously on CT. Thus, MRI may become the radiological technique of choice for the diagnosis of PVL in late infancy.

182.

A Hereditary Syndrome of Congenital Central Hypoventilation, Aganglionic Bowel and Pupillary Abnormality

L. METZ and H.Z. DARWASH (Calgary, Alberta)

Congenital central hypoventilation syndrome (CCHS) is a rare disorder where there is abnormal control of ventilation particularly during non-REM slow wave sleep. It is thought to be secondary to autonomic nervous system dysfunction. Associated abnormalities have included Hirschsprung's Disease and poor cardiac variability. One set of siblings with CCHS and Hirschsprung's Disease has been reported. We present another set of two siblings with CCHS and Hirschsprung's Disease, who also had unreactive pupils and facial weakness.

The first infant required intubation and ventilation at birth. He had unreactive pupils and absent corneal and gag reflexes and mild hypotonia, yet was moving all limbs and spontaneously opening his eyes. A barium enema suggested Hirschsprung's Disease. He died at 2 months. The second infant was born at 35 weeks gestation and had recurrent apnea necessitating intubation within the first hour. She had unreactive dilated pupils, absent corneal and gag reflex and mild hypotonia yet she opened her eyes spontaneously, had normal oculocephalic reflexes and moved all limbs well. At 12 weeks of age she has normal ventilation while awake but becomes totally apneic at onset of slow-wave (non-REM) sleep with absence of bradycardia even with oxygen desaturation to 50 - 60%. She has decreased cardiac variability in sleep and no response to carotid massage. She did however increase her heart rate with IV atropine. Pharmacologic testing of her pupils reveals a sympathetic lesion (no response to 4% cocaine) without deafferentation (no response to 0.1% phenylephrine) and a parasympathetic lesion with denervation supersensitivity (pupil constricts to 1/8% pilocarpine). She has a normal Shirmer's Test indicating normal tearing and a normal response to intradermal Histamine. A barium enema suggested Hirschsprung's of the entire colon and the rectum appears totally aganglionic on biopsy. Both these infants were initially erroneously considered to have suffered an asphyxial insult.

183.

The MELAS Syndrome: Light Microscopic and Ultrastructural Observations

E. SHAHAR, D.L. MacGREGOR and L.E. BECKOR (Toronto, Ontario)

The MELAS syndrome is a combination of mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes of unknown etiology. The light microscopy and ultrastructural investigations in a 17-year-old male with MELAS are presented. Since childhood, he would easily fatigue associated with episodes of recurrent vomiting. Academic skills were behind his age performance aggravated by sensorineural hearing loss. Since age 15 years, he had two stroke-like episodes documented with head C.T.; both with complete recovery. These

were associated with altered consciousness, recurrent vomiting, and partial complex seizures. Serum lactate levels were consistently elevated. The diagnosis of MELAS was confirmed by muscle biopsy showing pathognomonic "ragged-red" fibers. By electron microscopy, these represented large, subsarcolemmal and interfibrillary aggregates of mitochondria. Mitochondrial architecture consisted of the characteristic "paracrystalline" or globular inclusion bodies. Some mitochondria were elongated with loops and branches while others were oval or globular. Cristae were either markedly increased in number, mitochondria described as honeycomb-like or coral-like, or were empty of cristae and filled with glycogen particles. The myofibrillary architecture ranged from normal with subsarcolemmal aggregates of abnormal mitochondria to complete myofibrillary derangement associated with numerous, bizarre mitochondria. Swelling of endothelial cells was not observed in this study. Although the mitochondrial abnormalities and lactic acidosis suggested that the symptoms were due to cellular hypoxia, the exact pathogenesis of the stroke-like syndrome in MELAS syndrome has not been completely elucidated.

184.

Moya Moya Disease and Renal Artery Stenosis Presenting in Infancy: Case Presentation

C. ADAMS and D.A. McGREAL (Toronto, Ontario)

The patient was born at term following a normal pregnancy and delivery. At 4 weeks he had focal and secondarily generalized seizures. At 7 months, seizures associated with a transient left hemiparesis recurred. Development continued normally until at 14 months he became dysphasic and had a persistent right hemiparesis. Hypertension was noted and treated. A subsequent hypertensive crisis caused progression of his hemiparesis and cortical blindness.

Associated with the first 3 episodes were questionable otitis media infections. Lumbar punctures were always free of cells and sterile. Head CT scans from 4 weeks to 18 months showed hypodensities in both hemispheres. A carotid angiogram at 7 months was normal. At 17 months a repeat angiogram showed occlusion of both internal carotid arteries with basal ganglia collaterals. Renal artery stenosis was demonstrated on angiogram. At 18 months he had a left and later a right extracranial dural artery synangiosis.

The radiographic studies are shown. Three previous reports of renal artery stenosis and Moya Moya disease are discussed. The proposal of congenital and acquired forms of Moya Moya and the pathology of fibromuscular dysplasia and its similarity to the changes in Moya Moya are reviewed.

185.

Clinical Course and Investigations in Neonatal High Cervical Cord Injuries Resulting From Forceps Delivery

J.E. WARK, S.R. GEORGE, D. ARMSTRONG and H.E. WHYTE (Toronto, Ontario)

High cervical cord injuries due to forceps rotation comprise 25% of neonatal cord injuries, and their outlook has been considered hopeless. We describe the very different clinical course and the associated investigations in two such infants followed for 3 months.

Baby R.N. was flaccid and areflexic. Pain appreciation was present from 4 days of age, and from 11 days spontaneous movements of her limbs and weak though ineffective respiratory efforts were made. Baby S.G. was clinically identical to R.N. initially. A transient response to pain was noted from days 14 to 18, but spontaneous movements were never seen. No respiratory movements were observed and the child was much less responsive.

Cervical X-rays showed a C1-C2 dislocation in R.N. and a craniocervical dislocation in S.G. Metrizamide myelography within 12 hours of birth demonstrated diffuse high cervical cord swelling in both. Ultrasound of the cervical cord at 6 weeks showed severe narrowing in S.G. but not in R.N. Repeat myelography at 11 weeks in S.G. showed severe local cord thinning at the level of the previous swelling.

Somatosensory evoked potentials (SEPs) were recorded to median nerve stimulation in both patients on day one and at regular intervals thereafter. A cortical response was present in both on day 1, deteriorated over the first week, then showed good recovery in R.N. but not in S.G.

In conclusion, R.N. recovered some function below the level of injury, corroborated by imaging techniques and SEPs. S.G. had virtually no recovery of function and this was supported by ultrasound, myelography, and electrophysiology. Early investigations did not predict outcome, but by 6 weeks definitive clinical-investigative findings had emerged in each case.

186.

CT Scan Findings in Glutaric Aciduria — Type I

J.Y. YAGER, B. McCLARTY and S.S. SESHIA (Winnipeg, Manitoba)

Glutaric Aciduria Type I generally presents in infancy or early childhood with dyskinesia and mental retardation. But the clinical spectrum of the disorder is likely to be broader than currently recognized. Little attention has been drawn to CT scan findings in this disorder, and in particular, to changes in cerebral white matter. We, therefore, report the CT scan findings in an infant with Type I Glutaric Aciduria.

G.M., one of the twins, was born at 29 weeks gestation with a birth weight of 990 gms. The neonatal period was uneventful. He then presented at 43 weeks conceptional age (3 weeks corrected) because of an increasing head circumference. He was also hypertonic. Urine organic acid analysis showed a marked increase of glutaric acid and 3 hydroxyglutaric acid (courtesy Dr. L. Seargeant). CT scan showed generalized ventricular, cerebral, sulcal and basal cisternal dilatation. The subarachnoid spaces anterior to both temporal horns were large. Additionally, there was striking diffuse attenuation of the white matter. A CT scan done 18 weeks later showed severe generalized cerebral atrophy with sparing of subcortical gray matter and little evidence of cerebral white matter. The diagnosis of Type I Glutaric Aciduria was confirmed by the inability to detect glutaryl - CoA dehydrogenase activity in fibroblasts (courtesy Dr. S.I. Goodman).

The marked cerebral white matter attenuation on the initial CT scan in our case is similar to that seen with the leukodystrophies. Such a finding has not been emphasized in previous reports on children with Type I Glutaric Aciduria. Furthermore, the evolution of the CT scan findings in our case may suggest that the "conflicting" reports on CT scan findings in this disorder (Aicardi et al 1985) are likely related to the timing of the study. We suggest that Type I Glutaric Aciduria be entertained in the differential diagnosis of children with neurological disorders who show diffuse attenuation of cerebral white matter on CT scan.

187.

Vomiting in Children Following Head Injury

D. IZUKAWA, P. SHEAR, H. HUGENHOLTZ, M. LI and E.C.G. VENTUREYRA (Ottawa, Ontario)

Many children vomit following a head injury. Often emesis is the symptom on which a physician will base his or her decision to admit a child. The mechanisms that trigger emesis in some of these children and not in others are unknown. Experimental work with concussion in primates suggested that the incidence of emesis could be reduced by fasting the animal prior to concussion. Accordingly, we studied 96 consecutive children with a mild head injury (GCS 13-15) in order to ascertain the relationship of posttraumatic emesis to a variety of factors

including the interval between the injury and their previous meal or snack. Additionally, a retrospective study was carried out of all 29 consecutive moderate and severely injured children (GCS 8-12) among the 645 most recent head injuries.

This study reveals that posttraumatic emesis is more common following minor head injuries than following more severe head injuries ($p<0.05$). Posttraumatic emesis occurs more frequently in children over two years old ($p<0.001$) and in children injured within an hour of a meal or snack ($p<0.001$). Retching and vomiting generally subsides within 3 hours of onset, except in those children injured more than an hour after a meal or snack who experience posttraumatic emesis. In these cases, the vomiting may be quite protracted. (Mean = 7.5 hrs.)

Children over 2 years old with posttraumatic emesis who are neurologically stable following a minor head injury that occurred within an hour of a meal or snack can be expected to improve quickly. Their counterparts injured more than an hour after a meal or snack are likely to remain distressed much longer and are best admitted to hospital.

188.

A Progressive Multisystem Neurodegenerative Disorder, with Autonomic Failure, in Childhood

G.M. RONEN, A.G. LACSON, J. GREEN and G. JOHNSON (St. John's, Newfoundland)

We report the clinical and pathological findings in a boy with a unique neurodegenerative disorder, whose family history was negative, and whose investigations did not reveal any metabolic or known degenerative cause. He was well until age 4 when progressive sensorineural deafness began. At age 11 he presented with decreased visual acquity, atypical retinitis pigmentosa and mild degree of optic atrophy. Rapid deterioration in multiple functions occurred at age 13, leading to death within a few months. It started with sudden decline in vision, progressive gait impairment, with pyramidal tract signs and proprioceptive loss, and was followed by non-rhythmic breathing, urinary incontinence; flushed, hot, dry skin with periodic blotching and tachycardia. Diffuse lancinating pain developed and progressive respiratory irregularities led finally to death. Cranial CT was normal, EEG showed 7-8 theta frequencies, nerve conductions were slow and the echocardiogram showed concentric left ventricular myocardial hypertrophy.

Pathology showed: 1. Neuronal loss and astrocytosis of anterior horn cells, the lateral geniculate body, and many cranial nerve and other brainstem nuclei including the nucleus ambiguus and the dorsal motor nucleus of vagus; 2. Loss of neurons in the dorsal root ganglia; and 3. Myelin fiber loss and astrocytosis involving the optic, vestibular, cochlear and vagus nerves and some ascending and descending tracts.

