XXIVTH MEETING OF THE CANADIAN CONGRESS OF NEUROLOGICAL SCIENCES OTTAWA, JUNE 13 - 17, 1989 PROGRAM

Tuesday, June 13

Canadian Association for Child Neurology Annual Meeting

Health Sciences Centre, Ottawa

Manpower and Educational Needs	R. Haslam, Toronto P. Humphreys, Ottawa W. Logan, Toronto
Invited Lecturer of Canadian Association Of Child Neurology Communication Disorders In Preschool Children	Isabelle Rapin, New York
Clinical-Pathological Conference	H. Sarnat, Calgary C. Jimenez, Ottawa

Problem Cases – Presented for discussion by members of the Association

SATELLITE SYMPOSIUM - Multiple Sclerosis

Westin Hotel, Ottawa

Chairmen: B. Weinshenker and R. Nelson, Ottawa.

Morning

I. Epidemiology of Multiple Sclerosis	
MS in Saskatchewan	W. Hader, Saskatoon
MS in British Columbia	D. Sadovnick, Vancouver
MS in Newfoundland	W. Pryse-Phillips, St. John's
MS in families: Is MS a genetic disease?	G. Ebers, London
MS in the Faroes: Is MS a transmissable disease?	J. Kurtzke, Washington DC
Update on HTLV-1 and MS	G. Rice, London

Afternoon

II. Clinical Trials in Multiple Sclerosis	
The Canadian Cooperative Study of cyclophosphamide and plasma exchange in progressive MS: Rationale and assessment criteria	J. Noseworthy, London
Lessons to be learned from the natural history of MS	B. Weinshenker, Ottawa
MRI: How helpful will it be in clinical trials?	D. Paty, Vancouver
Do tests of immunological function have any role in clinical trials?	J. Antel, Montreal
A statistician's perspective on the design and conduct of clinical trials in MS	W. Taylor, Hamilton

Evening

Canadian Headache Society Dinner

Westin Hotel, Ottawa

Annual Business Meeting
Guest Speaker - Kenneth Welch, Detroit
"Spreading Depression in Migraine"
Banquet

Wednesday, June 14

Pre-Congress Courses

COURSE I: Neurological/Neurosurgical Complications of Pregnancy

Chairman: A. Guberman, Ottawa

Supported by a contribution from **Geigy Pharmaceuticals Canada**

Morning

Overview of Neurological Complications of Pregnancy	A. Guberman, Ottawa
Physiological Changes in Pregnancy, Eclampsia	P. Garner, Ottawa
Nerve Entrapments and Neuropathies of Pregnancy	B. Brown, London
Epilepsy in Pregnancy	I. Leppik, Minneapolis

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Afternoon

Headaches and Cerebrovascular Disease in Pregnancy	D. Wiebers, Rochester, MN
Neurosurgical Aspects of Brain Tumors, Aneurysms and AVMs in Pregnancy	N. Russell, Ottawa
Management of Chronic Disorders in Pregnancy: Multiple Sclerosis, Myasthenia Gravis, Wilson's etc.	R. Nelson, Ottawa

COURSE II: Pediatric Neurology for the Adult Neurologist

Chairman: K. Farrell, Vancouver

Morning

Headaches in Children	P. Humphreys, Ottawa
Brain Tumors in Children	J.C. Allen, New York
Clinical Approach to Degenerative Brain Disorders in Childhood	D. McGregor, Toronto
Coma and Brain Death in Young Children	S. Seshia, Winnipeg
Childhood Seizure Disorders	P. Camfield, Halifax

COURSE III: Current Concepts in Head Injury

Chairman: M. Schwartz, Toronto

Afternoon

Prevention and Protection	M. Schwartz, Toronto
Diffuse Brain Injury: Pathophysiology and Rationale for Therapy	J. Povlishock, Richmond
Multimodality Monitoring	R. Moulton, Toronto
Outcome after Head Injury	D. Stuss, Toronto
Rehabilitation Strategies	S. Garner, Hamilton

COURSE IV: Intensive Neurodiagnostic Monitoring

Chairman: G. Blair, Toronto

Afternoon

Intraoperative EEG Monitoring	F. Sharbrough, Rochester MN
Pre-surgical EEG Monitoring in Epilepsy	W. Blume, London
Polygraphic Monitoring in Myoclonic Epileptic Syndromes	C. Tassinari, Bologna
Specific Applications of Ambulatory Monitoring in Children with Epilepsy	P. Hwang, Toronto
EEG Monitoring in Sleep Apnea	J. Reiher, Sherbrooke
EEG Monitoring in Pseudoseizures	J. Bruni, Toronto

Thursday, June 15

Morning

PLENARY SESSION #1 - Guests of the Congress

Welcome
Gilles Hurteau
Dean, Faculty of Health Sciences
University of Ottawa

Opening of the Scientific Session
G. Bray
President
Canadian Neurological Society

Richardson Lecture
Canadian Neurological Society
Richard Johnson, Baltimore
"AIDS and The Nervous System"

Penfield Lecture
Canadian Neurosurgical Society
Phanar Perot, Charleston
"Acute Spinal Cord Injury: Advances in Research and Treatment"

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Canadian League Against Epilepsy Lecture
Ilo Leppik, Minneapolis
"Status Epilepticus: Recent Advances in Therapy"

Francis McNaughton Memorial Prize for clinical research in neuroscience

Kenneth G. MacKenzie Memorial Award

Afternoon

Free Communications

Platform 14:00 - 17:00

A. Neurobiology/Neuro-oncology
B. Neuromuscular
C. Movement Disorders
D. Pediatric Neurology/Neurosurgery
(including President's Prize Lecture)

Poster - 07:30 - 17:30
Authors standing by 07:30 - 08:30 & 13:00 - 14:00

Neurobiology/Neuro-oncology	(P1-P30)
Neuromuscular	(P31-P44)
Movement Disorders	(P45-P52)
Pediatric Neurology/Neurosurgery	(P53-P60)
Epilepsy	(P61-P76)
Neurophysiology	(P77-P81)

Friday, June 16

Morning

PLENARY SESSION #2 - Guests of the Congress

Opening of the Scientific Session
Gérard Leblanc
President
Canadian Neurosurgical Society

Speaker of the Royal College of Physicians and Surgeons of Canada
Neurosurgery
Bryce Weir, Edmonton
"Cerebral Vasospasm and Subarachnoid Hemorrhage"

Speaker of the Royal College of Physicians and Surgeons of Canada
Neurology
Ronald Worton, Toronto
"The Defective Gene and Protein Causing Duchenne Muscular Dystrophy"

Canadian Society of Clinical Neurophysiologists Lecture
Carlo A. Tassinari, Bologna
"Polygraphic Monitoring in Epilepsy"

Andre Barbeau Memorial Prize For Basic Research in Neuroscience

Afternoon

Free Communications

Platform 14:00 - 17:00

E. Behavioral Neurology/Evoked Potentials
F. Epilepsy/EEG (including Epilepsy
Canada Clinical Fellowship
award presented by Parke Davis - 15:30)
G. Neurosurgery
H. General Neurology/Multiple
Sclerosis/Cerebrovascular

Posters - 07:30 - 17:30
Authors standing by 07:30 - 08:30 & 13:00 - 14:00

Behavioral Neurology	(P82-P87)
Neurosurgery	(P88-P116)
Neuroradiology	(P117-P121)
General Neurology	(P122-P136)
Multiple Sclerosis	(P137-P143)
Cerebrovascular	(P144-P158)

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Saturday, June 17

Morning

PLENARY SESSION #3

Symposium - Issues in Neurological Education

Chairman: T. J. Murray

Opening Remarks and Update on Undergraduate Education	T. J. Murray, Halifax
Postgraduate Education	W. Pryse-Phillips, St. John's
Manpower and Opportunities	K. Brownell, Calgary
New Technologies	A. Guberman, C. Skinner, Ottawa
Evaluation	I. Hart, Ottawa
Neurological Education and Manpower in the United States	Matthew Menken, Princeton
Panel Discussion	All Participants
Comment & Conclusion	T. J. Murray, Halifax

Symposium - Legal Aspects of Neurosurgery/Neurology Practice

Chairman: B. Benoit

Supported by the Canadian Medical Protective Association

Current Trends in Canadian Malpractice Law	Mr. Justice T. David Marshall Executive Director Canadian Judicial Centre Ottawa
Importance and Relevance of the Medical-Legal Report	P. Forcier Assistant Director Medical Services, Régie de l'Assurance de l'Automobile du Québec
Legal Cases Involving Neurosurgeons and Neurologists	L. Ivan, Canadian Medical Protective Association
Responsibility of Physicians Acting as Expert Witnesses or Defendants	K. Evans, General Counsel Canadian Medical Protective Association
Panel Discussion	All participants

Afternoon

Symposium - Cerebrovascular Disease

Chairman: J. Norris

Sponsored by the Canadian Stroke Society

Canadian Stroke Society Prize Essay

Thrombolytic Therapy	David Levy, New York
PET Scanning in Stroke	A. Hakim, Montreal
Carotid Endarterectomy	S. Peerless, London

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XXIVth Meeting of the Canadian Congress of Neurological Sciences

Abstracts of the Scientific Program

Platform Presentations

Poster Presentations

Platform Presentations

THURSDAY, JUNE 15TH - P.M.

Neurobiology

1.

The Temporal Profile and Distribution of Ischemic Neuronal Injury Studied Using NMR and Histopathology

G. SUTHERLAND, H. LESIUK, J. PEELING, I.C.P. SMITH, D. WILKINS and J.K. SAUNDERS (Winnipeg, Manitoba and NRC, Ottawa, Ontario)

Regional changes in both MR microimaging and histopathology were observed following a (10 min) forebrain ischemic insult in rat. Five rats were imaged at 24, 48 and 72 hrs following ischemia and sacrificed via perfusion-fixation following completion of the last study. Additional groups of animals (n=5) were imaged at 1, 24, 48, 72 or 96 hr following ischemia and perfusion-fixed following the MRI study. ^{31}P spectra were obtained from a third set of animals (n=4), showing that the ischemic insult was associated with energy failure and a drop in pH from 7.1 to about 6.2. On reperfusion the high energy metabolites and pH rapidly returned to control values. The phenomena of selective neuronal vulnerability and ischemic maturation were readily observed with both MRI and histological evidence of neuronal injury appearing at increasing post-ischemic time intervals. The changes principally involved the CA1 sector of the hippocampus, the striatum, and in a few animals the deep cortical layers. In addition, the maximum changes were manifested at variable times in the selectively vulnerable brain regions (24 hr in the caudoputamen; 48 hr in hippocampus) supporting the hypothesis that intrinsic neuronal mechanisms are operant in the development of irreversible neuronal injury. Persistent post-ischemic energy failure or acidosis are not likely factors given the spectroscopic findings. As the MRI changes paralleled the histological findings, we conclude that the development of ischemic neuronal injury may be followed non-invasively with MRI.

(Supported by The National Research Council, The Canadian Heart Foundation, and the Upjohn Company of Canada)

2.

In Vivo 3H-MK-801: Focal Ischaemia Increases Binding

M.C. WALLACE, A. McCORMACK, G.M. TEASDALE and J. McCULLOCH (Toronto, Ontario; Glasgow, Scotland)

MK-801 is a non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptor with proven cerebroprotective efficacy in focal ischaemia. The delivery and distribution to ischaemic tissue is fundamental to its evaluation as a therapeutic agent in stroke. This study investigates the in vivo distribution of 3H-MK-801 in normal and ischaemic tissue.

Sprague-Dawley rats (n=48) were anaesthetised and ventilated. Half of the animals underwent middle cerebral artery occlusion (MCAO). 3H-MK-801 (10μCi) was given IV and the ligand concentration in brain regions was determined at several time periods by liquid scintillation counting. A similar group of animals (n=8) had cerebral blood flow determined by 14C-iodoantipyrine and tissue dissection. The last group (n=8) received an IV injection of 3H-MK-801 (100μCi) after MCAO, but regional concentration of ligand was determined by autoradiography. 3H-MK-801 moved rapidly into the normal brain, but slowly into ischaemic tissue. The ratio of 3H-MK-801 content of cortex to cerebellum, regions high and low in NMDA receptor content respectively, was 1.31±0.04 in normal tissue at 15 minutes versus 1.61±0.08 in ischaemic tissue at 120 minutes. Modelling studies indicate that MK-801 accumulation in ischaemic tissue cannot be attributed to reduced cerebral blood flow alone. Autoradiography demonstrated marked regional localization of ligand in ischaemic tissue. Ischaemic striatum [3H-MK-801] increased to 52±8 p mol/g (60 minutes) from 22±4 p mol/g (15 minutes) despite declining plasma levels and decreasing concentrations in the nonischaemic, contralateral hemisphere. This increase is 171±21% of the contralateral striatum. In vivo 3H-MK-801 accumulation in ischaemic tissue supports the proposal that glutamate release occurs in ischaemia. The pharmacology of MK-801 provides evidence that delivery to ischaemic tissue is possible and that localization of MK-801 may help target this therapeutic agent in ischaemic brain.

3.

Protective Action of Combined Prostacyclin: Dimethyl Sulfoxide In Focal Brain Ischemia

J.C. DE LA TORRE and M.T. RICHARD (Ottawa, Ontario)

Cerebral ischemia can trigger a series of biochemical eruptions that may increase the levels of tissue calcium, prostaglandins (PG) free radicals (FR) and 3-endorphins. We examined whether drugs that block calcium, PG, FR and endorphin release could modify cerebral blood flow (CBF) or brain tissue pathology after an experimental focal vascular lesion. Cats were randomly divided into six groups and were subjected to a standard middle cerebral artery occlusion (MCAO) performed using a transorbital approach. One hour after MCAO, cats received the following compounds intravenously: (i) saline (S) 1.5 ml/Kg or polyethylene glycol, 300 ug (P); (ii) naloxone (NX) 2 mg/Kg; (iii) nimodipine (NM) 1 ug/Kg/min x 60 min; (iv) dimethyl sulfoxide (DS) 1.5 g/Kg in a 40% solution; (v) prostacyclin (PGI_2) 0.2 mg/Kg/min for 25 min. or (vi) DS: PGI_2 combined. At 1 hour intervals, local CBF was recorded from the cortical tissue proximal and distal to MCAO using the hydrogen clearance method. Five hours after MCAO, cortical tissue was removed for catecholamine (SPG method) histofluorescence or perfused for tyrosine hydroxylase immunoreactive (TH-IR) axon examination. Treatment with NX, NM, P or S had no effect on either CBF or cortical tissue neurotransmitter morphology. PGI_2 showed a transiently modest but significant increase of CBF while DS provided moderate protection of catecholaminergic fibers and increased CBF by 27% after MCAO. The combination of DS/PGI_2 resulted in significant cytoprotection of cortical catecholaminergic fibers and generated a sustained CBF increase of 68% of control values. These findings suggest that combining DS with PGI_2 can yield a synergic effect with respect to cortical neurotransmitter and CBF protection after MCAO.

(Supported by the Canadian Heart Foundation)

4.

Spontaneous Recovery from the Encephalomyelitis in Mice Caused by Street Rabies Virus

A.C. JACKSON, D.L. REIMER and S.K. LUDWIN (Kingston, Ontario)

Recovery from rabies was studied in an experimental model. Young adult mice were inoculated in a hindlimb footpad with street rabies virus (fox salivary gland isolate). Ninety-seven percent of mice in an observation group developed clinical rabies with paresis of the extremities and spasticity, and thirty-seven percent recovered with neurologic sequelae. There was an acute inflammatory reaction in the brainstem and gray matter of the spinal cord, and degeneration of myelinated axons in the white matter of the cord and in dorsal roots. Rabies virus antigen was found in the central nervous system of all mice examined between day 5 and 13, and also in trigeminal and dorsal root ganglia. Surviving mice had neutralizing antibodies in serum and brain tissue, and 90% survived an intracerebral challenge with the CVS strain of fixed rabies virus. Spontaneous recovery from rabies encephalomyelitis was demonstrated with evidence of viral replication and pathologic changes in the central nervous system.

5.

Laminin is a Substrate for a Sensory Neuron Galactosyltransferase Activity that Promotes Neurite Growth

R.J. RIOPELLE and K.E. DOW (Kingston, Ontario)

Cell surface enzyme systems on neurons provide a potential mechanism to promote extension by adherence to and/or modification of appropriate substrates. Avian embryonic sensory neurons from ED8 chick glycosylated an appropriate acceptor substrate [N-acetyl glucosamine (GlcNac)]. These neurons extended processes on laminin and fibronectin substrata in the presence of NGF, but only on the laminin substrate was neurite formation partially inhibited in a dose-dependent manner by α-lactalbumin, which is an inhibitor of galactosyltransferase (GalTase) activity. In the presence of GlcNac, or the related polymer chitotriose, there was also dose-dependent inhibition of neurite outgrowth on the laminin substrate. Finally, dose-dependent partial inhibition of neurite outgrowth was seen in the presence of the catalytic substrate for GalTase — UDP-galactose. In all cases, there was no effect of additives on adhesion to the laminin substrate.

Laminin contains oligosaccharide domains that provide appropriate acceptor substrates for a neuronal surface galactosyltransferase with receptor and/or enzyme function.

(Supported by MRC Canada and Canadian Paraplegic Association)

6.

Enhanced Endoneurial Perfusion Following Adrenergic Sympathectomy

D.W. ZOCHODNE, Z. HUANG, K.K. WARD and P.A. LOW (Kingston, Ontario and Rochester, U.S.A.)

We studied the effects of adrenergic sympathectomy on peripheral nerve blood flow (NBF), microvascular resistance (MR), NE content and microvessel caliber in the sciatic nerve of normal rats. Sympathectomy was accomplished using a 5 week course of guanethidine sulfate which induces a selective autoimmune adrenergic neuropathy sparing somatic conduction. NBF and MR were measured using an endoneurial microelectrode sensitive to the rate of hydrogen clearance. NE was measured using HPLC with electrochemical detection. The sciatic nerve was then removed and frozen following perfusion with India Ink and endorneurial vessels measured using a computerized imaging technique.

In the guanethidine treated animals we observed elevated NBF (19.9±1.5 vs 14.8±0.7 ml/100g/min; N=20; p=0.003), decreased MR (7.18±0.47 vs 10.84±0.59; N=20; p<0.001) and depleted NE content (0.04±0.01 vs 0.79 ±0.11; N=11,10; p<0.001). Guanethidine animals had similar numbers of perfused microvessels compared to controls, but had a larger mean microvessel perimeter, mean microvessel luminal area and mean combined luminal area.

Our findings indicate that normal endoneurial microvessels have a degree of tonic vasoconstriction and that NBF may be subject to adrenergic regulation. Removal of adrenergic tone by sympathectomy increased NBF by permitting endoneurial vessels to dilate.

Neuro-oncology

7.

Stereotaxic Biopsy of Brain Tumors

A. SADIKOT, J.-G. VILLEMURE (Montreal, Quebec)

Over a ten year period spanning from March 1978 to March 1988, 396 stereotactic procedures were performed at the Montreal Neurological Institute. Of these, 158 procedures were performed for mass lesions, the primary procedural objective being biopsy in 145 procedures and cyst aspiration in 13 procedures. Each procedure was reviewed with respect to anesthetic technique, preoperative imaging modalities, stereotactic imaging modalities, approach for biopsy, location of target site(s), number of target sites, number of biopsy sites, number of samples taken, intraoperative pathologic diagnosis based on smear or frozen techniques, final pathologic diagnosis and procedure related morbidity. Diagnostic yield was high, with very good correlation between intraoperative diagnosis and final diagnosis. Overall procedural morbidity was 8.8% including procedural mortality of 2.5%. Nonfatal morbidity included minor complications such as scalp infections and transient postoperative psychosis, and major complications

such as intracerebral hemorrhage (symptomatic and asymptomatic), and reversible ischemic neurologic deficits related to stereotactic angiography. Fatal morbidity was related to intracerebral hematoma occurring at deep biopsy sites in patients with either lymphoma or glioblastoma multiforme. Of 56 procedures performed with the aid of stereotactic angiography, none had hematoma related complications. Absence of neovascularity and tumor blush on preoperative angiography does not guarantee against intracerebral hematoma as the majority of procedures resulting in hematoma did not show tumor vessels on preoperative angiography.

Stereotaxic biopsy provides an accurate histological diagnosis in most patients. When the morbidity is critically looked at, the procedure is not benign and should be done on the basis of specific indications.

8.

Interstitial Brachytherapy for Recurrent Solitary Brain Metastases

M. BERNSTEIN, N. LAPERRIERE, P. LEUNG and S. McKENZIE (Toronto, Ontario)

Conventional treatment of solitary brain metastases includes external radiation and surgical resection in selected cases. Often, however, the treated cerebral metastasis recurs before systemic metastases develop and limits the quality of life and survival of the patient. Once the brain metastasis recurs thereapeutic options are limited. Interstitial brachytherapy allows delivery of a high total dose of radiation to a localized recurrence with sparing of outlying already irradiated brain.

The authors present three patients with solitary brain metastases from adenocarcinoma of lung occurring after disease-free intervals of 2, 2.5, and 3 years. All three patients were treated with surgery and whole brain radiation. At time of recurrence of the brain metastasis (after intervals of 8, 12, and 16 months) there was no evidence of systemic disease. High activity removable Iodine-125 seeds were placed stereotactically to produce a minimum tumor dose of 70 Gy in each case. As of January 1989, the patients are alive and well at eight months, 7.5 months, and five months post-implant. Two patients have essentially negative CT scans while one patient does have a diffuse enhancing lesion at the site of the implant.

The approaches to treatment of metastatic brain tumors and the rationale for using brachytherapy in highly selected cases are discussed.

9.

The Role of CT-Documented Gross Total Resection In The Combined Modality Treatment of Malignant Gliomas

K.B. MALLYA, J.H. GALICICH, E. ARBIT and G. KROL (New York, U.S.A.)

In a consecutive series of 117 patients with malignant gliomas, survival and functional status were assessed relative to CT-documented extent of surgical resection. There were 63 males and 54 males; age ranged from 18 to 75 years (median, 57 years). Eighty-five patients (73%) had glioblastoma multiforme and 32 (27%) had anaplastic astrocytoma. Sixty-nine tumors (59%) were in the left hemisphere, 43 (37%) in the right and 5 (4%) were bifrontal. The preoperative Karnofsky ratings ranged from 40 to 100 with a median of 70. Eighty-one patients (69%) had CT-documented gross total resection and 36 (31%), sub-total resection. All patients received whole brain radiation therapy and 109 patients received chemotherapy. One patient died of myocardial infarction 23 days following surgery yielding a 30-day mortality rate of 0.8%.

At time of discharge, the Karnofsky ratings had improved significantly in the gross total resection group but not in the sub-total resection group ($p=0.001$, median Karnofsky ratings 90 vs 60). The median survival in the gross total resection group was 76 weeks (23 still alive) as compared to 40 weeks (1 alive) in the sub-total resection group. The longer survival of patients undergoing gross total resection was significant even after adjusting for age, preoperative Karnofsky status and histological grade of the glioma ($p<0.001$). There were 16 long-term survivors (>2 years) in the gross total resection group as compared to 1 in the sub-total resection group. Failure to achieve gross total resection was a major factor associated with poor functional status of patients in the postoperative period.

We conclude that, gross total resection of malignant gliomas when combined with adjuvant therapies offers the best prospect for long-term survival and improvement in functional status.

10.

Oligodendrogliomatosis: Revival of a Syndrome

R. MOUMDJIAN, A. SADIKOT, J.-G. VILLEMURE, D. MELANSON and Y. ROBITAILLE (Montreal, Quebec)

Beck and Russell (1942) coined the term oligodendrogliomatosis to characterize those oligodendrogliomas which diffusely disseminate in the subarachnoid spaces and sometimes metastasize. Bloomenfeld and Gardner (1945), after a literature review, thought that oligodendrogliomas were second only to medulloblastomas in their tendency to disseminate. A total of five cases from the Montreal Neurological Hospital were reviewed between 1960 and 1988, an occurrence much rarer than the reported 3.4% incidence of nondesquamating oligodendrogliomas.

Oligodendrogliomatosis occurs in young and middle-aged adults with no apparent sex predilection. Increased intracranial pressure, acute hydrocephalus, confusion and multisegmental neurologic deficits including sciatica and spinal block with paraparesis are the main presenting symptoms. The primary location tends to be relatively small with possibly a predilection for the suprasellar region, and widespread subarachnoid and intraventricular dissemination. Surgery may aggravate the neurological symptoms and prognosis is dismal despite multidimensional therapy.

Pathophysiology is discussed and salient radiological data (ventriculomegaly, periventricular calcifications and contrast enhancement on CT, suprasellar and paraventricular space-occupying lesions), CSF studies (high CSF proteins and CSF pleocytosis with elevated opening pressure) and histopathology (CSF cytology as well as mucinous degeneration within the tumor) emphasize their complementary features to confirm an early diagnosis and orient therapy more aggressively.

Neuromuscular

11.

P^{31}NMR Spectroscopy — A Valuable Tool to Detect Partial Expression of Myophosphorylase Deficiency

A.F. HAHN, W.J. KOOPMAN, R.T. THOMPSON and D. GRAVETTE (London, Ontario)

Exercise intolerance and exercise induced myalgias, stiffness, weakness and myoglobinuria are the cardinal manifestations of muscle phosphorylase deficiency. Because of remarkable variations in the severity of symptoms, the clinical diagnosis may be difficult. Diagnostic confirmations have relied on the forearm ischemic lactate test and the absence of histochemical reaction for phosphorylase in the muscle biopsy. Results of these tests may be misleading in cases of partial enzyme deficiency, since the histochemical stain will detect as little as 3-5 percent residual phosphorylase activity (Di Mauro 1986).

This difficulty arose in the investigation of a 44 year old man, who had typical symptoms and a positive ischemic exercise test, but whose muscle biopsy showed apparent normal histochemical reactions for phosphorylase and other glycolytic enzymes. An in vivo P^{31}NMR spectrometric examination showed the typical findings of McArdle's disease (Ross 1981). Subsequent study revealed a variable expression of

the disease in 4/9 siblings. P^{31}NMR spectra showed an alkalotic intramuscular pH during exercise and a striking drop in phosphocreatine, relative to 26 normal subjects. Phosphorylase activity was absent in the biopsy of a brother.

Observations of the P^{31}NMR spectroscopy, proved to be valuable in achieving the correct diagnosis. The spectra are being correlated with the activities of phosphorylase in the muscle biopsies.

12.

Imaging of Muscles

P. ASHBY (Toronto, Ontario)

Can CT or MR images of muscles provide useful information for the clinician? We have scanned a number of patients with neuromuscular disease and made the following observations. It is possible to image muscles which cannot be seen or tested clinically, or subjected to EMG (e.g. deep muscles of the neck, abdomen or pelvis). In myopathic disorders the signal density tends to be reduced in a uniform manner while the cross-sectional area of the muscle remains normal. The pattern of involved muscles may be quite distinct in certain diseases. In neurogenic disorders the cross-sectional area of the muscle is usually reduced and the remaining muscle tissue is in clumps of normal density. The distribution of involvement can be used to localize the lesion. It appears, therefore, that imaging of muscles could be useful in certain circumstances. For example in assessing muscles that cannot be clinically visualized especially in obese, uncooperative or ill patients; choosing a site for muscle biopsy or spectroscopy; recognizing certain specific disease processes from the pattern of muscle involvement, and assessing the effects of treatment.

13.

Myotubular Myopathy: Maturational Arrest or Persistence of Fetal Vimentin?

H.B. SARNAT (Calgary, Alberta)

Myotubular myopathy (MM) denotes a congenital myopathy usually transmitted as an X-linked recessive trait. It is characterized histopathologically by centronuclear myofibres with a core of sarcoplasm and a rim of myofibrils, resembling the architecture of fetal myotubes. Three neonatal cases of MM were compared with skeletal muscle from 4 human fetuses of 8-14 weeks and from 4 normal full-term neonates. The fascicular organization, perimysium, blood vessels, spindles, myelinated intramuscular nerves and motor end-plates are as well developed in MM as in neonatal muscle, but undeveloped or rudimentary in fetal muscle. Histochemical differentiation of myofibres with ATPase is advanced in MM, consistent with normal innervation; spinal motor neurons are normal in number, morphology, and RNA fluorescence. The cytoarchitecture of myofibres in MM resembles that of fetal myotubes, but is more mature in nuclear detail, spacing of central nuclei, registry of Z-bands in adjacent myofibrils, and in the sarcotubular system. Fetal muscle shows frequent mitoses of presumptive myoblast nuclei, myoblast fusion, and scattered degenerating myotubes as physiological cell death; none of these features are seen in MM. Immunoreactivity of vimentin and desmin in myofibres of MM is strong, similar to fetal myotubes and unlike neonatal muscle. It is concluded that MM is neither a primary maturational arrest of fetal muscle development, nor a disorder of innervation. It is proposed that MM is a disturbance of morphogenesis of myofibre architecture due to persistence of fetal vimentin, a transitory cytoskeletal filament protein responsible for preserving immature central positions of nuclei and mitochondria but not T-tubules or triads in developing myofibres and in MM.

14.

Monomelic Atrophy

J. ORYEMA and P. ASHBY (Toronto, Ontario)

Hirayama et al. (1959) were the first to describe a condition in which there was wasting and weakness of the muscles of one upper limb which became arrested after 1-2 years. They called it "juvenile muscular atrophy of unilateral upper extremity" but it is also known as "monomelic amyotrophy", "juvenile type of distal and segmental muscle atrophy of the upper extremities" and "benign focal amyotrophy".

About 150 cases have reported in Japan, 47 in India, 19 in Malaya, 6 in Australia, one in Denmark, one in Holland, one in Israel and 2 rather atypical cases in North America: one case affecting the lower limb and one case involving the proximal muscles of one upper limb.

It is not known whether the condition is less frequent in North America or is simply not reported. We report 5 typical cases attending a clinical EMG laboratory suggesting that the condition may be just as common in North America.

They were all male, onset 14-19 years. The weakness was predominantly unilateral in 4 (all on the right) and symmetrical in 1. Even those with unilateral involvement had minor neurogenic changes in the opposite limb.

The weakness progressed for 1-3 years and then stabilized. CT myleography showed focal cervical cord atrophy in two cases.

We conclude that monomelic amyotrophy may be just as common in Canada as in other countries in which it has been reported.

15.

Exercise Intolerance and Myoglobinuria in Becker's Muscular Dystrophy

A.F. HAHN, R.T. THOMPSON, D. GRAVETTE and W.J. KOOPMAN (London, Ontario)

A close relationship between serum levels of creatine kinase (CK) and myoglobin (MB) and physical activity was demonstrated in patients with Duchenne muscular dystrophy (Florence 1985). Minor exercise results in a prompt rise in serum MB and CK, yet exercise tolerance is limited and therefore myoglobinuria is not observed. The less affected patient with the allelic Becker's muscular dystrophy is much less restricted and may experience exercise induced myalgias. Episodic myoglobinuria has to our knowledge, not been described.

We have studied a family with an x-linked muscular dystrophy, expressed in 5 males of 3 generations. The proband, 15 years .old, showed marked calf hypertrophy, milkd weakness and exercise intolerance. Strenuous exercise induced myalgias and repeated episodes of myoglobinuria. Random serum CK was elevated to 9250 U/L, the biopsy of the vastus medialis showed changes of a chronic dystrophy. Histochemical stains excluded specific enzyme deficiencies. His brothers, 12 and 11 years old, showed similar features and serum CKs of 34000 U/L and 22000 U/L respectively. His maternal uncle, 41 years old, showed moderate hip girdle wasting and weakness, calf hypertrophy, a CK of 1500 U/L and had experienced exercise related myoglobinuria.

P^{31}NMR spectroscopy of the proband, showed an intracellular pH of 7.27 at rest, which dropped with an aerobic exercise to 6.24 with slow recovery to alkalotic values. Phosphocreatine/inorganic phosphate was normal at rest, but fell during exercise to subnormal values with slow recovery.

These observations raise the possibility that changes of muscle membrane permeability and muscle fibre damage may be secondary to abnormalities in energy metabolism.

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16.

Postoperative Ulnar Neuropathies

B. WATSON, W.F. BROWN and R. MERCHANT (London, Ontario)

Among the many causes of ulnar neuropathies centered about the elbow, are cases developing postoperatively. While some recover spontaneously others continue to produce troublesome symptoms and sometimes signs for many months. To determine the incidence and time of occurrence of this neuropathy we embarked on a prospective study of patients undergoing coronary bypass surgery.