We could not find a similar published report and present this case for discussion of the possible etiology and classification of this disease.

Multiple Sclerosis (Platform)

FRIDAY, JUNE 26TH, 1987 1345-1700

Co-Chairmen: DR. D.W. PATY (Vancouver)
DR. J. ANTEL (Montreal)

189.

Homonymous Field Defects in Multiple Sclerosis: A Clinical and Magnetic Resonance Correlation

M.R. HANSON, R.L. TOMSACK, E.J. FITZGIBBON and P.J. SWEENEY (Cleveland, Ohio)

While prechiasmal lesions in multiple sclerosis (MS) are common, documented retrochiasmal lesions are rare. We report 5 patients (4 women, 1 man; onset age: 23-46 years) with retrochiasmal lesions diagnosed by magnetic resonance imaging (MRI). All had homonymous visual field defects (VFD), 4 left, 1 right. VFDs were the presenting symptom in 3. MS was definite in 3 and probable in 2. Computed tomographic scans were positive in 3, correlating with the VFD in 2. MRI in 3 cases revealed symmetric, bilateral, periventricular lesions characteristic of MS. In 2, lesions were bilateral but heavily contralateral to the VFD. We conclude that these retrochiasmal lesions are rare and that they have little MRI correlation anatomically. MRI is crucial, however, in establishing the diagnosis. Reasons for the infrequency of documented retrochiasmal lesions include: (1) The vascularity is greater anterior than posterior to the chiasm. (2) Because of the separation of myelinated fibres, larger lesions are necessary to cause clinical defects. (3) The presence of co-existing prechiasmal lesions. Our study suggests that the latter 2 explanations are the reasons the VFDs are under reported.

190.

Tizanidine Versus Baclofen in the Treatment of Spasticity in Patients with Multiple Sclerosis: A Double Blind Study

B. BASS, B. WEINSHENKER, G.P.A. RICE, J. NOSEWORTHY, M.G.P. CAMERON and G.C. EBERS (London, Ontario)

Baclofen was compared to tizanidine in a randomized, double-blind, cross-over trial. Each medication was introduced over a 3 week titration period and then maintained at the highest tolerated dose for 5 weeks. The two treatment phases were separated by a 1 week drug withdrawal and a 2 week washout period.

Sixty-six patients entered the trial and forty-eight completed both treatment phases. Drug-related weakness was the commonest cause of patient dropout and exclusion from data analysis and this was more common in patients treated with baclofen. At the end of the trial, evaluating neurologists and physiotherapists thought that baclofen was superior on the basis of perceived efficacy and tolerance ($p<0.05$). Although the efficacy of either tizanidine or baclofen was judged as good to excellent by 24 and 39% of patients respectively, this difference was not statistically significant. Bedside assessment of change in limb tone favoured baclofen although these results were not statistically significant. Muscle weakness was the most common adverse effect. This was significantly more troublesome in patients treated with baclofen. Somnolence and xerostomia were commoner in patients treated with tizanidine.

Both baclofen and tizanidine appear to be useful adjuncts in the treatment of spasticity in patients with multiple sclerosis. Preference of either drug is tempered principally by their side effects.

191.

A Putative Role for Human Retroviruses in the Cause of Multiple Sclerosis

B. WEINSHENKER, J. FLYNN, P. PAYSON and G.P.A. RICE (London, Ontario)

Animal models and recent serological observations have suggested that a human retrovirus might be causally related to multiple sclerosis. Visna, a chronic neurological disease of sheep, bears significant clinical and pathological similarities to MS. This retrovirus is closely related to the human immunodeficiency virus. In patients with AIDS, direct involvement of the nervous system has been recently recognized. Serological studies of patients with MS and some chronic myelopathies (tropical spastic paraparesis) have suggested that a novel human retrovirus, possibly related to HTLV-I, might be etiologically related.

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We have examined sera of 201 patients with clinically definite MS, 29 with chronic idiopathic myelopathy, 51 with other neurological diseases and 29 healthy blood donors, and have found no antibody to either HTLV-I or HTLV-III, in an enzyme immunoassay. We have bolstered the sensitivity of these assays by developing a cell-based ELISA system, which has failed to identify conclusively any antibody to HTLV-I. Preliminary studies with an immunoblot technique have failed to identify antibodies to subcomponents of HTLV-I.

As we refine these assays, we are continuing to look for biochemical evidence (a reverse transcriptase) and morphological evidence (electronmicroscopic evidence) of a putative retroviral infection. We propose that the reported antibodies to various retroviruses in MS patients might reflect cross reactivities (molecular mimicry) between retroviral protein sequences and various central nervous system proteins.

192.

Predictive Tests in Isolated Optic Neuritis

T.E. FEASBY, G.C. EBERS, A.J. FOX and S. KARLIK (London, Ontario)

Patients with isolated unilateral optic neuritis (ON) may subsequently develop multiple sclerosis but the reported rate of conversion varies from 13-85%. We are trying to define this relationship better by long-term follow up in ON patients and by using tests to identify signs characteristic of M.S. in ON patients. These tests are visual (VER) and auditory (AER) evoked responses, spinal fluid protein electrophoresis to detect oligoclonal banding (OB), and MRI scanning of the brain.

We have seen 85 patients with acute isolated unilateral ON. After a mean follow-up time of 33.4 months, 22 (25.9%) have developed signs of clinically definite M.S. The mean time of conversion to M.S. was 26.4 months. The VER in the clinically unaffected eye was abnormal in 6/63 (9.5%) patients not progressing to M.S. and in 5/19 (26.3%) of those progressing to M.S. The AER was not a helpful predictor. Oligoclonal banding was found in 27/59 (45.8%) of those who did progress to M.S. and in 12/17 (70.6%) of those who did progress. These results suggest that while abnormalities of the VER and CSF electrophoresis may help to predict those at higher risk of clinical M.S., many patients who do not develop other clinical signs may also have M.S. We are exploring this possibility with MRI scans of the brain in all our new and follow-up ON patients. Preliminary results suggest that many of them have clinically silent M.S. lesions in the brain, but lesions in the optic nerve have been more difficult to image.

193.

Benign and Chronic Progressive Multiple Sclerosis: A MRI Study

R. KOOPMANS, D. LI, E. GROCHOWSKI, P. CUTLER and D.W. PATY (Vancouver, British Columbia)

The extent of pathology and the degree of disability in MS do not necessarily correlate.

The extent of disease as detected by MRI was compared with clinical severity in 25 benign patients (mean DSS = 1.66, mean age = 42.4, mean duration = 17.2) matched for age, sex and duration of disease with 25 chronic progressive (CP) patients (mean DSS = 6.02, mean age = 43.6, mean duration = 16.8). Benign = >10 years and DSS<3. A computerized quantitation method was used.

MRI was abnormal in 23 benign patients with a total of 285 lesions; 153 (53.7%) lesions were small and solitary (max. dia. <8 mm), 105 (36.8%) large and solitary (max. dia. >8 mm) and 27 (9.5%) were confluent. MRI was abnormal in all CP patients. With 316 lesions; 86 (27.2%) were small and solitary, 90 (28.5%) large and solitary; and 140 (44.3%) confluent.

In 19 (76%) benign patients the lesion load was less than in matched controls, although the range in benign patients (0-4,661 mm^2, mean = 1,219 mm^2) overlapped with the range in CP patients 140-11,910 mm^2, mean = 2,925 mm^2). In 24% (6/25) of pairs the disease load was greater in the benign patient.

Only half of the benign patients had confluency of lesions whereas this was true for all controls. When comparing patients with similar burden of disease (MRI) the CP patients could be distinguished by a higher degree of confluence.

Half of the benign patients with cerebellar and/or brainstem lesions had sub-clinical involvement. In CP disease this was not seen.

Subclinical infra-tentorial involvement, a low proportion of confluence and moderate lesion load were important characteristics of benign disease.

In contrast a high degree of confluence and of clinical expression was characteristic of the disabled patients.

194.

Magnetic Resonance Imaging (MRI) Studies of Experimental Allergic Encephalomyelitis (EAE)

J.H. NOSEWORTHY, J.J. GILBERT and S.J. KARLIK (London, Ontario)

The relapsing and progressive EAE guinea pig animal models provide suitable experimental material for studies designed to understand the tissue basis for the MRI-detected lesions in multiple sclerosis. We have extended our in vitro tissue nuclear magnetic resonance studies to include high field MRI studies using a 1.5 Tesla G.E. system. Using the head coil and a 5½ inch surface coil, 3 mm contiguous slices were obtained with a standard data set of 256 by 256 matrix (partial saturation: 600/20 and multiple spin echo 2000/20, 40, 60, 80) yielding pixel sizes of between 0.8 and 0.9 mm.

We found: (1) It is possible to visualize the CNS of juvenile (225 g) and adult guinea pigs at 1.5 T and do quantitative T1 and T2 measurements.

(2) Extremely small lesions (1 mm) can be detected by MRI in the spinal cord of animals with EAE using a standard clinical imager with the human head coil. Image resolution can be improved with specially designed coils.

(3) It is possible to perform serial MRI studies on animals with progressive EAE and these studies document the evolution of the disease process.

195.

Abnormal Pokeweed Mitogen Induced IGG Secretion in Progressive Multiple Sclerosis: Searching For its Prognostic Value in Stable MS

M. O'GORMAN and J. OGER (Vancouver, British Columbia)

It has been hypothesized that immunological abnormalities contribute to the central nervous system pathology observed in multiple sclerosis.

We have compared the level of immunoglobulin secreted by pokeweed mitogen (PWM) stimulated peripheral blood mononuclear cells (PBMNC) obtained from a) 50 chronic progressive (CP) MS patients, b) 16 stable MS patients and c) 56 healthy control volunteers.

The mean level of IgG secreted by the PBMNC of the CP-MS group (3902±474 ng) was significantly higher than the amount secreted by the healthy control group (2694±349, $p<.05$). The amount of IgG secreted by the PBMNC of the stable MS (2156±396 ng) patients was significantly lower ($p<.01$) than the amount secreted by the PBMNC of the chronic progressive group and did not differ from the control group.

The stable MS group was separated into 2 groups based on the clinical activity of their disease in a 6 month follow-up. The first group

presented with a clinical relapse within 6 months of the immune function test and the second group remained stable throughout the 6 month follow-up.

Pokeweed mitogen induced IgG secretion was higher in the 6 patients who went on to have a relapse (2757±429) than it was in the 10 patients whose disease remained clinically stable (1750±531). This difference is not significant and indicates only a trend. This may be due to the small sample size and we are therefore continuing our investigation of stable MS patients and we will present our updated results.

196.

Tizanidine Therapy for Spasticity in Multiple Sclerosis

Y. LAPIERRE, C. TANSEY, S. BOUCHARD, W.J. BARKAS, D. GENDRON and G. FRANCIS (Montreal, Quebec)

Spasticity is a frequent and often disabling symptom in MS patients. Current agents used as antispastic agents include Dantrolene Sodium, Baclofen and Diazepam. Tizanidine (5-chloro-4-(2imidazolin-2yl amino)-2, 1, 3- benzothialdiazole) is a new antispasticity agent that has purported central action. A double blind placebo controlled trial was performed to study the efficacy of this drug in MS patients. Sixty-six patients entered an eight week therapeutic trial and fifty-nine completed the trial. Patients were assessed at 0, 2, 3, 8 weeks of therapy for clinical effects. Electrophysiologic tests were performed at 0 and 8 weeks.