Patients were electrophysiologically and clinically studied preoperatively, as early as possible postoperatively, again at four weeks, and with late followups at six and twelve months. In our study to date approximately 20% developed ulnar neuropathies. All were apparent within one week of the operation, none of which were apparent preoperatively. All were mild and unaccompanied by symptoms. These neuropathies were characterized by mild conduction slowing across the postcondylar segment or cubital tunnel and in one case was associated with the later development of denervation in the ulnar innervation territory. No instances of conduction block were seen. In all cases somatosensory evoked potential studies were normal with no evidence of proximal conduction slowing across the roots or plexus. So far, none have developed clinically symptomatic or troublesome ulnar neuropathies although there was an unexpectedly high incidence of mild subclinical ulnar neuropathies.

17.

Peripheral Entrapment Neuropathies and Radiculopathies — Their Association

J. VEITCH and W.F. BROWN (London, Ontario)

Sometimes it is difficult clinically to distinguish between cervical radiculopathies especially those affecting the C6 or C7 roots and median entrapment neuropathies, or in the case of the C8 root, ulnar neuropathies. This study was designed to determine the incidence of electrophysiologically proven median and ulnar entrapment neuropathies in clinically evident cervical radiculopathies.

Electrophysiological studies looking for evidence of median and/or ulnar peripheral neuropathies were carried out in thirty-five C7, thirteen C6, and two C8 radiculopathies.

Electrophysiological, and in some cases clinical, evidence of median entrapment neuropathies were seen in close to 20% of C6 or C7 radiculopathies, while ulnar entrapment neuropathy at the elbow was seen in both C8 radiculopathies. In all these cases the dominant symptomatic neuropathy was the radiculopathy but associated more peripheral entrapment neuropathies were present much more commonly than would be expected from the incidence of these peripheral entrapment neuropathies in age-matched non-radiculopathy patients. Cases where radiculopathy and peripheral entrapment neuropathy coexist can present difficult diagnostic and therapeutic problems.

18.

Stretch Injuries of the Spinal Accessory Nerve

R.O. HOLNESS and T. BENSTEAD (Halifax, Nova Scotia)

Three patients with closed stretch injuries of the spinal accessory nerve are described. Two patients had associated stretch injury of the brachial plexus mainly affecting upper and middle trunks. The third patient had an isolated partial stretch injury of the spinal accessory nerve which worsened after a second injury. Stimulation of the spinal accessory nerve in the neck demonstrated small or absent compound muscle action potentials over trapezius. Needle electromyography showed fibrillation and motor unit potential alteration in sternomastoid and trapezius. In the two patients with associated brachial plexus injury, spinal accessory nerve function recovered over 6-12 months. No recovery was present in the third patient after 12 months. Closed injuries of the spinal accessory nerve have not been frequently recorded. The association of spinal accessory palsy with brachial plexus injury has not been previously completely documented and should be looked for when evaluating patients with traumatic brachial plexus lesions.

19.

Correlation of Spinal and Cortical Pathology with Distribution of Paralysis in Amyotrophic Lateral Sclerosis

J.A. KIERNAN and A.J. HUDSON (London, Ontario)

In amyotrophic lateral sclerosis (ALS) neurons are lost from the ventral horn, brainstem motor nuclei and precentral gyrus. The lower motor neurons may die as a result of transneural degeneration following loss of corticospinal afferents[1] or from an excitotoxic action[2] of the neurotransmitter used by the pyramidal cells of the cerebral cortex.

If cortical neurons are the first to die, one would expect abnormalities in regions of the motor cortex concerned with groups of muscles that were not yet paralysed at the time of death. If an excitotoxic mechanism is at work, the cortical neurons should not be lost until after the deaths of the motor neurons they supply, so one would expect to see normal cortical areas for groups of muscles in the early stages of paresis.

We are conducting a morphometric study in a series of patients with ALS who died with no evident paralysis of some parts of the body. If the hypothesis of transsynaptic degeneration of motor neurons is correct, we should find loss or abnormality of pyramidal cells in layer V of the parts of the precentral gyrus in which the spared groups of muscles are represented. It appears that in these cortical areas the numbers of neurons per sq. mm of sectioned cortex are the same in ALS and in age- and sex-matched controls. However, the volumes of the perikarya of pyramidal neurons are about half those found in the controls.

1. Hudson AJ, Kiernan JA. Lancet 1988; I, 652.
2. Plaitakis A, Caroscio, JT. Ann Neurol 22,275 (1987). Supported by ALSSOC.

20.

Contribution à l'étude du réflexe facio-facial. Son intérêt dans le diagnostic et le pronostic des lésions du complexe facial

N.T. TRAN et P. MOLINA-NEGRO (Montréal, Québec)

Les auteurs passent en revue les données récentes d'embryologie et d'anatomo-histologie portant sur l'existence, chez les animaux, des projections sensitives du nerf facial. Chez l'humain, les données de la neurophysiologie clinique et les travaux électrophysiologiques de MOLINA-NEGRO et collaborateurs depuis 1976, aboutissant à la reconnaissance de l'existence d'un réflexe facio-facial spécifique, sont autant de preuves sur l'évidence des afférences sensitives au sein du tronc facial.

Se basant sur les données qualitatives et quantitatives de ce réflexe facio-facial et après revision des études électrophysiologiques de 660 cas cliniques, les auteurs ont pu identifier des altérations électriques spécifiques qui sont toujours reliées à une lésion (infectieuse, traumatique, compressive, irritative), touchant la composante afférente ou efférente du complexe facial.

Le réflexe facio-facial constitue un moyen diagnostic simple, non-invasif et fiable qui contribue de façon spécifique à préciser la topographie des lésions du complexe facial. D'autre part, il sert à établir le pronostic et à suivre l'évolution de la paralysie faciale accompagnant souvent ces lésions.

Movement Disorders

21.

Is Autologus Transplant of Adrenal Medulla Into The Striatum A New And Effective Therapy For Parkinson's Disease?

E.G. FLORES, H. DECANINI, V.M. LEOS, A. MARTINEZ and M.D.C.Z. GONZALEZ (Monterrey, Mexico)

The autologus adreno-medulla transplant in the neostriatum is a new modality of surgical therapy developed recently to treat Parkinson's patients.

We presented the results in 24 patients operated at the Osler Clinic between the 1st of August of 1987 to 31st of August of 1988. Age varied between 37 and 73 years, duration of illness at the time of surgery was between 3 and 21 years. All patients had a complete neurological examination as well as a pre and post evaluation according to modified Columbia and Schwab, and England Scales. A neuropsychological assessment using Halstead and Reitan as well as MMPI Scales were also performed before and after surgery. All patients had CT-Scan, EEG, EMG, and test of adrenal reserve with Insuline to find if they could tolerate the adrenalectomy. All patients had CT-Scan of both adrenal glands. Preoperatory metabolities of Dopamine in the C.S.F., as well as measurements at different stages in the postoperative period. The surgical technique was similar to that described by Madrazo and coworkers.

The results were distributed in three groups.

Four patients conformed the first group and they showed improvement which lasted for approximately one year. These patients presented with a regression in the Columbia Scale of 1.5 stages and with improvement of up to 50% according to the Scale of Schwab and England. Forteen patients (Group II) presented slight to moderate improvement that lasted less than 6 months with a regression of less than 1 stage in the Columbia Scale; and less than 25% in the Schwab and England Scale. The remaining 4 patients (Group III) showed no improvement after surgery. One patient died 30 days after complications from surgery.

At present time eighteen patients had from 12 to 18 months of follow up and in only two, the improvement had lasted for more than one year. Incidentally these were the younger patients of our series (37 and 46 years of age) and also they were the only ones who did not have regular preoperative treatment with L-Dopa.

In 20 of 24 patients no improvement was observed when the follow up was considered for more than one year.

We have stopped performing this operation in September 1988 because we failed to show the promising results that Madrazo and coworkers announced in their previous reports.

22.

Treatment of Refractory Parkinson's Disease with Adrenal Medulla Autografts Utilizing Two Stage Surgery

K.C. PETRUK, A.F. WILSON, D.R. McLEAN, N. WITT, W.R. MARTIN and D.B. CALNE (Edmonton, Alberta and Vancouver, British Columbia)

The observation that transplantation of adrenal medulla tissue produces a significant functional improvement in parkinsonian animal models has led various clinical investigators to auto-implant adrenal medullary tissue into the corpus striatum of severely affected, drug resistant patients. In an attempt to improve clinical outcome, a two stage implantation procedure was designed to increase cell survival of grafted and intrinsic striatal cells.

Younger healthy patients (<65 years), refractory to current medical therapy or ones with incapacitating drug induced side effects were included in the present study. A two stage interhemispheric-transcallosal approach to the right caudate nucleus was used. Initial surgery involved the preparation of a transplantation cavity and the insertion of a ventricular catheter for serial CSF studies. Seven to 10 days later, adrenal medulla tissue harvest and caudate implantation was performed. This delayed transplantation technique may improve graft tissue survival and has important implications with respect to long-lasting blood-brain barrier disruption, post implantation medical therapy and long term clinical functional improvement. Results from the initial five patients receiving transplants will be presented.

23.

Adrenal To Caudate Implants In Advanced Parkinson's Disease

D. GRIMES, B. BENOIT, P. GRAY and K. GRIMES (Ottawa, Ontario)

Adrenal to caudate implantation has been reported to improve patients with Parkinson's disease. As part of a multicentre evaluation of this therapy, 2 patients (ages 53 and 60) with advanced fluctuating Parkinson's disease (disabled more than 70% of each day) received autologous adrenal to caudate implants. They had Parkinson's disease for 17 and 13 years respectively and had received all available treatment regimes.

Confusion and hallucinations were the major early post-operative problems. One patient had bifrontal subdural hygromas removed. The patients have now been followed for 9 and 6 months on their same preoperative drugs. One patient has had a 40% reduction in "off" time; his Parkinson rating when "off" decreased from 79 to 51 and his Schwab and England "off" score improved from 10 to 50 percent. He is still troubled with fluctuating confusion. The second patient has shown very minor improvements, with no continuing adverse effects. Neither patient demonstrates any evidence that the course of their disease has been altered.

Adrenal to caudate grafting is an experimental treatment for Parkinson's disease. The procedure is major; 1 of these 2 patients had significant motor improvement but it is not clear if this will be sustained and fluctuating confusion continues to be a problem. While these results allow a degree of optimism, new and different graft preparations must be developed if further brain grafting procedures are to be justified.

24.

Idiopathic Parkinson's Disease in Siblings — Consideration of Etiology

A.H. RAJPUT and B. THIESSEN (Saskatoon, Saskatchewan)

There is now sufficient evidence that the cause of idiopathic Parkinson's disease (IPD) is not genetic but is related to environments. The onset of pathological process is insidious and no trigger factor has been identified. The preclinical course is long (maybe several decades) but cannot be accurately ascertained. Thus the exposure to the offending agent is possible anytime before the clinical features begin. Any one of the numerous environmental factors could therefore be crucial in the etiology of IPD. It is necessary to devise strategies that would narrow the range of possibilities. One alternative is to analyze the environmental factors in IPD siblings.

The lifetime risk of parkinsonism in an individual is 0.025 and the risk of two siblings developing the same is 0.0006. Assuming that the cause of IPD in the affected siblings is the same, the exposure would have occurred during the period that they shared the same environments.

We have identified 6 families where 2 or more siblings had IPD (one 3 sibs). Only those IPD cases seen personally (AHR) were included in the study. In each family, the affected siblings were of the same sex. The (presumed crucial) simultaneous common exposure occurred during the first 11-24 years. In 3 families, there was a correlation between the duration of exposure and the age of onset. This observation indicates that the trigger factor is not a single event but rather cumulative effect of the offending agent — the larger the dose of exposure, the more severe the damage (early onset).

The advantages of studying sibships over other methods, e.g. two generation IPD families or regional general IPD cases will be discussed.

25.

Parkinsonism — Onset and Mortality Update

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

Introduction of levodopa marked a major event in treatment of chronic neurological diseases. The beneficial effect to the individual parkinson (PK) patients are well known but the impact on the general patient population and the social and health care systems is emerging slowly.

Because of universal health care and drug plan in Saskatchewan, there have been no barriers to treatment in these cases. The circumstances are therefore conducive to identifying a representative patient population to study the profile of the disease today.

Data on all patients attending Parkinson Clinic (PC) at University Hospital, Saskatoon since 1968 have been entered regularly in a computer registry. These include year of birth, sex, age at onset, type of parkinsonism, drug therapy, severity of disease (Hoehn & Yahr) and date of last visit or death.

During 21 years, 806 PK patients were evaluated and idiopathic Parkinson's disease (IPD) was diagnosed in 91% cases. The median age of onset in all PK cases was 63 years and in IPD it was 64 years. The clinical onset in 4.6% PK cases was during the first four decades and in 39% during the 7th decade. Nearly half of the patients at the first visit to PC had mild (Hoehn & Yahr, Stage I & II) disability. During the interval of study, 71% cases had received levodopa at some point. The mean duration until death was 13.1 years. Based on the incidence rate of 20.5 per 100,000 in general population, the current prevalence rate in Canada is estimated at 269 per 100,000. It is also evident that parkinsonism produces functional disability during active working life in most of the victims. Further details and pertinent discussion and comparison with past studies will be presented.

26.

Ferrous Sulfate, Sinemet Interaction in Patients with Parkinson's Disease

D. RANKINE, N.R.C. CAMPBELL, A. GOODRIDGE, T. KARA and B. HASINOFF (St. John's, Newfoundland)

Sinemet (a combination of l-dopa and carbidopa) is commonly used to treat Parkinson's disease. Ferrous sulfate has been shown to decrease l-dopa bioavailability in healthy individuals through binding of l-dopa by iron. In this study we examined the effects of administering ferrous sulfate 325 mg with Sinemet (100/25) tablets on l-dopa and carbidopa bioavailability and on symptoms and signs of Parkinson's disease in seven patients. The study was a randomized placebo controlled crossover design with a subsequent open phase. The administration of ferrous sulfate with Sinemet resulted in a decrease in l-dopa bioavailability (AUC) of 28% (P 0.01) and a substantial decrease in carbidopa bioavailability (AUC). Carbidopa was shown to bind iron in chemical studies. There was a statistically non-significant trend for Sinemet to be less effective clinically when it was administered with ferrous sulfate than when it was administered with placebo. The changes in levodopa bioavailability (AUC) with iron were also associated with non-significant changes in clinical status (r=0.46, p 0.05). The decreases in l-dopa bioavailability when Sinemet was given with ferrous sulfate were variable and not as large as those seen in the previous study on healthy individuals. The reduced bioavailability appears to be clinically significant in some but not all patients. The clinical significance of iron-l-dopa and carbidopa interactions will ultimately await further study.

27.

Pathology of Caudate Nucleus in Parkinson's Disease

B. LACH, D. GRIMES, B. BENOIT, A. MINKIEWICZ, A. GREGOR, M. SENKOWSKI (Ottawa, Ontario)

We present ultrastructural and biochemical changes in the biopsy specimens of the caudate nucleus of two patients with advanced Parkinson's disease, undergoing adrenal gland implanatation to the brain. A small biopsy specimen of a caudate nucleus obtained during passage to a deeply-seated frontal tumor was used as a control (CTR).

Both Parkinson patients displayed similar abnormalities differing only in severity. The neuropil of the caudate nuclei showed frequent dystrophic neurites filled with numerous dense bodies, myelin figures, mitochondria, polyglucosan bodies and neurofilaments. Some myelinated and unmyelinated fibers showed varicosities with focal accumulation of the content similar to that present in the dystrophic neurites, chiefly mitochondria. Preliminary morphometric studies indicated at least 20% reduction in the number of mitochondria in the neuropil of the caudate nucleus in one patient. The number of astrocytes and macrophages was clearly increased in one patient. The synapses were frequently separated from the post-synaptic terminals by electron-dense processes of either microglial or satellite cells. The neurons appeared entirely normal. The HLPC assessments of the levels of neuro-transmitters measured in one patient were as follows: (nannograms/mg of proteins): Dopamine 0.49 (CTR 3.97), DOPAC 0.67 (CTRC 1.47), HVA 0.006 (CTR 5.14). Light microscopic and immunohistochemical examination (GFAP, neurofilament, Tyrosine hydroxylase, Ricinus communis lectin, HLA-Rd antigen and ubiquitin) of a frozen biopsy specimen of a similar size showed no evident abnormalities.

Ultrastructural demonstration of frequent dystrophic changes and decreased numbers of mitochondria in the neuropil of the caudate nucleus, suggests abnormal transport in Parkinson's disease. Although these changes are not specific, their presence or absence may have prognostic potential in the assessment of severity of disease and the prediction of the outcome of transplantation in the future management of patients selected for this procedure. Electronmicroscopic and highly sensitive biochemical methods are necessary for demonstration of subtle pathological changes in the caudate nuclei in these patients.

28.

Potentiation of the Effect of Bromocriptine by D_1 Agonists in MPTP Monkeys

B.G. MANCILLA, P.J. BÉDARD and R. BOUCHER (Quebec, (Q.C.) P.Q.)

Dopamine receptors have been classified in two subtypes: D_1 and D_2 receptors (Kebabian & Calne, 1979, *Nature*, 277: 93-96). The D_1 receptor stimulates adenylate cyclase and D_2 receptors inhibits adenylate cyclase. In the regulation of metabolism of dopamine an interaction of both dopamine receptors has been postulated (Saller & Salama, 1986, *J. Pharmacol. Exp. Ther.*, 236: 714-720). The possibility of a functional interaction between these receptor subtypes has been shown by recent highly selective D_1 and D_2 agonist and antagonist in biochemical, electrophysiological and behavioral studies (Clark & White, 1987, *Synapse*, 1: 347).

To date, the SKF38393 is the only suggested selective D_1 agonist which has been studied extensively. However in MPTP-treated monkeys SKF38393 does not reverse the motor deficits and can inhibit the positive effects of the D_2 agonist LY171555 (Nomoto et al. 1988, *Neurosci. Lett.*, 57: 37-41); SKF38393 does not readily penetrate into the brain, it has a short half-life and it may be metabolished to another compound which has D_2 antagonist properties (Jenner et al. 1988, *Eur. Jour. Pharm.*, 136: 197-206).

Recently another putative D_1 agonist the benzegaline CY208243 has been described (Makstein et al. in press), and this has been shown to

have antiparkinsonian activity in MPTP-treated monkeys (Jenner et al. 1988, *Eur. Jour. Pharm.*, 136: 197-206).

In MPTP monkeys, we studied the effect of bromocriptine (D_2 agonist) and CY208243 (D_1 agonist) in assessment of locomotion activity and motor deficits (Laval University Disability Scale for BPTP-monkeys).

Preliminary results, suggest that there is a synergism between bromocriptine and CY208243. This may open new avenues in the treatment of Parkinson's disease.

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29.

The Use of Selective Denervation for Spasmodic Torticollis in Cervical Dystonias

G. BOUVIER (Montreal, Quebec)

During the past eleven years, 180 patients suffering from spasmodic torticollis or cervical dystonias were treated exclusively by denervating at the periphery the muscles involved in the dystonia. Following clinical examination the muscles were identified by bilateral simultaneous electromyography and local blocks. Denervation was carried out under light anaesthesia without curare, using stimulation to identify the roots, the rami and the nerves. The majority of these patients (60%) suffered from rotational torticollis and, usually, denervation involved the posterior cervical group down to C6 on the side towards which the head is turning, together with the contralateral (agonist) sternocleidomastoid muscle. The antagonist muscles, especially the opposite sternocleidomastoid muscle are often inhibited. It has been established that with early physiotherapy total (30%) or very marked relief (57%) of movements is obtained while preserving normal or near normal movements of the head from residual muscles. The posterior cervical group of muscles are innervated by C1 C2 and the posterior primary divisions of C3 C4 C5 and sometimes C6 and C7.

In laterocollis, where all the involved musculature is on the same side, the trapezius and occasionally the levator scapulae may participate. While some patients can do without their trapezius, it is essential in others for good shoulder stability and movements and this should be ascertained by blocks, while doing an electromyogram. Save for this limitation, the results are also very satisfactory in simple laterocollis. In postero-laterocollis, and in retrocollis there is usually bilateral involvement of the posterior musculature. The posterior rami have been interrupted down to C5 bilaterally in five instances but we usually limit it to C4 on one side. The results are less complete, specially if both trapezei contribute to the movement.

Avulsion of the distal portion of the nerves appears to be important to prevent return of innervation.

30.

Use of Botulinum-A Toxin in Spasmodic Torticollis: Three-year Follow Up

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

Two hundred and ten patients with spasmodic torticollis were treated with botulinum-A toxin for the past three years. These included 82 males and 128 females. Seventy-two per cent of treated patients continued to attend for repeated injections. Seven hundred and fifty-five treatments were given in total, and the mean dose per treatment per patient was 135 mouse units (±31 SD). Torticollis, evaluated by the scoring protocol described in our previous studies, fell from a mean of 11 (±4) before to an average of 5.7 (±3) after repeated treatment ($p<0.05$). Pain scores fell from a mean of 6 to 2 ($p<0.05$). The mean follow up interval was 14.6 weeks (±5), reflecting the duration of benefit. Patients reported onset of improvement 6 days (mean) after injections. Adverse reactions, occurring in 30 patients, were mild and transient. Botulinum-A toxin remained effective after repeated injections up to three years with few and insignificant side effects.

Pediatric Neurology/Neurosurgery

31.

Congenital Inflammatory Myopathy

M. SHEVELL, B. ROSENBLATT, K. SILVER, S. CARPENTER and G. KARPATI (Montreal, Quebec)

Congenital inflammatory myopathy is a rarely reported cause of neonatal hypotonia, weakness and arthrogryposis that is not yet clearly defined as a nosologic entity. Three cases of congenital inflammatory myopathy are presented and the literature regarding this entity summarized. Central nervous system involvement (microcephaly/intellectual delay) may or may not be present. Creatine kinase values are elevated, the EMG is myopathic and the muscle biopsy, revealing both an inflammatory infiltrate and muscle fiber atrophy, is diagnostic. Possible etiologies include intra-uterine viral infection or acquired auto-immune dysfunction. Treatment with steroids may result in some motor improvement but has no effect on CNS involvement if present. Despite a common time of presentation and muscle pathology, these patients have a hetergeneous clinical profile and often the diagnosis of a congenital muscular dystrophy syndrome is suggested. The presence of a congenital inflammatory myopathy in such patients may provide an important etiologic clue into these disorders that warrants further investigation.

32.

Dancing Eye Syndrome: Magnetic Resonance (MRI) Findings and Unusual Biochemical Characteristics

L. DE MEIRLEIR, P. LENOIR, B. DESPRECHINS, S. PEETERS, F. GORUS and H. LOEB (Brussels, Belgium)

The syndrome of dancing eyes or myoclonic encephalopathy of infancy (MEI) is a rare disease, probably of auto-immune origin. The syndrome can occur in association with viral infection or neuroblastoma. Outcome is variable. No specific pathological features in cerebellum or brainstem has been identified in this syndrome. Brain CT-scans are rarely abnormal. We present clinical data of an 11 month old boy, who was first admitted with irritability, fever, myoclonia and opsoclonus. He made a complete recovery within one week. A relapse occurred 5 months later and was followed by a persistent debilitating cerebellar ataxia and further aggravation with bouts of myoclonia during viral infections. Steroid treatment did not improve the ataxia, but seemed to suppress the bouts of myoclonia. During the acute episodes serum alkaline phosphatases were very elevated (up to 4000 IU/l) and returned to normal in the chronic phases.

An MRI of the brain after one year clearly demonstrated atrophy of the cerebellum, mainly of the vermis. These findings and the unusual increase of the alkaline phosphatases, and its possible relationship with the entity known as transient alkaline phosphatasemia, which is sometimes associated with mental retardation, will be discussed.

33.

Mother-Infant Anti-CNS Antibody Reactivity

A.V. PLIOPLYS (Toronto, Ontario)

During pregnancy, it is possible that mothers may produce IgG antibodies, directed against CNS antigens, which upon crossing the placenta might cause neurologic impairment in the offspring. Since anti-CNS

reactivity may be present in normal individuals, it is important to establish background rates in healthy mothers and infants.

101 maternal-infant pairs were studied. Serum samples were obtained from the mothers at the time of hospital admission for delivery. Cord blood samples were taken from the infants at the time of birth. In all cases, these were uncomplicated pregnancies and deliveries. This study was approved by hospital ethics review committees. The serum samples were screened against Western blots of normal, human, adult, autopsy-derived frontal cortex (FC) and cerebellum (CER) tissue specimens using standard techniques (JNNP 50:1514, 1987). To detect the presence of antibodies directed against embryonic CNS antigens, the serum samples were also screened against Western blots prepared from embryonic day (E) 17 and adult mouse cerebral cortex specimens.

In the case of IgG, in mothers the incidence of immunoreactive banding against FC was 2% and against CER was 1%. In the infants there was no banding detected. When screened against E17 mouse CNS tissue, the incidence of IgG banding in both mothers and newborns was 10%, whereas against adult mouse cortex the respective incidences were 9% and 12%. These results indicate that there is a very low incidence of background IgG anti-CNS reactivity in term mothers using human CNS as substrate. This suggests that the techniques used would be appropriate ones to investigate the presence of maternally derived IgG anti-CNS antibodies as potential pathogens in infants born with CNS disease. However, results from the use of adult or fetal mouse CNS tissue as substrate would be more difficult to interpret because of the approximately 10% background IgG reactivity.

34.

Isolated Cerebral Angiitis In Childhood

D. MATSELL, D. KEENE, C. JIMINEZ and P. HUMPHREYS (Ottawa, Ontario)

Isolated cerebral angiitis, a rare inflammatory condition of the nervous system, characterized by vasculitis of the small vessels, has not, to the best of our knowledge, been described in childhood. It usually presents with a diversity of neurological symptoms in the fifth to eighth decades of life.

An 8 year old male presented with a left sided facial weakness, diplopia, nystagmus and head tilt leading to an initial diagnosis of posterior fossa tumor (PFT). CT Scan failed to confirm the diagnosis, but demonstrated multiple enhancing lesions of the cerebrum. MRI showed multiple diffuse hyperintense foci of white matter. Four months after presentation he developed sudden onset of severe headaches, followed by quadraparesis, ocular palsy, inability to speak, and loss of gag reflex. CT Scan demonstrated a pontine hemorrage. Cerebral angiography was normal. Surgical evacuation was done with intra-operative arterial biopsy which revealed perivascular cutting with a mononuclear infiltrate. Despite intravenous methyl prednisolone intracranial bleeds occurred. Cyclophosphamide was added. A few months later the patient became ambulatory and was discharged home. Over the next 5 months subtle neurological deterioration occurred; seizures developed and the patient died in status. Autopsy showed leptomeningeal vasculitis and pervascular inflammatories of the small vessels of the central nervous system without evidence of systemic vasculitis.

We present this case to document the occurrence of cerebral angitis in childhood; to emphasize the consideration of this disorder in children presenting with a diversity of neurological signs and symptoms; and the lack of sensitivity of present modalitis of neurological investigation in its diagnosis.

35.

Narcolepsy-cataplexy and Different Forms of Hypersomnia in Early Childhood

S. NEVSÍMALOVÁ and B. ROTH (Prague, Czechoslovakia)

The first symptoms of narcolepsy-cataplexy and hypersomnia usually appear in adolescents or in adults. Over the past 5 years we have observed 10 children (5 with narcolepsy, 5 with different forms of hypersomnia) who developed the disease before the age of 12 years. In 4 children the first signs appeared during the first (3x) or second (1x) years of life, in 2 others between 4-5 years. Most of them had risk factors during pregnancy or delivery with signs of minimal brain damage in the clinical and psychological picture, and paroxysmal EEG activity accompanied by febrile, affective, or in 1 child epileptic, convulsions. Morbid sleepiness with onset in early childhood showed a tendency to improvement, or disappearance until the age of 6-8 years.

On the other hand, the clinical picture of 4 other children in whom the disease began between 10-12 years does not differ from typical adult cases.

A detailed EEG and polysomnographic study as well as the results of HLA (DR2) tests in both age groups are discussed.

36.

Congenital Foix-Chavany-Marie Syndrome in Two Patients: An Unusual Cause of Speech Delay in Children

S. CHRISTIE, S. WHITING and P. HUMPHREYS (Ottawa, Ontario)

A syndrome of facio-pharyngo-glosso-masticatory diplegia with automatic voluntary dissociation due to bilateral anterior opercular lesions was first named by Foix, Chavany and Marie in 1926. Several cases have been reported since. All have been caused by multiple infarcts.

Developmental Foix-Chavany-Marie syndrome in 41-year-old identical twins was reported by Graff-Radford et al. in 1986. MRI showed bilateral perisylvian cortical dysplasia consistent with incomplete opercula formation and polymicrogyria.

We report two additional patients with this syndrome.

S.L., a thirteen year old female, and M.P., a five year old male, both presented with severe expressive language delay. S.L. ahd facio-lingual diplegia with relative sparing of involuntary emotional expression and likewise, M.P. had lingual paresis with relative sparing of involuntary tongue movement.

In both patients, CT scans showed heterotopic foci of grey matter consistent with cortical dysplasia in the perisylvian fissures, bilaterally.

This syndrome should be considered in children presenting with expressive language delay and oral-facial paresis.

37.

Different Allelic Mutations Cause Tay-Sachs Disease in French-Canadians

P. HECHTMAN, J. BAYLERAN, B. BOULAY, E. ANDERMANN, R. GAGNE and E.E. KOLODNY (Montreal, Quebec)

Genes causing infantile Tay-Sachs Disease (TSD) occur in high frequencies among Ashkenazi Jews and French Canadians (FC). Southern analysis of the genomic DNA obtained from two FC patients led Myerowitz and Hogikyan to conclude that the mutations in the two groups are different with the FC mutation characterized by a deletion which includes the first exon of the hex A α subunit locus. We have examined DNA from seven FC TSD families. Five of these patients came from the region of the lower south shore of the St. Lawrence River. The sixth comes from Québec City and the seventh from Minnesota. In the latter patient, a compound heterozygote, the TSD gene is traceable to FC ancestry on the maternal side through great-grandparents who migrated from the Estrie region of Québec. In all patients from the lower south shore region, an intronic probe recognized only a 23 kb EcoR1 digestion fragment indicating homozygosity for the α locus deletion. Examination of the pedigrees reveals surnames common to all families although common ancestors link only two pairs of nine known parents. By contrast, the absence of a 23 kb band in the proband and parents from Québec City indicates that a different type of

mutant allele is segregating in this family. Fibroblasts obtained from this patient have no hexosaminidase A activity nor do they synthesize an antigen which cross reacts anti-α antiserum. The patient from Minnesota also produced only a 9 kb EcoR1 digest fragment recognized by the intronic probe. This fragment is found in normal as well as Jewish TSD DNA. Thus, founder effect, which may explain the high frequency of the TSD gene in a single region of Québec, cannot account for all cases of TSD in the FC population. In this regard, FC pedigrees with TSD probands have been identified in three other regions of Québec, remote from the Gaspé. DNA samples from obligate heterozygotes from the lower north shore of the St. Lawrence, from the Gatineau and from the Montreal region are currently being analyzed to determine the extent of heteroallelism in this population.

38.

Coronal Craniosynostosis: Forehead Release Versus Forehead Advancement

S.T. MYLES (Calgary, Alberta)

A number of different operative techniques have been suggested for treatment of coronal craniosynostosis, whether unilateral or bilateral.

In the past 10 years, I have tried the lateral canthal advancement procedure, as well as tongue-in-groove advancement of the supra-orbital bar, in 11 children with unilateral or bilateral coronal craniosynostosis. While the initial cosmetic result has been satisfactory, excessive vertical growth of the frontal bones has occurred subsequently in several children, causing relative turricephaly.

In 9 children, with unilateral or bilateral coronal synostosis, the supra-orbital bar and re-shaped frontal bones have been replaced as free grafts, without advancement. The cosmetic results have been excellent, provided the operative procedure was carried out at 2 to 3 months of age. This procedure, which I have termed "forehead release", requires less operative time, and blood loss has been reduced, compared to forehead advancement.

39.

Vascular Malformations of the Brain Stem

E.C.G. VENTUREYRA (Ottawa, Ontario)

Four vascular malformations of the brain stem in children are presented: 3 males, 1 female, ages from 3 to 17 years. Vascular malformations were located in the thalamus (1), pons (2), medulla oblongata (1). Three cases presented with intrinsic brain stem hemorrhages and 1 with repeated subarachnoid hemorrhages. Clinical presentation was characterized by sudden onset of severe motor deficit (3), gaze palsy (1), incomplete Wallenberg Syndrome (1). Level of consciousness was impaired initially in only 1 patient. Two presented with a history of minor head injury preceding onset of neurological deficits.

MRI Scan was the most reliable test in demonstrating presence of offending lesion showing evidence of recent and remote hemorrhages. CT Scanning demonstrated presence of blood in brain stem or subarachnoid spaces. Infusion of contrast material did not contribute in diagnosis.

Cerebral angiography failed to demonstrate the vascular malformation in 3 cases.

Direct surgical intervention, evacuation of blood clot, excision of vascular malformation, was used in 3 cases. One was treated with sterotaxic radiosurgery.

Despite negative angiographic findings active vascular malformations were obvious in 2 of 3 cases operated upon. Intraoperative electrophysiological monitoring with brain stem auditory evoked responses (BAER) proved valuable in increasing safety of surgical procedure. Immediate improvement of previously impaired BAER was observed and recorded.

No mortality or morbidity associated with direct surgical intervention was encountered. Histologically all lesions were compatible with "vascular malformation". One diagnosed as "cavernous angioma" confirming preoperative diagnosis. Post surgical intervention results were very gratifying. All patients returned to their regular activities with only mild neurological abnormalities.

Results, technical details will be discussed.

40.

Remote Effects of Selective Posterior Rhizotomy in Spasticity

D.D. COCHRANE, P. STEINBOK and A. SYKANDA (Vancouver, British Columbia)

This report describes the local and remote effects of selective posterior root section for the treatment of spasticity in children affected by spastic diplegia.

During the past 18 months, 9 children affected with spastic diplegia secondary to prematurity, have undergone selective posterior rhyzotomies of the L2 through S2 roots for the treatment of spasticity. In all cases, changes in muscular hypertonicity, reflex hyperactivity and joint mobility have occurred. Initial hypotonicity, areflexia and apparent weakness were apparent in all. The tone and reflex changes occurred in proportion to the number of abnormal rootlets found and sectioned at operation. By 6 weeks, all children showed improvement in sitting and standing postures, freedom of volitional movement and ease of nursing care.

In addition to the anticipated lower extremity changes, 5 of the 7 followed patients demonstrated remote effects following the procedure. These included increased use of the upper extremities, increased voice volume, decreased bronchospasm, decreased drooling and improved attentiveness. These changes were not reflected in changes in the clinical examination.

The nature of these remote effects will be discussed.

FRIDAY, JUNE 16TH — P.M.

Behavioral Neurology

41.

Creutzfeldt-Jacob Disease With PET-Scan Changes Mimicking Those Seen in Huntington's Disease

M.F. MAZUREK, E.S. GARNETT, A.R.M. UPTON and J.T. GROVES (Hamilton, Ontario)

A neuroradiological hallmark of Huntington's disease (HD) is diminished glucose metabolism in the striatum as imaged by positron emission tomography (PET) scanning. The potential diagnostic usefulness of this finding will depend not only on its reliability in identifying cases of HD but also on its specificity in distinguishing HD from other disorders. We have recently observed HD-like changes on PET scan in a 46-year-old gentleman with pathologically-confirmed Creutzfeld-Jacob disease.

The patient had been neurologically well until the age of 46, when he developed a progressive neurological syndrome characterized by severe dysarthria, supranuclear gaze palsies, abnormal saccadic eye movements, gross trunkal and limb ataxia, a marked choreoathetotic movement disorder and extensor plantar responses. Aside from mild memory impairment the patient was intellectually intact when first seen. There was no family history of neurological disease. Exhaustive serum studies were normal. The cerebrospinal fluid showed moderately elevated protein but was otherwise normal. The CT scan was normal as was the MRI scan. A PET scan performed 5 months after the initial onset of symptoms revealed marked hypometabolism of fluorodeoxyglucose in the striatum, a pattern that was judged to be indistinguishable from that

seen in HD. The patient died one month after the PET scan. Neuropathological examination of the brain showed findings typical of spongiform encephalopathy.

Creutzfeld-Jacob disease can present a pattern of PET scan abnormalities identical to those seen with HD.

42.

Patterns of Neuropeptide Changes in Alzheimer's Disease Cerebral Cortex

M.F. MAZUREK and M.F. BEAL (Hamilton, Ontario; Boston Massachusetts)

Most of the peptide immunoreactivity in cerebral cortex derives from morphologically similar populations of locally-projecting intrinsic cortical neurons. Despite this apparent homogeneity of peptide-containing cortical neurons, there is evidence that tissue concentrations of the various neuropeptides might be differentially altered in Alzheimer's disease (AD). We have studied this issue in a single set of postmortem cerebral cortex samples that we dissected from 14 histologically-confirmed cases of AD and 17 age-matched controls. Pooled aqueous and acid extracts of tissue were reconstituted in buffer and the following peptides were measured by radioimmunoassay: somatostatin, corticotropin releasing factor (CRF), neuropeptide Y (NPY), cholecystokinin (CCK), vasoactive intestinal polypeptide (VIP) and substance P. Concentrations of both somatostatin and CRF were significantly reduced by 42-65% in 9 of 11 cortical areas examined, and by 18-33% in the remaining 2 cortical regions. The other neuropeptides were much less dramatically affected. NPY, which is almost 100% colocalized with somatostatin in cerebral cortical neurons, was significantly decreased by only 22-33% in 4 of the 11 areas studied, and was normal elsewhere. CCK and VIP were significantly reduced by 22-44% in 5 of the 11 areas studied, and was normal elsewhere. CCK and VIP were significantly reduced by 22-44% in 5 of the 11 cortical regions and normal in the others. Substance P levels were decreased by 21-35% in 8 of the 11 areas.

These results indicate that the Alzheimer disease process produces highly similar reductions in cortical concentrations of somatostatin and CRF, while levels of the other cortical peptides, despite their being contained in morphologically similar neurons, are less markedly affected.

43.

Automatic Semantic Priming Alterations in Dementia of the Alzheimer's Type and Pseudodementia

H. CHERTKOW, D. BUB and A. BRUEMMER (Montreal, Quebec)

In a lexical decision task, pairs of words or non-word letter strings are briefly presented to subjects, who must rapidly decide if they have seen a word or non-word. When a pair consists of two semantically related words (e.g.: cat-dog) response times on the second (target) word will be faster than when the first word in the pair is unrelated (e.g.: lamp-dog). This phenomenon, termed semantic priming, reflects a reliable influence of word association which occurs automatically and even unconsciously at the level of long-term semantic memory, on seeing a written word. Semantic priming effects (time to respond to "dog" when preceded by an unassociated word *minus* time to respond to "dog" when preceded by an associated word), are unaltered by normal aging.

Deterioration of semantic memory occurs commonly in Dementia of the Alzheimer's Type (DAT). We have previously shown that such semantic impairment can be accompanied by a pathological increase in the amount of semantic priming, termed Hyperpriming (Chertkow, Bub, and Seidenberg, Brain and Language, 1989).

We have now further tested groups of subjects for semantic priming effects on a lexical decision task. Of 19 DAT patients (mean age 74), 13 showed increased priming effects greater than 50 msec (mean 98 msec). These 13 were significantly more impaired in terms of semantic memory deterioration measured by other off-line tasks, than the other DAT patients. Forty-one of 42 age-matched neurologically normal control subjects (mean age 72 years) had priming effects in the range of 50 msec or less (mean 28 msec). The pattern of response indicated that the priming was indeed automatic. Three dementia patients subsequently found to have reversible "pseudodementia of depression" showed semantic priming effects in the normal range.

We suggest that Hyperpriming on a lexical decision task may delineate a subgroup of DAT patients with semantic impairment. Since it appears to be an automatic, unconscious phenomena, it is possible that Hyperpriming may not occur in pseudodementia due to reversible depression. It may require actual organic deterioration of semantic memory such as in DAT.

44.

Spatial Disorientation in Persons with Early Alzheimer's Disease

L. LIU, L. GAUTHIER and S. GAUTHIER (Montreal, Quebec)

To better understand spatial disorientation in persons with Alzheimer's disease (AD), spatial tasks were administered to 15 individuals in the early stages of AD (3 and 4 of the Reisberg Scale) and 15 control subjects. The two subject groups were comparable in sex distribution, age and years of education. The spatial tasks were classified as requiring basic, higher cognitive or functional spatial skills. Basic spatial skills were observed through performances on tasks that required figure-ground perception, visual and tactual shape recognition, visual and tactual size discrimination, position in space, spatial relations and left-right discrimination. Higher cognitive spatial skills were observed in tasks requiring spatial mental representation, spatial problem solving and spatial memory. Functional spatial skills were evaluated by having subjects lead the way to destinations in familiar and in unfamiliar environments. The general findings were that the AD group was impaired in all tasks of higher cognitive spatial orientation skills compared to the controls. Four of the eight basic spatial orientation skills were intact, namely visual recognition of shape, both visual and tactual discrimination of size and left-right discrimination. It was possible that the poor performance on the other basic spatial tasks was due to impairment of higher cognitive processes. For example, tactual shape recognition may have required mental representation of the shapes, thus this test would not exclusively examine basic spatial skills. While the AD group was impaired in functional spatial orientation in the new environment, functional spatial orientation in the familiar environment was intact. The results of the tests agree with the common observation that higher cognitive functions and the ability to integrate new information deteriorate early in AD. Further studies of spatial disorientation would contribute to the clinical assessment and management of persons with AD.

(This study was supported in part by the Alzheimer Society of Montreal)

45.

Lymphocyte Function in Autism

A.V. PLIOPLYS, A. GREAVES, K. KAZEMI and E. SILVERMAN (Toronto, Ontario)

Blood samples were obtained from a total of 17 patients with autism. There were 16 males and 1 female. The age range was from 7 to 23 years with a mean age of 17. The diagnosis of autism conformed to the DSM-III and DSM-III-R criteria for autism. There were no identified neurobiologic causes of autism in any of the studied population. Parental signed consent was obtained prior to phlebotomy. This study was approved by ethics review committees.

Peripheral blood lymphocytes were separated on a Ficoll-hypaque density gradient. Patients had normal numbers of T and B cells and T cell subsets. Although CD4:CD8 ratios were normal for the whole group (2.09±0.97) 6 patients had elevated ratios (>2.2) and 5 had decreased ratios (<1.5). There was an abnormally increased percentage

of DR+ (activated) T lymphocytes in the whole group (7.73±5.75%; normal <2%) which was more marked in the patients with low (<2) CD4:CD8 as compared to patients with high (>2) CD4:CD8 ratios (10.71±2.87% vs 5.12±6.5%). With increasing age there was a decreasing percentage of DR+ lymphocytes. Mitogen-induced proliferation (concanavalin-A and phytohemagglutinin) was normal as was the autologous mixed lymphocyte reaction (AMLR) for the whole group. However, the AMLR was significantly decreased in 5 patients with CD4:CD8<1.5 as compared to 9 patients with a normal or elevated CD4:CD8 ($p<0.05$). No patient had any interleukin-2 (IL-2) receptor+ cells.

Autistic patients have an abnormally increased percentage of DR+ but not IL-2 receptor+ lymphocytes suggesting "incomplete" activation, a finding which is seen in autoimmune diseases. The decrease in activated cells with increasing age suggests that there may be an autoimmune process which is more active earlier in life.

46.

Role of the Cerebellum in Cognitive Thought

M.I. BOTEZ, J. LEVEILLE and T. BOTEZ (Montreal, Quebec)

Twenty-two patients with cerebellar well-delimited lesions of various etiologies underwent a neuropsychological assessment and single photon emission computed tomography (SPECT) studies. Twenty-two normal subjects individually matched with the patient group for age, sex, and level of education served as controls.

The cerebellum interferes with some cognitive functions, namely, the speed of information processing, the programming of a logical sequence of events, abstract thinking and visuo-spatial abilities. This study confirms that the speed of information processing is mainly a subcortical function. The cerebello-frontal and cerebello-parietal loops interfere indirectly with cognitive functions. Our SPECT studies established the existence of a new form of diaschisis which represents the functional and/or metabolic background for the understanding of the cognitive role of the cerebellum framed on the merging concept of cortico-subcortical circuits determining human behavior.

These studies revealed that: i) four patients with unilateral cerebellar infarction display contralateral frontoparietal hypoperfusion; the "reverse" cerebellar-cerebral diaschisis is described; ii) patients with Freidreich's ataxia and olivo-pontocerebellar atrophy could display either a limited cerebellar hypoperfusion of varying degrees (7 cases) or a cerebellar hypoperfusion associated with unilateral or bilateral fronto parietal or parietal hypoperfusion (11 cases). The cerebellar frontal and cerebellar parietal loops underlying the role of the cerebellum in cognitive thought were therefore confirmed by SPECT studies.

FRIDAY JUNE 16TH — P.M.

Evoked Potentials

47.

Clinical Experience with Cortical Magnetic Stimulation

A.A. EISEN, W. SHYTBEL and S. BOHLEGA (Vancouver, British Columbia)

Motor evoked potentials (MEPS) were elicited using a Dantec magnetic coil. Potentials were recorded referentially from a variety of muscles, whilst under minimal voluntary contraction. Over 100 control subjects aged between 15 and 85 years have been studies without significant side effects.

Normal cortex to target muscle latencies measured: 20.2 + 1.6 msec (thenar), 14.2 + 1.7 msec (extensor digitorum communis), 9.4 + 1.7 msec (biceps), and 27.2 + 2.0 ms (tibialis anterior). Central motor delay (CCT) between the cortex and lower cervical spine measured 6.5 + 2.0 ms (using F wave subtraction) and 6.0 + 1.2 ms (stimulating the root of the neck with the coil). CCT between the cortex and dL5 measured 12.1 + 3.8 ms. Mean spinal cord motor conduction velocity measured 75.9 m/sec. MEP amplitude expressed as a percentage of the maximum M wave was never less than 20% of the M wave. A value of less than 15% is considered abnormal.

The following patients have been studied: ALS (N=45), MS (N=40), Parkinson's disease (N=18), Huntington's disease and their relatives (N=22), Stroke (N=2), Guillain-Barre syndrome (GBS) (N=2). In Parkinson's and Huntington's diseases, the MEP and CCT were normal. In ALS there was modest slowing of CCT (mean 7.7±2.1 ms). The hallmark was a very small MEP; unrecordable if bulbar features were prominent. In MS CCT was often very delayed. Compared to the SEP abnormal MEPS were seen more frequently. In 2 patients seen 3 months after hemiplegic stroke, despite good functional recovery, the MEP was small and delayed. In GBS it was possible using MEP latencies to document proximal motor slowing.

48.

Cerebellar Evoked Potentials Recorded from the Rat

R.J. HURLBERT, M.G. FEHLINGS, G. NIZNIK, R.D. LINDEN and C.H. TATOR (Toronto, Ontario)

Currently no single electrophysiological test monitors integrity of all spinal cord tracts. Somatosensory and motor evoked potentials, though useful, may not adequately reflect the integrity of the ventral funiculus. It has been suggested that cerebellar evoked potentials might fulfill this function. Therefore, in the present study, we have recorded and characterized the cerebellar evoked potentials (CEPs) in a rat model. Under alphachlorolose and urethane anesthesia, the dura over the right paramedian lobule in 17 animals was exposed with a burr hole placed 2 mm inferior to the occipital protuberance and 2 mm to the right of midline. Laminectomies were performed at C5-T1 and T9-10. CEPs were elicited by applying constant current anodal stimuli (10 mA,50 us, 8.2 Hz) to the cerebellar cortex; 512 responses were recorded from microelectrodes in the T9 spinal cord at a bandwidth of 30-3000 Hz and averaged.

The CEPs consisted of five negative and four positive waves. The mean latencies (and SD) for N1, P1, N2, P2, N3, P3, N4, P4, and N5 were 1.10 (0.05), 1.31 (0.07), 1.60 (0.08), 1.94 (0.09), 2.30 (0.10), 2.63 (0.12), 2.91 (0.19), 3.45 (0.30), and 3.81 (0.29) ms respectively. Similarly, the mean amplitudes were 15.10 (17.11), 10.41 (4.04), 35.67 (13.17), 48.17 (23.04), 40.88 (17.72), 22.13 (9.65), 9.37 (7.06), 15.00 (6.11), and 6.56 (4.20) uV. Fifteen animals were evaluated with cord lesions made with a #11 scalpel blade at the C6 level. Dorsal column lesions and posterior hemisection had little effect on CEPs while ventral hemisection extinguished the response. This paper represents the first characterization of CEPs in rats. The results indicate that CEPs are conducted through ventral funiculi of the rat spinal cord. This technique is potentially of great value for experimental spinal cord injury research and for the neurophysiological monitoring of patients with acute cord injury or those at risk for the same.

49.

Longitudinal VEPs and Neurological Outcome of Full-Term Birth Asphyxia

M.J. TAYLOR, S.C. MUTTITT, L.J. MacMILLAN and H.E. WHYTE (Toronto, Ontario)

Birth asphyxia is a major cause of neonatal mortality and morbidity, yet it is difficult to accurately predict neurological outcome. We have found VEPs to be useful in short-term prognosis; the current study compares the VEPs recorded serially, in the initial days of life and at 3, 6, 9, 12 and 18 months, with the neurological outcome at 18 months. VEPs were recorded to binocular LED stimulation from Oz, referenced to Fz; ERGs were recorded from an infraorbital lead referenced to Fz.

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The studies were completed in 46 full-term asphyxiated neonates who were classified clinically as mild, moderate or severe asphyxia, as defined by Apgar score <3 at 10′, or a combination of Apgar <6 at 5′, fetal distress by cord gases, late decelerations, meconium staining and/or neurological abnormalities.

It was found that the VEPs were most usefully classified into normal (i.e., normal or only transiently abnormal (returning to normal within one week)) or abnormal (prolonged absence or abnormalities) studies. The most useful VEPs prognostically were those recorded during the first week of life, as the VEPs tended to normalize eventually (6 weeks to 9 months later) regardless of outcome. They were most useful in neonates who were moderately asphyxiated, whose outcome is most difficult to predict clinically. In this group the VEPs had a positive predictive value of 91% (sensitivity 91%, specificity 94%). Thus we conclude that early VEPs demonstrate good correlation with long-term neurological outcome in full-term birth asphyxia.

50.

Using the Derived Narrow-band ABR to Assess Ototoxicity

S.G. COUPLAND, C.W. PONTON, S.L. MIKI and J.J. EGGERMONT (Calgary, Alberta)

The audiogram can be electrophysiologically estimated by one of three methods: (i) by using frequency-specific stimuli such as filtered clicks, tonepips or tonebursts and estimating threshold of wave V at different frequencies (Kodera et al., 1977) (ii) through using the broad-band click one can infer that overall hearing is normal or abnormal based upon latency and amplitude parameters (Galambos and Hecox, 1977); unfortunately, this technique provides little information about frequency-specific hearing loss or the shape of the audiogram (iii) by the use of a broad-band click stimulus combined with high-pass filtered noise allows one to derive narrow-band responses and obtain an accurate estimate of the audiogram (Don, Eggermont, and Brackmann, 1979). We will report the results of 2 years experience using the derived narrow-band ABR technique to monitor frequency-specific changes in pediatric oncology patients at-risk to develop ototoxicity. This patient group is especially at-risk to develop high-frequency sensorineural hearing loss resulting from combinations of chemotherapeutic agents (cis-platinum) and aminoglycosides. The high-pass noise masking ABR screening protocol determines the derived narrow-band ABRs to 60 and 30 dbHL clicks at octave intervals having center frequencies of 11.3, 5.6, 2.8, 1.4, .7, and .2 kHz. respectively. Pediatric oncology patients are seen prior to and during chemotherapy regimen and on a near monthly basis for several months following treatment (until ABR changes have stabilized). We have successfully detected abnormalities in the higher frequencies in a significant proportion of cases *before* they were documented behaviorally using pure-tone audiometry. The superiority of the derived-band ABR over the standard broad-band click ABR in the assessment of frequency-specific hearing impairment will be demonstrated.

Epilepsy

51.

Hemispherectomy: Indications

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

Hemispherectomy is the procedure of choice to treat medically refractory seizures in patients suffering from hemiplegia. Decision to carry out hemispherectomy is based on the critical analysis of the patient's clinical seizures, neurological examination, radiological and electroencephalographic investigation. In the Montreal Neurological Institute (MNI) series of 55 hemispherectomies, etiologies for the brain damage responsible for the seizures were birth trauma (19 pts), inflammatory disease (26 pts), head injury (5 pts), Sturge Weber Syndrome (3 pts), CVA (1 pt), and developmental abnormality (1 pt). In cases of chronic encephalitis and Sturge Weber syndrome, consideration to carry out hemispherectomy early, before maximum hemiplegia, is indicated. Most patients had more than one seizure pattern but focal motor seizures predominated in 36 patients, epilepsia partialis continua in 8 patients, sensory-motor in 4 patients and generalized tonico-clonic in 7 patients. The radiological investigation, with skull x-ray, CT scan and MRI demonstrated atrophy of different degree, occasionally bilateral but worse on the side of the affected hemisphere. Electro-encephalography showed diffuse background abnormality, with low amplitude, widespread slow waves, spikes or sharp waves on the affected side. In over half of the cases, the abnormalities were lateralized to the affected hemisphere only, while in the others generalized spike and wave activity were seen – interpreted sometimes as reflecting the integrity of the good hemisphere. Independent multifocal epileptic abnormalities were often recorded from the disease hemisphere.

The objective of the investigation in hemispherectomy candidates is to determine the degree of damage of the affected hemisphere and the degree of integrity of the "good" hemisphere. In well selected patients, hemispherectomy controls or reduces significantly the seizure tendency in 85% of the cases. The earlier the procedure is carried out and seizure control obtained, the greater will the benefit be to the patient.

52.

The Prognosis of Epilepsy Surgery in Childhood

D.R. FISH, L.F. QUESNEY and T. RASMUSSEN (Montreal, Quebec)

The prognostic factors for a good response to epilepsy surgery were studied in 118 children. The median age at operation was 13 years (range 6 months to 15 years), and median follow-up 15 years (range 2-37 years). 73 patients had temporal lobectomies and 45 patients had frontal lobe excisions. Overall 56 patients became seizure free or averaged 2 or less seizures per year. The following were associated with a more favourable outcome: temporal lobectomy, ECoG spiking restricted to one lobe, and the finding of a focal structural lesion at operation. 14 out of 18 patients with temporal lobe excisions and a previous febrile seizure had a good outcome. There was a tendency for a less favourable outcome in patients with secondary generalization, multiple partial seizure patterns, or generalized background EEG abnormalities. All patients had multiple EEGs, and 51 had ictal recordings. The correlation between preoperative EEG and ECoG, pathology and outcome will be discussed.

53.

Is Carbamazepine-10, 11-Epoxide Neurotoxic?

A. AL-QUDAH, P. HWANG, S. SOLDIN and E. GEISBRECHT (Toronto, Ontario)

Carbamazepine-10, 11-epoxide (CBZ-E) is a major metabolite of carbamazepine (CBZ). CBZ-E has received recent attention because of its possible adverse side effects. Schoeman et al. (Dev. Med. Chi. Neu, 1984, 26:756-764) reported that a CBZ-E plasma level above 9 μM/L is more often associated with side effects than lower levels. We retrospectively reviewed health records of 88 children aged 6-16 years (mean: 12.1) on CBZ therapy for at least 3 months. CBZ-E and other antiepileptic dugs (AEDs) plasma levels were measured concurrent with their neurologic evaluation. Three groups of patients were identified. Monotherapy group (n = 48), polytherapy group without neurotoxicity (n = 36) and polytherapy group with neurotoxicity (n = 4). All 4 neurotoxic patients had plasma levels of CBZ and other AEDs within the therapeutic range but their plasma CBZ-E values were high (mean = 15.8 μM/L, range 11-23). The incidence of neurotoxicity on polytherapy group was 4/40 (10%) whereas none of the patients on monotherapy

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was toxic. CBZ-E plasma levels of the polytherapy group (11.3 μM/L) was significantly higher than the CBZ-E plasma levels of the monotherapy group (6 μM/L) ($p < 0.01$), t-test).

We conclude that CBZ-E may contribute to the neurotoxicity of the CBZ. We recommend monitoring plasma levels of CBZ-E in children on combination of CBZ and other AEDs.

54.

The Influence of Microsomal Metabolism on Valproate Toxicity Assessed *in Vitro* Using Human Lymphocytes

K. FARRELL, F.S. ABBOTT, J.S. WADDELL, A.K. JUNKER and S.P. SPIELBERG (Vancouver, British Columbia; Toronto, Ontario)

The incidence of severe valproate (VPA) hepatotoxicity is higher in patients receiving polytherapy. Several antiepileptic drugs induce cytochrome P-450 mediated hepatic microsomal metabolism. Microsomal metabolism is involved in the formation of 4-ene VPA, a metabolite which induces hepatic steatogenesis in rats. We have examined the effect of microsomal metabolism on the toxicity of VPA using an *in vitro* human lymphocyte system.

Isolated human lymphocytes from 17 healthy adult volunteers were incubated with VPA in the presence and absence of microsomes prepared from the livers of phenobarbital-induced mice. Cell death was measured by trypan blue dye exclusion. A concentration-dependent toxicity was observed in the presence of microsomes and an activating system containing NADPH. The mean cell toxity at 1,000 ug/mL VPA was 15.5±3.0% in the presence of microsomes and 0.3±0.5% in their absence. Minimal toxicity was observed when the activating system was omitted (1.4±0.9%), the microsomes were inactivated by boliling (0.8±1.1%), or when 5 mM cimetidine was added to the incubation medium (2.0±0.8%). The VPA toxicity at 1,000 ug/mL was greater using microsomes from phenobarbital-induced mice compared to phenobarbital-induced rats. The difference in toxicity using microsomes from mice and rats is consistent with the species difference in the microsomal mediated formation of 4-ene VPA.

These data are consistent with the involvement of microsomal metabolism in the formation of a toxic VPA metabolite. This method of measuring VPA toxicity may be useful in studying the mechanisms underlying severe VPA hepatotoxicity.

55.

Add-on Trial of Clobazam in 36 Intractable Epileptic Patients, with Plasma Level Correlations

A. GUBERMAN, A. SHERWIN and K. BLASCHUK (Ottawa, Ontario; Montreal, Quebec)

Clobazam, a 1,5-benzodiazepine with a double ketone radical has been used as an anti-epileptic drug in Europe for over 10 years. It has been shown to be effective in a variety of intractable seizure types but tolerance with escape from seizure control is reported in up to 1/3 of cases.

We have used clobazam as an add-on drug in 36 uncontrolled epileptic patients including 24 with complex partial and generalized tonic-clonic seizures, 2 with complex partial seizures alone, 3 with generalized tonic-clonic seizures alone and 3 with Lennox-Gastaut syndrome. 26 patients were idiopathic, 10 of known etiology. 10 patients had had previous neurosurgery for epilepsy control or removal of arteriovenous malformation.

Five patients had to abandon the drug within 2 months due to side effects and in 3 of these the drug was clearly ineffective. In 5 other patients the drug was stopped due to ineffectiveness and 2 of these also had side-effects. There were 12 patients with complete control of seizures, most of whom had a combination of complex partial and/or generalized tonic-clonic seizures. Mean follow-up in this group was 10 months (range 5-18). An additional 9 patients had a greater than 50% reduction in seizures with mean follow-up of 10.5 months (3-16). The mean daily dose in responders was 41.4 mg. Three additional patients escaped from initial control within the first 6 months. No serious side-effects were seen and the most common side-effect was drowsiness in 11 cases.

Plasma levels of clobazam and its active metabolite N-desmethyl clobazam were measured in several patients and related both to response and toxicity. Plasma levels of concurrent anti-epileptic drugs were not altered on clobazam.

Clobazam is a very effective well-tolerated add-on agent especially in patients with complex partial and/or generalized tonic-clonic seizures. Tolerance was less of a problem than in most previous studies.

56.

Clobazam in Treatment of Childhood Epilepsy – A Double Blind Cross-Over Study

D. KEENE, S. WHITING and P. HUMPHREYS (Ottawa, Ontario)

The purpose of this paper is to report the results of a double blind cross-over study comparing Clobazam to placebo in the treatment of childhood epilepsy.

The patients between the ages of 6 months and 18 years of age, with greater than 4 seizures a month, were considered for entry into this study as long as they did not have any underlying degenerative Central Nervous System (CNS) disorder or poor drug compliance. Prior to entry parental consent was obtained. After a one month pre-study period in which seizure frequency was recorded, the patients were entered into the study which consisted of 2 parts (active drug or placebo) each 3 months duration with a 1 month cross-over phase. Monthly clinic visits with pill counts were done, as well as SGOT, CBC, Thyroid Studies and EEG every 3 months. Success was considered if there was 50% reduction of frequency in the major seizure form in either phase over pre-study seizure frequency. During the Clobazam phase 51 patients (52%) had greater than 50% reduction in their seizure frequency in comparison to pre-study phase. During the placebo phase no patients had a significant reduction in their seizure frequency in comparison to pre-study phase. The mean Clobazam dosage in the success group is 0.75 mgm/kg compared to 0.65 mgm/kg in the nonsuccess group. Sex, age, seizure type, intellect did not appear to differentiate between Clobazam responsive patients from those nonresponsive. In only 2 patients significant deterioration behaviour occurred while on the drug which required the patients to drop out of the study prematurely. No other significant side effects occurred during this study.

This study would support the use of Clobazam as an add-on drug in the treatment of refractory epilepsy in childhood.

EEG

57.

Alpha, Theta and Alpha-Theta Coma EEG Patterns

G.B. YOUNG, W.T. BLUME and V. JACONO (London, Ontario)

The purpose of this study was to examine the individual and relative importance as well as the evolution of 3 specific EEG patterns: alpha coma (AC), alpha-theta coma (ATC) and theta coma (TC).

Inclusion criteria were: 1. coma at time of EEG; 2. predominant alpha and/or theta frequencies throughout the recording; 3. no alteration of initial pattern by stimuli or passive eye opening. Cases of barbiturate intoxication were excluded.

Cases were classified as AC if the predominant frequency was in the alpha band, TC if a theta rhythm predominated and ATC if both alpha and theta were equally represented.

There were 7 AC patients, 14 ATC and 16 TC patients. No significant difference was found for age, sex and etiology among the 3 groups. Two AC, 3 ATC and 3 TC patients recovered consciousnessness ($p > .05$).

AC, ATC and TC patterns lasted less than 7 days in all but 4 patients. Among the 8 survivors subsequent EEGs from each group showed continuous and variable rhythms with reactivity to stimuli. Those who died in each group showed burst-suppression or suppression patterns without reactivity.

We conclude that there is no difference among AC, ATC and TC patterns with respect to their clinical importance and evolution. Although each pattern was associated with a high mortality, none was reliable for predicting outcome. Prognostically useful recordings can usually be obtained within one week from coma onset, when the AC, ATC or TC pattern has subsided.

58.

Status Epilepticus Partialis With or Without Overt Ictal Clinical Manifestations. Relevance of Analysis of EEG Abnormalities

F. GRAND'MAISON and J. REIHER (Sherbrooke, Quebec)

In patients with status epilepticus partialis (SEP), the more subtle the ictal clinical manifestations, the more essential EEG monitoring becomes. How prolonged need it be?

Our review of EEG-monitored SEP in 100 patients establishes that most seizures are larval or clinically subtle, and that EEG documentation is necessary to distinguish ictal and post-ictal stupor from non-epileptic stupor.

Furthermore analysis of ictal (IAs) and interictal (IIAs) abnormalities reveals that the following cascading sequence is stereotyped and of utmost practical value in patient management:

a) Continuous seizures without IIAs
b) Closely spaced seizures, post-ictal exhaustion (PIE) without IIAs
c) Closely spaced seizures, PIE and sparse IIAs
d) Sporadic seizures, PIE and abundant IIAs
e) Sustained repetitive IIAs, not to be mistaken for IAs
f) Sporadic IIAs
g) Resolution of IIAs.

While the persistence of repetitive IAs calls for mandatory EEG monitoring and vigorous I.V. treatment, the emergence of IIAs heralds the beginning of a favorable seizure outcome. The most frequent initial IIAs are periodic lateralized epileptiform discharges (PLEDs) with afterdischarges. Prominent afterdischarges being associated with a high incidence of recurrent seizures, further EEG monitoring is advisable. With resolution of afterdischarges and arrest of seizures, sporadic EEG sampling becomes optional, and IV anticonvulsant therapy no longer warranted.

59.

Evoked Potentials Versus MSLT for Assessing Sleepiness in Narcolepsy-cataplexy

R.J. BROUGHTON and M. AGUIRRE (Ottawa, Canada and Monterrey, Mexico)

A direct comparison was made between the amplitude of the evoked potential component P3 using the P300 paradigm and the sleep latency on the Multiple Sleep Latency Test to assess the degree of sleepiness in 11 untreated patients with narcolepsy - cataplexy compared to matched controls. There were 6 males and 5 females in each group aged 22-63 (mean 45.5, sd 14.6, in narcoleptics). Repeated P3 measures (lasting approx. 7 min.) were done immediately before standard 20 min. MSLT naps at 1000, 1200, 1400, 1600, and 1800 hrs. Significant group differences were seen in both variables with a lower amplitude component P3 and shorter mean sleep latency in narcoleptics. Using discriminant analysis and F tests, both the P3 amplitude and the mean sleep latency were found to distinguish the 2 groups at the $p < .0001$ level for collapsed 5-nap data. They also showed parallel circadian time of day effects with greatest sleepiness in the afternoon. Both tests, however, misclassified some subjects as coming from the other group with rather more misclassifications occurring by P3. Even single tests provided some degree of differentiation of groups. It was concluded that EPs have considerable promise for the rapid diagnosis of excessive daytime sleepiness narcolepsy and probably also in other neurological sleep disorders.