A statistically significant benefit was noted in spastic muscle groups in the legs with concomitant significant reduction in hyperactive stretch reflexes and ankle clonus. Side effects most frequently cited included dry mouth and drowsiness. Two patients developed elevated liver function test that decreased with cessation of therapy. Other clinical details, side effects and electrophysiologic data will be presented.

Tizanidine appears to reduce clinical spasticity and hyperreflexia in MS patients although no change in functional status was detected. Tizanidine may well serve as an alternative antispastic agent, alone or in combination with other agents.

197.

Age-dependent Changes in Nuclear Magnetic Resonance (NMR) Relaxation Times in Guinea Pig Central Nervous System

J.H. NOSEWORTHY, J.J. GILBERT and S.J. KARLIK (London, Ontario)

The clinical course of the experimental allergic encephalomyelitis (EAE) animal models of multiple sclerosis is largely age dependent in that it is possible to induce a relapsing model of EAE in guinea pigs immunized as juveniles whereas a progressive course can be predictably developed in adult animals. In order to assess the changes in the NMR relaxation parameters that occur with postnatal maturation of the guinea pig CNS we measured the T1 and T2 relaxation times and the tissue specific gravities at each level of the CNS in strain 13 guinea pigs from 1.5 weeks of life (100 g) until adulthood (7.0 weeks, 400 g).

NMR relaxation times were dependant on the anatomic location. T1 and T2 relaxation times progressively shorten during the early postnatal period and thereafter stabilize and remain constant throughout early adulthood. This was accompanied by a significant decrease in tissue water content. Thus the factors which determine NMR relaxation times (e.g. tissue water content) appear to change in a predictable fashion during early postnatal development in the guinea pig. Conversion of the EAE model from the relapsing to the progressive form appears to coincide with the age-dependent stabilization of NMR relaxation values.

198.

A New Approach to the Classification of BAER in Multiple Sclerosis

M. JAVIDAN, A. FARID, D.R. McLEAN and K.G. WARREN (Edmonton, Alberta)

To improve the interpretation and classification of Brainstem Auditory Evoked Responses (BAER) in Multiple Sclerosis (MS), discriminant analysis was performed on 162 BAERS in patients with definite MS and 60 BAERS in normal controls.

The best discriminating latency and amplitudes were weighted to produce a function which led to a final score. The function developed was: 1 x wave V amplitude — 0.43 x wave V latency + 0.41 x wave IV amplitude — 0.32 wave I amplitude + 0.29 x wave II latency.

Sensitivity was 75% and specificity was 88% with overall 79% correct classification.

This function was applied to 106 BAERS in probable MS patients and 102 BAERS in possible MS patients as unclassified cases to identify an abnormal response. The classification criterion assumed a 0.5 probability of group membership. 62% of BAER in probable MS and 49% of BAERS in possible MS patients were classified as abnormal. This computerized technique can be used to minimize errors in classification of BAERS in patients with MS.

199.

A Trial of Namalwa Interferon in the Treatment of Chronic Progressive (CP) Multiple Sclerosis (MS) I. Clinical and MRI Analysis

L.F. KASTRUKOFF, S.A. HASHIMOTO, J.J. OGER, S.L. SACKS, D.K. LI, A.J. PETKAU, J. BERKOWITZ and D.W. PATY (Vancouver, British Columbia)

One hundred and one clinically definite MS patients with a CP course were treated for six months with daily subcutaneous namalwa interferon (Wellferon) (5 x 10^6 IU) in a randomized, double-blind, placebo-controlled study. Disease activity was assessed both clinically and by serial MRI scans. Quantitation of lesions in two planes was achieved using a computer-assisted measurement system. A correlation between disease activity assessed clinically and by MRI of the brain was not observed. No significant difference was observed between the interferon and placebo treated groups after two years of follow-up using either clinical or MRI criteria. Similarly, no significant differences were observed at 3, 6, 9, 12 or 18 months although a number of patients were observed to register their "best" clinical score at 9 months. A small sub-population of patients was observed to improve transiently with interferon. Characteristics of this population are under investigation.

Namalwa interferon was generally well tolerated but severe fatigue and/or malaise were among the more common side-effects. Severe hematologic and biochemical abnormalities were not observed.

200.

Vascular Headache: A Presenting Symptom of Multiple Sclerosis

M.S. FREEDMAN and T.A. GRAY (Toronto, Ontario)

Vascular headache of migraine type may be a presenting symptom of multiple sclerosis (M.S.). If the headache is severe and accompanied by neurological signs it may cause difficulties in differential diagnosis.

We reviewed the records of 1,113 patients with M.S. seen at St. Michael's Hospital from 1967-1987. Forty-four cases were found whose initial attack or subsequent exacerbations presented with headache which was severe, long-lasting and accompanied by gastrointestinal, visual disturbances, or other migrainous symptomatology.

Patients with head pain which was either paraoxysmal in nature of other neuralgic character, or associated with optic neuritis were excluded.

Of the 44 cases, 30 were female and 14 were male. The average age at presentation with their headache in both groups was 31, with similar ranges. 18 patients had headache during their first clinical attack of M.S. while 26 suffered headaches with exacerbations. 17 patients had headaches with attacks of demyelination which could be localized to the posterior fossa. All but 3 patients carried a diagnosis of clinically definite M.S.

All patients were asked to complete a questionnaire inquiring into previous headaches, family history, details of their documented episode, and recurrences, with or without further attacks of demyelination. Preliminary data indicate that at least 5 patients never suffered from migraines prior to the onset of their M.S. At least 12 patients went on to have headaches of similar nature with further M.S. attacks.

Although migraine has been reported in association with M.S. it has not been well described as a presenting symptom. Since perivascular inflammation can be a striking feature of demyelination the concurrent release of vasoactive substances might provoke a migraine. Our results indicate that migraine headache may be a presenting symptom of M.S. in at least 4% of cases.

Evoked Potentials (Poster)

FRIDAY, JUNE 26TH, 1987 0730-1700

201.

Somatosensory Evoked Potentials in Newborns and Infants

S.R. GEORGE and M.J. TAYLOR (Toronto, Ontario)

Somatosensory evoked potentials (SEPs) are rarely used clinically in neonates or young infants due to the difficulty in obtaining reliable results. This study presents methodological and normative SEP data in this age range.

SEPs were recorded in 29 normal infants (0-11 weeks) from C3′ and C4′ in response to median nerve stimulation. High stimulation intensities, up to 20mA, were required to elicit a motor response of the thumb or the fingers; this was easily tolerated by the babies. Stimulation rate was 1.1Hz and duration was 200μs. In order to obtain a reliable response three different bandpasses were used: bandpasses of 5-1500Hz and 5-3000Hz with a 40K gain and a bandpass of 30-3000Hz with a 100K gain. The sweep was 200ms and at each bandpass at least 2×64 sweeps were averaged.

Notes were made whether the child was awake or asleep during each average and whether eye movements behind closed lids or sucking movements were observed.

To interpret results all three recordings were compared. The narrow bandpass (30-3000Hz) accented the P22 and the following N35, predominantly when the baby was awake, whereas the wider bandpasses (5-1500Hz, 5-3000Hz) accented the N20, P22 and a late wave at about 100ms allowing the evaluation of the sleeping child. Short periods of data acquisition (64 trials with 1.1Hz) proved to be better than longer sampling duration, as sleep stages in young infants change rapidly and can affect the cortical SEP.

In every child a P22 (comparable to the adult P22) and a N35 could be demonstrated; normative data will be presented.

202.

Central Pontine Myelinolysis: CT and BAER Correlates of Acute and Recovery Phases

D.S. GRAY, M.A. LEE AND W.A. FLETCHER (Calgary, Alberta)

Central pontine myelinolysis (osmotic demyelination syndrome) is usually associated with severe electrolyte disturbance or other debilitating disease. Recovery is uncommon.

We report a young alcoholic male who over a two week period developed a dense spastic quadraparesis with bulbar involvement and pseudo-bulbar affect. There was no electrolyte disturbance or systemic disease. Over a period of sixty days, he recovered the ability to walk unassisted, swallow normally, and perform normal activities of daily living.

At the time of maximal weakness, CT scan revealed a large hypodense area in the pons. Brainstem auditory evoked responses (BAER) demonstrated bilateral symmetric delay of wave forms III-V. Ten days later, the clinical and radiologic findings were unchanged but BAER latencies were normal. After complete clinical recovery forty-five days later, BAER latencies remained normal but the CT appearance of the pontine lesion was unchanged.

These findings confirm that CT and BAER investigations are helpful in the diagnosis of central pontine myelinolysis. In addition, the suggestion is made that CT and BAER may not accurately reflect the functional status of the patient beyond the acute phase of the disease.

203.

Posterior Tibial Somatosensory Evoked Potential Abnormalities in Patients with Cystic Fibrosis

P. HUMPHREYS, P. THORP, J. VAJSAR, W. BATTEN and N.E. MacDONALD (Ottawa, Ontario)

Cystic fibrosis patients at autopsy typically demonstrate dystrophic changes in the posterior column tracts and nuclei, with frequent axonal spheroids, particularly in the nucleus gracilis. Exceptionally such patients have had an ataxic syndrome in life, usually accompanied by low serum vitamin E levels; most, however, are asymptomatic. It is not clear whether these neuroaxonal changes in cystic fibrosis are part of the disease, or related to vitamin E malabsorption. We undertook an investigation of posterior column function, using median and posterior column function, using median and posterior tibial nerve somatosensory evoked potential (SEP) studies in 9 patients with cystic fibrosis.

The patients ranged in age from 8 to 18. Nutritional status varied from normal to undernourished; all were receiving vitamin E supplementation. Clinical neurologic assessment was normal in all patients; once had only subjective symptoms of numbness in the feet. Results of SEP recordings were compared statistically with those from a group of 9 age-matched controls. The following data were analyzed: 1) median nerve conduction velocities; latency, amplitude, configuration of SEP's from Erb's point, neck and scalp, 2) posterior tibial nerve conduction velocities; latency amplitude, configuration of SEP's from lumbar spine, neck (when obtainable) and scalp.

Statistically significant differences were found only for posterior tibial nerve scalp recording amplitudes: left P1/N1 2.11 ± 0.73 μV (control 5.09 ± 3.37 μV), $p = .019$; left N1/P2 2.11 ± 1.00 μV (control 4.54 ± 1.59 μV), $p = .002$. There was no significant side-to-side difference in both posterior tibial and median nerve studies. These findings lend support to the concept of a ubiquitous dysfunction in somatosensory pathways from the lower limbs in cystic fibrosis patients, and are in agreement with known pathological findings.

204.

Intraoperative Monitoring of Brainstem Evoked Potentials, Electrochleography and Direct Auditory Nerve Action Potentials During Posterior Fossa Surgery

R.D. LINDEN, C.H. TATOR, V. MRAZ, L. KENNEDY, I. BELL and D. CHARLES (Toronto, Ontario)

One of the complications of surgery for the removal of an acoustic neuroma is the loss of hearing. Morphological preservation of the eighth cranial nerve does not always indicate preserved hearing. The auditory brainstem response (ABR), electrocochleography (ECOG) and direct recording of compound action potential from the auditory nerve (CNAP) have been recommended as intraoperative monitoring techniques. The optimal method for monitoring has not yet been determined. Therefore, we compared the ABR, ECOG and CNAP as intraoperative monitoring methods.