(Supported by the Medical Research Council of Canada)

60.

Pupillography Does Not Detect Excessive Sleepiness in Narcolepsy-cataplexy

J. NEWMAN and R.J. BROUGHTON (Ottawa, Ontario)

Pupillometry has been widely quoted as a sensitive and accurate measure of sleepiness since pioneering studies in narcolepsy by the Mayo Clinic group. However, each of the reports of such changes from various centers are flawed by experimental weaknesses. These include lack of normal control groups, inappropriate statistics and other. We decided to do a controlled study. Six male and four female narcoleptics (mean age 48.6, sd 13.6) were compared to sex and age (mean 49.0, sd 13.8) matched controls and had pupillometry measures done for 15 min. immediately prior to standard Multiple Sleep Latency Test naps scheduled at 1000, 1200, 1400, 1600, and 1800 hrs. The pupil measures involved a repetition of: 8 min. dark adaptation, response to 11 tone stimuli, rest period, and response to 10 light stimuli. Stanford Sleepiness Scale was filled every 30 min. Although narcoleptics were subjectively (higher SSS scores, $p < .025$) and objectively (shorter mean sleep latency on MSLT, $p < .002$) sleepier than controls, there were no pupillometric differences in resting pupil diameter or in reflex responses to light or to sound stimuli, as the literature might predict. The only difference was a larger number of spontaneous oscillations in narcoleptics ($p < .001$). This was also the only effect of sleepiness in sleep derived normals in a recent report (Herz et al. 1988). It appears that the pupillogram, as currently used, is *not* a reliable measure of sleepiness.

Neurosurgery

61.

Photon Beam Treatment of Arteriovenous Malformations Using Dynamic Radiosurgery

A. OLIVIER, E. PODGORSAK, A. DELOTBINIERE, L. SOUHAMI, B. PIKE and G. BERTRAND (Montreal, Quebec)

Dyanamic radiosurgery using a linear accelerator was developed at McGill University. Its principle resides in the continuous and simultaneous rotation of both the head and the accelerator photon beam around a common isocenter which provides sharp fall off of the radiation outside the target volume.

Target determination and dose-structures correlations are established with specially designed stereoactic software.

Our experience with the first 30 cases of arteriovenous malformations treated by this modality at the Montreal Neurological Institute and McGill University is presented. Results for 10 patients having had angiography at or around 1 year post-treatment is available. 5 patients have had total occlusion of the arteriovenous malformation, 3 patients have had occlusion in the order of 85-90% and 2 patients in the order of 50% or less. Complications have been oedema and hemiparesis in one patient and rebleeding in 2 patients.

The combined use of stereotactic DSA and MRI permits the use of small target volume in relation to lesion volume, thus decreasing the risk of necrosis to neighbouring structures.

62.

Impact of Recent Technological Advances On Endovascular Therapy of Brain Arteriovenous Malformations and Fistulas

J.E. DION, F. VINUELA, G. DUCKWILER, N. MARTIN, S. JORDAN and J. BENTSON (Los Angeles, California)

PURPOSE: Over the past few years, there have been numerous technological improvements relating to therapeutic endovascular procedures performed for AVMs and AVFs, including: new, flexible microcatheters not dependent on balloon navigation for proper placement, (Tracker, Progressive Suppleness Pursil Catheter), alternate embolic agents, improved detachable systems, continuous computerized EEG monitoring with superselective amytal provocative test, MRI, improved digital angiographic systems. The purpose of this study was to determine if these advances had substantially increased both the safety and efficacy of brain AVM and AVF embolization procedure.

MATERIALS & METHODS: The authors describe their experience in 40 patients (65 embolizations) and contrast the results with their prior experience in embolization of over 125 brain AVMs.

RESULTS: Over the past eight years, the permanent neurological morbidity for AVM embolization has fallen from 18.8% to 7%. Mortality rate decreased from 4.3 to approximately 2%. The percentage of obliteration of nidus superior to 75% has risen from approximately 35 to 60%. When surgery followed embolization, the operation was performed with significant economy of time and blood loss. Lesions too large for radiotherapy were reduced in size and rendered treatable.

CONCLUSION: Embolization of brain AVMs and AVFs remains at the present time an adjunct to surgery and radiotherapy, which are facilitated. Calibrated-leak balloon systems should be avoided whenever possible. No immediate technical complications such as ruptured vessels occurred in the present series. The advent of new technologies and increasing operator experience seem to have reduced morbidity (and possibly mortality), while percentage occlusion of nidus has increased.

63.

Arterial Wall Changes in Cerebral Vasospasm

J.M. FINDLAY, B.K.A. WEIR, K. KANAMARU and F. ESPINOSA (Kingston, Ontario)

A unilateral right-sided subarachnoid hemorrhage (SAH) was created in 12 monkeys which were then followed angiographically for 7 to 14 days. The right middle cerebral arteries (MCAs) developed significant VSP, maximal 7 days after hemorrhage, while the left MCAs remained unchanged from baseline. At sacrifice the MCAs were harvested for fixation and scanning and transmission electron microscopy (SEM and TEM). Four normal left MCAs were vasoconstricted *in vitro* prior to fixation with prostaglandin $F_{2\alpha}$. Vessels in maximal VSP 7 days from arteries vasoconstricted *in vitro*, both groups demonstrating a 57% reduction in lumen caliber and a five-fold increase in vessel wall thickness. On TEM, however, arteries in SAH induced VSP possessed degenerative ultrastructural changes in the tunica intima and media. These changes were still evident at 14 days, despite considerable resolution of VSP. These findings, as well as those from other pathological studies of animal and human cerebral arteries in VSP, suggest that the arterial narrowing and vessel wall thickening seen within several weeks of SAH is due primarily to vasoconstriction, but unlike physiologic constriction, is associated with degenerative ultrastructural changes in the endothelium and vascular smooth muscle cells. These morphological abnormalities may be markers of temporarily irreversible smooth muscle contraction. Long term arterial stenoses due to exuberant intimal proliferation and fibrosis occur in some patients, for uncertain reasons.

64.

The Effect of Timing of Intrathecal Fibrinolytic Therapy on Cerebral Vasospasm in a Primate Model of Subarachnoid Hemorrhage

J.M. FINDLAY, B.K.A. WEIR, K. KANAMARU, M. GRACE and R. BAUGHMAN (Edmonton, Alberta; San Francisco, U.S.A.)

The effect of intrathecal recombinant, tissue plasminogen activator (rt-PA) administered at times from 0 to 72 hours after subarachnoid hemorrhage (SAH) on the development of cerebral vasospasm (VSP) in primates was examined. Thirty monkeys were randomized into one of 5 equal groups: a control group which underwent SAH alone, and 0, 24, 48 and 72 hour treatment groups which received 0.75 mg of sustained-release gel rt-PA at those times after baseline cerebral angiography and right-sided SAH. Seven days later angiography was repeated and the animals sacrificed. One animal in the 72 hour group developed a delayed ischemic deficit on day 7 after SAH. In the control and 72 hour groups significant VSP occurred in most of the major, right-sided cerebral arteries ($p < 0.05$), but no significant VSP developed in the 0, 24 and 48 hour groups. While a large subarachnoid clot remained in the control animals, most clot had been cleared in all treatment groups. Clearance of subarachnoid hematoma with intrathecal rt-PA within 72 hours of SAH is effective in preventing VSP in primates.

65.

Pharmacological Studies on Relaxation of Spastic Primate Arteries

K. KANAMARU, B.K.A. WEIR, J.M. FINDLAY, C.A. KRUEGER and D.A. COOK (Edmonton, Alberta)

Vascular responses to acetylcholine (ACh), histamine (His) and the calcium ionophore A23187 were studied in rings of primate middle cerebral arteries (MCAs) (N=16). In preparations with an intact endothelium, which has been precontracted by prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), His and A23187 produced significant relaxation. The same concentrations of His and A23187 did not relax vascular tissues in which the endothelium had been mechanically removed. ACh did not produce significant endothelium-dependent relaxation of primate MCA rings, but did relax rings of primate common carotid artery. On the other hand, His and 23187 induced significant relaxation in both preparations. Pretreatment with chlorpheniramine, an H_1-receptor antagonist, prevented His-induced relaxation, however, cimetidine, an H_2-receptor antagonist, had no inhibitory action. It thus seems that histamine mediates relaxation of intact MCA mostly by an H_1-receptor mediated release of endothelium-derived relaxing factor (EDRF). In a further series of experiments, seven days after unilateral placement of clot in the Sylvian cisterns of primates, the MCAs from both sides were removed and vascular responses were compared. His- and A23187-induced relaxations were substantially reduced on the clot side of MCA. On the non-clot side of MCA, these relaxations were completely preserved. However, endothelium-independent relaxation induced by glyceryl trinitate (GTN) occurred in both preparations. Constrictions induced by KCl and $PGF_{2\alpha}$ were also reduced on the clot side of MCA. These results suggest that subarachnoid hemorrhage influences both constriction and endothelium-dependent relaxation of affected arteries. The small contraction which can be elicited in spastic arteries can be fully relaxed by GTN *in vitro*.

66.

Genetic Probing of Cerebral Aneurysms

R. LEBLANC, A.M. LOZANO, M. VAN DER REST and R. GUTTMAN (Montreal, Quebec)

It has been suggested that patients with cerebral aneurysms may have a relative deficiency of type III collagen, predisposing them to

aneurysm formation and rupture, and suggesting that cerebral aneurysms may be genetically determined lesions. If type III collagen deficiency is important in the etiology of cerebral aneurysms it should be demonstrable in patients with a clear family history of cerebral aneurysms and in patients with multiple aneurysms.

To test this hypothesis, we established skin fibroblast cell cultures of 5 patients who had a total of 13 cerebral aneurysms including one patient with 3 aneurysms whose mother had 2 cerebral aneurysms and whose sister had one. The HLA antigens were identified in 8 members of this family who also underwent elective angiography. Collagen studies were performed in duplicate on two separate cultures. Three control cell lines as well as cell lines from a patient with Ehlers-Danlos type IV (E-D IV) syndrome, were analyzed simultaneously, also in duplicate.

Cultured skin fibroblasts were labelled with [^{3}H]-proline. Collagens and procollagens were precipitated and run on gel electrophoresis after reduction to analyze procollagen chains. Quantitation of the ratios of type III to type I procollagen synthesis was achieved by integration of the intensities of the pro-α1(III)/pro-α1(I) bands on fluorograms of electrophoretic gels of medium proteins.

There was no difference in types I and III procollagen levels in the cells from the aneurysm patients and in those from the control cell lines, but there was a clear deficiency of type III collagen in the E-D IV patient. There was no association between specific HLA antigens and the presence of cerebral aneurysms.

These data do not support the hypothesis that either familial or multiple sporadic cerebral aneurysms are caused by a deficiency of type III collagen. Normal type III collagen levels do not exclude the presence of cerebral aneurysms in family members, nor does a specific HLA antigen identify those at risk.

67.

Cortical Mapping Under General Anesthesia (GA)

R. LEBLANC, M. ABOU-MADI, A. OLIVIER and D. TROP (Montreal, Quebec)

Cortical mapping under local anesthesia (LA) is well established in the resection of epileptogenic brain tissue. We have also used it extensively for the first stage treatment of cerebral arteriovenous malformations (AVMs) involving eloquent brain regions, where cortical mapping under LA is followed by clipping of the major feeding arteries. In some epileptic patients, and in brain tumour patients, it is sometimes not feasible to operate with LA because of poor cooperation or fear of major intraoperative seizures. For AVMs LA often precludes definitive resection at the initial operation which must then be accomplished at a later stage under GA with induced hypotension. The present study describes a technique of balanced GA in which a pneumatic tourniquet is applied to the arm contralateral to the craniotomy allowing cortical mapping to be performed under GA. The tourniquet effectively isolates the arm opposite to the craniotomy from the effects of neuromuscular blocking agents, preserving motor response to cortical stimulation. GA is induced with fentanyl, droperidol, and methohexital or thiopental and is maintained with nitrous oxide in oxygen with increments of fentanyl and atracurium as needed. Thirty minutes before cortical mapping neuromuscular blockage is allowed to wear off. Three minutes prior to stimulation of the cortex the cuff is inflated above systolic blood pressure to produce vascular occlusion and atracurium is administered to achieve motor paralysis of the body.

Using this technique we have been able to satisfactorily map out the sensory-motor strips in patients undergoing craniotomy for cerebral AVMs, brain tumours, and resection of epileptogenic cortex.

Examples will be shown demonstrating that this technique is useful for the treatment, under GA, of cerebral AVMs, brain tumours and fronto-temporal seizure disturbances where identification of the sensory-motor strip is required for safe resection.

68.

Microscope Assisted Lumbar Discectomy in an Ambulatory Care Setting: Medical and Economic Considerations

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

Our experience with microscope-assisted lumbar discectomy, now includes over 150 cases. Because of high patient acceptance of the procedure, several management innovations have been gradually introduced. When a number of patients were deemed fit for discharge the day following surgery, it became apparent that a selected group of patients could be treated exclusively in an ambulatory care setting. Added impetus resulted from economic considerations related to bed closures, and add-on funding which accrues to out-patient surgery.

We report our pilot project of an initial 10 patients, and compare medical and economic factors with an equal number treated on an in-patient basis. An out-patient CT scan and/or myelogram is done prior to surgery. The patient is then admitted early on the day of operation, maintained in the Recovery Room after the procedure, and discharged at 0800 hours the following morning.

Analgesic requirements were minimal, and there was no need for community nursing services. A post-operative survey indicated a high degree of patient satisfaction, with this form of management. Our experience would indicate that this is safe, and justified for both medical and economic reasons, in a selected group of patients.

69.

A Survey of Pre-operative and Post-operative Electromyographic Recordings in Patients Undergoing Microvascular Decompression for Primary Hemifacial Spasm

G.S. MOSBY, P. MOLINA-NEGRO, J. HARDY and G. OUAKNINE (Montreal, Quebec)

Seventy-two cases of microvascular decompression (MVD) performed for the diagnosis of primary hemifacial spasm, involving sixty-five patients at two institutions over a fifteen-year period, were reviewed in a retrospective manner. Of these cases, forty have been followed in an ongoing prospective manner, with respect to their pre-operative and post-operative electromyographic (EMG) studies of the trigemino-facial ("blink") and facio-facial reflexes, according to the method described by Molina and classified according to the system proposed by Molina and Esteban, with modification. Of the forty cases, the authors have data and preliminary results of 28 cases involving 24 patients (four of which required re-operation). Of the 28 cases of MVD with minimum one year follow-up, fifteen were clinically cured or substantially improved (53.6%). Twelve were shown to be unchanged (42.9%) and one case was noted to become worse (3.6%). Of the fifteen cases found to be cured or improved, six (40%) were shown to have a pre-operative EMG classification indicating afferent and efferent defects of the facial nerve. Conversely, no patient from this classification failed to improve clinically and in seven of the twelve clinically improved cases for which complete post-operative EMG results were available, (58.3%) were noted to have complete normalization of their trigemino-facial and facio-facial reflexes on EMG, compared to one of eleven (9.1%) of the clinical failure group. The authors believe this study is significant in that it strongly suggests a predictive role for EMG study of both the trigemino-facial and facio-facial reflexes in the selection of patients for MVD for primary hemifacial spasm.

70.

Intraspinal Injection of Exogenous Schwann Cell and Fetal Spinal Cord Suspensions After Spinal Cord Injury: Morphological and Behavioral Assessment

M. KHAN, K. LEFEBVRE, M. POLITIS, G. GOPLEN, R. GRIEBEL and K. KHAN (Saskatoon, Saskatchewan)

The post-traumatic glial environment of the spinal cord does not support axonal elongation from intrinsic CNS axons. The present study represents a series of experiments aimed at replacing the reactive glial and/or degenerating neuronal circuitry by injecting exogenous cell suspensions into injured spinal cord. Spinal cords of 200 gram rats were exposed to a 400 gm/cm weight drop lesion at T8. In the first study, Schwann cell-enriched suspensions were obtained from the right sciatic nerve of the same animal and injected into the dorsal columns on either side of the lesion. Control rats received intraspinal injections of fibroblasts or saline. By 3 weeks post-op, animals treated with Schwann cells showed increased strength of withdrawal reflexes, improved function on the inclined plane, and the presence of myelinated axons in the dorsal columns rostral to the injury site. No such changes were seen after intraspinal injection of autologous fibroblasts. Studies are in progress to determine the relative beneficial effects of intraspinal injection of suspensions obtained from fetal/neonatal spinal cord and peripheral nerve after injury of adult host cord tissue.

General Neurology

71.

Pathology of "MELAS" and "MERRF". Morphological and Biochemical Studies

B. LACH, D. PRESTON, S. SERVIDEI, G. EMBREE, S. SWIERENGA and S. DIMAURO (New York, U.S.A.)

We present pathological findings in three family members with maternally inherited mitochondrial encephalomyopathy. The mother died at the age of 54 with multi-infarct dementia, quadriplegia, deafness and ataxia, approximately 18 years after onset of MELAS (myopathy, encephalopathy, lactic acidosis and stroke-like episodes). One of her two daughters with non-progressive MERRF syndrome (myoclonus epilepsy with ragged-red fiber myopathy, RRF) since the age of 16, died suddenly at the age of 23. Another daughter showed a transition of MERRF to MELAS and died at 24, after several years of progressive disease characterized by dementia, deafness, ataxia, strokes and focal seizures.

Ultrastructural examination revealed extensive accumulation of mitochondria in pericytes and smooth muscles (SM) of vessels in all patients. The endothelial basal lamina was often markedly thickened. RRF were found in the mother and one daughter while mitochondrial vascular abnormalities and obliteration of capillaries were the only changes in the daughter biopsied early in the course of MERRF. All the patients showed excess of mitochondria in the myocardium and visceral SM. Smaller numbers of abnormal mitochondria were also found in many other tissues, and they persist in the tissue cultures. Mitochondrial enzyme deficiency was not found biochemically. The brains of patients with MELAS revealed obliterative vasculopathy with laminar cortical necrosis. The mother also showed multiple intracerebral microaneurysms. The brain of the daughter with MERRF was microscopically unremarkable; however, abnormal mitochondria in vascular wall cells were demonstrated ultrastructurally. It is postulated that generalized mitochondrial abnormalities in members of this family are most dramatically expressed in the cells of vascular walls. Involvement of the endothelium, pericytes and smooth muscles of the vessels is responsible for development of vasculopathy affecting predominantly CNS. Ischemia of the affected tissues leads to clinical manifestations of MELAS and MERRF, and probably contributes to development of RRF myopathy.

72.

Mitochondrial Function in Friedreich's Ataxia

A. ABDOLLAH, E. ANDERMANN, P. MATTHEWS and D.L. ARNOLD (Montreal, Quebec)

Deficiencies of various mitochondrial enzymes have been implicated in Friedreich's ataxia based on indirect evidence from study of non nervous system tissue. Phosphorous magnetic resonance spectroscopy (MRS), which provides a means of assessing mitochondrial function non-invasively *in vivo*, has demonstrated impaired mitochondrial function in muscle in patients with mitochondrial disorders, including those primarily involving brain. We therefore obtained proton MRI/phosphorous MRS examinations of brain and muscle in 8 patients with typical Friedreich's ataxia. MRI, concentrations of phosphate-containing metabolites and intracellular pH were normal in both brain and muscle of all the patients except one. This patient had an atrophic cerebellum on MRI (not a feature of Friedreich's ataxia) and an elevated inorganic phosphate concentration in his muscle (a feature of mitochondrial disorders).

Thus phosphorous MRS provides no evidence that the basic defect in Friedreich's ataxia leads to significant and widespread mitochondrial dysfunction. On the contrary, it suggests that the presence of such abnormalities in patients suspected of Friedreich's ataxia should raise the suspicion of another phenotypically similar disease.

(Supported by the Canadian Association for Friedreich's ataxia)

73.

Current Prevalence of Amyotrophic Lateral Sclerosis and Parkinsonism-Dementia Complex on Guam

J.C. STEELE, L. LAVINE, A. WORKMAN, *B. SCHOENBERG, M. ALBERT, G. GLOSSER, N. WOLFE and L. KURLAND (Agana, Guam; Bethesda, Boston, Rochester, U.S.A.)

Thirty-five years ago, door-to-door surveys by Kurland and Mulder showed remarkably high rates of amyotrophic lateral sclerosis (ALS) in Umatac and Merizo, adjacent villages in southern Guam. We recently resurveyed these villages in respect to ALS and parkinsonism-dementia complex (PDC). A census of the entire population was carried out and 95% of all residents 40 years and older had detailed neurological and psychological testing.

In Umatac, 211 of 813 residents were 40 years and over. Of those, 19 (9%) suffered ALS and/or PDC and/or dementia. Seven patients, four of them women, had parkinsonism with or without dementia. Eight others, all women, had only dementia. Eleven of these 15 patients with parkinsonism and/or dementia were between 52 and 65 years of age. Two patients had ALS and two had both ALS and PDC (i.e., mixed). Only three people in the village were older than 75 years, and all were demented women.

Among Merizo's 1,515 residents, 394 were 40 years and over. Of these 12 (3%) suffered ALS and/or PDC and/or dementia. Six women and one man had dementia alone, and two men had parkinsonism with dementia. Six of the nine were older than 78 years, and the youngest (dementia alone) was 61 years. Two men (69 and 79) had mixed ALS/PDC. Only one patient, born in 1950, was identified to have pure ALS. Twenty-one residents were older than 75 years and seven suffered PDC.

These results confirm earlier impressions that the clinical manifestations of ALS/PDC have altered over time. The incidence of ALS has decreased, but PDC remains prevalent and dementia without parkinsonism, among women, is now as remarkably common as was ALS among men in the 1950s. In Umatac, the prevalence of dementia corresponds to the prevalence in the mainland United States of those aged 85 years. The average age at onset or ALS/PDC is now at least 10 years older than in earlier studies, and this suggests a cohort effect from a period source exposure several decades ago.

The strikingly different rates and ages at onset of ALS/PDC between these villages is likely to relate to different exposure to the etiological agent(s) of this unusual disease, a paradigm of neurofibrillary degeneration.

74.

The Epidural Stimulation in the Treatment of the Refractory Angina

S.N. MARTINEZ, R.M. GAGNON, C. ROY, D. RENE, D. SAVARD, Y. GOULET and M. MORISSETTE (Montreal, Quebec)

Since 1979, at Notre-Dame Hospital, we are using epidural stimulation as treatment for chronic pain. At this day, 215 patients have been treated this way but since March 1988 only, we have been using this technique in refractory angina.

The long term effects of this epidural stimulation for our patients suffering of ischemial neuropathy and from observations from different colleagues around the world brought us to adopt this treatment in the application of the stimulation in refractory angina cases. The 3 parameters retained concerning the efficacity of the epidural stimulation on the autonomic system are: the increase of the blood pressure at fingers level, the increase of the temperature at the skin level and the increase of the micro-circulation (natrium-fluorescein injection).

The anginose pain is at "sustained sympathetic" character such as ischemical neuropathy cases. The mechanisms by which the epidural stimulation takes off and improves the hemodynamics of the sanguine flood at the heart level are not very well known. We think that the effect of the stimulation equals to a functional sympathectomy.

Three patients suffering from refractory angina have had an implantation of epidural electrode. After 1-2 weeks of stimulation, the 3 of them observed a real improvement of the anginose syndrome (confirmed by the effort test) with decrease of the nitroglycerin consumption and a better quality of life.

From patients chosen carefully, we believe that the epidural stimulation seems a valuable approach for the treatment of such a disabled anginose syndrome. To our knowledge, this is the first time the epidural stimulation as treatment for the refractory angina has been used in Canada.

75.

Neurological and Neuropsychological Effects of Chronic Hypoxia

D.A. GUZMAN, I. PETERKIN, D.T. STUSS and C. GUZMAN (Ottawa, Ontario)

Patients with COPD have documented neuro-behavioural dysfunction. Previous studies compared COPD patients only with healthy controls, thus not isolating the deficits solely attributable to chronic hypoxia. This study is unique in matching a chronically hypoxic COPD case group (n=9) to a non-hypoxic COPD control group (n=9).

Case and control groups were well matched for age, education, language, nature of disease and smoking history. Case-control characteristics differed only in mean arterial pO2 (52.1 mm Hg *vs* 70.3, $p < .001$) and in mean arterial pCO2 (53.7 mm Hg *vs* 40.4, $p < .01$).

Evidence of known motor manifestations of COPD were found equally in both case and control groups on neurological examination. EEGs revealed diffuse slowing in 3 of 8 cases tested; none of the 7 controls tested showed any such slowing. CT scanning demonstrated a more marked cerebral cortical atrophy in cases than in controls.

Two major areas of deficit in behavioural functions were discovered. Case patients were significantly slower in speed of mental processing, as on the Trail-Making Test Part B (219 seconds to completion *vs* 88.7 seconds, $p < .005$), and on the Paced Authority Serial Addition Task (78.1 correct out of 240 *vs* 133.6 correct, $p=.01$). These results significantly correlated with arterial pO2 ($p < .01$).

Secondly, the chronic hypoxic group had significantly impaired memory, both immediate as on the Digit Span (9/15 *vs* 11/15, $p < .005$), and short-term memory on the Wechsler Memory Scale (Memory Quotient 105 *vs* 127, $p < .01$).

COPD does cause measurable neurobehavioural deficits. These are directly related to the chronic hypoxia. Deficits reflect both diffuse brain dysfunction (speed of information processing) as well as the known sensitivity of the hippocampus to oxygen debt (memory disturbance).

Cerebrovascular

76.

Rescue of Ischemic Brain by Selective Venous Retroperfusion of Arterial Blood

J.E. DION, J. FRAZEE, S. JORDAN, S. KAR, F. VINUELA, R. RAND and ELLIOT CORDARY (Los Angeles, California)

PURPOSE: Human myocardial ischemia has been successfully reversed by coronary sinus retroperfusion. The purpose of the present experiment is to evaluate the feasibility, safety, efficacy of venous retroperfusion of arterial blood for the rescue of ischemic brain in the baboon.

MATERIAL & METHODS: Nine baboon experiments were performed; six determined the techniques and safety of retroperfusion, three the ability of retroperfusion to reverse cerebral ischemia. Using halothane anesthesia, specially developed balloon catheters were passed into both sigmoid sinuses. During retroperfusion, arterial blood was continuously circulated by an external pump from a femoral artery to one jugular catheter while balloons at catheter tips repeatedly occluded both jugular bulbs in a cyclical fashion. Ischemia was produced by temporary middle cerebral artery occlusion by a snare and by selective embolization of large particles in the distal intracranial internal carotid artery. Brain mapping monitored the onset and reversal of ischemia.

RESULTS: Brains were examined to determine injury from retroperfusion. Retroperfusion exceeded 49ml/min, with a median intrasinus pressure increase of 29 mmHg (0-143 mmHg) in all experiments. Venograms demonstrated complete or partial filling of the superior sagittal sinus in each experiments. Four experiments without ischemia established maximal balloon occlusion cycles, perfusion flow rate and sinus pressure changes (in two additional experiments death occurred secondary to anesthetic or surgical complications). The animals were clinically neurologically normal after retroperfusion, confirmed by MRI scans in two. EEG suppression following middle cerebral artery occlusion was reversed with retroperfusion in all three ischemia experiments. Autopsy demonstrated no parenchymal hemorrhage.

CONCLUSION: These results suggest that, as in the heart, retroperfusion is feasible and may rescue ischemic brain; further study is warranted.

77.

Transcranial Doppler in Acute Ischemic Stroke

Y.M. LUO, R.L. BONDAR and J.W. NORRIS (Toronto, Ontario)

Using daily transcranial Doppler (TCD) examination of each cerebral hemisphere, we investigated 50 patients with acute ischemic stroke for the first 10 days after their admission to an acute stroke unit.

The peak blood flow velocity of the middle cerebral artery (MCA-BFV) in the stroke side was compared to the unaffected side. In 32 patients the MCA-BFV in the affected hemisphere was normal compared to the unaffected side and normal controls. In the remaining 18 patients, MCA-BFV were either increased or decreased in the infarcted hemisphere. All those with abnormal BFV were severe strokes with predominantly cortical lesions on CT scan.

Of 12 patients with decreased BFV, 8 had ipsilateral carotid occlusion. Of the 6 patients with increased MCA-BFV, 5 were embolic strokes and SPECT scanning confirmed cerebral hyperperfusion. Outcome was better in patients whose BVF returned to normal within the first week.

Our preliminary data suggest that TCD may aid in the diagnosis of cerebral embolism, and be a useful predictor in outcome.

78.

Management of Massive Cerebellar Infarction – Our Experience

M. KHAN, R. GRIEBEL, M. SUNDARAM, G. GOPLEN, K. CHANDLER and K. LEFEVRE (Saskatoon, Saskatchewan)

Massive cerebellar infarction is the result of an occlusion of the vertebral basilar trunk or one of its branches and is associated with high mortality and morbidity rates. Most authors recommend urgent suboccipital craniectomy and resection of the swollen and/or hemorrhagic cerebellar tissue as the treatment of choice. This procedure is not free of serious complications, since it has to be performed in elderly people with comprised circulatory systems which comprise the vast majority of patients with cerebellar infarctions. The rapid and progressive deterioration with coma and death can be attributed to, 1) associated extensive brain stem infarction, 2) direct compression of the brain stem by swollen cerebellar tissue in association with tonsillar or upward transtentorial herniation, or 3) total or partial obliteration of the 4th ventricle resulting in obstructive hydrocephalus. During the recent years we have encountered 20 patients with large cerebellar infarctions. Twelve patients showed evidence of acute obstructive hydrocephalus on CT scan examination. These patients were treated by controlled external ventricular drainage. The remaining 8 patients were managed conservatively. There was one death in each group as a result of progressive brain stem infarction. The clinical course and outcome of these 20 patients will be reported. Our results would suggest that prompt treatment of the acute obstructive hydrocephalus may obviate the need for posterior fossa decompression in most patients with massive cerebellar infarction.

Multiple Sclerosis

79.

Inhibition of Anti-myelin Basic Protein Neutralization by Cerebrospinal Fluid of Patients With Chronic Progressing Multiple Sclerosis.

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

Autoantibodies to myelin basic protein (anti-MBP) can be detected by radioimmunoassay in free (F) and bound (B) forms in the cerebrospinal fluid (CSF) of multiple sclerosis (MS) patients with active disease. Acute relapses are characterized by an elevated, above unity, F/B anti-MBP, while in contrast, patients with chronic progessing MS have a low, below unity F/B anti-MBP. As patients with acute relapses enter into remission, the F/B anti-MBP gradually decreases, and eventually when remission is complete, anti-MBP becomes undetectable.

An anti-MBP neutralizing effect by CSF from MS patients in clinical remission was demonstrated in 29 of 31 autologous and homologous experiments. Elevated CSF anti-MBP from patients with acute relapses were neutralized by increasing amounts of CSF with undetectable anti-MBP from patients in clinical remission. This did not occur when CSF with undetectable anti-MBP from non MS controls were substituted for the remission sample while CSF with elevated anti-MBP from prositive controls produced a cumulative effect.

Chronic progressing MS is characterized by persistence of elevated CSF anti-MBP over long periods of time. Inhibition of anti-MBP neutralization was observed in the CSF of 21 of 23 MS patients with progressive disease. If CSF with known neutralizing ability, from a patient in remission, was firstly reacted with CSF from a patient with progressive MS, the resulting "mixture" substituted for the remission sample did not produce anti-MBP neutralization. CSF from MS patients with progressive disease produced inhibition of anti-MBP neutralization.

80.

Computerizing Clinical Data in MS Clinics

D.R. STUDNEY and D.W. PATY (Boston, U.S.A.; Vancouver, British Columbia)

A unique, powerful and cost-effective computer system for neurological clinical research has been developed and extensively tested in several Canadian Multiple Sclerosis (MS) clinics. The major distinguishing features of this system include; behavior as a computerized medical record rather than a database system, derivation from public-domain Computer Stored Ambulatory Record (COSTAR) software which has had world-wide distribution and clinical use, extensive search and analysis capability, and provision for confidential data pooling among cooperating users for clinical epidemiology and clinical trials.

To use the system, a microcomputer of the IBM PC/AT or equivalent type with at least 10mb of available disc storage space is required. Clinical data including all signs, symptoms, physical exam and test results are entered in plain text and are self-encoded by the system's extensive internal directory with subsequent filing on an intrinsic time axis. There is no practical upper and lower limit on the number of patients or amount of clinical data which may be entered; these may be captured concurrently with clinical care or input retroactively as required without undermining the time base accuracy.

Clinical information may be retrieved both on an individual case basis or by comprehensive searches of aggregate demographic and clinical data. The format of reports and display documents as well as the context of searches is specified by the individual user, and in general does not require programming ability.

This system (MS-COSTAR) has proved to be an effective and reliable means of supporting a wide range of clinical research in MS, and may have value in the study of similar chronic disorders where long term and precisely-documented clinical observation is important.

Poster Presentations

THURSDAY, JUNE 15TH

Neurobiology

P1.

The Effect of Direct Current Fields on Injured Spinal Cord Axons is Polarity Dependent

M.G. FEHLINGS and C.H. TATOR (Toronto, Ontario)

Direct current (DC) fields appear to promote the recovery of acutely injured mammalian spinal cord axons. In vitro experiments suggest that polarity is of critical importance to the mechanism of action of DC fields on neurites. In the present experiment the effect of DC field polarity was studied *in vivo* in a rat model of cord injury. After a 53 g clip compression injury of the cord at T1, the rats were randomly and blindly allocated to one of three groups of 10 rats each; one group received implantation of a DC stimulator (14 uA) with the cathode caudal to the injury site; a second received implantation of a similar stimulator with the cathode rostral to the lesion; a third group received a sham (0 uA) stimulator. 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 recorded and the axonal tracer horseradish peroxidase (HRP) was introduced into the cord at T6. The total number of HRP-labelled cells was counted in

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sections through the brainstem and motor cortex and a computer-assisted morphometric analysis of axons at the injury site was performed.

The inclined plane scores ($p<0.0001$), MEP amplitude ($p<0.02$), counts of neurons retrogradely labelled by HRP ($p<0.0001$), and axon counts at the injury site ($p<0.01$) were significantly greater in the group treated with a DC field with the cathode caudal to the lesion than in the sham-treated group or in the group in which the DC field was of reversed polarity. These results show that the polarity of the field is critical to the effect of a DC field on the acutely injured cord. The polarity dependence suggests that DC fields may attenuate intracellular influx of cations and thus reduce the extent of posttraumatic axonal degeneration.

P2.

Nerve Growth Factor and Two Proteins Associated with Neuronal Growth

V.M.K. VERGE, W. TETZLAFF, M.A. BISBY and P.M. RICHARDSON (Montreal, Quebec; Calgary, Alberta)

Observations regarding nerve growth factor (NGF) and two proteins that influence neuronal size and shape have been correlated in rat lumbar dorsal root ganglia (DRG). mRNAs for the growth-associated protein known as GAP43 and the middle subunit of neurofilament were analyzed by quantitative *in situ* hybridization with cDNA probes.

Although GAP43 expression is strongly increased by peripheral nerve injury, approximately $^2/_3$ of the lumbar sensory neurons in normal rats were also seen to contain relatively high concentrations of GAP43 mRNA. When adjacent sections of DRG were analyzed by GAP43 *in situ* hybridization and NGF receptor radioautography, grain densities over individual neurons were strongly correlated for the two populations. Given other observations in tissue culture, these findings suggest that endogenous NGF induces the expression of GAP43 in NGF-responsive sensory neurons. Furthermore, we speculate that differences among sensory neurons in basal levels of GAP43 may account for known differences in sprouting behaviour.

Expression of neurofilament is decreased following peripheral axonal injury in concert with decreased neuronal volume. Neurons with high-affinity NGF receptors atrophy more severely than those lacking receptors. The down-regulation of neurofilament in axotomized sensory neurons is counteracted by chronic infusion of NGF into the lumbar subarachnoid space.

NGF is implicated in the control of a cytoskeletal and regulatory protein both of which help to determine neuronal responses to injury.

(Supported by MRC (Canada)).

P3.

Axonal Regeneration in Two Strains of Mice

L. XIN, F. GERVAIS, E. SKAMENE and P.M. RICHARDSON (Montreal, Quebec)

Regeneration in the peripheral nervous system has been studied for two inbred strains of mice with known differences in macrophage behaviour (Journal of Leukocyte Biology *36* (1984) 357-364). Both fifth lumbar dorsal roots were crushed in adult A/J mice or C57BL/6J mice and the right sciatic nerve was cut to accelerate axonal regeneration in the corresponding root (Brain Research *411* (1987) 406-408). Two weeks later, the numbers of thinly myelinated new axons were counted in the dorsal roots near their junction with the spinal cord.

In both strains of mice as in rats, regeneration of crushed dorsal root axons was stimulated fourfold by sciatic nerve transection. More importantly, the assay with or without enhancement indicated that regenerating axons were five times more abundant in A/J mice than C57BL/6J mice. The difference between strains in axonal regeneration could reflect different neuronal responses to axonal injury or different endoneurial environments. The observations are consistent with other evidence that macrophages are implicated in peripheral nerve regeneration but are open to alternative interpretation. The detailed genetic information available for these two strains provides a valuable tool in studying mechanisms of regeneration.

(Supported by the Rick Hansen Fund)

P4.

Postnatal Mammalian Spinal Neurons and Motoneurons in Culture

C. KRIEGER and S.U. KIM (Vancouver, British Columbia)

Cultures of dissociated cells from mammalian spinal cord (SC) have been used for the study of mechanisms relevant to diseases affecting motoneurons (MNs). Generally, embryonic neurons have been used for such studies, however the use of postnatal neurons may be more appropriate as postnatal neurons may be closer in their properties to adult human neurons than embryonic neurons.

We have prepared monolayer cultures of neonatal rat and mouse SC as well as MNs using mechanical dissociation and trypsinization. MNs were purified by retrograde labelling from muscle *in situ* with fluorochromes followed by fluorescence-activated cell sorting. Neurons demonstrated acetylcholinesterase activity as well as neuron specific enolase and neurofilament immunoreactivity and these cells could be detected for at least 2 weeks *in vitro*. Labelled MNs could also be identified by these neuronal markers and these cells survived and extended processes in culture.

These observations indicate that postnatal MNs and SC neurons are capable of survival in culture. These methods may provide a useful technique to study diseases affecting the mammalian motoneuron.

(Supported by the Canadian MRC and the ALS Society of Canada)

P5.

Maternal Thiamine Deficiency and Brain Development

H. FOURNIER and R.F. BUTTERWORTH (Montreal, Quebec)

Studies of the effects of maternal thiamine deficiency in experimental animals have shown that developing rat brain is considerably more susceptible to thiamine deprivation than is that of the adult. Our aim was to study the metabolic basis for this susceptibility. The activity of three thiamine-dependent enzymes involved in carbohydrate metabolism (pyruvate dehydrogenase complex, PDHC; α-ketoglutarate dehydrogenase, αKGDH; and transketolase, TK) were measured in homogenates of brain tissue from thiamine-deficient mothers and their offspring. The study revealed region-selective delays in the establishment of adult patterns of thiamine-dependent enzymes as a result of maternal thiamine deficiency. PDHC activities in cerebral cortex of 13 days-old pups were significantly reduced (by 20% $p<0.05$); αKGDH activities were also reduced in cerebral cortex at the same age (by 30% $p<0.05$). In the case of TK, enzyme activities were significantly reduced in all three brain structures. Following thiamine rehabilitation, defective enzyme activities were restored to normal in all cases. Thiamine-dependent enzymes are important for the establishment of adult patterns of cerebral energy metabolism and possibly also in myelination. Thus, maternal thiamine deficiency resulting in reductions of thiamine-dependent enzymes at a vulnerable period in brain development could have serious metabolic consequences leading to permanent neurological dysfunction in the offspring.

(Supported by MRC in Canada and FRSQ)

P6.

Evidence for Decreased Cerebral GABA Synthesis in an Animal Model of Wernicke's Encephalopathy

R.F. BUTTERWORTH and M. HEROUX (Montreal, Quebec)

Treatment of rats with the central thiamine antagonist, pyrithiamine, results in severe neurological symptoms and neuropathological changes similar in nature and distribution to those encountered in Wernicke's Encephalopathy in man. GABA content of brain tissue from PT-treated rats was reduced in thalamus (by 45%, $p<0.01$), cerebellum (by 18%, $p<0.05$) and pons (by 30%, $p<0.05$). Activities of the thiamine-dependent enzyme α-ketoglutarate dehydrogenase (αKGDH) were reduced in parallel with the GABA changes and alanine concentrations were found to be concomitantly increased. Activities of glutamic acid decarboxylase remained within normal limits as did affinities and densities of high affinity ^{3}H-muscimol binding sites. Thiamine administration to symptomatic animals resulted in reversal of neurological abnormalities and in normalization of GABA and alanine levels and of αKGDH activities in cerebellum and pons. These results suggest that the reversible symptoms of PT treatment result from impaired GABA syntheses in pontine and cerebellar structures. Similar mechanisms may play a role in the pathogenesis of the reversible symptoms of Wernicke's Encephalopathy in man.

(Supported by MRC Canada and FRSQ)

P7.

The Application of Nonlinear Dynamics to Motor Pathophysiology

D. BORRETT, H.C. KWAN and T.H. YEAP (Toronto, Ontario)

Since a nonlinear dynamical system can be characterized by a collection of interacting elements that have properties of threshold, excitation and inhibition, its analysis is of direct relevance to the neurosciences. When suitable synaptic weights between the cellular elements are specified and the system is set in an initial condition, it will evolve in a deterministic fashion towards an equilibrium state (attractor). We conceive of a movement as relaxation of a dynamical system into a fixed point attractor, with the limb trajectory being determined by the characteristics of the relaxation process. We have modelled a system that displays the physical property of bradykinesia by a generalized alteration in the excitability of the constituent elements. In a similar fashion, other disorders affecting the motor system such as tremor, rigidity and chorea can be modelled by specific alterations in the parameters of the system. Since neurotransmitters such as dopamine may diffusely alter neuronal responsiveness, the conceptualization of movement in the nonlinear dynamical idiom is relevant to the understanding of the pathophysiology of disease affecting the motor system.

(Supported by the Toronto East General Hospital Research Foundation, and the Medical Research Council of Canada)

P8.

Phenotypic Transformation by Hypercholesterolemia of the Arterial Wall: A New Model for the Study of Cellular Angiogenic Response in Atherosclerosis Using the Rabbit Cornea

Y.G. COMAIR and S. BREM (Montreal, Quebec)

The pathogenesis of atherosclerosis is complex and multifactorial. Key initiating events leading to migration and proliferation of smooth muscle cells are difficult to study using present models of atherosclerosis. Emphasis has been placed on the role of endothelial damage in promoting these changes. In order to investigate the effect of hypercholesterolemia on the phenotypic expressions of smooth muscle cells, a new model was developed. Twelve normal rabbits and 11 diet induced hypercholesterolemic rabbits (3 weeks, 2% added cholesterol Rabbit Chow) underwent autografts of the right carotid artery media into a corneal pocket fashioned in each eye. The procedure was well tolerated. In hypercholesterolemic rabbits, the angiogenic response was brisker and more severe compared to normal rabbits as assessed by frequency of response (85% vs 33%), average vessel number at day 7 (42 vs 10) and vessel length (1.75 mm vs 0.75 mm). No angiogenic response was noted over empty pockets placed in each eye as a control. A lipid infiltration was noted in hypercholesterolemic animals preceding the angiogenic response and progressing to the formation of a plaque like appearance. This was absent in normal animals. Histological examination revealed a strong infiltration by inflammatory cells with neovessels and cellular lipid accumulation. In the normal animals there was preservation of the implant with occasional neovessels and minimal inflammatory cells.

We conclude that a short hypercholesterolemic diet is sufficient to induce phenotypic changes of smooth muscle cells resulting in expression of angiogenic-chemotactic factors independent of endothelial cell injury. This new model proves to be valuable in the study of these early events and their modulation.

P9.

Loss and Restoration of ATP after Rat Brain Ischemia Using NMR Spectroscopy

J.C. DE LA TORRE, T. FORTIN, J. SAUNDERS and J. McTAVISH (Ottawa, Ontario)

Nuclear magnetic resonance (NMR) spectroscopy was used to measure high energy cerebral metabolites following induction of partial or zero blood flow to the brain. A rat model of ischemia developed in this laboratory was used to reduce mean cerebral blood flow (CBF) levels by 60-100% of control values. Two variables were examined: the time course needed for brain adenosine triphosphate (ATP) and phosphocreatine (PCr) to fall or disappear after partial or total ischemia and their restoration following post-ischemic reperfusion. All rats were prepared by ligating both subclavian arteries (to abolish vertebral artery supply to brain) and by placement of bilateral common carotid artery (CCA) occluders as we have previously described.[1] After full recovery, rats were anesthetized and cranial scalp and muscles were removed. Rats were placed in a Bruker Biospec 4.7 T/30 cm spectrometer and baseline values for intracellular pH, ATP, PCr and inorganic phosphate (Pi) were taken. Results show a small but apparent reduction of ATP and PCr with an inverse rise in the Pi peak 60 min after partial ischemia was induced (associated mean CBF value: 46 ml/100g/min). By contrast, ATP/PCr signals disappeared and a large Pi peak appeared 8 min after total ischemia (associated mean CBF value: "0" ml and a flat EEG). Brain intracellular pH at this time was 6.5. When both CCA were released, ATP/PCr signals reappeared within 25 min. and progressively normalized while Pi peak gradually shifted to its original position. These findings show that neuronal viability as reflected by ATP/PCr levels is not permanently impaired after short duration severe ischemia if rapid post-ischemic reperfusion can be established.

(Supported by the Canadian Heart Foundation)

1. de la Torre J, Fortin T, Thakar J. Soc Neurosc Abstr 1988; 14: 1211.

P10.

The NMDA Receptor in Focal Ischaemia: Is It Important?

M.C. WALLACE, D. DEWAR, A. KURUMAJI, G.M. TEASDALE and J. McCULLOCH (Toronto, Ontario; Glasgow, Scotland)

The implication of excitatory amino acids in cerebral ischaemia has led to the use of N-methyl-D-Aspartate (NMDA) receptor antagonists as therapeutic agents. This study investigates the NMDA receptor recognition site and its associated ion channel and explores the functional integrity between the receptor and channel after experimental focal ischaemia.

Adult Sprague-Dawley rats (n=17) underwent middle cerebral artery occlusion (MCAO). Three animals underwent sham occlusion. In vitro receptor binding was carried out at 6, 12 and 24 hours after the onset of ischaemia. NMDA binding was done with [3H]-glutamate (200nM) and [3H]-MK-801 (10nM) was used to assess binding of the associated ion channel. Non-specific binding was determined in the presence of 100uM NMDA and 100uM MK-801 respectively. Films exposed to brain sections after binding were quantified by densitometry. Homogenate binding with [3H]-MK-801 (10nM) was performed on tissue obtained from animals (n=16) 12 hours after MCAO. Regions of brain demonstrating overt infarction did not have significant changes in either [3H]-glutamate or [3H]-MK-801 binding. Homogenate binding with [3H]-MK-801 in ischaemic cortex demonstrated a small reduction (94±16fmoles/mg protein), but retained its sensitivity to exogenous glutamate (10μ) which provoked a 400 fold increase in binding.

The integrity of the NMDA receptor and its retained capability to open its associated ion channel long past the onset of ischaemia has been demonstrated in this study. Although this study does not determine therapeutic window for NMDA antagonists in focal ischaemia, the integrity of the receptor is not the limiting factor regarding these agents' therapeutic effectiveness.

P11.

Water Suppressed Localized Proton Magnetic Resonance Spectroscopy of Human Brain *In Vivo*: Preliminary Observations

D.L. ARNOLD and P.M. MATTHEWS (Montreal, Quebec)

Although localized phosphorous magnetic resonance spectroscopy of human brain *in vivo* has been possible for several years, localized proton spectroscopy has only recently become feasible owing to the technical difficulty of suppressing the signal from the protons of water, which overwhelms the signal from low concentration metabolites that are of interest for spectroscopy. Using a Philips Gyroscan operating at 1.5 Tesla, we are now able to acquire localized water-suppressed proton spectra routinely in a clinical setting. Localization is based on a selective refocused stimulated echo while water suppression is achieved using a combination of binomial excitation and saturation by DANTE pulses.

Proton spectra of normal human brain show three main peaks attributable to choline, creatine/phosphocreatine, and n-acetylaspartate. Using the standard reference for proton spectroscopy, water is located at 4.8 ppm and these peaks are located at approximately 3.2, 3.0, and 2.0 ppm, respectively. A resonance at 1.3 ppm has been unequivocally identified as arising from lactate on the basis of its T2, spin-spin coupling and phase modulation with different echo times. A number of minor peaks can also be seen which have yet to be definitely identified. The method is in principle quantitative allowing metabolite concentration changes in pathological conditions to be identified.

P12.

Extinguishing Lipofuscin Autofluorescence Facilitates Immunofluorescence Histochemistry on Human Brain Tissue

W. STAINES, B. LACH and T. HOKFELT (Ottawa, Ontario; Stockholm, Sweden)

A very great deal is known about the distribution of neurotransmitter synthetic enzymes and neuropeptides in the brains of experimental animals under both normal conditions and after experimental manipulations meant to model certain aspects of human disease conditions. To a degree, this greater understanding of animal brain is due to the greater ease of techniques with which questions of immunolocalization may be addressed. One of the great barriers to working with postmortem human brain encountered by ourselves and others is the lipofuscin-derived autofluorescence which tends to overwhelm the specific immunofluorescent signal when the tissue is examined or photographed. We have found that the application of Sudan Black IV to the sections in either its native or acetylated form extinguishes the autofluorescence of lipofuscin and greatly facilitates detection and photography of the immunofluorescence histochemical signal under study. There appears to be no or little attenuation of the antigenicity of the neuropeptides or transmitter synthetic enzymes. "Before and after" examples will be presented on the application of the procedure to immunofluorescence histochemistry of somatostatin and neuropeptide Y in human postmortem forebrain.

Neuro-oncology

P13.

Rapid Cellular Kinetics of Intracerebral Tumor Angiogenesis Using a Monoclonal Antibody to Bromodeoxyuridine

S. BRIEN, D. ZAGZAG and S. BREM (Montreal, Quebec; New York, U.S.A.)

The microvasculature of brain tumors is an attractive target for angiostatic therapies. Previous methods to quantitate angiogenesis *in situ* have relied on histologic parameters of VEC cytology, hyperplasia and density, but failed to give a measurement of DNA synthesis or EC proliferation.

The recent development of a monoclonal antibody to the thymidine analogue, BUdR, enables the rapid intracerebral detection of S-phase cells. An immunohistochemical stain to BUdR, in the rabbit brain tumor model of angiogenesis (Am J Pathol *131*: 361, 1988), provides a reproducible assay of neovascularization and demonstrates the interdependency of the VEC and TC compartments. Endothelial proliferation is prominent at the tumor periphery with a labeling index (LI) of 25.8±12.8%, compared to the LI at the tumor center, 1.7±3.0%, in contrast to the non-tumor bearing contralateral hemisphere, less than 0.001%. Similar labeling indices were obtained with tritiated thymidine as a control. The high rates of endothelial proliferation correspond to the high LI of the TC, 26.6±8.4% at the periphery and 7.7±3.8% in the tumor center. DNA synthesis in the tumor cells is inversely proportional to the distance from the nearest capillary.

The quantitative cytokinetics demonstrate the close interdependence between tumor cell and vascular endothelial cell proliferation. BUdR can be used to measure angiogenesis and its inhibition *in situ*.

P14.

Radiographic and Autopsy Findings in Sagittal Sinus Thrombosis Due to L-Asparaginase

N.J. LOWRY and B. ROZDILSKY

Eleven days prior to death, this 9 year old started treatment for acute lymphatic leukemia. The protocol was that of the Children's Cancer Study Group and consisted of prednisone, vincristine, L-asparaginase, intrathecal methotrexate and allopurinol. Nine days later she became unable to walk and developed urinary incontinence. She was oriented and her cranial nerve exam was normal; her optic discs were normal. She had exaggerated deep tendon reflexes in her lower limbs with bilateral extensor plantar responses. A spinal cord epidural hematoma was the suspected diagnosis and a myelogram was performed. The myelogram was normal. CSF — no cells. Normal protein. (0.13 G/L), prothrombin time was normal 10 sec (control 10). Partial thromplastin time was 28 sec (control 30). A CT brain scan was ordered but within 12 hr of the myelogram she deteriorated and became comatose with fixed dilated pupils and absent brainstem reflexes. CT showed extensive edema of the left hemisphere with some small areas of hemorrhage in the left frontal area. Her clinical condition remained unchanged and she died four days later. Autopsy revealed thrombosis of the sagittal and transverse sinuses with cerebral edema and herniation. In 1981 Steinhertz et al. first reported the occurrence of two cases of cerebral

venous sinus thrombosis due to asparaginase. One presented with hemorrhagic infarction, they felt the cause was hypercoagulability due to low levels of antithrombin III. Both their cases had a subacute onset and anteriographic diagnosis led to successful treatment with IV heparin and fresh frozen plasma. This rare but treatable complication should be considered when unusual neurologic symptoms present in patients treated with L-Asparaginase.

P15.

The Astrocytic Lineage in Medulloblastoma

B.L. MARIA, D. WONG and V.I. KALNINS (Toronto, Ontario)

The assessment of the astrocytic lineage in medulloblastoma has been limited by the paucity of immature cell markers and rests largely on the detection of the glial fibrillary acidic protein (GFAP). Astrocyte progenitor cells from the mouse neopallium express the vimentin-type intermediate filaments (proastroblast stage) before they acquire GFAP (astroblast stage) *in vivo* and *in vitro*. The purpose of the current study was to determine if cells of the astrocytic lineage obtained from medulloblastoma express these stage-specific markers and are similar to immature astrocytes of the developing mouse brain. Astroglia were cultured from the tumor specimens of a focally GFAP-positive posterior fossa medulloblastoma at initial presentation and at the time of clinical recurrence, two months later. More than 80% of cells in both tumors contained vimentin while fewer than 1% of cells contained GFAP. In both tumors, occasional clusters of malignant GFAP-positive cells and clusters of cells negative for vimentin and GFAP were identified. One hundred percent of cultured astroglia from both tumor specimens contained vimentin and less than 30% of cells expressed GFAP. When cells were cultured in the presence of dibutyryl cyclic AMP (dBcAMP), time-lapse video microscopy showed that they developed fine cytoplasmic processes by cavitation of a fan-like expanse of cytoplasm, by leaving a trailing process behind as they moved and by direct extension of a forward moving process from the cell soma. DBcAMP also reversibly suppressed proliferation, increased the number of cells with GFAP and increased the amount of vimentin and GFAP per cell. These results suggest that astrocyte progenitors which are derived from medulloblastoma and cultured *in vitro* may be at a developmental stage which corresponds to the proastroblast stage in the developing mouse brain. Medulloblastoma cells in tumor sections which contain vimentin but no GFAP may be in maturation arrest *in vivo* at the proastroblast stage of normal astrocyte development while vimentin and GFAP-negative islands of cells may represent astrocyte progenitor cells at an earlier stage of differentiation (eg. glioblasts).

P16.

Incidence and Clinico-Pathological Features of Meningioma

G.R. SUTHERLAND, M. ROHRINGER, D.F. LOUW and A.A.F. SIMA (Winnipeg, Manitoba)

The incidence of intracranial meningioma in Manitoba was reviewed, from 1980 through 1987. One hundred and ninety-three tumors were diagnosed with a male to female ratio of 1:2 and corresponding to crude incidence rates of 2.3/100,000 for all meningiomas and 0.17/100,000 for malignant meningiomas. Among malignant meningiomas, the male to female ratio was 1:1. The age specific annual incidence rate increased with age up to the eighth decade, where it peaked at 8.4/100,000. The distribution of histopathological subtypes was 74 (38%) meningotheliomatous, 64 (33%) transitional, 14 (7%) malignant, 14 (7%) fibroblastic, 7 (4%) psammomatous, 4 (2%) angioblastic, and 16 (8%) unknown. The diagnosis of malignant meningioma was based on the World Health Organization criteria with only grades III and IV tumors included in this subtype. Clinical features did not allow for differentiation of benign from malignant neoplasms. Individuals with malignant tumors were, however, more likely to suffer paresis (50%) and less likely to be without any deficit (14%) than their benign counterparts. The radiographic appearance of "mushrooming" was observed only in patients with malignant meningioma. In addition, the malignant tumors were not calcified and all had evidence of peritumoral edema. During the eight-year study interval, ten (71%) of the 14 malignant cases recurred. Tumor recurrence was accompanied by dedifferentiation from a more benign histology in four patients (2%).

P17.

Comparison of Metabolite Levels in Human Epileptic Brain Tissue and Brain Tumors Using ^{1}H NMR Spectroscopy

G. SUTHERLAND, J. PEELING, M. DONNELLY and J. GIRVIN (Winnipeg, Manitoba; London, Ontario)

High resolution ^{1}H nuclear magnetic resonance (NMR) spectroscopy has been used to quantify the levels of numerous small metabolites (alanine, glutamate, glutamine, gamma-aminobutyric acid (gaba), N-acetylaspartate (naa), aspartate, taurine, glycine, acetate, creatine, cholines, myo-inositol) in surgical biopsy material obtained from patients with epilepsy and intracranial neoplasms. Tissue was immediately frozen in liquid nitrogen, extracted with perchloric acid, neutralized, and lyophilized. Each sample was dissolved in D_20 containing 0.75 mM TSP as an internal concentration and chemical shift reference. ^{1}H NMR spectra were assigned by comparison with spectra of pure compounds, and quantified by integration. Spectra were similar for brain tissue from active and inactive surface electrode sites except in these cases where the tissue showed evidence of either dysplasia or infarction. Metabolite levels in hippocampal tissue, which was generally gliotic, differed from the levels in surface tissue. Spectra of tumors differed markedly from those of tissue samples obtained from epileptic patients. Mannitol, administered perioperatively, was observed only in the spectra of tumor samples, in keeping with their known endothelial permeability. Although the spectra of the tumor samples were highly variable, some significant differences were observed between meningiomas and gliomas. Gliomas were highly variable, with levels of all metabolites decreasing towards the center of the neoplasm, corresponding to pathologically defined necrosis. The absence of naa and gaba in the tumors reflects the neuronal origin of these metabolites. Elevated alanine and taurine, an increased glutamine/glutamate ratio, and decreased levels of the other observed metabolites, indicate a significant difference in metabolic processes in tumors compared to brain.

P18.

Co-existence of Neuropeptide-Y and Somatostatin in P19 Embryonal Carcinoma-Derived Neurons

D.J. MORASSUTTI, W.A. STAINES and M.W. McBURNEY (Ottawa, Ontario)

The mouse P19 embryonal carcinoma (EC) cell line has been shown to differentiate into neurons, astrocytes, and fibroblasts in response to retinoic acid (RA) treatment. The differentiated cell types obtained are dependent on the concentration of RA present, suggestive of naturally occurring gradients of growth substances *in vivo*. A definitive neuronal phenotype is first present 6 days following induction with RA and it has previously been shown that catecholaminergic and GABAergic subpopulations exist. Synapse formation has been demonstrated as early as 15 days following RA exposure.

In an effort to further characterize these EC-derived neurons, we found that they also contain a subpopulation which is immunoreactive for neuropeptide-Y (NPY), as well as another population which is immunoreactive for somatostatin (SOM). Most interestingly there exists another subpopulation in which NPY and SOM co-exist. This co-existence is initially weak, and found only occasionally at 7 days, but becomes firmly established by 14 days. The observation that these two neuropeptides are found together within neurons, and indeed the pro-

portion of double to single labelled cells, is similar to that found in the rodent forebrain. This suggests that these EC-derived neurons follow a developmental path similar to that of CNS neurons. Since EC cells offer the opportunity for genetic manipulation prior to the induction of neuronal differentiation, this cell line offers a unique opportunity for the study of the molecular events involved in CNS neurotransmitter phenotype development, *in vitro*.

P19.

Primary Malignant Brain Tumors in a Northern Community in Canada

M. KHAN, R. GRIEBEL, M. SUNDARAM, G. GOPLEN, K. CHANDLER and K. LEFEVRE (Saskatoon, Saskatchewan)

This presentation deals with several aspects of Primary Malignant Brain Tumors (PMBT) in a community of half a million people in Northern Saskatchewan (North of the 50th parallel). A retrospective 5 year (1982-1986) study revealed that there were 170 PMBT for an annual incidence of 7 per 100,000 population with an almost equal incidence rate for male and female (52% male). Twenty-two percent of patients were under 16 years. Ninety-four percent of patients were of caucasian origin although accounting for 75% of the population. Several etiologic factors were considered including previous head injury, family history, use of steroids, CNS infection, area of residence, occupation, blood groups, smoking, alcohol, radiotherapy, hypertension, diabetes, cerebrovascular disease and race. Apart from the racial association, all other factors were insignificant. Nine histological tumor types were considered including high grade glioma, low grade glioma, medulloblastoma, ependymoma, ganglioglioma, choroid plexus papilloma, microglioma and primary lymphoma. The relationship between various tumor types, age, location and other demographic features will be presented.

P20.

Meningioma and Pregnancy

G. HADDAD, F.S. HADDAD and J.G. VILLEMURE (Montreal, Quebec; Beyrouth, Lebanon)

We reviewed the association of meningiomas and pregnancy. All the cases of meningiomas that were operated at the Montreal Neurological Institute (M.N.I.) from 1960 to 1985 and all those operated by Dr. Fouad Haddad in Lebanon between 1955 and 1988 were reviewed. The MNI cases numbered 519 and included 81 women between the ages of 15y and 45y. Of these, 4 were pregnant (4.9%). Dr. Haddad's cases numbered 346, including 119 women in the above age bracket. Twenty-three of these were pregnant (19%). Of the 23, 7 (30%) had their symptoms exacerbated by pregnancy, 15 (65%) developed symptoms during pregnancy and 1 (4%) developed symptoms post-partum. In the MNI cases, 2 (50%) developed symptoms during pregnancy and two (50%) had their symptoms exacerbated by it. The control group for the Haddad limb of the study consisted of 42 married women aged between 15y and 45y who underwent surgery for gliomas during the same period. Nine of these were pregnant (21.5%). Of these, 1 (11%) had her symptoms aggravated by and 4 (44%) developed symptoms during pregnancy, 3 (33%) appeared post-partum.

Our conclusions are that even though meningiomas are as prevalent during pregnancy as gliomas, they tend to be exacerbated or revealed by pregnancy more often than gliomas. The difference in prevalence between the MNI and FSH figures is most likely due to the difference in natality rate between Canada and Lebanon. Further analysis and review of the literature is provided.

P21.

Isolated Cerebellar Lymphomatoid Granulomatosis

M.G. HAMILTON, B.I. TRANMER, B. CURRY and A.J. BELZBERG (Calgary, Alberta)

Lymphomatoid granulomatosis is a lympho reticular disorder characterized by angiocentric and angionecrotic cellular infiltrate. CNS involvement has been reported to occur in as many as 20% of patients but isolated CNS involvement has only rarely been reported.

We present a 60 year old male who presented with a one year history of occipital headache, a four month history of severe nausea and vomiting and 30 lb weight loss, a one month history of severe positional vertigo and a two week history of progressive right arm and leg inco-ordination. Physical examination demonstrated a right head tilt, right beating nystagmus, abnormal smooth pursuit eye movements, blink-jaw-to-right synkenesis, right arm dysmetria and marked ataxia. The remainder of the examination was normal.

A CT of the head demonstrated a large irregular nodular ring enhancing lesion in the right lobe of the cerebellum. A CT scan done 4 months before presentation was normal.

A posterior fossa craniectomy with biopsy and decompression of the lesion was accomplished. The patient required V-P shunting in the operative period. Microscopic examination was consistent with lymphomatoid granulomatosis. Viral hybridization studies were positive. The patient is currently undergoing therapy.

In summary, we present a 60 year old male presenting with cerebellar lymphomatoid granulomatosis. Isolated CNS involvement has only rarely been recognized. The controversy regarding the relationship of lymphomatoid granulomatosis to lymphoma and a possible viral origin will also be discussed.

P22.

Radiation Induced Malignant Schwannoma of the Brachial Plexus

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

Malignant schwannomas comprise less than 4% of such lesions, and are usually associated with von Recklinghausen's neurofibromatosis. Consequently, malignant schwannomas of the brachial plexus are an extremely rare entity.

A 55-year-old woman, who had undergone a right simple mastectomy followed by thoraco-axillary irradiation 20 years previously, developed a rapidly growing mass in her ipsilateral axilla. An open biopsy revealed a malignant schwannoma, and at a subsequent procedure, and 8×6×4.5 cm tumor was removed en-block from the posterior cord of the brachial plexus. Serial quick section analysis of the cord, indicated total removal. Sural nerve cable grafting was then carried out.