The ABR was elicited preoperatively and post-operatively by presenting 70 dB nHL clicks at a rate of 11.1/s. An intensity series was performed (50,30,10,dB nHL) by presenting the stimuli at 44.4/s. Intraoperatively, a cotton-wick electrode made of Pt5T wire (medwire corporation) was placed transtympanically to record the ECOG and a similar electrode made of Ag5T was used to record the CNAP. The effects of stimulus intensity and repetition rate on the ECOG and CNAP were determined. The ECOG electrode is out of the operative field, and is therefore easier to use than the CNAP. Both methods provide real-time feedback to the surgeon because reliable responses may be recorded with a small number of averages (N = 10) to stimuli at high presentation rates (88.8/s). The CNAP response can aid in nerve localization. The ABR can be used to monitor brainstem function.

Our conclusion is that optimal recording requires monitoring of the ECOG, CNAP and ABR.

205. WITHDRAWN

206.

Developmental Changes in Somatosensory Evoked Potentials

M.J. TAYLOR (Toronto, Ontario)

Somatosensory evoked potentials (SEPs) provide neurologists with an assessment of the neuraxis from peripheral nerve through to sensory cortex; their value is particularly relevant in paediatric neurology as a sensory clinical exam can be difficult in young infants and children. The clinical utility of SEPs, however, requires knowledge of the alterations in waveform which occur with growth and development. This study presents SEP data from 136 normal children (4 mos - 18 yrs) and 50 adults (20-35 yrs). Recordings were done with a standard clinical paradigm (30-3000 hz bandpass, 40k gain, 50ms sweep, 256 trials/ave), stimulating the median nerve, recording over cervical spine (C7) and contralateral sensory cortex (C3′ and C4′). SEPs were easily recorded in all children across the age range studied. Differing nonlinear maturational patterns were seen with peripheral and central aspects of the nervous sytem. The cervical components (N12, N13) changed little in latency until 2-3yrs, the cortical N20 decreased in latency until 2-3yrs and P22 decreased until 6-8yrs, after which age, respectively, all latencies increased until adulthood. The greatest latency changes occurred with N12 and N13, the least with N20; the maturation seen in the subcortical components (P14, P16, N18) was intermediate between peripheral and cortical components. Waveform morphology and interpeak latencies also changed with age; adult morphology was achieved early (<1yr) but central conduction time (N13-N20) reached adult values only at 6-8 yrs. This study provides normative values for paediatric EP labs and a functional assessment of pathways known from neuropathological data to myelinate and mature at varying rates.

207.

Latency, Morphological and Distributional Changes in VEPs with Various Stimuli

M.J. TAYLOR and J. FARRELL (Toronto, Ontario)

VEPs are elicited in clinical settings increasingly by light emitting diode goggles (LEDs) rather then stroboscopic white flash (flash) in circumstances where pattern reversal stimulation is not feasible (ie, in an ICU or O.R.). This study investigated VEP differences to pattern, flash and LED stimulation. VEPs were recorded in 12 adults (6 female) from Fz, Cz, Pz, Oz, 01, 02, P3, P4, T5 and T6 all with a noncephalic reference, and from 01, 02, 0z referenced to Fz, in response to monocular and binocular stimulation (bandpass 1-100Hz, sweep 500ms, gain 10k, 64 trials/ave). ERGs were also recorded from infraorbital leads and did not differ in latency with type of stimulation. At the anterior electrodes the most prominent wave was a large positive peak at 200ms; this decreased somewhat in amplitude posteriorly, particularly with pattern stimulation. The N70 and P100 occipital components were clearer with all stimuli with the Fz reference. As has been reported, pattern VEPs have earlier, smaller, less variable P100s than flash VEPs, and females have earlier, larger P100s (this was more marked with flash and LED stimulation). However, there were also large differences between flash and LED VEPs; the latter were smaller amplitude posteriorly, had a larger frontal component, the P100 was usually bifid with a small peak at 100ms and a second larger peak at a longer latency than the P100 to the flash. With the noncephalic reference the LED VEPs had three distinct positive components between 100-250ms, whereas with the other two stimuli types there were only two. This study emphasizes the need for establishing normative values for each type of visual stimulation used in a clinical lab in order to make valid conclusions about VEP normality or abnormality.

208.

Evoked Potentials and Thoracic Outlet Syndrome

G. BLAIR, G. VANDERLINDEN, C.H. TATOR, R.D. LINDEN and L. VANDERLINDEN (Toronto, Ontario)

There is an urgent need to develop an objective test for the diagnosis of thoracic outlet syndrome (TOS). Evoked potentials have been reported to be a powerful, additional aid in this diagnosis. Both median and ulnar nerve somatosensory evoked potentials (SSEP) must be recorded. Further, a higher diagnostic yield may be obtained if the SSEPs are recorded while the patient's stimulated arm is in an abducted and externally rotated position. Unfortunately there is only one report in the literature wherein this type of analysis has been performed. We therefore, analyzed these potentials in normal subjects and in patients with suspected TOS. Ten normal adults (5 male, 5 female) and nineteen patients were examined. SSEPs were recorded in response to stimulation of the median and ulnar nerve at the wrist. Responses were recorded while the subjects stimulated arm was by their side (anatomic position) and, in an abducted position. One thousand constant current stimuli were delivered at a repetition rate of 4.72/s, at an intensity 10% above twitch threshold. Recordings were replicated. Electrodes were placed at Erb's point, the fifth cervical vertebra, Fz, C3′ and C4′. After a 4 ms delay, the response to the stimulus was recorded for 50 ms. The filter band pass was 30 Hz to 3 KHz.

The potentials recorded with ulnar nerve stimulation had a longer latency and were smaller in amplitude compared to responses recorded with median nerve stimulation. There was no significant difference

between the waveforms if the stimulated arm was placed in the abducted or anatomic position. Analysis of the waveforms recorded from the patients demonstrated that evoked potentials can be helpful in the diagnosis of TOS. Postoperative recordings often demonstrated clear improvements in the recorded waveforms.

Our study indicates that evoked potentials, if recorded with proper technique, are an important test in the diagnosis of TOS.

209.

Somatosensory Evoked Potentials in Normal Pressure Hydrocephalus

I. DANYS, C MELMED, A. COLOHAN and S. BREM (Montreal, Quebec)

In Normal Pressure Hydrocephalus (NPH) the clinical triad of gait disorder, incontinence and intellectual deterioration, along with the computed tomographic (CT) demonstration of ventricular dilatation without corresponding cortical atrophy, remain the best basis for the diagnosis and prediction of the benefit of shunting. The relationship between NPH and somatosensory evoked potentials (SSEP) has not been reported previously.

Fourteen patients with NPH were examined using SSEP. Right and left median nerve stimulation was performed in all cases. Responses at Erb's point (EP) C7, and contralateral somatosensory cortex (N19-P22) were analyzed. In ten of these patients, SSEP were recorded from the lumbar root entry zone (LP) and somatosensory cortex (P/N37) after right and left posterior tibial nerve stimulation.

On median nerve stimulation 12/14 patients had delayed P22 relative to EP and a widened N19-P22 complex. Findings were >2.5 standard deviations (SD), compared to normal subjects and age matched controls. In the lower extremities, the cortical response was abnormally delayed in 9/10 patients; and in 6/9 patients where central conduction time from LP to P/37 could be calculated, it was significantly prolonged >2.5 (SD).

To date 7/14 have undergone ventriculoperitoneal shunting. Clinical and CT follow-up were used to grade response as good, fair, or nil. 5/7 patients had good or fair clinical improvement. SSEP improved in these five patients but not the two who showed no clinical improvement.

SSEP recordings may provide a useful non-invasive technique in the evaluation of suitability of patients for shunting in NPH and in following their course after shunting. SSEP abnormalities may also provide more information regarding the underlying pathophysiology in this poorly understood clinical entity.

210.

The Effect of Electrode Position on Flash Visual Evoked Potentials in the Newborn

B.A. LUPTON, P.K. WONG and A. HILL (Vancouver, British Columbia)

An optimal technique for the assessment of the neonatal visual evoked potential (VEP) has not been estabished. Thus, the precise position of the occipital electrodes may affect latency, amplitude and morphology of the signal. The present study investigates the effect of electrode position on these parameters in the neonatal VEP using a multiple electrode technique.

The VEPs were performed at the bedside using a stroboscopic light source and a multichannel recorder. Thirty-one VEPs were recorded at 37-43 weeks post-conceptional age in 22 term infants with hypoxic-ischemic encephalopathy. Fifty-six VEPs were recorded in 52 premature infants (birth weight <1500g) at 30-43 weeks post-conceptional age. Twenty-nine of the preterm infants who had no clinical or radiographic evidence of neurological abnormalities, served as a control group. Electrodes were placed at the central occiput, Oz, and right and left occipital positions 10% of the circumference from Oz.

The VEP was present in 80/87 cases in at least one electrode position. However, it could be identified at all occipital electrodes in 59/87 cases only. Asymmetry of signal was common. In two cases, the response was absent at Oz but present at a more lateral electrode. The latency at the lateral electrodes varied by >2% from that at Oz in 59% of recordings and by >10% in 31% of recordings. The amplitude of the response at Oz was greater than at the lateral electrodes by a factor of 2.36. Similar results were obtained in the control group.

These data demonstrate that only minimal changes in electrode position (>1.5cm) significantly alter the latency, morphology and amplitude of the neonatal VEP. Asymmetry of signal parameters was common. This asymmetry may reflect focal intracranial lesions, discordance between internal and external brain landmarks, or asymmetry of brain maturation.

Consideration of this data indicates that a single electrode does not provide the most accurate representation of the neonatal VEP regarding presence or absence of signal as well as latency, amplitude and morphology of the response. Thus, the information provided by the multiple electrode technique for neonatal VEP should improve the prognostic value of this investigation.

General Neurology (Poster)

FRIDAY, JUNE 26TH, 1987 0730-1700

211.

A Trial of Namalwa Interferon in the Treatment of Chronic Progressive Multiple Sclerosis (MS) II: Serial Immunologic Studies

L.F. KASTRUKOFF, J.J. OGER, W.W. TOURTELLOTE and D.W. PATY (Vancouver, British Columbia)

One hundred and one patients with clinically definite MS and a chronic progressive (CP) course were treated for six months in a placebo-controlled study of namalwa interferon (Wellferon). Serial immune studies were performed over 12 months. Peripheral blood lymphocytes (PBL) were examined with a panel of monoclonal antibodies and FACS IV analysis and did not vary significantly from the placebo group. In the IF group, the percentage of Leu 1 and 3a ⊕ PBL increased significantly at 1 month but returned to base line by 3 months while the percentage of Leu 2a ⊕ cells decreased steadily through the treatment phase becoming significant at 6 months. NK cell functional activity was significantly elevated in the IF group by 48 hours. It remained elevated for 1 week and then returned to base line only to become significantly elevated again at 6 months. NK functional activity correlated with changes in Leu 11 ⊕ but not Leu 7 ⊕ PBL. Intrathecal immunoglobulin synthesis appeared to increase in some patients associated with interferon treatment. IF treatment significantly reduced PWM induced IgG secretion after 1 week compared to a placebo group. This remained depressed for the duration of the treatment phase. No change on Con A suppression was observed. Results of this study will be related to clinical changes.

212.

Neurologic Presentation of Neuroleptic Malignant Syndrome

R.A. O'BRIEN and G.B. YOUNG (London, Ontario)

There has been recent interest in neuroleptic malignant syndrome (NMS) as the entity has been better characterized. NMS is still poorly recognized, however, by most physicians.

We present two recent cases. The first, a 24-year-old schizophrenic man, previously had a febrile illness when on phenothiazines. On this occasion he received both chlorpromazine and haloperidol while in jail.

He developed severe NMS with myoglobinuria and resultant renal failure requiring hemodialysis. The second, a 63-year-old man with agitated psychosis, developed NMS with associated status epilepticus after haloperidol therapy.

Proposed pathogenesis, complications and treatment are reviewed.

213.

Unusual Neurological Presentation and Pathogenetic Considerations in a Case of Streptococcus Bovis Meningitis

R.A. PURDY, E.H. DYSART and J. ARDITTI (Halifax, Nova Scotia)

A 32-year-old woman presented with meningitis. She was fully alert and demonstrated complete bilateral third nerve palsies, failure to abduct the right eye (old), increased lower limb reflexes and bilateral Babinski responses. Past history revealed mastoiditis and recurrent meningitis since childhood, recent right nasal rhinorrhea and hypertension.

Investigations revealed chronic right petrositis and a congenital defect in the right petrous bone extending to the middle ear. The rhinorrhea was proved to be cerebrospinal fluid (CSF), and the hypertension was associated with hypokalemia.

At surgery, an extradural approach resulted in closure of a pseudomeningocele in the right petrous bone defect. The right mastoid bone and middle ear were explored to allow plastic repair of the CSF leak. The patient made a remarkable recovery with no recurrence of meningitis or rhinorrhea and normalization of her blood pressure and potassium.

Streptococcus bovis is an exceedingly rare cause of adult meningitis. The unusual and rather dramatic clinical features in this case will be discussed with appropriate clinical anatomical correlations, review of the pertinent literature and discussion of the possible relationships of chronic CSF leakage and hypertension.

214.

Panhypo-Hypothalamism of Spongiform Encephalopathy

M.H. MacEACHERN, E. ATACK, K. KUWAYTI and B. LACH (Ottawa, Ontario)

A previously healthy, successful 53-year-old businessman presented with somnolence, hyperphagia, and progressive dementia.

Initial laboratory screening revealed low serum thyroxine (T4) levels. Further endocrine work-up diagnosed panhypo-pituitarism on a hypothalamic basis. No abnormality was evident by brain CT scan or Magnetic Resonance Imaging. CSF analysis showed elevation of protein at 900 mg/L (150-450). A right frontal brain biopsy was nondiagnostic, however a transmissible spongiform encephalopathy was diagnosed by biolologic transfer to hampsters. Further electron microscopy on patient's biopsy revealed peculiar intranuclear vacuolar inclusions.

Panhypo-hypothalamism represents an unusual and dramatic form of presentation of spongiform encephalopathy.

215.

A Combination of Mixed Connective Tissue Disease and an Anterior Spinal Artery Syndrome

H. JABER, G. KLEIN and B.D. McLEOND (Calgary, Alberta)

In contrast to systemic lupus erythematosus, neurologic involvement in mixed connective tissue disease (MCTD) is relatively unusual. The commonest type of involvement is trigeminal neuropathy, with occasional reports of other cranial neuropathy, headaches, peripheral neuropathy, aseptic meningitis, and rarely other manifestations.

Spinal cord involvement has only been reported twice before. One patient had transverse myelitis, and the other a cauda equina syndrone.

We report here a patient with MCTD who presented with spinal cord involvement. This was compatible with occlusion of the anterior spinal artery in the mid-thoracic region. As far as we know, this has never been reported before.

216.

The Onset of Classic Migraine in Pregnancy

G. MacLEAN, A. GUBERMAN and J.G. D'ALTON (Ottawa, Ontario)

Migraine is reported to improve or disappear in up to 90% of women during pregnancy. Most series include mainly patients with common migraine.

A series of 28 patients with onset of classic migraine in pregnancy is described. Mean age was 26 and symptoms onsetted in the third trimester in 18 (64%) and the second trimester in 7 (25%). While 8 were previously migraine free, 18 had a history of common migraine and only 2 had previous classic migraine attacks. A visual aura, alone or in combination with other symptoms, occurred in 89% and in 5 patients was not associated with headache. Less frequently encountered were a hemi-sensory disturbance, hemiparesis, aphasia, agraphia, prosopognosia and vertigo. Two patients with hemiplegic migraine had a complicated course. Frequency of attacks varied from one to multiple.

Classic migraine often onsets de-novo in pregnancy and should be differentiated from transient ischemic attacks.

217.

Misdiagnosis of Headache Patients

R.S. McLACHLAN (London, Ontario)

The most important aspect of the neurologic assessment of headache is the history of the illness. The history alone usually allows the physician to distinguish between benign headache and that with a more serious etiology. Of over 2,000 patients seen for headaches in a general neurology practice in Oshawa and London, Ontario, the wrong diagnosis was made from the history in eight (that I know of). An estimated 95% of the headache patients had migraine, muscle contraction (tension) headache, or a combination of the two. The eight misdiagnosed patients were felt to have a history most consistent with common migraine in three, muscle contraction headache in two, and combination headache in three. Six were seen in office consultation and two in the emergency department. Five had chronic persistent or recurrent headache over more than one month and 3 had persistent headache for 2-3 weeks. Diagnoses were chronic subdural hematoma (2), ethmoid sinusitis (2), subarachnoid hemorrhage, hydrocephalus secondary to third ventricular glioma, unruptured occipital AVM, and vasculitis of unknown etiology. The clue to proper diagnosis came from physical examination in two patients (papilledema; cranial bruit), from laboratory investigations carried out because of persisting headache in three patients, and because the patient looked unwell on three occasions. Routine CT scans, skull x-rays, blood tests and other investigations are unnecessary in assessing patients with headaches. However, by taking this approach, one should be aware that rare mistakes in diagnosis will be made.

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218.

Hereditary Syndrome of Dissociated Suprabulbar and Bulbar Ocular Motor Control

K. JORGENSON and H.Z. DARWISH (Calgary, Alberta)

The accurate control of ocular movements is achieved through the integration of neural signals from the extensive brainstem, cerebellar, and cerebral circuits that regulate ocular motor control through the saccadic, smooth pursuit, optokinetic, and vestibulo-ocular and vergence systems. We describe a hereditary central nervous system syndrome with the following features: (1) a bizarre eye movement disorder characterized by intermittent disregulation of horizontal gaze; (2) a lingual apraxia; (3) generalized mild hypotonia more marked in the shoulder girdle regions in a 2 year 8 month female and her 9 month male sibling.

The 2 year 8 month old female sibling presented at 15 weeks of age with an inability to look straight ahead and fixate. There were large amplitude nystagmoid movements accompanied by side to side head movements on lateral gaze. She had mild generalized hypotonia most pronounced in the shoulder region and a minimal delay in acquisition of gross motor milestones. She now has a 6 month delay in motor skills and a severe delay in expressive language. Receptive language and cognitive development are normal for age. Abnormal eye movements persist at 2 years 8 months and like her younger sibling are characterized by: (1) normal vertical eye movements; (2) relatively normal smooth pursuit with head held; (3) saccadic eye movements in either lateral direction which are of excessive amplitude and result in forced lateral gaze in the intended direction; (4) rapid head movements in an attempt to correct fixation result in unopposed "dolls eye" response; (5) absence of optokinetic nystagmus.

Clinically the described eye movement disorder does not fit the definition of typical ocular motor apraxia and appears distinct from previously described congenital ocular motor apraxias of the Cogan type where there is an impaired ability to generate saccades and decreased amplitude of voluntary saccades. The observed abnormalities would suggest a lack of integration of neural signals from the frontal eye fields.

219.

Involvement of Hippocampus in Creutzfeldt-Jakob Disease

H. MIZUSAWA, A. HIRANO and J.F. LLENA (Bronx, New York)

The hippocampus is generally believed to be only rarely affected in Creutzfeldt-Jakob disease. In a systematic study of the hippocampus in 6 cases of Creutzfeldt-Jakob disease, the stratum moleculare lacunosum had definite spongiform change with gliosis in 5 cases. The stratum radiatum had spongiform change with gliosis in 3 of the 5 cases and the stratum pyramidale had spongiform change in 2 cases. The presubiculum, parasubiculum and entorhinal cortex were involved in all the cases. These results suggest that involvement of the hippocampus may not be uncommon in Creutzfeldt-Jakob disease and that the stratum moleculare lacunosum and the stratum radiatum are the sites preferentially affected.

220.

Alzheimer's Disease Presenting as an Autosomal Dominant Trait in Three Generations

A.D. SADOVNICK and P.A. BAIRD (Vancouver, British Columbia)

A family will be presented in which dementia of the Alzheimer type (SDAT) appears to be inherited as an autosomal dominant trait. Eleven individuals in 3 generations were affected. The sex ratio among affecteds is 5 females: 6 males. The disease had onset in the early 40's with death by age 50. Four of the 11 affected people had the diagnosis confirmed by detailed neuropathological examination. The proband, who is still alive, has undergone Positron Emission Tomography (PET) examination with results compatible with SDAT.

The occurrence of autosomal dominant inheritance of SDAT is relatively rare, but it does appear to occur. Such families must be carefully counselled with respect to recurrence risks for subsequent generations. In our family, there are presently 16 members of a fourth generation, aged 13-36, and 4 members of a fifth generation, aged 2-10. All these individuals may be at a 50% risk for developing SDAT. Genetic counselling in this situation raises many of the issues relevant in counselling individuals at risk for Huntington disease.

The purpose of this presentation will be to present details of a family with well-documented SDAT which appears to segregate in an autosomal dominant manner. Genetic counselling for this, and other such families, will also be discussed.

221.

Three Forms of Semantic Memory Loss in Dementia

H. CHERTKOW, D. BUB and D. CAPLAN (Montreal, Quebec)

Semantic Memory (SM) is the portion of Long Term Memory containing the permanent representation of one's knowledge about objects and concepts. Models of SM function are as yet poorly specified. Research has suggested that SM deteriorates in Senile Dementia of the Alzheimer's Type (SDAT) and this may be a major cause of the prominent Anomia of SDAT patients. The present work seeks to produce the basic elements of a processing model of SM by examining patterns of performance in SDAT patients.

Ten patients with SDAT were selected because of prominent Anomia without evidence of perceptual impairment, dyslexia, or other aphasia. SM loss was documented by coexistent loss of Picture Naming and Comprehension for a host of items. SM loss was confirmed by inability to answer perceptual and functional questions about the item, in verbal and visual modalities.

The performance of these patients supports a model of SM processing in which there are two separate stages: 1) a single amodal Concept Store of knowledge, and 2) a prior stage of Identification Procedures (IPs) for visual objects only, which must be semantically identified before the Concept Store can be accessed.

Three forms of SM loss were found. Group A (5 patients) showed deterioration of their Concept Store. Independant evidence also indicated occasional loss of IPs. On items with preserves IPs, more knowledge was retained for pictures of items than their verbal names. On items with loss of IPs, there was equal loss of knowledge for words and pictures. Group B (3 patients) showed a pattern of preserved IPs on all items, while Group C (2 patients) showed a pattern of loss of Concept Store plus loss of all IPs.

This model may help to clarify the nature of the Semantic Memory, as well as the nature of Anomia and conceptual breakdown in SDAT.

222.

Creutzfeldt-Jakob Disease in a Pathologist

L.D. SITWELL, D. ATACK, E. ATACK, B. LACH and D. IZUKAWA (Ottawa, Ontario)

A 75-year-old male, retired pathologist, at a medical school, presented with sudden onset of left homonymous hemianopia. EEG showed diffuse slowing. CT scan and CSF were normal. He subsequently underwent rapid mental deterioration followed by the onset of seizures, myoclonus, coma and death.