The histological features of the lesion, combined with the appropriate time interval from radiation treatments, and its extreme rarity as a de novo tumor, led us to conclude that this neoplasm was probably induced by radiotherapy.

P23.

The Risk of Spinal Cord Compression in a General Oncology Population and the Factors Affecting Outcome

J. KESTLE, M. RATHBONE and M. LEVINE (Hamilton, Ontario)

The development of spinal cord compression (scc) in a patient with cancer is a devastating complication associated with substantial morbidity. We were interested in evaluating whether an educational package for cancer patients at high risk of scc would be effective in bringing them to medical attention earlier in the natural history of their cord compression. To assess the feasibility of such an approach, 142 patients with scc who presented to five centres in Southern Ontario were studied in order to 1) determine the cancers at highest risk for scc and 2)

describe the clinical outcome, survival and prognostic factors in patients with scc.

The primary sites with the highest risk for scc were renal and prostate cancer. There were 8.0 cases of scc per 100 new cases of renal cancer and 4.3 cases of scc per 100 new cases of prostate cancer. Most patients (74%) had known metastases prior to scc. One hundred and twenty-one patients (85%) had difficulty walking, 116 (82%) had weakness and 109 (77%) had pain at presentation. Eighty-five patients were treated with steroids and radiotherapy and another 57 patients also had surgery. Of those treated surgically (90%) underwent posterior decompression.

Forty per cent of patients were ambulatory before treatment compared to 49% afterward (p=0.06). Seventy-four per cent of patients were catheter free before treatment compared to 62% afterward (p=0.03). The ambulatory and bladder outcomes in the patients treated surgically were not different from those treated non-surgically. Median survival was 17 weeks.

The baseline ambulatory status was the most important determinant of the ambulatory outcome. The post-treatment ambulatory status was the most important determinant of survival.

Baseline ambulatory status must be controlled in studies of therapy for scc. Although survival was short, the poor quality of life, the high cost of care of the non-ambulatory patients and the observed association between post-treatment ambulation and survival would seem to justify further attempts to improve the ambulatory outcome. Two approaches are suggested: 1) development of methods for earlier diagnosis of scc, and 2) assessment of anterior decompression as a first line treatment for scc.

P24

Criteria for the Intra-operative Diagnosis of Invasion in Pituitary Tumours

J. KESTLE and S.W. SCHATZ (Hamilton, Ontario)

A number of authors have reported a high incidence of microscopic invasion of dura by pituitary tumours but variability in the reported incidence of gross invasion reflects a lack of uniform diagnostic criteria. We have defined criteria specifically for the intra-operative diagnosis of invasion and have applied them prospectively to determine the incidence of invasion in our patient population, to describe the clinical features of the patients with invasive tumours and to assess the prognostic implications of invasion. Invasion is diagnosed during trans-sphenoidal surgery if there is obvious growth of tumour through the dura of the sellar floor or extravasation of contrast material into the subarachnoid space on the intra-operative adenomagram.

Fifteen consecutive patients had pituitary adenomas diagnosed by trans-sphenoidal surgery between December 1987 and November 1988. Eleven (73%) met our criteria for invasion — 8 through dura below, 2 through arachnoid above, 1 through both. There were 5 null cell adenomas (4 invasive), 5 prolactinomas (3 invasive), 2 gonadotroph cell adenomas (both invasive), 2 growth hormone cell adenomas (both invasive) and one functioning corticotroph cell adenoma (non-invasive).

Five of the patients with invasive tumours were men (median age 62 years), six were women (median age 51 years). The cardinal symptom was impairment of vision in 4 patients, endocrinopathy in 2 and headache in 2. Two patients experienced pituitary apoplexy. One patient's tumour was discovered during investigation of facial cellulitis. There was one invasive microadenoma. All other tumours eroded the floor of the sella (8), expanded beyond the chiasmatic cistern (7) and/or extended to cavernous sinus (3). The pre-operative serum prolactin level ranged from 141 to 4,505 ug/L for the invasive prolactinomas and from 147 to 1,846 for the non-invasine prolactinomas.

To date we have observed no features distinguishing the outcome of the patients with invasive tumours.

Conclusions: By our criteria, invasion was common. It was seen even in a microadenoma. Null cell adenomas and prolactinomas had the highest rate of invasion. Women with invasive tumours were older than expected. Assessment of the prognostic significance of invasion requires continued follow-up.

P25.

The Addition of Line Fibers in the Photodynamic Therapy of Primary Malignant Brain Tumours

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

We have treated 40 patients with primary brain tumours with intraoperative photodynamic therapy (PDT) using an argon dye pump laser and pre-operative administered hematoporphyrin derivative or diehematoporphyrin ether. In 8 recent cases, in addition to cavitary photo-illumination, we have used diffusion or line fibers to increase the amount of light energy administered to the tumour tissue.

These 8 cases had a mean age of 60 years. Two had glioblastoma and 6 had malignant astrocytoma; 5 had recurrent tumour and 2 were de novo.

Two received very little cavitary light; the remaining 6 received 1350-2700 J for a power density of 45-90 J/cm^2. The light energy delivered by fiber ranged from 60 to 675 J in the 8 cases with a light dose of 60-945 J/cm.

Six patients of the 8 are alive at time of reporting. Four patients had no post-operative complications; two had transient worsening of their neurologic deficit.

One patient who received the lowest light dose died of rapid disease progression. The two patients who received a light dose of more than 450 J/cm had acute post-operative complications. The patient who received the highest fiber light dose died of intracerebral hemmorhage. The other patient had a infraction in distribution of a photo-illuminated cerebral artery.

We concluded that the addition of diffusion fibers or line fibers can significantly increase the volume of tissue illuminated and that doses of light up to 300-400 J/cm were well tolerated. Direct photo-illumination of major arteries should likely be avoided.

P26.

Photo-dynamic Therapy of Malignant Brain Tumours

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

We are reporting our experience with intraoperative photodynamic therapy (PDT) in 40 patients with malignant primary supratentorial tumours. All patients received either hematoporphyrin derivative (HPD) or dihematoporphyrin ether (DHE) 18-24 hours preoperatively. Light (630 nm) was delivered by an argon dye pump laser; the total cavitary light energy delivered ranged from 440 to 3888 Joules and the light energy density ranged from 8 to 68 J/cm^2. In 8 patients a line fiber(s) was used to administer interstitial light as a supplement to the cavitary photo-illumination. The additional light dose ranged from 60-945 J/cm.

The 30 day post-operative mortality rate was 5% and the serious morbidity rate was 7.5%. Follow-up has ranged from 1 to 28 months. In the interval between PDT and death, the deaths per observation year was 1.03 for the whole group and 0.96 when the 2 post-operative deaths are excluded. In the interval between first diagnosis and death the rate was 0.50 deaths per observation year. The median survival after PDT was 259 days with a 1 and 2 year actuarial survival rate of 30% and 13%, respectively.

In 9 patients a complete CT scan response was identified post-PDT. These patients tended to have a tumour geometry (eg. cystic) that allowed complete or near complete light distribution to the tumour. The median survival for this group was 410 days with a 1 and 2 year actuarial survival of 57% and 28%, respectively. In the 31 cases who did not have a complete response the median survival was 196 days with a 1 and 2 year actuarial survival of 20% and 8%, respectively.

Photodynamic therapy of malignant brain tumours can be carried out with acceptable risk. The limits of the technique appear to be related to problems of adequate tumour illumination.

P27. Withdrawn

P28.

Metastatic Intradural Extramedullary Carcinoma: Case Report and Review of the Literature

A.J. BELZBERG, K.M. HUNTER and I.H. JADUSINGH (Calgary, Alberta)

The patient presented with symptoms and signs of cervical radiculopathy and myelopathy. Myelography and computer axial tomography of the cervical spine and brain demonstrated a solitary discrete tumor nodule in the cervical subarachnoid space. At operation, gross examination of the tumor was consistent with schwannoma. Pathological examination revealed renal cell carcinoma. Postoperative abdominal ultrasound exposed a mass involving the kidney.

A review of the literature yields few case reports of intradural extramedullary spinal metastasis originating from a primary tumor outside the central nervous system. In the reported cases over the past twenty-five years, the most common primary tumor was carcinoma of breast, followed by lung, melanoma and uterus. In most of the reported cases, spinal subarachnoid metastasis represents a tertiary deposit seeded by malignant cells in the CSF from secondary lesions elsewhere in the central nervous system. This theory does not account for the pathology in this case report. Alternative theories of metastatic spread have included extension along perineural lymphatic ducts, transdural invasion, and hematogenous dissemination.

P29.

Regional Nerve Injury Following Intra-arterial Cis-platinum and Radiation Therapy for Bladder Cancer: A Follow-up Study

G. MacLEAN, D. PRESTON, L. EAPEN, D. STEWART, C. DANJOUX, P. GENEST, N. FUTTER, D. MOORS, A. IRVINE, J. CROOK, S. AITKEN, L. GERIG, R. PETERSON and P. RASULI

Patients treated for invasive bladder cancer with concurrent internal iliac artery Cis-platinum infusion and radiation therapy have been reported to have a high incidence of somatosensory disturbance, occurring in conjunction with treatment (Journal of Clinical Oncology, February, 1989). Of 25 patients treated in such fashion, 11 have been symptomatic. This is a report of a detailed neurologic examination and electrophysiologic study on 10 of these 11 patients and on 4 additional patients, 3 of whom received sequential rather than concurrent treatment.

The sensory deficit appeared to be mainly large fibre and axonal in nature, with the distribution of sensory loss in some patients suggesting a peripheral neuropathy, while in other patients having a more definite dematomal distribution. Seven of 14 patients recovered within 12 months, another 3 were only mildly symptomatic at 20 months, and the remaining 4 had considerable dysaesthesia more than 20 months following therapy. Marked asymmetry was noted in 2 of these patients, both of whom had only ipsilatearal Cis-platinum infusion on at least one occasion.

The total dosage of Cis-platinum, and the total amount of radiotherapy, did not correlate with the development of symptoms or signs.

We postulate a direct neurotoxic effect of Cis-platinum, relating to the intra-arterial infusions.

P30.

Malignant Intravascular Lymphoma: Immunochemical Markers in 3 Cases

G. MacLEAN, R. OROZCO-FLORIAN and V. SANGALANG (Halifax, Nova Scotia)

Malignant intravascular lymphoma (neoplastic angioendotheliomatosis) is a rare disorder with pathological features of intraluminal proliferation of atypical mononuclear cells in blood vessels involving multiple organs. The central nervous system and skin show predominant involvement and there is relative sparing of the reticuloendothelial system. We report on 3 patients encountered at our center during the past 4 years with this disorder. Brief clinical summaries are provided with photographs of relevant pathological material. In 2 of 3 patients, the illness was characterized by subacute onset of a progressive dementia with multifocal neurological signs and persistent increase in CSF protein. The third patient presented with progressive myelopathy and at autopsy was found to have extensive involvement of spinal cord and nerve roots. Recent reports support histogenesis from lymphocytes rather than endothelial cells. Immunocytochemical studies on these 3 cases are reviewed.

Neuromuscular

P31.

Late Pseudo-exacerbation of Myasthenia Gravis Due to Ectopic Thymoma Invading Lower Cranial Nerves

G. MACLEAN and A. GUBERMAN (Ottawa, Ontario)

An underlying thymoma, locally invasive in 1/3 of cases, is found in 10% of patients with myasthenia gravis. Ectopic cervical thymomas occasionally occur but rarely extend above the hyoid. We report a case of cervical thymoma invading the jugular foramen and lower cranial nerves initially mistaken for an exacerbation of myasthenia gravis diagnosed eight years previously.

The patient presented at age 57 with typical bulbar, ocular and generalized signs of myasthenia gravis confirmed by electrical studies, edrophonium testing and elevated acetylcholine receptor binding anti-bodies. Her course was stormy but she eventually responded to pyridostigmine, prednisone, plasmapheresis and azathioprine. A thymectomy by "sternal-split" procedure nine months after diagnosis identified only residual thymic tissue.

Seven years after diagnosis a right cervical mass appeared with worsening dysphagia and dysarthria initially attributed to myasthenia. CT showed a large right parapharyngeal mass invading the base of the skull near the jugular foramen. Examination demonstrated a hoarse voice, wasting and fasciculations of the right side of the tongue, right palatal weakness, and wasting and weakness of right trapezius and sternocleidomastoid. The excised mass was identified as thymoma by a panel of 10 pathologists and she received a course of cobalt therapy.

We were unable to find other reports of ectopic thymoma invading cranial nerves in patients with myasthenia gravis. The cause of this patient's dysphagia and dysarthria was readily distinguishable from worsening myasthenia on the basis of physical examination.

P32.

Congenital Muscular Dystrophy Associated with "Leukodystrophy" and Normal Intelligence

N.J. LOWRY and D.G. MUNOZ (Saskatoon, Saskatchewan)

Fukuyama in 1960 first reported the association of central nervous system abnormalities with the occurrence of congenital or early onset of muscular dystrophy. The patients he described had mental retardation, microcephaly and muscular dystrophy. In the 1970's, CTS in Fukuyama's type muscular dystrophy were reported as demonstrating marked lucencies in frontal white matter. Subsequent pathology reports showed that the hypomyelination was a development abnormality and not a degenerative or leukodystrophic process. Brooke in his 1985 book alluded to cases of congenital dystrophy with abnormal white matter on brain CT scans but with normal intelligence. We have recently encountered a brother and sister with congenital muscular dystrophy, I.Q.'s of 115 and 110 and a marked "leukodystrophic" CT scan. We conclude CT's should be performed in all cases of congenital muscular dystrophy

including those with above normal intelligence. The clinical, radiological and muscular pathological aspects of this autosomal recessive condition will be presented in detail.

P33.

Muscular Dystrophy with an Atypical Phenotype — A Case Report

M. YEUNG, G.M. KLEIN, L. BARCLAY, A.K.W. BROWNELL and C.J. PENNEY

A man of 50 presented with a 3-4 year history of muscle weakness. Examination revealed profound wasting and weakness of biceps and triceps muscles in both arms, with mild weakness of hip flexors, and knee flexors and extensors in both legs. Cranial nerves, shoulder girdle muscles, and distal arm and leg muscles were all clinically normal. There were no joint contractures, and no evidence of cardiac involvement.

A serum creatine phosphokinase level was elevated at 2650 IU. A muscle biopsy of the left Vastus lateralis muscle was typical of a dystrophic process. An electromyogram was entirely compatible with a dystrophic process, and showed changes that were more extensive than were clinically apparent.

The clinical picture is reminiscent of Emery-Dreifuss Muscular Dystrophy. However this entity is characterized by early joint contractures. This man has a phenotype which is not typical of any other described muscular dystrophy.

P34.

Myotonic Dystrophy; the Partial Syndrome Revisited

W. PRYSE-PHILLIPS, E. IVES, A. MacKENZIE and D. ADAMS (St. John's, Newfoundland; Ottawa, Ontario)

Myotonic Dystrophy (MyD) is a dominantly-inherited multi-system disease with an unusually high prevalence in Labrador. The existence of a "partial syndrome" of this condition was suggested following a study of the affected kindred in 1978, when it was also suggested that the presence of fragments of the syndrome held genetic implications similar to those of manifesting the complete syndrome.

A further study of the kindred is ongoing. At this time, the changes in the manifestations among ten affected and six partial syndrome subjects after a ten year interval will be presented. No patient in the former group has been reclassified, but among those with a partial syndrome, two are now clearly affected, three remain in this category and one is now considered to be normal. The implications of these clinical findings and of the results of linkage studies with new probes including ApoC2 will be discussed.

P35.

Restricted Inflammatory Myopathy: Distal Limb Distribution

A. SULAIMAN, G. KARPATI, S. CARPENTER and D. GENDRON

Polymyositis is a form of chronic idiopathic inflammatory myopathy that typically presents with symmetrical weakness of limb-girdle muscles and neck flexors. An atypical presentation of selective or preferential distal muscle involvement has been described in a few patients. We report two additional patients (1 male age 59, 1 female age 18) with a chronic inflammatory myopathy selectively affecting forearm muscles, intrinsic muscles of the hand, and to some extent tibialis anterior (in the first patient only). The weakness and wasting of these muscles was present for *1* year in the first patient and *7* years in the second patient before diagnosis. Both patients had initial myalgia but no dysphagia or skin rash, or systemic illness. Serum creatine phosphokinase activity was elevated approximately two-fold in both patients. Electromyography showed small-amplitude motor unit potentials of brief duration and fibrillation potentials in the affected muscles. Microscopy revealed necrosis with phagocytosis and regeneration of muscle fibers as well as mononuclear inflammatory cell infiltrates in connective tissue septa and between muscle fibers. Features of inclusion body myositis were absent. Strength of the involved muscles moderately improved in both patients after several months of corticosteroid treatment.

Distal polymyositis should be distinguished from inclusion body myositis which often presents with prominent distal limb weakness. While inclusion body myositis is resistant to therapy, distal polymyositis appears to be corticosteroid responsive.

P36.

Neuromyopathy with Colloid (Hyaline) Inclusions in Muscle Fibers

S. CHRISTIE, B. LACH and D. PRESTON (Ottawa, Canada)

A 31 year old adopted male presented with a chronic progressive motor polyneuropathy. The patient was noted to have a gait disorder and developmental delay since infancy, and quadriparesis was diagnosed at the third year of age. By nine, he had developed distal wasting and weakness, and loss of deep tendon reflexes consistent with Charcot-Marie-Tooth disease. He has had gradual, slow deterioration in motor function and three episodes of acute deterioration, each associated with a febrile illness. EMG and nerve conduction studies done in 1980 and 1987 were consistent with axonal polyneuropathy.

Nerve biopsy revealed very severe loss of myelinated and unmyelinated fibers and axonal degeneration. The muscle biopsy showed markedly atrophic rounded fibers and endomysial fibrosis. Enzyme histochemistry demonstrated Type II fiber preponderance (approximately 90% of total). Electronmicroscopy revealed rounded intracytoplasmic inclusions (IC's) measuring up to 5-10 u in diameter, present in many muscle fibers. They were surrounded by a single membrane occasionally studded by ribosomes. The content of IC's consisted of moderately electrondense, uniformly homogenous, most likely proteinaceous substance. Channels of dilated endoplasmic reticulum (RER) contained identical material. Some IC's were enclosed within the membranes of cellular nuclei. In addition to IC's, many fibers showed typical "cytoplasmic bodies," abnormal mitochondria, clear vacuoles, occasional Z-disk streaming, and degeneration of end-plates. Multiple immunohistochemical stains for intermediate filaments, actin and myosin as well as routine histological methods were not helpful in chemical characterization of IC's.

Ultrastructural properties of IC's in our case are similar to "colloid" or "hyaline" inclusions found in normal and diseased motor neurons. To our knowledge this form of IC's have not been reported in muscle fibers. Electronmicroscopy indicate their origin from RER and nuclear envelope. At this point, it is not known whether IC's represent a hallmark of a specific disease or they are formed in muscles as a result of chronic denervation.

P37.

Fragile X Syndrome and Amyotrophic Lateral Sclerosis — A Case Report

H.B. DESAI, J.R. DONAT and D. MUNOZ (Saskatoon, Saskatchewan)

Fragile X syndrome is a common cause of mental retardation. Its frequency is estimated at about 1 per 2000 males and it is the second most common genetic cause of mental impairment after Trisomy 21. It is characterized by a fragile site at Xq 27-28, X linked mental retardation, and a characteristic phenotype including macroorchidism. We report the clinical and pathological features of a patient with fragile X syndrome who developed amyotrophic lateral sclerosis (ALS) at an unusually young age. Although the occurrence of these two diseases could be a mere coincidence, it raises the possibility of an association similar to that existing between Down's syndrome and Alzheimer's disease.

P38.

Thiamine Status in Alcoholic Polyneuropathy

M.L. D'AMOUR, R.F. BUTTERWORTH, J. BRUNEAU and G. POMIER LAYRARGUES (Montreal, Quebec)

The etiology of alcoholic polyneuropathy has not been definitively established. Thiamine deficiency or multiple vitamin deficiencies have been suspected but not proven. To evaluate the thiamine status in alcoholic polyneuropathy, 20 alcoholic subjects admitted to a Detoxication Unit without signs of Wernicke disease or other causes of neuropathy were studied. Each had a determination of blood transketolase level, a neurological and electromyographic (EMG) examination. Twenty normal age-matched subjects served as controls. Dosage of red blood cell transketolase (TKA), a thiamine-dependent enzyme was measured in the absence of and in the presence of excess thiamine pyrophosphate (TPP), the enzyme cofactor. The incremental increase of transketolase resulting from TPP addition (TPP-effect) is generally less than 15% in normal subjects. Abnormal values of TKA and/or TPP effect were observed in 35% of patients. In patients and controls, mean TKA values were respectively 169 and 193 mU/L, TPP effect 13.3 and 9.7%.

EMG evaluation showed reduced conduction velocities for several different nerves in alcoholic patients; median motor 61.5 vs 65 M/sec., $p=.05$; ulnar motor 61.2 vs 66.8, $p<0.006$; peroneal 48.3 vs 56, $p<0.004$; posterior tibial 48.2 vs 53, $p<0.002$; median sensory 56.1 vs 63.4, $p<0.001$; ulnar sensory 55.9 vs 60.2, $p<0.03$; sural 51.8 vs 55.5 NS. Amplitude values followed a similar pattern. Few signs of active denervation were observed. Abnormal EMG values were observed in 38% of patients. In the case of peroneal nerve, reduced conduction velocities were negatively correlated with TPP effect values.

These findings suggest that altered thiamine status may play a role in the pathogenesis of alcoholic polyneuropathy

(Supported by La Fondation Jean Lapointe)

P39.

Demyelinative Neuropathy with Hypermyelination in IgM Paraproteinemia. Immunoelectronmicroscopic Study

B. LACH, D. ATACK, P. RIPPSTEIN and A. GREGOR (Ottawa, Canada)

We present an ultrastructural and immunohistochemical study of a sural nerve biopsy in a 78 year old lady with benign IgMK paraproteinemia and a severe sensory motor neuropathy of three years duration. Significant clinical and laboratory findings include: glove and stocking distribution of sensory loss, inability to walk without support, denervation pattern on EMG, IgM Kappa paraproteinemia: serum level 6.30 G/L(N:0.6-3.50), and a normal bone marrow and bone scan.

Sural nerve revealed severe loss of myelinated and unmyelinated fibers as well as focal axonal degeneration. Among the remaining fibers, many showed disproportionally thin myelin for the size of axons, occasional onion-skin formations, and shortened internodes in teased fiber preparation. Numerous fibers were hyper-myelinated with excessive layers of myelin lamellae as well as an abundance of redundant convolutions and loops of well-formed and abnormal myelin. The myelinated fibers often displayed splitting of the outer layers of the intraperiod myelin line, resulting in a characteristic appearance of a "light myelin". Immunofluorescence and immunoelectronmicroscopy demonstrated deposition of heavy M^- and light Kappa chains in the layers of the myelin undergoing splitting. IgM Kappa of the patient's serum reacted with the myelin of normal PNS. Only IgM Kappa globulins were localized on fragments of myelin and some vesicular structures within the Schwann cell cytoplasm. The axons were negative for immunoglobulins.

Our immunohistochemical study indicates that the separation of myelin lamellae and demyelination in this disease is directly caused by the monoclonal IgM "paraprotein" antibody. Schwann cells are able to internalize the antigen-antibody complexes formed on the surface of myelinated fibers. The antibodies against some components of myelin probably provoke excessive myelin production or lead to inefficient myelin turnover, resulting in hypermyelination reminiscent of a tomaculous neuropathy.

P40.

Is there CNS Demyelination in Chronic Inflammatory Demyelinating Polyneuropathy?

A.F. HAHN, W.J. KOOPMAN and D.G. LEE (London, Ontario)

There is continuing controversy whether the lesions in the demyelinating neuropathies involve the central nervous system. Several clinical and pathological reports have suggested that patients with chronic inflammatory demyelinating polyneuropathy (CIDP) may have CNS demyelinating lesions. This might be explained if an immunologic response were directed against an antigen common to the central and peripheral nervous systems. Two recent papers on CIDP (Thomas, et al., 1987; Mendell et al., 1987) reported the presence of CNS lesions on MRI scans.

We studied 18 patients with the diagnosis of CIDP. MRI scans were done on all patients with a 1.5 tesla unit. Ten scans were normal and 5 showed punctate white matter lesions in the cerebral hemispheres which were thought to be ischemic. These latter 5 patients were 56-75 years old. Only one scan showed lesions (3) which might be thought to be demyelinating and even these were atypical, none being periventricular in location. Visual evoked responses were done in 5 patients and were normal except for one eye which showed a slight delay in latency.

Our results do not deny the occurrence of CNS demyelination in CIDP but they do suggest that it is uncommon.

P41.

Vasculitic Peripheral Neuropathy — Report of Two Unusual Cases

J.Y. CHU, A.E. KARASIK and L. RESCH (Toronto, Ontario)

The peripheral nervous system is affected in 50 to 75% of patients with systemic vasculitis, but much less frequent in the other vasculitic syndromes (0-25%). We report two unusual cases of vasculitic peripheral neuropathy: one associated with allergic vasculitis (Henoch-Schoenlein Purpura) and another with isolated peripheral nerve vasculitis.

Case 1 is a 74 year old man with six weeks history of progressive weakness and numbness of his feet and hands. Four months prior to its onset, he had developed purpura of his lower limbs with skin biopsy showing leukocytoclastic vasculitis. He did not respond to two short courses of low dose prednisone therapy. Clinical examination and electrophysiological studies confirmed moderately severe sensori-motor peripheral neuropathy. Sural nerve biopsy showed vasculitis. He improved with high dose prednisone therapy and is now controlled on maintenance dose of prednisone.

Case 2 is a 72 year old man with a two month history of weakness and numbness of his hands and feet. Examination revealed moderate distal weakness and impaired vibration sense with depressed reflexes in lower limbs. Electrophysiological studies confirmed moderate sensorimotor peripheral neuropathy. Sural nerve biopsy showed epineural vasculitis. Extensive investigations failed to show any evidence of systemic vasculitis. He responded to prednisone therapy over the next twelve months and is currently ambulatory without assistance.

The clinical course, laboratory investigations, electrophysiological studies and pathology will be presented in detail. The current literature will also be reviewed.

P42.

Thoracic Myelopathy Presenting as Peripheral Neuropathy

P.R. BOURQUE and A.J. WINDEBANK (Rochester, Minnesota, U.S.A.)

Patients with thoracic intraspinal tumors may present with a clinical picture suggestive of peripheral neuropathy. We describe four such cases. The presenting symptoms were leg paresthesia in three and asymmetric paraparesis in one. A thoracic radicular sensory disturbance was eventually present in three. None showed hyperreflexia or Babinski signs. All had normal nerve conduction studies. The EMG showed mild distal leg denervation in 2 (abductor hallucis and tibialis anterior muscles) while one patient had definite ongoing denervation/reinnervation in both quadriceps femoris muscles, which were atrophied. The final diagnoses were: T8 neurilemmoma, T6 meningioma, and T8-9 and T7-8 disc herniations.

The possibility of a thoracic myelopathy should be considered in patients with leg sensory disturbances, even if pyramidal signs are lacking and there is mild EMG evidence of denervation.

The suggestion of lower motor neuron dysfunction several segments below the site of compression is of interest. Its cause may be ischemic, as has been postulated with high cervical or foramen magnum lesions leading to denervation in C7-T1 myotomes.

P43.

Postoperative Ulnar Neuropathy

B.G. BENOIT, N. RINTOUL, D.M. ATACK, D.N. PRESTON and N.A. RUSSELL (Ottawa, Ontario)

Ulnar neuropathy is a well recognized complication of general anesthesia. In establishing its incidence and the contributing factors we have analysed the charts of 106 patients having this diagnosis during 1984-1988. In 31 cases the ulnar neuropathy occurred after an operation under general anesthesia, and 19 of these required neurolysis.

Most of the patients were male (24/31) and obese. The mean age was 52 years and the left side was most frequently involved. The associated operations included cholecystectomy, hernia repair, TURP and laparotomy. Usually the supine position was used and the symptoms appeared immediately after awakening from anesthesia. Little information was available regarding arm position, site of vascular lines and location of B.P. cuff.

The ulnar nerve is vulnerable to direct pressure, prolonged elbow flexion and prolonged pronation of the forearm, especially if diabetes or obesity are also present. Simple preventive measures can eliminate this complication.

P44.

Parturition Palsy: Bilateral Femoral Neuropathy as an Unusual Complication of Position Assumed During Childbirth

P.J. SWEENEY and A.J. WILBOURN (Cleveland, U.S.A.)

A 33-year-old primipera spent over five hours of her labor in a semi-sitting posture with her thighs forceably hyperflexed against her chest. Delivery was ultimately by caesarian section.

Afterwards, she noted marked weakness bilaterally in her quadriceps muscles. Clinical examination confirmed the above plus absent knee reflexes, and decreased anterior thigh sensation, all bilaterally.

Serial EMG studies demonstrated severe bilateral femoral neuropathies, consisting of both conduction block and axon loss.

Significant improvement began asymmetrically within three months post-onset, as conduction block resolved.

Differential diagnosis of this parturition complication, and its medicolegal implications, will be discussed.

Movement Disorders

P45.

Controlled-Release Sinemet (CR 4) in Advanced Fluctuating Parkinson's Disease

D. GRIMES, P. GRAY and K. GRIMES (Ottawa, Ontario)

Twenty-one patients with longstanding (mean 14 years) Parkinson's disease complicated by end of dose failure were treated with a new slowly dissolving matrix (levodopa 200 mg - carbidopa 50 mg) preparation. These patients received regular Sinemet from 4 to 9 (mean 6) times daily. The mean initial dose of Sinemet was 708 (250 to 1600) mg daily. After 12 weeks of follow-up, 9 patients demonstrated clear benefit as evidenced by improved mobility, less "off" time, less dyskinesias and improved coordination. The mean daily dose of slow release Sinemet was 988 (500 to 2300) mg and the number of doses had decreased to 4 (range 3-6) daily.

Nine patients had an increase in dyskinesias which was improved with Sinemet or Bromocriptine reduction. The following other adverse effects were noted: increased bradykinesia (3), hallucinations or vivid dreams (3), dyspnea (2), nausea (1), abdominal cramps (1), chest pain (1) and leg discomfort (1). Five patients stopped the drug because of adverse effects.

The following drug adjustments were beneficial: increased individual drug doses, especially early in the day; an early morning or late evening dose helped morning and overnight slowness respectively. Patients frequently noted the slower onset of action of the slow release preparation but those who responded were pleased with their improved, more predictable mobility.

Slow release Sinemet is simple to use, worthwhile preparation, which may benefit about 50% of patients with advanced fluctuating Parkinson's disease.

P46.

Induction of Symptomatic Scoliosis by Dopamine Agonist Therapy in Advanced Parkinson's Disease

K.A. GRIMES, J.D. GRIMES and S. ALSHAMMRI (Ottawa, Ontario)

Two patients (ages 62 and 79) with stage 3.5 Parkinson's disease (PD) complicated by end of dose failure had bromocriptine (30 mg daily) added to Sinemet (700 mg) therapy. Over the next year both patients developed increasing scoliosis and leaning to one side with more gait difficulty. This disability was constant; fluctuations and dyskinesias were improved in both patients. The scoliosis was documented with plumb line, photography, and spinal radiographs. In both patients the right side was the side of onset and most severely involved. One patient leaned to the left and one to the right. Bromocriptine was stopped; over two weeks both patients had marked functional improvement in postural asymmetry and gait, however end of dose failure recurred. On specific measures, scoliosis cleared almost completely in one patient and was moderately improved in the other. Dopamine agonists may cause or aggravate scoliosis and postural instability in Parkinson's disease and may have to be withdrawn. The mechanism is unclear but it may be related to asymmetrical nigral degeneration and striatal hypersensitivity as is seen in animal models of PD.

P47.

Early Drug Limiting Adverse Effects with Deprenyl Therapy in Patients with Advanced Parkinson's Disease

K. GRIMES, D. GRIMES and P. GRAY (Ottawa, Ontario)

Sixteen patients (mean age 69 years) with advanced (stages 3-4 Hoehn and Yahr) longstanding Parkinson's disease had the monoamine

oxidase type B inhibitor, Deprenyl (5-10 mg daily), added to their antiparkinsonian drug therapy. All patients continued on Sinemet (mean 668 mg daily) and 7 patients also received low dose bromocriptine. All other available antiparkinsonian drugs and treatment regimes (low protein diet) had been previously attempted. Fourteen of 16 patients had end of dose failure. Initial Deprenyl dosage was 5 mg daily, and was increased to 5 mg B.I.D. after 10 days.

Drug limiting adverse effects developed within 3 weeks in 7 patients. The symptoms that necessitated Deprenyl withdrawal were: confusion (3 patients); hallucinations (2) and dizziness (2). In addition 2 patients complained of increased gait upset. Three patients stopped the drug because of lack of improvement. A maximum benefit of mild improvement was recorded in 4 of 6 patients who continued on Deprenyl.

The results of Deprenyl adjunct therapy in this group of 16 patients were disappointing. The drug was withdrawn because of adverse effects in 44 percent of patients and only 4 patients had benefit. This drug should be given cautiously and with limited expectations to patients with advanced Parkinson's disease. Preexisting confusion or hallucinations are contraindications.

P48.

Frozen Shoulder and Parkinson's Disease

H.R. BALIAN, M.N. HASSAN and G.R. KRAAG (Ottawa, Ontario)

Preliminary data from 120 consecutive patients with Parkinson's Disease (PD), showed a frequent occurrence of shoulder joint dysfunction (SJD).

Over the past 2 years, 10 patients (6 females and 4 males) aged 55 to 88 years, either presented with or developed SJD in keeping with a frozen shoulder or peri-arthritis. Six patients (3 females and 3 males) presented initially with shoulder joint stiffness, pain and limited range of motion of one side. These patients were treated with local steroid injections, anti-inflammatory agents and physiotherapy with partial improvement. Parkinson's disease was diagnosed 2 to 12 months later, with 4 cases exhibiting unilateral, and the other 2 bilateral but asymmetric signs, mainly bradykinesia and rigidity. Treatment with anti-parkinsonian agents resulted in complete clearance of shoulder joint symptoms.

In the remaining 4 patients, SJD developed after a mean period of 6 years following the diagnosis of PD. These patients had bilateral and symmetrical PD signs manifested by rigidity, bradykinesia and tremor. Adjustment of anti-parkinsonian medications coupled with short courses of anti-inflammatory agents produced symptomatic relief.

Our study shows that frozen shoulder occurs quite commonly in PD and it may either precede or follow the diagnosis. The spontaneous development of a frozen shoulder may herald the onset of PD.

P49.

Parkinson's Disease and Amyotrophic Lateral Sclerosis — A Family with Six Affected Members Over Three Generations

D.C. HOWSE and P.M. MacLEOD (Kingston, Ontario)

Early onset Parkinson's disease (PD) has been associated with the use of well water for drinking in childhood. A Parkinson's like disorder and amyotrophic lateral sclerosis (ALS) have been linked to an environmental toxin in Guam. We describe a family in which five members over three generations developed PD with the age of onset ranging from 38 to 64. A sixth member developed typical ALS at age 88. All affected members were raised in the Crowe Lake area of Eastern Ontario and all drank well water in childhood. An additional member developed intellectual impairment with mild cerebral atrophy beginning age 45 without evidence of PD or ALS. The only child of one Parkinsonian patient is institutionalized with seizures and mental retardation.

The frequency of neurological disease raises intriguing questions about the interplay between genetics and environmental influences.

P50.

Electrophysiological Predictive Testing in Huntington's Disease

A.A. EISEN (Vancouver, British Columbia)

Symptoms of Huntington's disease (HD) are rarely evident before the 3rd to 4th decades; therefore predictive testing, although raising ethical issues, is important. A variety of neurophysiological tests have been shown to be abnormal in HD and recently some have been applied to at risk subjects.

We have measured short (R1) and long (R2) latency components of the stretch reflex, the electromyographic silent period (S-X interval) and central motor conduction (CCT) in HD and their first degree relatives. Nine patients aged 32-64 years (mean 43 years), 13 at risk subjects aged 26-68 years (mean 23 years) were studied.

R2, normally easily recordable, was absent in 7/9 patients, and 3/13 at risk subjects. The normal thenar muscle S-X interval measured 111±10.8 msec (range 96-147 msec). Seven patients and 5 at risk subjects had shortened S-X intervals (84 msec). Taken in combination these tests were abnormal in 88.9% of patients with HD and 53.8% of at risk relatives. Thenar MEP latencies and CCTs were normal in both groups.

The silent period although incompletely understood involves transcortical, glycinergic and gabaminergic dependent, inhibition of voluntary contraction. This is presumed to be defective in HD and some at risk subjects. Absence of R2 in HD and at risk subjects is probably a direct consequence of diminished somatosensory inflow involving thalamic and cortical projections.

These tests may usefully complement others such as use of DNA markers in the prediction of HD.

P51.

PET Demonstrates an Early Nigrostriatal Lesion in Wilson's Disease

B.J. SNOW, M. BHATT, W.R.W. MARTIN and D.B. CALNE (Vancouver, British Columbia)

We studied 5 patients with Wilson's disease, using ^{18}F-6-fluorodopa positron emission tomography (6FD PET) and MRI, to investigate the structure and dopaminergic function of the striatum. PET scans were analyzed using a graphical method to calculate striatal uptake of 6FD; the results were compared with 9 normal subjects. One patient was neurologically normal and had normal PET and MRI. Three patients had parkinsonian features. Their striata were normal on MRI, but PET revealed significantly reduced striatal uptake of 6FD. One patient had dystonia; MRI demonstrated high signal from the putamen, and PET revealed significantly reduced uptake of 6FD. The results demonstrate a predilection for damage from copper deposition to occur in the presynaptic dopaminergic system before any striatal abnormality is seen on MRI; this pattern is associated with clinical parkinsonism. When the striatum was abnormal on both MRI and PET, dystonia occurred. This is consistent with the concept that reduced dopaminergic input into an intact putamen causes parkinsonism, while direct putamenal damage causes dystonia.

P52.

Neurological Deterioration During Treatment of Wilson's Disease

W.J. LOGAN (Toronto, Ontario)

It is well known that patients with Wilson's Disease can deteriorate after treatment with Penicillamine (Pen) has been initiated. There has been concern that Pen may contribute to this deterioration by mobilizing copper from the liver and temporarily exposing the brain to a higher copper level or by forming a neurotoxic complex with copper. In an attempt to determine the pathogenesis of this deterioration and to evaluate the efficacy of alternative therapy a study was undertaken in a

patient who had progressive deterioration after Pen was instituted.

A 17-year-old female was diagnosed as having Wilson's Disease after she presented with neurologic and academic symptomatology and was found to have Kayser Fleischer rings. Pen was begun increasing to 1 gram per day. The patient began to have increasing difficulty with speech, feeding and motor control. This progressed over 4 months until she was anarthric aphagic and rigid and only had involuntary movements of her extremities. Pen was discontinued. Zinc gluconate (Zn), triethylene tetramine (Trien) and Pen were then used individually and in combination while urinary copper excretion was determined and the patient's clinical course was monitored.

Trien was almost as effective in inducing cupriuresis as Pen. Zn did not result in urinary copper excretion. When Zn was combined with Trien there was considerable copper output but somewhat less than with Trien alone. CSF copper arose from 2 uMol/L on Trien alone to 2.8 uMol/L after one week treatment with Pen alone, dropping to 2.2 uMol/L one week later during treatment with Trien alone.

These results support the suggestion that Pen may contribute to neurologic deterioration in Wilson's Disease by increasing brain exposure to copper. Trien with or without Zn in an effective cupriuretic agent which may be preferable to Pen in this situation.

Pediatric Neurology

P53.

Further molecular genetic and genealogic studies on the Friedreich's Ataxia gene in the Quebec population

A. RICHTER, S.B. MELANCON, M. ROY, C. MEUNIER, S. CHAMBERLAIN and M. FARRALL (Montreal, Quebec; London, England)

Friedreich's Ataxia (FA), the most common form of the inherited ataxias has autosomal recessive inheritance. The biochemical cause of this progressive disorder is unknown. Recent molecular genetic studies localized the FA gene to the pericentromeric region of chromosome 9 in British, Italian and German families (1). This finding has recently been confirmed in French families (2). Our extensive investigation of other British, Quebec as well as Louisiana Cajun families, these latter displaying later onset and slower progressing disease, unequivocally confirmed the locus to chromosome 9, using the probe MCT 112 (D9S15), despite the observed clinical variation (3).

We have extended our investigation by studying linkage in a total of 13 two generation or incomplete three generation Quebec FA families, each with a minimum of 2 affected sibs. Genomic DNA from 87 individuals, including 32 patients, was analyzed, using the restriction enzymes MspI and/or AccI in combination with the D9S15 probe. Evidence for linkage was observed, generating a LOD score (likelyhood odds ratio) ($\hat{z}$) of 4.28 with recombination fraction of 0.00 between the probe and the FA gene.

The genealogy of 5 of these families has now been connected to the original founder couple believed to have introduced the FA gene into New France in 1634.

We are presently involved in attempts to connect the rest of the Quebec FA families in order to establish whether all cases of FA in Quebec families of continental French origin could be attributed to this couple.

1. Chamberlain S et al. Nature 1988; 334: 248.
2. Fujita R et al. Genomics 1989; 4 110.
3. Chamberlain S. et al. Am Hum Gen (in press).

P54.

Lebanese Juvenile-Onset Tay-Sachs Disease is a Lysosomal Enzyme Targeting Mutation

P. HECHTMAN, B. BOULAY, J. BAYLERAN and E. ANDERMANN (Montreal, Quebec)

Juvenile Tay-Sachs disease (JTSD) was reported in three Christian-Lebanese immigrant families in Canada by Andermann. We now report on the mutation mechanism in one of these consanguineous families based on a study of the maturation of hexosaminidase A (hex A) subunits and of the properties of residual hex A in fibroblasts obtained from two affected sibs. Fibroblasts have 16% hex A activity toward sulfated hex substrate (4MUG) and 3.3% activity toward sulfated substrate (4MUGS) relative to control cells. In the two mutant JTSD cell lines 39% and 49% of 4MUGS cleaving activity cochromatographs with hex A compared to 0% in Infantile TSD cells and 100% in normal control cells. Enzymatic activity is reduced in the JTSD cells because the hex A α subunit precursor fails to mature and is degraded in an early compartment. The α subunit precursor is not phosphorylated nor can its secretion be induced by NH_4Cl in the culture medium. This mechanism was also shown to be associated with the ITSD phenotype in an Italian proband. In the Lebanese JTSD a small amount of hex A α escapes degradation. Although the residual subunit hex A activity (measured chromatographically using 4MUG) is significantly less in the JTSD cells than in fibroblasts obtained from patients with the B1 variant form of ITSD, the properties of this residual enzyme activity in fibroblasts with the JTSD genotype indicate that the enzyme is capable of 4MUGS hydrolysis at normal lysomal pH (pH optimum of normal and JTSD hex A 4.0) whereas the mutant hex A in two unrelated B1 ITSD variant patients (pH optimum 2.4) would be inactive in the lysosome. Mutant hex A activity in both JTSD and B1 ITSD fibroblasts is abnormally thermostable suggesting that in both mutant genotypes the residual hex A is completely processed. We suggest that B1 mutations produce a catalytically inert enzyme but that the maturation of enzyme is unaffected by this allele. The JTSD mutant allele found in the Lebanese patients, however, behaves like a cis-regulatory mutant which reduces the quantity of α-subunit surviving the maturation process but doesn't alter its catalytic properties.

P55.

Effects of the Ketogenic Diet on Clinical Manifestation of Rett Syndrome

J. WARK, D. MacGREGOR and P. HWANG (Toronto, Ontario)

Of a group of 23 girls with Rett Syndrome known to the Hospital for Sick Children, Toronto, all had abnormal EEG's, although 5 had such mild seizures that they did not require AED's; 7 others had such severe seizures that resort was had to the use of the ketogenic diet to attempt to control them.

In the group that had the ketogenic diet, compliance was a major problem, and two children stopped before efficacy could be assessed. Striking changes were observed in 3 of the remaining 5 girls, with respect to their stereotypic behaviours, gross motor abilities, and responsiveness to the environment. Thus, 2 were remarkably more interactive, but the third showed increased stereotypic behaviour and some deterioration of gait. Video documentation before and after the diet substantiates the reality of the effects, and is also of interest as a visual demonstration of the clinical features of Rett Syndrome. In a condition whose pathogenesis is completely obscure, the impact of these biochemical changes is of considerable importance and strongly suggests further avenues of investigation.

P56.

Detection of the Carrier State in Metachromatic Leukodystrophy by MRI and Evoked Potentials

C.E. NIESEN, A.K. HOPE, E. COHEN, J.T.R. CLARKE and D. MacGREGOR (Toronto, Ontario)

We evaluated the carrier state in first degree relatives of five known metachromatic leukodystrophy (MLD) patients. Eleven documented

heterozygotes (leukocyte arylsulfatase A Activity = 40-50% of normal values) were studied using MRI scans, performed on a 1.5 T system with T_1W and heavily T_2W sequences, and trimodal evoked potentials (EP). No siblings were tested.

All relatives, 4 males and 7 females, ranging in age from 23-70 years (mean age = 32 years), were asymptomatic and had normal physical examinations. None had a history of neuorologic disease. MRI sequences in 10/10 relatives failed to show any abnormal white matter changes, but abnormal EP's were recorded in 4/8 heterozygotes. These four relatives exhibited abnormal auditory responses (increased interpeak latencies of waves I-III) and two of them had abnormal peripheral and central somatosensory responses. All male heterozygotes tested had abnormal results (3/3).

To our knowledge, this is the first report of a large group of heterozygotes evaluated by MRI. Despite its popularity and high imaging resolution, MRI was not sensitive in detecting MLD heterozygotes. EP testing was more useful for revealing the sub-clinical changes in the heterozygotus state, particularly male, of this leukodystrophy.

P57.

Brainstem Auditory Evoked Potentials in Neonates with Chiari II Malformation in Relation to Ventriculoperitoneal Shunting

J. VAJSAR, A.J. HOPKINS and G.M. RONEN (St. John's, Newfoundland)

The brainstem auditory evoked potentials (BAEP) is a noninvasive electrophysiological measure of the functional integrity of the brainstem. To determine the effect of the ventriculoperitoneal shunting on the brainstem function in neonates with Chiari II malformation and hydrocephalus we compared the BAEPs recorded in such patients before and after the surgery.

The BAEPs were recorded from the vertex electrode with reference to the ipsilateral mastoid in 15 full term neonates with Chiari II malformation and hydrocephalus. Click stimuli of 0.1 msec were presented at 11.29 Hz. Peak latencies for wave I and V were measured and interpeak latency (IPL) I-V was calculated. The second BAEP recording after the surgery followed the first one in 6 days on average (range 2-15 days). Comparison of the BAEPs prior and after the shunting procedure showed 2 types of responses. In the first one (6 neonates), the initially absent wave V appeared after the surgery. In the second type (9 neonates), we measured a decrease in: absolute wave V latency (mean = 1.63 msec), absolute wave I latency (mean decrease = 0.19 msec) and I-V IPL (mean decrease = 1.51 msec). Repeated measures ANOVAs were used to evaluate changes in absolute peak latencies and I-V IPL between the two recordings. The analysis was significant at less than 0.01 level of probability for wave V and I-V IPL.

The results indicate that the brainstem function in neonates with Chiari II malformation and hydrocephalus is improved after the shunting procedure.

P58.

The Survival and Functional Status of Children with Stroke: A Clinical Study of 77 Children (Hôpital de l'Enfant-Jésus) 1978-1988

S. DESBIENS and S. VERRET (Quebec City, Quebec)

A stroke or cerebrovascular accident is a neurological condition with sudden onset caused by an acute vascular lesion of the brain such as hemorrhage, embolism, thrombosis or rupturing aneurysm (Dorland). This is an unfrequent but well known problem in children and young adults.

Several studies went through the clinical problem of these children since the basic review from Mayo Clinic by Schoenberg in 1978. However the survival and mostly the functional status of these patients were less often evaluated. This is the purpose of the present study.

During a 10 year period (1978-1988), 77 patients, 0-19 years of age with stroke were diagnosed and treated at l'Hôpital de l'Enfant-Jésus within the Department of Neurological Sciences. Follow-up was conducted in every patient until January 1989.

We will briefly comment on the clinical picture etiology and investigation. Ten patients died in acute phase of the illness.

The functional status of the survivors was established according to a modification of the scale employed by us and Bloom for the follow-up of children with brain tumors.

From our clinical survey we concluded that:

Children who survive a stroke have a good quality of life. Patients knowing that they have an arteriovenous malformation (AVM) in their head live a stressful life.

If agressive treatment of increased intracranial pressure is started early at the onset of the problem, death can be prevented and if occurs, it is more related to the cause than to the stroke. There is no useful therapy in idiopathic ischemic stroke of childhood. The risk of recurrency is very low and permits to be optimistic about the future. AVM should benefit from appropriate therapy considering the psychological burden of living with it in its head.

P59.

CAT Scans for Children with Headache Without Neurologic Signs

J. DOOLEY, P. CAMFIELD, M. O'NEILL and A. VOHRA (Halfiax, Nova Scotia)

We reviewed the use of CT scans for children referred because of headache over a 1 year period to a secondary and tertiary pediatric centre. Both the IWK Children's Hospital, Halifax, (the tertiary centre for Nova Scotia) and the Colchester Regional Hospital, Truro, (the secondary centre) have CT scanners. Headache referrals to the pediatric neurology service of the IWK Hospital and the only pediatrician at CRH were reviewed. No patient had signs of abnormal intracranial pressure or progressive neurologic abnormality.

CT scans were ordered for 4/117 patients seen by the 2 pediatric neurologists (1 choroid plexus papilloma, 1 venticular dilatation without increased ICP, 2 normal performed for parental anxiety) and 3/40 patients seen by the pediatrician (3 normal, 1 for parental anxiety). During the same year 34 CT scans were ordered at the CRH by family physicians for children with headache (all normal). No patient has developed intracranial disease during 6 months follow-up. Of children with headaches seen by a Pediatric Neurologist or a Pediatrician only 4.5% had a CT scan. Overall of 191 children with headaches only 1 (0.5%) had a CT scan which resulted in intervention. We conclude that CT scans are seldom indicated for children with headaches without neurologic signs and probably should only be ordered following an appropriate consultation.

P60.

Neuroblastoma and Fetal Exposure to Phenytoin: Chance Association or Evidence for Oncogenicity?

S. AL-SHAMRI and A. GUBERMAN (Ottawa, Ontario)

There is likely a two to three-fold increased risk of malformations such as cleft-lip and palate, ventriculoseptal defect, distal digital hypoplasia and other digital anomalies and microcephaly in children exposed to phenytoin in utero. The rarely-seen full-blown "fetal hydantoin syndrome" also includes other minor malformations and in some cases mental retardation. The oncogenic potential of phenytoin has been little-discussed in the neurology literature.

We present the case of a $2^1/2$ year old boy who presented with an abdominal mass leading to a diagnosis of stage IV neuroblastoma. Birth and development were normal and there were no cogenital malformations detected. His mother had been on phenytoin with relatively low

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blood levels throughout gestation and for 8 years prior. She had also been taking carbamazepine throughout the pregnancy.

Ours is the tenth reported case of a malignant childhood tumor in the offspring of mothers on phenytoin during gestation. Seven of these cases were associated with features of the fetal hydantoin syndrome and only 2 were definitely known to be physically normal. In 7/10 cases the mother was also taking phenobarbital or a derivative. The tumors involved were: 5 neuroblastomas; 1 ganglioneuroblastoma, 1 melanotic ectodermal tumor, 1 ependymoblastoma, 1 mesenchymoma and 1 Wilms' tumor.

Our case offers further support for the oncogenic potential of phenytoin. It is hoped that by drawing the attention of neurologists to this association further case reports, experimental evidence as well as retrospective reviews of patients with neuroblastoma and other pediatric tumors for exposure to phenytoin will be forthcoming to add to the evidence suggesting an oncogenic as well as teratogenic potential for phenytoin.

Epilepsy

P61.

Hippocampal EEG-like Rhythms *In Vitro*: Relation to Epileptiform Activity

J.H. SCHNEIDERMAN (Toronto, Ontario)

Spontaneous rhythmic field potentials (RFP) were recorded from the CA3 region of guinea pig hippocampal slices in standard artificial cerebrospinal fluid (ACSF). These potentials were small (30-120 uV) and difficult to distinguish from background noise with standard recording techniques. However, filtering and power spectral anlaysis (PSA) revealed activity distinct from that in the bath in 63/73 slices. The remaining slices were not viable since they did not respond to stimulation or burst in 3.4 mM Penicillin (PEN).

In ACSF, power was maximal at the lower end of the frequency resolution (0.8 to 1.6 Hz) and fell off smoothly to frequencies around 20 Hz. Although peaks at various frequencies were present in individual spectra, no consistent peaks were identified in averaged spectra. However, distinct peaks appeared around 6 Hz as small amounts of PEN were added (0.085 to 0.17 mM). Peak power increased further and shifted towards lower frequencies in a dose-dependent fashion as PEN was raised to 0.51 mM. The spontaneous synchronous bursts which occurred in 3.4 mM PEN were always heralded by a brief period (1-5 min) of non-stationary increases in RFP. In a few slices the build-up in RFP stabilized and bursts did not occur until after a few bursts had been triggered by extracellular stimulation. PSA revealed peaks around 2 to 3 Hz in these slices. Spontaneous epileptiform bursts also occur in slices perfused in the absence of Mg++. However, PSA revealed increased power in all frequencies in low Mg++ (0.1 to 0.5 mM) or shifts to higher frequencies. Concentrations of Mg++ interfering with synaptic transmission blocked the RFP in normal medium and in low PEN and prevented bursting in high PEN.

PSA revealed RFP responsive to pharmacologic and ionic manipulations which could provide a model for studying the mechanisms underlying EEG rhythms. Different changes in the RFP preceed epileptiform bursting depending on the mechanisms underlying the bursts.

P62.

Suppression of Secondarily Generalized Seizures by Lesioning the Substantia Innominata

R.S. McLACHLAN and F. BIHARI (London, Ontario)

The subpallidal region centered on the substantia innominata (SI) has been implicated in the mechanism of secondarily generalized seizures from neocortex in rats, as well as in the generalization of amygdala kindled seizures in cats. We studied the effect of lesioning SI on secondarily generalized seizures induced by electrical stimulation of the prepyriform cortex (PPX) in rats following the establishment of an experimental interictal focus in the neocortex. Focal interictal spike activity was produced by applying a 1 mm^2 pledget of litmus paper soaked in aqueous penicillin G to one hemisphere of urethane anaesthetized Wistar rats. Ipsilateral bipolar stimulation of PPX was then carried out to induce secondarily generalized electrographic seizures. Following lesioning of SI using a DC current, seizures induced by electrical stimulation of PPX were abolished or decreased in duration and amplitude in 10 of 13 animals. This was not a non-specific effect of lesioning since lesions of PPX had no effect on seizures induced by SI stimulation in 7 additional animals. The results support the hypothesis that SI has a facilitatory role in the generalization of seizures from a neocortical focus. Whether this effect occurs via wide-spread cholinergic efferents to the cortex or by purely subcortical mechanisms remains to be determined.

P63.

Retrospective Study of Epileptic Seizures Following Cerebral Infarction

G. McCARRAGHER and A. GUBERMAN (Ottawa, Ontario)

The incidence of single or recurrent epileptic seizures as a sequela following cerebral infarction has been estimated as 10-20% in most studies. Seizures occurring in patients with cerebrovascular disease and previous ischemic brain damage are often difficult to differentiate from recurrent stroke and may per se predispose to additional ischemic neuronal damage. We have identified 50 patients with cerebral infarction who developed one or more epileptic seizures and have retrospectively examined variables including CT appearance and EEG which could serve as predictors for the risk of seizures post-infarction.

In our series 12/46 of the seizures occurred within the first month post-infarct, 14/46 1 month-1 year post-infarct and 20/46 greater than 1 year post-infarct. Seizures were generalized tonic-clonic in 18/43; partial in 25/43. All infarcts were hemispheric, anterior in 45/48, cortical in 48/50 and large in 25/38. The infarct was felt to be embolic in 13/25 cases where this could be determined. Thirty-five of the patients had left-sided infarcts. EEG subsequent to seizures was epileptiform in 12/46 cases.

Although we cannot make any statement about the incidence of epileptic seizures following cerebral infarction in this study, we can identify certain features of cerebral infarction which are more common in those patients who ultimately develop seizures. A "high-risk" profile could be described as a large, anterior, cortical, left-sided embolic infarction. Although a control population was not specifically used, clinical experience and information from stroke registries suggests that these characteristics are over-represented in our post-infarct seizures group. A large prospective study would be of benefit to define predictors of epilepsy more precisely and allow judicious prophylactic use of anti-epileptic drugs in cerebral infarct patients.

P64.

CT Scan Findings in Children with Epilepsy

D. KEENE, V. BRIGGS and P. HUMPHREYS (Ottawa, Ontario)

A review of the clinical data, EEG and CT Scan findings of 315 consequitive children with epilepsy was done. The clinical data included age of onset of seizures, type of seizure, findings on examination, intellectual status, degree of seizure control. EEG's were classified according to background and epileptiform abnormalities. CT Scans were independently reviewed and classified by the Radiologist.

230 patients had normal or normal variants on CT Scan. 85 had abnormalities on CT; 8 space occupying lesions; 9 lucent areas; 10 porencephalic cysts; 35 atrophy; 7 calcifications; 1 macrogyria; 5 agen-

esis of the corpus callosum; 2 subarachnoid cysts and 8 with microcephaly.

In the normal group, 56% had partial seizures; 7% had generalized tonic clonic seizures; 30% tonic; 2% myoclonic; 4% atonic; 1% mixed. 71% had normal intellect. 92% had a normal neurological examination. Seizures occurring more often than once per two months was noted in 15% of these patients. EEG background was normal in 68% with epileptiform abnormalities being found on 63%.

In the abnormal group 61% had partial seizures; 3% generalized seizures; 23% tonic clonic seizures; myoclonic seizures 5%; atonic seizures 2% and mixed 5%. 49% had normal neurological examination. 28% had normal intellect. 54% had poor seizure control. EEG background activity was normal in 31%. EEG epileptiform abnormalities were found in 62%.

Those patients who had an abnormal neurological examination, poor seizure control or abnormal EEG background, were felt to be more likely to have abnormal CT Scans.

P65.

Seizures from the Secondary Sensory Area

W.T. BLUME, J.P. GIRVIN and D.C. JONES (London, Ontario)

We report precise electrophysiological and pathological documentation of right secondary sensory seizures over a six-year period without apparent etiology in an otherwise healty 19 year old right handed woman.

Simple partial seizures consisted of numbness and tingling of lips, fingertips, and more rarely diffusely or throughout her head.

Complex partial seizures occasionally issued from simple partial seizures. Most began with a non-specific ill-localised sensation; then loss of consciousness, staring fearfully, a moan or cry, uttering brief sentences, grinding teeth, profuse salivation, automatisms, variable limb posturing, writhing, hyperventilation would occur. She would gradually emerge with a motor speech difficulty but not dysphasia. Olfactory, gustatory, abdominal, auditory deja-vu and visual phenomena were never present. No facial or arm myclonus was ever observed.

EEGs showed no focal spikes and no specific alteration with either of her clinical seizures. Subdural electroencephalography using lines and then grids showed simple partial and complex partial seizures arising from the right secondary sensory region with variable propagation principally with variable right lateral temporal spread but no inferior temporal involvement.

Effect of ablative surgery and pathology will be illustrated and discussed.

Although the secondary sensory area has been well outlined by stimulation studies in humans and other primates, spontaneous seizures originating from this area are rarely reported in humans. Much of their simple and complex partial symptomatology could be mistaken for temporal originating attacks possibly leading to unnecessary and unhelpful temporal lobectomy.

P66.

Localization of Epileptic Foci in Children

W.T. BLUME, M. KAIBARA and J.P. GIRVIN (London, Ontario)

Laboratory data from all 48 patients aged 16 years or less undergoing regional corticectomy for uncontrolled partial seizures were reviewed.

A radiologically apparent lesion was present in the lobe of operation in 32 patients (67%) whereas ipsilateral radiological abnormalities were noted in an additional 3. The most active spike focus corresponded to the operated lobe in 31 patients (65%). Adjacent and ipsilateral principal spikes appeared in an additional 12 patients (24%). Clinical seizures were EEG-recorded in 31 patients (65%). Of these, the seizures of 21 patients (44% of total) arose from the operated lobe whereas those of an additional 7 patients arose from either an adjacent lobe or were at least ipsilaterasl to the operated site. The seizure origin corresponded to the most active spike region in 22 of 28 patients with both phenomena (79%) and were adjacent or ipsilateral in the remaining 6 patients. Focal EEG delta activity appeared over the operated lobe in 22 of the 48 patients (46%) and was adjacent or ipsilateral to the operated lobe in an additional 7 patients.

We conclude that although recent advances in radiology have been valuable adjuncts in identifying the epileptogenic lobe, scalp EEG remains a reliable guide as outlined above. In no instance was false lateralization obtained by EEG when normal apiculate phenomena were exluded.

P67.

Magnetic Resonance Imaging Findings in a Boy With Acquired Epileptic Aphasia

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

Acquired epileptic aphasia (Landau-Kleffner Syndrome) is characterized by acquired receptive and expressive aphasia and seizures. This rare disorder presents during childhood and is often associated with poor recovery of language function. The underlying anatomical substrate and etiology have not been established. We describe abnormalities on magnetic resonance imaging (MRI) in a boy with acquired epileptic aphasia.

The patient was right-handed, healthy and had normal development until 5 years of age when he developed sudden onset of profound receptive and expressive aphasia. There was a history of upper respiratory infection immediately preceding the onset of aphasia. Shortly thereafter he had several generalized tonic-clonic and complex partial seizures. The seizures were controlled easily with anticonvulsant medication. However, the aphasia did not respond to treatment with several anticonvulsants medications including phenytoin, valproic acid, clobazam, intravenous diazepam, or corticosteroids.

The EEG demonstrated a slow, dysrhythmic background and frequent multifocal and generalized spike waves which originated most commonly from the temporal lobes (L>R). Computed tomography of the head was normal. Laboratory investigations for metabolic and infectious causes, including cerebrospinal fluid analysis, were normal.

Magnetic resonance images of the brain were obtained with a superconducting magnet of field strength 1.5 Tesla. Single echo T2 weighted spin echo coronal images demonstrated increased signal intensity in the medial aspect of the left temporal lobe, most marked in the cortical tissue. There was no mass effect associated with this finding. There was a smaller area of increased signal intensity in the medial aspect of the right temporal lobe. The signal changes were interpreted to result from increased tissue water associated with gliosis.

Although an inflammatory cause has been proposed for acquired epileptic aphasia, there is little data to support this hypothesis. The history of an antecedent infectious illness and the MRI findings in this boy are suggestive of a post-infectious encephalopathy. Furthermore, the location of the abnormality on the MRI scan in the mesial temporal lobe rather than the neocortex may imply that problems with verbal memory may play a role in the pathogenesis of acquired epileptic aphasia.

P68.

Focal Inhibitory Seizures and Speech Arrest in a Patient with a Cerebral Neoplasm: Case Report and Literature Review

R.A. PURDY, R.O. HOLNESS, V. SANGALANG and A. OLIVIER (Halifax, Nova Scotia and Montreal, Quebec)

Focal inhibitory seizures are rare events requiring clinical differentiation from more common causes of motor paralysis, including the postictal paralysis of Todd. The mechanisms of such seizures have been

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debated, however, their existence has been confirmed. Speech arrest is a more common clinical event in patients with seizure disorders.

We report the case of a 33 year old, left handed, man who presented with recurrent episodes of motor paralysis beginning in his right foot, marching to his right lower face and followed by an inability to speak. No convulsive activity was noted and was not seen on the single occasion that a seizure was witnessed by a neurologist. Five years prior to presentation the patient had a generalized tonic-clonic seizure and subsequently a low grade astrocytoma was biopsied in the left frontal lobe and treated with radiotherapy.

Neurological examination was initially normal. His EEG demonstrated a left frontal-temporal slow wave dysrythmia without epileptic activity. CT and MR scans demonstrated a large mass lesion in the left hemisphere. Subsequent CT guided sterotaxic biopsy was performed and local radiation therapy was given to a high grade frontal lobe glioma. The patient initially responded but deteriorated neurologically over four months and expired. Neuropathological examination demonstrated extensive tumor in the left hemisphere and corpus collosum.

Recent work of Lüders et al (1987) complements classical cortical stimulation studies and demonstrates that negative motor responses arise from peri-Rolandic areas. These studies suggest possible mechanisms to account for inhibitory seizures and speech arrest.

A discussion of the pertinent literature and detailed clinical, neuroimaging and neuropathological data will be presented on our patient.

P69.