Autopsy revealed distinct spongiform encephalopathic changes, mainly

in the occipital lobes, indicating Creutzfeldt-Jakob disease. To our knowledge, this represents the first documented case of Creutzfeldt-Jakob disease in a pathologist. Possible modes of transmission will be discussed.

223.

Carbazepine Overdose: Five Episodes with Clinical and Pharmacological Observations

D. WEAVER, P. CAMFIELD and A. FRASER (Halifax, Nova Scotia)

Since there are few reports of massive carbamazepine (CBZ) intoxication, 5 episodes in 4 patients are presented. Clinically, there were 4 distinct stages: I. (CBZ levels >105 umol/L) - coma, and status epilepticus in 1 patient which responded to IV diazepam and phenytoin; II. (65-105 umol/L) - combativeness, hallucinations, choreiform movements; III. (45-65 umol/L) - drowsiness, ataxia; IV. (<45 umol/L) - potentially catastrophic relapse in 2 patients presumably the result of renewed absorption as gut motility returned. In 2 patients this relapse was prevented by 3-5 gastric lavages in the first 10 hours after ingestion. Pharmacokinetics were studied in 2 cases. Case 1 had epilepsy treated with CBZ and fortuitously had previous half-life determinations when not intoxicated. Following ingestion of 20 g she showed: prolongation of CBZ half-life from 13 to 25 hours presumably secondary to ongoing absorption; elevation of CBZ-epoxide/CBZ ratio from approximately 1/10 to 1/1 with peak epoxide level of 67 umoles/L; emergence of the CBZ-epoxide to CBZ-diol transformation as a new rate limiting step. In Case 2 a 20 g overdose was her first exposure to CBZ. Her CBZ half-life was 24 hours; the CBZ-epoxide/CBZ ratio never exceeded 1/3 and peak epoxide level was 22 umoles/L. Autoinduction of hepatic CBZ metabolism in Case 1 may explain these pharmacokinetic differences.

We propose that treatment include repeated gastric lavage and detection of an insoluble tablet coagulum as methods to prevent unexpected relapse, electrolyte monitoring, avoidance of cathartics, and treatment of seizures with diazepam. Cardiac arrhythmias may require hemoperfusion.

224.

Neurofibrillary Tangles in Heterotopic Cerebral Gray Matter in L'Hermitte-Duclos Disease

E. SCHNEIDER, B. LACH and B.G. BENOIT (Ottawa, Ontario)

Neurofibrillary tangles (NFT) composed of paired hellical filaments (PHF) are the ultrastructural hallmark of Alzheimer's Disease (AD). NFT's of AD have also been observed in several unrelated pathological conditions, including hamartomatous disorders such as hypothalmic gangliocytoma and tuberous sclerosis. Similarly, straight neurotubules are the most consistent ultrastructural finding in progressive supranuclear palsy (PSP).

We describe the presence of typical NFT's and straight neurofilaments in heterotopic gray matter in a 46-year-old, intellectually normal male with L'Hermitte-Duclos Disease who died of myocardial infarction. At autopsy, the left cerebellar hemisphere showed a typical, large dysplastic gangliocytoma. Associated findings included megalencephaly (2200 gm) with focal pachygyria, heterotopic cortex in the white matter of the frontal, parietal and temporal lobes, and bilateral small foci of heterotopic gray matter in the leptomeninges. The heterotopic large neurons (reminiscent of motor neurons), in proximity to the orbital gyri of the frontal lobes, contained frequent NFT's and straight neurofilaments. Some neurons also showed granulo-vacuolar degeneration. No other areas of the brain exhibited these changes. Electromicroscopic examination revealed tight collections of straight, 15 nm diameter tubules intermingled with occasional twisted tubules 10-17 nm in width with 700-800 nm periodic constriction.

Our findings indicate that NFT's and straight neurofilaments of types seen in Alzheimer's Disease, Pick's Disease or progressive supranuclear palsy may also develop non-specifically. They may reflect a metabolic and/or genetic abnormality inherent to the neuronal cells in which they are found. The possible role of an environmental or transmissible factor in their genesis becomes less likely under these conditions.

225.

Interhemispheric Communication in the Absence of Forebrain Commissures

J. SERGENT (Montreal, Quebec)

The "split-brain" syndrome results from the severance of forebrain commissures and it is characterized by an incapacity of the cerebral hemispheres to exchange information and by the coexistence of two independent cognitive systems in the same cranium. Research on commissurotomized patients, for the most part, has focused on the disconnection and has treated the two hemispheres as independent entities. Eight separate experiments were conducted on two commissurotomized patients who were tachistoscopically presented with bilateral simultaneous information such that neither hemisphere received sufficient information to make a final decision. Only by combining the information initially segregated between the two hemispheres could a correct response be produced. Both patients performed significantly above chance in seven of the tasks (spatial orientation, calculation, lexical decision), suggesting that the information divided between the hemispheres could be united, related, and acted upon in a unified manner. This performance was achieved despite each hemisphere being unaware of the information received by the other, as typically observed in "split-brain" patients. The results indicate the coexistence of perceptual disunity and behavioural unity in commissurotomized patients.

General Neurosurgery (Poster)

FRIDAY, JUNE 26TH, 1987 0730-1700

226.

Papillary Meningioma Superimposed on Recurrent Arachnoid Cyst

G.P. MURRAY, W.J. HOWES and A.G. LACSON (Halifax, Nova Scotia)

Meningiomas are an uncommon paediatric tumour accounting for less than 2% of all meningiomas. Recently, a rare histological form of meningioma characterized by a papillary pattern and aggressive malignant behavior has been described and considered a distinct clinicopathologic entity. To date, very few of these tumours have been described in the literature.

We recently encountered an unusual case which we report here. This female patient first came to our attention at age 4 months, because of symptoms stemming from a right sylvian fissure arachnoid cyst which was treated by a shunting procedure. At age 19 months, she returned due to shunt blockage and surgical excision of the cyst was performed. She remained asymptomatic until age 8 years, 7 months, at which time she again began to experience symptoms suggestive of a further recurrence. CT scan demonstrated a large cystic lesion at the site of the previous arachnoid cyst. At surgical exploration, we encountered a cystic tumour with an extremely vascular wall. Histological examination of resected tumour tissue showed a papillary meningioma superimposed on a recurrent arachnoid cyst. Review of the original surgical specimen of areas of the arachnoid cyst wall showed changes suggestive of meningioma en plaque. Such an occurrence of these two lesions has not been previously reported to our knowledge.

The detailed case report, along with radiological and pathological findings at the time of initial surgery and subsequent recurrence is provided. We also discuss treatment in this patient and review results of treatment in the other small number of cases of papillary meningiomas described in the literature.

227.

Comparison of Computarized Axial Tomography Scanning and Post-Mortem Findings in Fatal Head Injuries

M. KHAN and M. SHADY (Saskatoon, Saskatchewan)

Although the value of computed tomography (CT) scanning is well established in the diagnosis of head injuries and their complications, certain types of post-traumatic brain damage still remains unrecognized with this method of investigation. The objectives of this study are to compare CT scanning and post-mortem findings in fatal head injuries, to identify lesions affecting the fatality in head injuries not detected on CT scanning and thus limitations of the CT investigations in fatal head injuries. Thirty-three cases of fatal head injuries were admitted to University Hospital in Saskatoon over a 2 year period and subjected to serial CT head scannings, using a G.E. 8800 scanner and subsequent post-mortem examinations. Eighty percent of patients were males and motor vehicle accidents accounted for 60% of head trauma. The mean age at death was 40 years. Most patients died from severe head injuries with a Glasgow Coma Scale of 8 or less on admission. There was a 90% correlation in surgical mass lesions and brain swelling, and 100% correlation in midline shift between CT and post-morten findings. Skull fracture correlation was 60% while correlation between CT and post-mortem findings for brain stem and deep white matter lesions was below 10%. CT head scanning is an excellent tool in the diagnosis of intracranial mass lesions following severe head injury, but has certain limitations in terms of identifying brain stem and shearing injuries in the deep white matter which adversely affects outcome. It is quite conceivable that with high resolution CT scanning, these limitations will be minimized.

228.

Acute-On-Chronic Subdural Hematoma

M. KHAN and K. CHANDLER (Saskatoon, Saskatchewan)

Acute, subacute and chronic subdural hematomas have been well documented in the past. Management of these entities varies according to the size of the hematoma and whether the hematoma is in a coagulated or liquified form. While drainage of these hematomas accounts for a significant number of neurosurgical procedures carried out, the phenomena of Acute-On-Chronic Subdural Hematomas (AC-SDHS) has only recently been defined through the advent of CT scanning. However, the pathophysiology of this entity remains ill-defined. There have been several patients who have presented with AC-SDHS at University Hospital in Saskatoon, Saskatchewan, suggesting that AC-SDHS may be a factor in the protean presentation of most chronic hematomas.

We propose to assess the clinical presentation, management and neurologic outcome of a representative sample of 12 patients with AC-SDHS. This information would be used to develop a hypothesis of the pathophysiology of AC-SDHS and relate them to operative and computed tomography findings. In our study, we have found that relatively minor trauma is very significant in the production of an acute hemorrhage within a pre-existing chronic subdural hematoma.

Recommendations for further studies to verify the exact etiology and pathophysiology of AC-SDHA will be made.

229.

Chronic Subdural Empyema: A Case Report

A. BELZBERG and M. LONG (Calgary, Alberta)

Classically, subdural empyema (SDE) presents with a constellation of symptoms including fever, headache, meningismus, seizures, focal neurological deficits and an altered level of consciousness. Rapid deterioration usually follows and it is associated with a high mortality rate. A "subacute" form of SDE has been described as a post-operative complication of subdural hemorrhage, and if presentation is greater than four to six months post-evacuation, the term "chronic" SDE is applied.

We report a case of a 64-year-old male who presented with occipital headache and left lateral rectus palsy of two months duration. He was otherwise asymptomatic. Pre-operative computerized tomographic and angiographic investigations suggested the diagnosis of mengingioma en plaque. Surgical exploration revealed an SDE. We believe that the term "chronic" SDE is appropriate for describing patients such as ours. Our case report demonstrates that chronic SDE can occur without previous surgery for subdural hemorrhage.

230.

Telemetric ICP Monitoring: A Clinical Experience

R. GRIEBEL, P.M. BLACK, P. CHAPMAN and E. COSMAN (Saskatoon, Saskatchewan)

Telemetric monitoring of intracranial pressure offers the benefits of reduced rate of infection, unrestricted patient mobility and long term monitoring capability. The Cosman designed telesensor can be incorporated into cerebrospinal fluid (CSF) shunt systems and allows the neurosurgeon ready access to intraventricular pressure, CSF pulse waves and fluid dynamics.

A 7 year experience with telesensor shunt monitoring has been accrued at the Massachusetts General Hospital and a population of 86 telesensor monitored neurosurgical patients are reviewed. The telesensor was of clinical value in determining shunt malfunction and able to distinguish proximal from distal shunt obstructions in most instances. Intracranial pressure (ICP) telesensor monitoring via blind-ended ventricular catheters was used in 14 instances to follow ICP after posterior fossa surgery and reliably indicated sustained pressure elevations that required shunting.

The telesensor has also provided a venue for the study of CSF dynamics in patients with both shunted and unshunted ventricles, providing insight into the effects of CSF siphoning with positional changes in shunted patients.

Telesensor monitoring appears to provide valuable information to the neurosurgeon regarding intracranial pressure, shunt function and CSF dynamics with little, if any, risk to the patient.

231.

Complications of CT Guided Stereotactic Surgery

O.N.R. DOLD, J.D.S. McKEAN, P.B.R. ALLEN and K.E. ARONYK (Calgary, Alberta)

Over a four year period 184 stereotactic procedures were carried out on 166 patients using the Brown Robert Wells stereotactic system. The overall case mortality rate was 1.8%, the morbidity rate 4.2%.

One hundred ten biopsies of deep seated lesions were carried out in 101 patients. Three patients died, two patients sustained major morbidity and four patients transient morbidity, for case mortality and morbidity rates of 3.0% and 5.9% respectively. Hemorrhage was the most common complication. Of 13 patients who underwent 15 thala-

motomies only one patient had a complication, an intracerebral hematoma producing a transient dysphasia for a case morbidity rate of 7.7%. No complications occurred in the following procedures: insertion of deep brain stimulator, 24 procedures in 21 patients; cyst aspirations, 17 procedures in 14 patients; intracerebral hematoma aspiration, 7 procedures in 7 patients; abscess drainage, 6 procedures in 5 patients; interstitial radiation implants, 4 procedures in 4 patients; insertion of depth electrodes, 1 procedure in 1 patient.

In conclusion, although CT guided stereotactic surgery is a useful technique for diagnosis and therapy of CNS disorders it is associated with significant risk.

232.

Case of Intracerebral Epidermoid and Review of Literature

G. deVEBER and H.S. SMYTH (London, Ontario)

Epidermoids are rare tumors and are ususally extra-axial — only rarely are they intra-parenchymal.

A 36 year old female presented with a 12 year history of generalized seizures and no other symptoms. Her neurological examination was normal. CT scan showed a large non-enhancing bifrontal tumor of varying densities. Biopsy showed laminated keratin contents. At surgery, a large waxy tumor with a pearly sheen was found and resected from both frontal lobes. There was no communication with the ventricular system. Pathology revealed a lining epithelium of stratified squamous cells and abundant keratin contents typical of epidermoid inclusion cyst. Post-operatively, the patient remains seizure-free with no deficit.

The unusual location and relatively asymptomatic presentation are significant. Theory of etiology (inclusion cyst) is related to this location and reviewed along with the previously reported cases of intracerebral location for the unique presenting features of this rare group (later age of presentation, seizures).

Epidermoid tumor should be added to the differential diagnosis of intracerebral mass lesions.

233.

Symptomatic Subependymoma of the Fourth Ventricle

T.P.G. DOORLY, E.F. GAFFNEY, J.J. DINN and J.P. PHILLIPS (Toronto, Ontario)

Symptomatic subependymomas of the fourth ventricle are rare with some 50 cases reported in the literature. Histologically subependymomas are often considered to be slowly growing, benign tumours. However symptomatic subependymomas of the fourth ventricle have a relatively poor prognosis with an operative mortality of 40 to 70% depending on histological type, tumour size and attachments, and relationship to the brainstem.

We report the case of a 37 year old male who presented 6 years after treatment of a testicular seminoma with a tumour in the region of the fourth ventricle. Histological examination at the time of surgery established the unexpected diagnosis of subependymoma. The tumour was completely excised and the patient remains symptom-free 3 years after surgery.

The clinical presentation, histopathology and treatment of symptomatic subependymomas of the fourth ventricle are reviewed. Recognition of this tumour at the time of surgery is important because some are amenable to radical excision with mininal morbidity and a good long term prognosis.

234.

Slit Ventricle Syndrome with Aqueduct Stenosis — Third Ventriculostomy as Definitive Treatment

R. REDDY, D. FEWER and N. HILL (Winnipeg, Manitoba)

Shunt dependent hydrocephalic patients with raised intracranial pressure and small ventricles (slit ventricle syndrome) are difficult to manage in spite of the use of high pressure shunts, antisiphon devices and subtemporal decompression. This a preliminary study of the use of third ventriculostomy in patients with slight ventricle syndrome (SVS) and aqueduct stenosis who were unresponsive to the above measures.

Four patients, all females and between 9 and 29 years of age, underwent ventriculoperitoneal shunts initially for aqueduct stenosis. Numerous hospitalizations and shunt revisions ensued. Presenting features of shunt malfunction consisted of severe headaches with or without rapid deterioration of the level of consciousness and Parinaud's syndrome, in the presence of very small ventricles. Three of the patients underwent subtemporal decompression and the insertion of high pressure shunts and antisiphon devices. As the patients continued to decompensate in spite of these measures, they underwent wide opening of lamina terminalis under direct vision, using the subfrontal approach (Stookey and Scraff operation), aided by operating microscope and bipolar cautery. Three of the procedures were preceded by deliberate occlusion of the existing shunt system, to enable the third ventricle to dilate. No operative mortality of morbidity was encountered.

One patient required shunt revision early in the post operative period. One patient (asymptomatic following surgery), died as a result of an automobile accident. The other 3 patients were asymptomatic at the last follow up (mean 32 weeks).

We suggest that third ventriculostomy is effective in the treatment of a select group of patients with non-communicating hydrocephalus and SVS.

235.

Concussion: Initial Deficits and Recovery of Function

H. HUGENHOLTZ, D.T. STUSS, L.L. STETHAM and M.T. RICHARD (Ottawa, Ontario)

Twenty-two patients with concussion, ages 16 to 57, were assessed five times over a period of three months, the initial investigation occurring within seventy-two hours of the trauma. The severity of the concussion was classified according to Ommaya and Genarelli's criteria. Investigations included a neurological examination and neuropsychological reaction time (RT) tests. The RT tests included single and choice RT variations. The concussion patients were compared to age, sex and education matched control subjects. Time of day of testing was equated.

None of the concussed patients had significant neurological deficits; none were hospitalized. There were no significant differences in the number of errors on the RT tests, indicating both groups were equally proficient in completeting the tasks. On the single RT test, requiring a predetermined response to a specific signal, there was no significant difference between the groups, although the concussion group was approximately 28 ms slower on average than the control group. On the choice RT test, demanding an increased amount of information processing, there was a significant group by visit effect. The concussion patients were significantly slower than the normal control group, particularly in the testing sessions in the first three weeks after trauma. Three months after the concussion, there was no significant difference between the two groups. Analysis of the response curves over time suggested two processes: an improvement in the concussion group; a slowing in the normal control group, likely due to decreased motivation. Within the concussion group, there was no correlation of RT with the severity of the concussion.

Even mild closed head injuries can cause significant attentional and information processing impairment in the absence of any apparent neurological problems. Specific neuropsychological tests are necessary to reveal the deficit. A significant impairment appears to last for several weeks. There is a gradual improvement in time, suggesting a recovery process.

236.

Combined Suboccipital-Transmeatal Approach for Acoustic Neuromas

G. MOH and J.J. DUFOUR (Montreal, Quebec)

From 1980 to 1986, 67 combined procedures using the suboccipital transmeatal approach to the CP-angle have been performed in collaboration between neurosurgery and ENT, including 44 acoustic neuromas and 23 vestibular neurectomies. In acoustic neuromas, using the modified lateral decubitus ("park bench position"), the transmeatal stage with opening of the posterior wall of the internal auditory meatus, removal of the intracanalicular tumor portion and identification of the distal seventh and eight cranial nerves was performed by the ENT-surgeon immediately after exposure of the CP-angle. The neurosurgeon then performed the endocranial removal of the tumor and micro-dissection from the subarachnoid portions of the facial and cochleo-vestibular nerves. There was no mortality in this series, and CSF-fistulae occurred in 2 cases.

Regarding the facial nerve function, no facial paralysis occurred in 15 cases of small tumors (0.1-1.9 cm), 13% (3 cases) permanent facial paralyses were observed in 23 medium-sized tumors (2.0-3.9 cm), and 83.3% (5 cases) in 6 large tumors (above 4 cm in diameter).

Intraoperative auditory evoked brainstem potentials (BSAEP) were monitored in most cases where serviceable hearing was present (Speech Reception Threshold $\leq$50dB and Discrimination Score $\geq$50%): from 11 cases with serviceable hearing preop and complete tumor removal, useful hearing was preserved in 3 cases postoperatively (27%). Monitoring of BSAEP was considered as a very useful guide for hearing preservation but neuro-anatomical parameters are equally important.

The authors believe that the combined suboccipital transmeatal approach improves the preservation of facial and cochlear nerves and increases the completeness of tumor removal of the intracanalicular portion in most cases of acoustic neuromas.

By Title Only

237.

Popular Concepts of Whiplash Symptoms: Further Evidence Against Malingering

J.B. AUBREY, A.R. DOBBS, B.G. RULE and W.J. VANAST (Edmonton, Alberta)

Nonimpact rotational acceleration injury of the head and neck ("whiplash") is frequently followed by complaints of decreased memory, concentration, and orientation as well as changes in mood, sleep pattern, sexual drive and ambition.

Because commonly used psychologic tests are often normal, these patients are accused of malingering.

Rather than choose symptoms that evoke derision or cynicism, patients are likely to enhance or embrace widely known complaints that fit popular notions about this type of accident.

To document head injury concepts extant in lay circles, 40 university students were asked to rate a list of symptoms after rear-end and other collisions. When loss of consciousness did not occur, affective or cognitive symptoms were rated as never occurring or very mild. When asked to estimate collision force for each CNS symptom, very high speeds were thought to be necessary, even when the scenario involved direct (impact) trauma to the head. There was little support for delayed symptoms.

These data suggest that "whiplash" patients with persistent symptoms do not derive their complaints from generally-held lay concepts. This further supports our opinion that the complex symptomatology after "whiplash" injuries is not due to malingering.

A larger study involving a broader range of the population is now in progress.

238.

Roma Amyot and the Genealogy of French Canadian Neurology

G.M. REMILLARD (Montreal, Quebec)

Roma Amyot (1899-1980) trained in neuropsychiatry with André Thomas and de Clérambault in Paris from 1926 to 1929. André Thomas published a treatise on "Les maladies de la moelle épinière" in 1909. His last publication appeared when he was 90 years old: The neurological examination of the infant with Yves Chesni and Mme S. Saint-Anne Dargassies. It had an international distribution.

Under his influence, Amyot acquired books illustrating the roots of neurological knowledge in French Canada before Penfield founded the Montreal Neurological Hospital and before the American Academy of Neurology was started.

Amyot's Montreal teacher, a student of the Déjérines, A. Prévost held the "chaire de neurologie" at the University of Montreal from 1917 to 1926 and had trained in France for 7 years (1907-1913).

Doctors G. Villeneuve and later E.P. Chagnon were trained alienists who tought nervous and mental diseases from 1894. Neurological knowledge was also transmitted by oculists, aurists, medical and surgical clinicians and pathologists on their "retour de France" mainly in the last quarter of the 19th century.

American and anglo-saxon influence through McGill University existed but neurological development by and large proceeded independently until 1930 when a merger was initiated by Cone, Penfield with the french-canadian neuropsychiatrists.

239.

Cerebellar Atrophy in Outpatient Epileptics: A Neurobiological Study

M.I. BOTEZ, R. ELIE, T. BOTEZ, E. ATTIG and R. LALONDE (Montreal, Quebec)

This study has been carried out in two groups of outpatient epileptics, i.e.: 33 patients with normal CT scans. (group 1) and 31 patients with cerebellar and brainstem (CBS) atrophies (group 2).

The assessment of the possible etiological factors of CBS atrophy (length of the disease, number of epileptic seizures, phenytoin treatment and the number of peiods of phenytoin treatment and the number of periods of phenytoin intoxication in the past) showed that the main etiology of CBS atrophy in chronic epileptics is the long-lasting phenytoin consumption associated or not with periods of phenytoin-overdosage.

Serum folate and cerebrospinal (CSF) thiamine levels were lower in group 2 than in group 1. A higher percentage of patients with lower vitamin B_{12} levels was found in group 2 than in group 1. CSF folate, blood thiamine levels and the percentage of thiamine pyrophosphase activity showed no difference between the groups.

The Ottawa-Wechsler I.Q. scale and the measurements of visual and auditory reaction (RT) and mouvement time (MT) showed: (i) lower performances on the I.Q. scale in group 2 as compared with group 1; (ii) the analysis of composite scores on the I.Q. scale showed that the behavioral impairment was selective, involving mainly the visuo-constructive abilities and the speed of psychomotor performances; (iii)

patients with CBS atrophies were definitely slower on the RT measurements whereas no significant difference was observed for MT evaluations. There were no significant differences between the two groups as concerning age, education and number of epileptic seizures.

It is concluded that the neuropsychology of the cerebellum does exist at least concerning two major functions: the visuo-spatial abilities for concrete tasks and the speed of information processing. The cerebellar thalamo-cortical and the cerebellar-limbic loops underlying the behavioral disorders with cerebellar damage are reviewed.

240.

Problems with Payment of Medico-Legal Reports

W.J. VANAST (Edmonton, Alberta)

On occasion, lawyers avoid responsibility for payment of medico-legal fees by asking physicians to bill the patient directly ("as we do not have instructions to pay on her behalf"). Sometimes patients are instructed to pay physicans directly. Lawyers may withhold payment until they receive proceeds from their actions ("we have no objection to the cost of your report provided you will wait until the insurers pay", or alternatively "we do not have sufficient funds in trust to ensure that the physician's account for the report will be promptly paid"). Some lawyers deny responsibility for payment ("a lawyer is simply an agent of his client and any expense incurred by the lawyer is in fact incurred on behalf of his client as it is solely the client and not the lawyer who is liable to pay for it").

To avoid any compromise of the physician-patient relationship, we reject requests to bill the patient directly. Direct payments from patients are not accepted. When court appearance is requested, we advise beforehand of our fees per hour.

In B.C. the Law Society takes the position that it is not professional misconduct for a lawyer to dispute the amount of a doctor's bill, hence the Society will not investigate a complaint relating to delay or failure to pay a bill.

The stress and disruption produced by the frequent medico-legal work inherent in neurologic and neurosurgical practice suggests that more attention to such issues should be played in our post graduate and annual scientific programs. Joint meeting with legal colleagues would help to solve some of our mutual problems.

241.

Chronic Benign, Almost Daily Headache Definition, Distinct Patterns and Prognosis

W.J. VANAST (Edmonton, Alberta)

Most headache patients referred for consultation have Chronic Benign Headache (CBH), combining features of common migraine and tension headache. Despite failure of most therapies, little research is directed at this disorder. Specific criteria for patient inclusion in CBH studies are required.

We confine several CBH projects to women with at least a three year history of headache, at a relatively stable frequenty for six months prior to consultation, at an average frequency of 15 days per month — a pattern we call Benign, Almost Daily Headache (BADH). For each male BADH patient, 6 females are seen.

When age at consultation (AAC) is plotted against age at onset (AAO) distinct patterns emerge in BADH females: young women (40) with early AAO (3-36) older women (50) with early AAO, and older women with late AAO (40). BADH studies should not mix these groups.

When studies of young BADH women are limited to AAC 20-40, and AAO 10-25, 50% of all BADH females are eligible. We contacted 47 such patients 1-2.5 years after initial consultation (IC). Only 2 were worse, and these had a low IC headache frequency (ICF) of 15-17 days per month. A paradoxical relationship between ICF and average improvement was noted: 61% for 31 patients with ICF 25-30; 34% for 3 patients with ICF at 20; 13% for 13 patients with ICF 15-17. There was no relationship between our treatments and improvement.

This suggests that headache severity over time may have a bell-shaped configuration, with consultation requested near the peak, followed by spontaneous improvement.

These data should be considered in the evaluation of new therapies.

242.

Canadian Arctic Neuroethnology: The Multiple Uses of Induced Cerebral Ischemia

W.J. VANAST (Edmonton, Alberta)

Canadian arctic history provides a rich lore of neurologic events amongst the Inuit, the white explorers and their interactions. In early written accounts, native events involving ischemia received much publicity. A seal skin thong about the neck was sometimes used to end the suffering of starving children (a sacrifice considered a credit to the mother who resorted to such action) and for suicide by older natives no longer able to hunt.

To derive pleasure, children would suspend each other by their parka hoods, kicking their legs to signal when they should be let down. If a child was alone, or too heavy for the remaining child spectators, tragedy would ensue.

Shamans used the seal skin thong in several ways. If a tribe member was afflicted with poor hunting or other adversity, the thong was placed around his head. Various hypotheses about the situation, the animals possibly offended, or taboos broken were then posed, and the answer determined in the affirmative or negative depending on the ease with which the head could be lifted.

Father Guy Marie Rosseliere of Pond Inlet, a famous prehistoric Inuit anthropologist, has recorded a Shamanic song in which the assistant is thanked for tightening the cord about the Shaman's neck, thus allowing him to have his visions and "travels" to far away places.

243.

EEG and Clinical Manifestations of Frontal and Temporal Lobe Seizures

L.F. QUESNEY, A. OLIVIER, F. ANDERMANN and P. GLOOR (Montreal, Quebec)

The EEG and clinical manifestations of complex partial seizures were studied in a selected population of 19 temporal lobe and 19 frontal lobe patients investigated with intracerebral depth electrodes. A total of 96 temporal and 279 frontal lobe seizures were included in this study.

Results:

1) Seizure onset: 80% of temporal lobe seizures originated in the amygdaloid and or hippocampal structures. 39% of frontal lobe seizures exhibited a focal or regional seizure onset in the frontal lobe. The remaining frontal lobe seizures disclosed either a unilateral diffuse (27%), generalized (29%) or bifrontal (5%) seizure onset. **2) Seizure duration and spread:** The mean duration of temporal and frontal lobe seizures was 86 and 30 seconds respectively. Preferential siezure spread to homologous contralateral brain regions was noticed. **3) Clinical Presentation:** The initial behavioural manifestations of temporal lobe seizures included mainly: warning (76%), motionless stare (24%), automatism (22%) and head-body turning (24%). The initial clinical features in frontal lobe seizures included: head-body turning, tonic posturing of extremities, motionless stare and automatism. Automatic behaviour was observed in 50% of frontal lobe seizures coinciding with seizure

spread to the temporal lobe(s). However, in 4 patients, ictal automatism was observed in association with seizure discharge restricted to one or both frontal lobes.

244.

Adenocarcinoma of the Lung and Management of Brain Metastases: A Case Presentation

J. SCHNITTKER, K.H. SHIN, H. THOMAS and A. CLARK (Calgary, Alberta)

Adenocarcinoma of the lung constitutes 10% of all bronchogenic carcinomas. With high dose radiation therapy, the rates of locoregional tumor control is relatively high. Like small cell carcinomas, the adenocarcinoma of the lung associates with high incidence of brain metastases. On many occasions, such brain metastases can occur without locoregional recurrence and other metastases. In such selective situations, aggressive radiotherapy to the brain is fully justified and a cure is a definite possibility.

We present a 45 year old lady with an adenocarcinoma of the right upper lung treated in 1983 by radiation therapy [5800 centigray (cGy)] who is in complete local control to date. Unfortunately, she developed multiple brain metastases in 1984 and this was treated again by means of radiation therapy (5500 cGy). She has been disease free for over 2 years. We are of the strong opinion that in selected cases like ours, an aggressive treatment is warranted for a possible cure. Also we are of strong opinion that serious consideration should be given for prophylactic whole brain irradiation for adenocarcinoma of the lung.

245.

Is Long term Survival a Realistic Goal for Patients with Brain Metastases?

E. ARBIT and J.H. GALICICH (New York, New York)

Cerebral metastases occur in 25% of patients with cancer; of these 50% are solitary. Traditionally brain metastases were considered to represent a preterminal event. However, the prognosis for patients with a single brain lesion has improved significantly if surgical resection is done followed by radiation therapy. Judging by local recurrence rate after this treatment course, complete eradication of the metastasis is achieved in over 86% of cases. This observation is further substantiated by the fact that most cases treated by surgery and radiation die systemic rather than neurologic deaths. Hence, the ability to control the primary disease is the most important single prognostic factor determining survival.

In our series of 226 patients operated upon for a single brain metastasis, 10% lived more than 2 years, 5% more than 3, and 4% more than 6. The overall median survival was 8.9 months; for carcinoma of lung 14 months, breast 9, kidney 10.6, melanoma 6.2, colon 11.2, unknown primary 7.4, sarcoma 3, and testicular 5.9 months. The combined therapy group had a significantly longer survival than historical controls treated with radiation alone (the median survival for ca. of lung 9 months, colon 9 weeks, and melanoma 9 weeks).

We conclude that in a selected group of patients with controlled primary disease, surgery plus radiation can yield long term survival.

246.

Primary Primitive Neuroectodermal Tumors in The Spinal Axis: A Report of Two Cases

A. SHUAIB, F.E. LeBLANC, K.M. HUNTER, K. SHIN and B. CURRY (Calgary, Alberta)

Primary primitive neurectodermal tumors (PNET) in the spinal axis are extremely uncommon, are seen in children and present with spinal cord compression or a radiculopathy. This report deals with two cases; one presenting with a Brown-Sequard Syndrome, and the other with an S1 radiculopathy.

Case 1: A 22 year old male was seen with a two month history of progressive left-sided weakness. Examination revealed weakness and decreased perception of temperature and pain in the left arm and leg. Myelogram showed an intradural obstruction of C1 and C2 level. Removal was complete and histology was consistent with PNET. The patient received 3500 cGy/4.5 weeks to the neuroaxis and 5500 cGy/6.5 weeks to the tumor mass. Two years later the patient presented with multiple metastases involving the bones and bone marrow, lymph nodes, pleura and spinal extradural space. He died shortly thereafter. At autopsy no intracranial malignancy was found.

Case 2: A 47 year old male presented with a six month history of weakness and numbness involving the left leg. Myelogram revealed an intradural lesion adherent to the left S1 spinal root. Removal was complete and histology was consistent with PNET. Despite 5500 cGy in 6 weeks to the lumbosacral region there was recurrence of tumor at C2, C7 and T11 levels. Following subtotal removal of tumor at C2 and T11 the patient is alive with paraplegia and neurogenic bladder. Two cranial CT scans to date have revealed no evidence of neoplasm.

Summary: *Although PNET presents rarely in the spinal cord, local and systemic recurrence as was seen in our cases would indicate that PNETs in the spinal axis are as invasive as elsewhere in the body and should be treated in the entire CNS axis aggressively.*

247.

Recognition of Progressive Neurological deficit in Treated Spinal Dysraphic States

F.B. MAROUN, J.C. JACOB and W.D HENEGHAN (St. John's Newfoundland)

Spinal dysraphism, a complex developmental abnormality of the central nervous system is a well established clinico-pathological entity. After the initial treatment of the overt lesions, emphasis is shifted almost entirely to a various means of rehabilitation. However in a large number of patients, slow progressive neurological deficit is evident. Several cases will be presented to emphasize the progressive nature of the disease. The value of early MRI will be discussed.