Study of Partial Inhibitory Seizures in Childhood Epilepsy

M. OGUNI, H. SATO, K. HAYASHI and Y. FUKUYAMA (Tokyo, Japan)

Partial inhibitory seizures are a rare seizure type that is not included in the International Classification of Epileptic Seizures (1981). We have studied this seizure pattern in 7 patients with epilepsy who displayed clinical and EEG features resembling atypical benign partial epilepsy of childhood (Aicardi, 1981). When the patient was asked to keep both arms outstretched in front of the body, simultaneous video and EMG polygraphic recordings showed that dropping of an arm was synchronous with a single sharp and slow wave complex over the contralateral centrotemporoparietal region. In these examinations, the EMG discharges of the deltoid muscle were interrupted corresponding to dropping of the arm. In all cases, these interruptions appeared to start simultaneously with the top of the sharp wave component and stopped at the top of the wave component of the sharp and slow wave complex.

The partial inhibitory seizures were observed very frequently. These occasionally progressed to atonic absence seizures, when epileptic discharges appeared in a bilateral synchronous and rhythmic fashion.

The severity of this inhibition correlated with the amplitude of the contralateral epileptic discharge in one patient; i.e. higher amplitude corresponded with more intense inhibition and lower amplitude with less intense inhibition.

These results led us to the conclusion that the sharp and slow wave complexes over the Rolandic region would exert an inhibition of the contralateral motor control, suggesting the inhibitory nature of this type of epileptic discharge.

P70.

Myoclonic Status Epilepticus Following Cardiac Arrest

G.B. YOUNG, J.J. GILBERT and D.W. ZOCHODNE (London and Kingston, Ontario)

We present clinical, EEG and neuropathological features of 9 fatal cases of myoclonic status epilepticus following cardiac arrest. Five men and 4 women ranged in age from 18-87 years. All died without recovering consciousness following initial resuscitation.

Myoclonic seizures began 3-72 hours post-arrest, lasted 4-72 hours and were poorly responsive to standard anti-epileptic drugs. Seizures consistently involved various cranial nerve-innervated muscles in a symmetrical manner; diaphragm and limbs were variably affected.

EEGs were performed during myoclonus in 7 cases. Three showed burst-suppression with jerks during bursts. Two showed suppression, one had alpha coma and one had periodic bifrontal spikes.

At autopsy all had severe nerve cell damage to the cerebral and cerebellar cortices. All but one has ischemic cell change in thalamus, basal ganglia and spinal grey matter.

We conclude that our patients died of the initial anoxic-ischemic insult rather than status epilepticus and we suggest that clinical and EEG features are helpful in guiding treatment.

P71.

Fragmentary Myoclonus in Sleep Disorder Patients With Excessive Daytime Sleepiness

O. G. LINS and R.J. BROUGHTON (Recife, Brasil and Ottawa, Ontario)

Over the last 6 years the presence of brief fragmentary myoclonus has been described in association with excessive sleepiness in a variety of sleep disorders (Broughton et al. Electroenceph Clin Neurophysiol 1985, 61: 123-133). It consists of very brief generally <150 msec hypersynchronous potentials on surface EMGs which affect different body regions in asynchronous and asymmetrical manner. Visible movement may or may not occur. It was reported that these potentials resemble those of the physiological myoclonus ("twitching") of REM sleep but do not occur in clusters in REM sleep, as does the normal twitching with which it seems superimposed.

A comparison was made between a group of 12 patients with a polysomnographic diagnosis of fragmentary myoclonus and matched normals. EMG potentials over 50 uV were quantified as present or absent in all 2 sec miniepoques. It was found that patients with fragmentary myoclonus had on average over 3 times the amount as control subjects. Moreover, in the latter group it was more or less restricted to stage 1 for several min after sleep onset plus REM sleep, whereas in those afflicted it was present in all sleep stages.

(Supported by the Medical Research Council of Canada)

P72.

Early Discontinuation of Anticonvulsants Following Neonatal Seizures

S. PARNES (Ottawa, Ontario)

The optimal duration for the treatment of neonatal seizures is not known. As studies in newborn animals have shown that chronic exposure to anticonvulsants may have deleterious effects on brain growth, it would seem prudent to avoid unnecessary exposure of the newborn to anticonvulsants.

Cases of neonatal seizures evaluated at the Children's Hospital of Eastern Ontario in 1985-1986 were reviewed. These babies were treated serially with Phenobarbital, Dilantin, Lorazepam, and/or Paraldehyde in doses needed for acute seizure control. Maintenance anticonvulsant was then given for 2 weeks or less. Of the 32 patients in whom 2-year follow-up is available, 8 had a recurrence of seizures off medication, 4 patients recurred with infantile spasms, 1 with benign febrile seizures, 2 with partial seizures, and 1 with a generalized post-hypoxic seizure. It is likely that only the recurrences in those who did not have infantile spasms might have been prevented if the patients had remained on medication, and this would have required maintenance anticonvulsant for up to 2 years.

Because the rate of recurrence was relatively low and because recurrences might have been preventable in only 12% of patients, early dis-

continuation of anticonvulsants following neonatal seizures is recommended.

P73.

"Near-Miss" Sudden Unexpected Death in Epilepsy

F. JACQUES, A. GUBERMAN and G. JONES (Ottawa, Ontario)

Sudden, unexpected death in epilepsy (SUDE) occurs in as many as 1/100-1/500 epileptic patients. Although a high-risk patient profile has been defined, underlying pathophysiological mechanisms are poorly understood. Our investigation of a patient who nearly died from pulmonary edema following 2 generalized tonic-clinic seizures within the space of 1 hour have allowed us to speculate on the possible pathophysiological factors involved in the SUDE syndrome.

The patient was a 32-year-old otherwise healthy woman with recently-diagnosed idiopathic generalized tonic-clonic nocturnal seizures. She had 2 convulsive seizures spaced over approximately 1 hour and less than 1/2 hour later suddenly suffered severe respiratory distress due to pulmonary edema without evidence of aspiration. Serum phenytoin and carbamazepine levels were subtherapeutic. She was ventilated for 6 days and given inotropic support. Blood gases revealed a marked mixed acidosis and moderate hypoxia. She had bilateral pulmonary infiltrates with no elevation of jugular venous pulse. Later pulmonary arterial pressure was elevated and pulmonary capillary wedge pressure borderline elevated. No cardiac arrhythmias were detected. She recovered completely within 9 days and her seizures have subsequently been well-controlled over 1 1/2 years. MRI scan of the head was normal.

Findings in this case support neurogenic pulmonary edema rather than cardiac arrhythmia as the cause of the SUDE syndrome. Another potential pathogenetic factor which cannot be ruled out is aspiration of gastric contents.

P74.

A Preliminary Study of Development in Children of Epileptic Mothers

M. LYSYK and E. ANDERMANN (Montreal, Quebec)

Growth and development in offspring of epileptic mothers remains an area of concern and controversy. It has already been demonstrated that these children have an increased risk of major and minor congenital malformations. However, other abnormalities in physical, mental and psychosocial development are not as well recognized.

In this study, the cognitive, motor (gross and fine) and sensory abilities of preschoolers ranging in age from 2 yrs 9 mo to 5 yrs 6 mo were evaluated. The children were randomly selected from those whose mothers were followed during pregnancy at the Neurogenetics Unit of the Montreal Neurological Institute. To date, 9 children have been assessed.

All evaluations were performed at the homes of the children to allow for an informal assessment of the home environment, including the physical and emotional climate. The evaluator was aware only of the names, ages and addresses of the children prior to commencing the evaluations. Pregnancy, birth and developmental histories were also obtained during the visits.

The developmental assessment tool used was the Miller Assessment for Preschoolers (MAP). This is an individually administered tool consisting of 27 items standardized for children aged 2 yrs 9 mo to 4 yrs 8 mo. It provides an overview of the child's developmental status with respect to other children the same age.

Preliminary findings from the MAP show that 8 of 9 children are functioning in the top 25% or better as compared to the standardization sample, with a mean percentile score of 78.2 (n=8). In four of the children, the birth, pregnancy and delivery history revealed some complications (e.g. maternal seizures, umbilical cord around neck). However, in all but one, the subsequent development was not significantly affected.

These findings appear to confirm those of previous studies, employing different developmental scales (Denver, Griffiths).

P75.

Trends in Pregnancy Outcome in Epileptic Women Over Two Decades: Relationship to Maternal Anticonvulsant Therapy

M. OGUNI, L. DANSKY, E. ANDERMANN, C. WOLFSON, A. SHERWIN and F. ANDERMANN (Montreal, Quebec)

We have studied the correlation between maternal exposure to anticonvulsant drugs during pregnancy and subsequent prevalence of abnormal pregnancy outcomes (major congenital malformations and spontaneous abortions) in the offspring. The patient material consisted of 109 pregnant epileptic women who had pregnancies followed prospectively at the Montreal Neurological Hospital between 1981 and 1988. The purpose of this study was to compare the prevalence of abnormal pregnancy outcomes in this cohort with the previous study by Dansky et al. (1982) from the same institution.

Our results have shown a significant decrease in the prevalence of major malformations, including positional deformities and hernias, as compared with the previous study: 4 (7%) of all newborns have major anomalies, and 9 (10.3%) of all pregnancies terminated in spontaneous abortions, as compared to 24.1% and 5.2% respectively in the data of Dansky et al.

Monotherapy was more frequent in this study (62% vs 38%; $x^2<0.01$). The mean number of drugs used during pregnancy was significantly smaller in the present study (1.4 vs 1.8). Phenytoin, phenobarbital and primidone were prescribed less frequently in the present study (39%, 17% and 6% vs 76%, 43% and 17%), whereas carbamazepine and valproic acid were used more frequently (50% and 20% vs 20% and 8%). Three of the four major malformations in this study were observed among children exposed to VPA in the first trimester. Plasma levels of VPA during pregnancy were higher in mothers of malformed babies (109±34 vs 64±26).

In conclusion, the type and number of drugs used during pregnancy, as well as the plasma concentrations, may determine the frequency of abnormal outcomes. In recent years, the tendency to monotherapy, introduction of newer anticonvulsant drugs, and decreased use of barbiturates have resulted in the reduction of abnormal pregnancy outcomes.

P76.

Education of Schoolchildren to Prevent Social Disability Related to Epilepsy

B. LAMBERT, G.M. RÉMILLARD, B. ZIFKIN, N. GIARD and F. PICARD (Sept-Iles, and Montreal, Quebec)

In this comic strip colouring book, NEURO 88, a remote control electronic toy dog, has been left alone because his master, Alberta, has just had a seizure.

Two schoolchildren, Luc and Sophie, spot him. Albert has programmed NEURO 88 to speak only to children because many adults do not understand epilepsy and make fun of him. The children are fascinated by this unusual toy. He comes to life as they play with his controls.

NEURO 88 explains to them that the symptoms of epilepsy are temporary and due to excessive electrical discharge in the brain. He reminds them that other children may have allergies or wear spectacles, that nobody is perfect.

NEURO 88 shows them how generalized tonic-clonic seizures involve jerking movements of the entire body. He also describes absences and partial seizures. Luc and Sophie are fascinated. They ask how they can help someone who is having a seizure. NEURO 88 explains to them that they should remove objects which could be harmful and that they can place something soft beneath the person's head. After the seizure is over, they could remain calm, not make fun of the person and remain until normal activities can be resumed.

Luc and Sophie now recall that one of their classmates wears a medic-alert bracelet with "EPILEPSY" engraved on it. Now they know what this means. NEURO 88 suggests that one can always get in touch with local epilepsy associations which, like him, provide information on epilepsy.

Neurophysiology

P77.

VEPs in Acute Onset Cortical Bindness in Children

M.J. TAYLOR and D.L. McCULLOCH (Toronto, Ontario)

VEPs were recorded in 45 children (4m-17 yrs) who were clinically diagnosed as cortically blind following an acute insult. All the children had no significant visual or neurological problems prior to the insult which included trauma (n=8), cardiac (post cardiac surgery or cardiac arrest) (n=16), other post-operative complications (n-5), meningitis (n=4), encephalopathy (n=4), hypoxia (n=3), and other (5). Flash VEPs were recorded during the acute stage of cortical blindness in most patients; later recordings were either flash or pattern VEPs, depending on the age and visual status of the child. Multiple VEP studies were done in 29 children. VEPs were graded as normal, abnormal or absent.

The VEPs remained fairly stable over repeat studies in most patients. Some improvement in VEPs was seen in 12 of the children who progressed from cortical blindness with absent VEPs, to only poor visual function and abnormal VEPs on follow-up. Normal flash VEPs in the acute stage were followed by abnormal VEPs to smaller pattern stimuli in 3 children, associated with somewhat decreased visual acuity (e.g., 6/15 - 6/30). However, all children that had normal VEPs acutely recovered at least useful visual function; none with abnormal or absent VEPs acutely were visually normal on follow-up. Abnormal VEPs were most often associated with subsequent visual impairment, but less often blindness. Absent VEPs usually predicted continued blindness or very poor recovery of visual function (ie., light perception only). Hence, in a child who is cortically blind due to an acute insult, VEPs can be useful in predicting whether the blindness will or will not be transitory.

P78.

Central Pathway Involvement in Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay

J. DE LÉAN, J.-P. BOUCHARD and J. MATHIEU (Quebec City and Chicoutimi, Quebec)

Evoked potential studies have been reported in Friedreich's ataxia and in several other inherited cerebellar ataxias. Central pathway conduction has never been investigated in autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS).

Somatosensory (SEP), brainstem auditory (BAEP) and pattern-reversal visual (VEP) evoked potentials were recorded in 67 patients with ARSACS and in a group of 60 healthy subjects. The mean age of the ataxic patients was 25 years with a range from 5 to 56 years.

SEP revealed a marked attenuation of the clavicular potential consistent with degeneration of some spinal ganglion neurons. In addition, the cortical response was dispersed and delayed indicating slowed conduction in the central sensory pathways. BAEP showed a significant delay in the I-III interpeak latency suggesting a degeneration process in the spiral ganglion neurons. The III-V interpeak latency was normal. VEP revealed a dispersed and delayed cortical response. These results will be presented with a longitudinal approach and discussed in light of the electrophysiological abnormalities reported in other inherited ataxias.

There is a high incidence of asymptomatic auditory and visual pathway involvement in ARSACS. These findings reveal a widespread process of axonal degeneration in the primary sensory neurons as well as in the central nervous system.

P79.

Frequency Specific Analysis of Maturation in the Human Auditory System Using Derived Band ABR's

C.W. PONTON, S.G. COUPLAND, J.J. EGGERMONT and R. WINKELAAR (Calgary, Alberta)

The auditory brainstem response (ABR), as described by Jewett and Williston (1971), consists of a series of five to seven peaks that occur in the first 10 milliseconds following the presentation of an acoustic stimulus such as a click. The temporal interval between wave I and wave V in the ABR, referred to as central conduction time, reflects synaptic delays and neural conduction time from the distal end of the auditory nerve to the level of the mid pons in the brainstem as well as traveling wave delay in the cochlea. In developmental ABR studies, it has been shown that the I-V interval for click-evoked ABR's decreases as function of age, reaching asymptote to adult latencies values at about three to five years of age. In studies that have used frequency-specific stimuli such as band-pass filtered clicks to evoke the ABR, it has been demonstrated that the I-V interval for low frequency stimuli attains adult latency values earlier than for high frequency stimuli (Teas et al., 1982). The present investigation assessed frequency specific maturation of the auditory system using the high-pass noise-masking technique (Don and Eggermont, 1978; Eggermont and Don, 1980) to obtained derived band ABR's on full-term and premature infants. By four months of age, no significant difference was found between adults and infants in the I-V interval from low CF derived ABR's. However, the I-V interval was still significantly longer for infants than for adults in the high CF derived ABR's. Thus, confirming the findings of Teas et al., (1982) it was found that in the human auditory system, low frequency channels mature *earlier* than high frequency channels.

P80.

Evoked Potentials in Cerebral Dysgeneses

S.G. COUPLAND and H.B. SARNAT (Calgary, Alberta)

Visual and auditory evoked potential studies were performed over a four year period in 24 children with defined cerebral malformations. Diagnoses were confirmed by CT-scan, supplemented in some cases with MRI, cranial ultrasound, or neuropathological examination. Of 8 cases with callosal agenesis, one was associated with colpocephaly and 2 had Aicardi syndrome. Seven cases of holoprosencephaly included 2 of the alobar type, 3 of the semilobar or lobar types, and 2 additionally presented a congenital vertex encephalocele. Single cases each of septo-optic dysplasia, lissencephaly, pachygyria, megalencephaly without gross morphological abnormality, hemimegalencephaly, focal dysplasia of the frontal lobe, microcephaly with multifocal dysplasias, optic nerve hypoplasia, and cerebellar hypoplasia also were available for study. Ninety multimodality evoked potential studies were performed in these 24 cases over the study period: 14 ERGs were recorded in 9 patients; 52 flash-VEPs in 21 patients; 24 click-ABRs in 16 patients. The VEPs and ABRs were delayed in about half of our cases of callosal agenesis, but ERGs were normal except in 2 cases of Aicardi syndrome. Flash VEPs were abnormal in 6 of 7 cases with holoprosencephaly; in 3 cases the VEP was nonrecordable and in 3 the waveform morphology was grossly distorted. ABRs recorded in these holoprosencephalic children had a delayed wave V and prolonged I-V central brainstem pathway conduction times. ABR central conduction time delay was also observed in our patients with lissencephaly, pachygyria, and generalized megalencephaly. Conduction time delay through the optic nerves and retrochiasmal visual pathways was also evident in these cases and also in the case of hemimegalencephaly. VEPs were delayed or extinguished in septo-optic dysplasia and in optic nerve hypoplasia, but the ABRs were found to be normal in septo-optic dysplasia. Evoked potential studies, though not specifically diagnostic of cerebral malformations, provide confirmation of functional distur-

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bances associated with anatomical anomalies of cerebral development and help disclose small unsuspected associated lesions. Evoked potentials are a useful supplement in the investigation of children with cerebral dysgenesis.

P81.

Cortical Source Localization Through Topographic Visual Evoked Potential Mapping and Single Photon Emission Computed Tomography (SPECT)

S.G. COUPLAND, C.W. PONTON and D. MUELLER (Calgary, Alberta)

Use of new imaging techniques such as MRI, PET and SPECT have provided new insights into functional neurophysiology of healthy and diseased brain. Recent investigations have established that regional distribution of hexa-methyl-propylene-amine-oxime (HMPAO) is proportional to regional cerebral blood flow (rCBF) and reliably identified areas of abnormal perfusion in cortical areas of seizure patients. Our intention was to (i) study the sensitivity of HMPAO in detecting areas of increased rCBF activity in *normal* visual cortex and (ii) compare the area of visual cortex localization identified by HMPAO deposition with the scalp field topography of the VEP. Two human subjects monocularly viewed half-field (left or right, upper or lower) pattern reversing checks (45 minutes of arc) with a field radius of 20° at 2 reversals/second for a two minute period during infusion of HMPAO. On separate occasions pattern VEPs were recorded from up to 16 channels using several different montages to the same stimulus configuration. Resultant scalp field distribution maps (global field power) and current source derivation analytic techniques were used and correlated with rCBF localization of visual activity. There was a high degree of correlation between VEP scalp-field localization and HMPAO regional distribution. The results of these investigations will be presented and compared to previous evoked potential studies of hemi-field stimulation.

FRIDAY, JUNE 16TH

Behavioral Neurology

P82.

Alzheimer's or Binswanger's Disease?

A. KERTESZ, M. POLK and T. CARR (London, Ontario)

Recently white matter hyperintensities have been seen in demented and stroke patients on magnetic resonance imaging (MRI). We studied patients selected on the basis of clinical diagnosis of Alzheimer's disease (AD) (n=27), vascular dementia (9) and normal age matched controls (12). Out of the 27 Alzheimer patients, 13 were reclassified as Binswanger's disease (BD) on the basis of objective scoring of the white matter hyperintensities. The images were evaluated without knowing the patient's condition. Images were scored on a scale of 0-4 for ventricular enlargement, sulcal atrophy, periventricular rim, or hyperintensity, periventricular caps, and unidentified bright objects (UBOs) (unidentified by clinical event or comparable CT evidence of infarction).

Neuropsychological evaluation included the Mattis Dementia Rating Scale with a cut-off score of 128, the Wechsler Memory Scale (WMS-R), block design, digit symbol, Raven's Progressive Mattrices, word fluency, verbal and performance intelligence (WAIS-R), and the Western Aphasia Battery (WAB). Multivariate statistics indicated that the sentence comprehension task from the WAB and the paired associate task from the WMS-R were significant discriminators of AD and BD. The status of these two entities pathologically, radiologically and clinically will be discussed. It is concluded that white matter hyperintensities, as seen on the MRI, contribute to the heterogeneity of clinically diagnosed AD. BD, as diagnosed on MRI, may represent a hypertension related entity that requires different treatment from AD, although it may coincide with AD. It is distinguishable from normal aging.

P83.

A Randomized Trial Evaluating the Effect of Cognitive Behavioral Therapy on Home Behavior in Boys with Attention Deficit Hyperactivity Disorder (ADHD)

D.L. FEHLINGS, G. DAWE, W. ROBERTS and T. HUMPHRIES (Toronto, Ontario)

Cognitive Behavioral Therapy (CBT) attempts to teach the child to stop and think before he acts. This study hypothesizes that by focusing on home behavior in the child's sessions, and directly instructing the parents in CBT in the natural home setting, that parental ratings of the child's inattentiveness, impulsiveness, and hyperactivity will improve compared to a supportive therapy control group.

Twenty males (age: 7-13 years) with a diagnosis of ADHD, were included in the study and randomized to CBT or a supportive therapy group. Children on ritalin or with conduct disorder were excluded. Treatment consisted of 12 individual child sessions and 8 family sessions in the home.

The following represent pre-post differences in treatment effects for the first ten families enrolled in the study (6 CBT, 4 supportive) analyzed by ANOVA. CBT was associated with a significant improvement in parental ratings of hyperactivity (Werry Weiss Scale) ($F=5.98$, $P < 0.04$). The Attention Problem Subscale of the Behavior Problem Checklist revealed a minor but nonsignificant treatment effect ($F=2.25$, $P<0.17$) favouring the CBT group. The parents' and teachers' ratings on the Self Control Rating Scale, and the child's ratings on the Piers Harris Self-Esteen Scale improved similarly in both groups. These results suggest that parents' perceptions of the child's hyperactivity in the home can improve significantly following Cognitive Behavioral Therapy.

P84.

Ideomotor Apraxia in Huntington Disease

P.A. SHELTON and D.S. KNOPMAN (Winnipeg, Manitoba; Minneapolis, U.S.A.)

Ideomotor apraxia is a disorder of the performance of previously learned complex movements which cannot be ascribed to abnormalities in elementary motor function. The pattern of errors suggests, rather, abnormal selection and sequencing of component movements. It results from destruction of parietal or premotor association cortex of the dominant hemisphere or disconnection of these areas and in Alzheimer's disease (DAT), suggesting these motor functions are dependent on cortical processing.

Evidence indicates the basal ganglia are involved in the programming of simultaneous or sequential movements. Therefore we assessed the incidence of ideomotor apraxia prospectively in individuals with Huntington Disease (HD) (N=9) and compared their performance to a group with probable DAT (N=6). The groups differed in age (HD 50.9±15.7 yrs; DAT 81.3±3.7 yrs) and in duration of symptoms (HD 10.4±5.2 yrs; DAT 5.6±3.3 yrs) but both were in mid-course and had equivalent Functional Disability Rating (HD 3.44; DAT 4.00; $p >0.087$). They were evaluated with MMSE, an auditory comprehension test, constructional ability and several measures of praxis. Only unequivocal apraxic errors were included in the Apraxia Score. Ideomotor apraxia occurred in 33% (3/9) of HD and was moderately severe in 11% (1/9); mild apraxia occurred in only 17% (1/6) of DAT. All measures of apraxia in HD correlated with the subjective rating: Apraxia Score (Spearman $r=0.92$, $p<0.0004$), total apraxic errors ($r=0.84$, $p<0.004$). Therefore, ideomotor apraxia occurs at least as frequently in HD (mean errors=6.0) as in DAT (mean errors=2.5) at this

stage in the course (Wilcoxon rank sum $p>0.18$). Errors in movement imitation were associated with apraxia in HD ($r=0.72$, $p<0.042$) but movement recognition was normal. Degree of apraxia correlated significantly with duration of disease ($r=0.68$, $p<0.043$) but not with other measures of cognitive function or motor disability.

P85.

A Working Model for the Assessment of Patients with Memory Disorders

J. WILLMER, D.A. GUZMAN, D. STUSS, J. NAVARRO and E. BAZILE (Ottawa, Ontario)

The assessment of patients with memory problems can be a difficult and time consuming task and diagnosis of many conditions is by a combination of excluding known easily detectable conditions, clinical judgment and close follow-up. Accurate diagnosis is essential for providing good prognostic information to relatives and caregivers, for evaluation of new therapeutic modalities and for the purposes of research.

More than 300 patients have now been assessed using a standard protocol. All patients are examined by a neurologist, neuropsychologist, psychiatrist, social worker and nurse. Standard investigations including CT scans, EEG's, neuropsychological tests and a bettery of hematological and biochemical studies are carried out. Results are recorded in a standardized fashion. Diagnosis is then reached by consensus after discussing all the data as a group. Patients are all followed on a 6-12 month basis to determine the accuracy of the original diagnosis.

Demographically, our population had roughly equal numbers of each sex. Ages ranged from 33 years to 90 years with a mean of 68.5 years. Functionally patients ranged from normal to severely demented. The diagnoses made were broken down as follows: normal (15%), depression (6%), dementia of the Alzheimer type (47%), multi-infarct dementia (2%), mixed dementia (3%), other known cause (9%), unknown (18%).

Information obtained has been useful in providing clinical support to community caregivers. In addition a database has been set up for use in current and future research projects. We believe that the clinic model presented is both a means of achieving more accurate diagnoses, better and more cost effective utilization of medical service, and an effective instrument for follow-up assessment and care.

P86.

Cognitive Delay in Duchenne Muscular Dystrophy

A. AL-QUDAH, J. KOBAYASHI, S. CHUNG, M. DENNIS and R. WORTON (Toronto, Ontario)

The exact etiology of cognitive delay in Duchenne muscular dystrophy (DMD) is unknown. Histopathological and CT scan studies described structural brain changes. To our knowledge, no brain MRI studies have been done on DMD patients to delineate further these structural brain changes. We have prospectively studied four DMD patients by MRI of the brain, verbal I.Q., genomic DNA analysis, and clinical evaluation.

The first patient (13 years) had normal MRI, I.Q. of 85 and no DNA deletion. The second patient (14 years) had mild atrophy-like changes on MRI, I.Q. of 85 and no DNA deletion. The third patient (18 years) had mild atrophy-like changes on MRI, I.Q. of 113 and large DNA deletion encompassing exons 3-30. The fourth patient (19 years) had normal MRI, I.Q. of 87 and small deletion encompassing exons 41-43.

There was no significant correlation between the I.Q. and the MIR findings, genomic DNA analysis, and the severity of the disease.

With these first MRI studies in DMD, we concluded that they did not show any significant anatomical brain changes other than the mild atrophy like changes in 2 patients. We believe this is an important finding to consider in investigating the etiology behind cognitive delay in DMD in the future.

P87.

Sensory and Perceptual Processes Underlying Visual Object Recognition

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

In spite of its automaticity, visual object recognition is a highly complex skill that comprises many component processes. The senses provide a pattern of varying light intensities from which structural information must be derived for object recognition. Objects can normally be recognized irrespective of their orientation, size, level of illumination, but this requires that a correspondence be established between the initial representation and the stored representation that specifies the object's structure. This is achieved through a series of transformations and normalisations aimed at correcting deviations of the early descriptions from the stored representations. The nature and efficiency of these operations were examined in normal, commissurotomized, hemispherectomized, and unilaterally brain-damaged subjects in an attempt to obtain converging information about the respective contribution of the cerebral hemispheres to early stages of object recognition. The "sensory" tasks consisted of measures of visual acuity, contrast sensitivity, and visual-field mapping; the "perceptual" tasks involved the matching of same views of objects and faces, of different views of same objects and faces, of low-pass stimuli, as well as recognition of disoriented stimuli requiring a mental rotation operation. Both individual and group analyses were carried out to examine the pattern of performance across tasks. The results of the sensory tests indicated a selective deficit in low-frequency resolution among right-hemisphere damaged subjects independent of visual acuity and visual-field defect. This deficit was significantly correlated with performance on perceptual tasks, but differently so depending on the nature of the task. However, this sensory deficit was not sufficient to explain the whole perceptual performance. Left hemisphere damaged patients were defective on perceptual but not on sensory tasks, and the pattern of their results was qualitatively different from that of normal subjects.

Neurosurgery

P88.

Taking Aim at the Giant Pituitary Tumor — One Arrow or Two?

J.P. KRCEK and F.E. LEBLANC (Calgary, Alberta)

Fifteen cases of giant (>2 cm suprasellar extension) pituitary tumor were reviewed for presentation, magnitude and direction of extension, choice of operative approach, postoperative complications and efficacy of the surgical treatment that was chosen. Six patients had two-stage procedures, seven had bifrontal approach only and two had trans-sphenoidal approach only. Only one patient underwent post-surgical radiotherapy. In this series, eleven patients were male, two of whom had prolactin-secreting tumors. None of the four females had prolactinomas. If cure is defined as complete tumor extirpation with absence of clinical or anatomical recurrence for a minimum of 2 years, as well as full recovery of visual fields; twelve of the fifteen patients met such criteria, for a surgical efficacy of 80%. One patient died one year after a bifrontal extirpation of a giant prolactinoma, the result of operative hypothalamic infarction.

P89.

Brain Tumor Biopsy Using a Noninvasive Stereotactic System

T. DOORLY, A. NORTH and R. PERRIN (Toronto, Ontario)

Most stereotactic systems in current use are invasive, using pins to fix the frame to the skull. To minimize patient discomfort and the risk of dislodging the frame, surgery has to closely follow the radiological studies to localize the target. Once removed, repositioning these frames

in a reproducible manner is difficult. Further procedures cannot be safely performed without first repeating the radiological studies with the frame applied.

We have recently used the noninvasive, Laitinen stereotactic system to biopsy brain tumors in 20 patients. The Laitinen system consists of a stereoadapter and a phantom base. The stereoadapter is mounted on the patient's head by means of 2 ear plugs and a nasion support only. Our preliminary experience with this system will be presented. We have found that Laitinen system to have certain advantages. It is noninvasive, is quick and easy to apply and is well tolerated by the patient. The system can be easily taken off and reapplied at a later date with a high degree of accuracy and reproducibility. It is CT and MRI compatible and appears suitable for use in a wide range of stereotactic and functional neurosurgical procedures.

P90.

Microsurgical Anterior Cervical Discectomy

T. DOORLY and J. PHILLIPS (Toronto, Ontario; Dublin, Ireland)

In the 3 year period to April 1985, 42 patients underwent microsurgical anterior cervical discectomy for cervical disc prolapse. Interbody fusion was not employed in any of these patients. The results of a 3 year follow-up are presented.

There were 24 males and 18 females with a mean age of 50 years. In 13 patients (31%) symptoms commenced following a significant cervical injury. Only 31% of all patients had symptoms for longer than 1 year. Radicular symptoms and signs were present in 67%. In 39 patients only 1 disc was involved radiologically. In the other 3 patients 2 adjacent discs were involved.

A standard microsurgical technique of discectomy and osteophytectomy was employed. In this series there was no operative mortality. There were no injuries to the carotid or vertebral arteries, the trachea, esophagus or spinal cord. There were no nerve root injuries, no postoperative hematomas requiring evacuation and no wound infections. Ten patients complained of transient worsening of neck or arm pain, or transient dysphagia. Two patients did not improve at all following surgery. Five patients had a modest improvement but remained with some limitation of activity. The remaining 35 patients (83%) had either complete or near-complete relief of symptoms and returned to full activity.

Microsurgical anterior cervical discectomy without interbody fusion is easy to perform, safe for the patient, and at least as effective as fusion procedures in current use. We consider this operation as the surgical treatment of choice for cervical disc prolapse.

P91.

The Relationship Between Axon Counts and Neurological Function after Experimental Spinal Cord Injury

M.G. FEHLINGS, M. LEWICKI and C.H. TATOR (Toronto, Ontario)

The relationship between the number of surviving axons at the injury site and the extent of clinical neurological recovery after spinal cord injury (SCI) is not known. In the present study, this relationship was examined in rats with graded severity of clip compression injury of the cord at T1. The rats were randomly assigned to one of the following injury groups (n=5 each): normal (laminectomy only), 2 g, 17 g, 30 g, 50 g and 100 g clip injuries. Clinical neurological function was assessed by the inclined plane method. A morphometric assessment of axons at the injury site was performed by a computer-assisted line sampling technique.

The inclined plane scores varied as a linear function of SCI ($r=0.93$; $p<0.0001$). The mean axon count was 370,000±27,000 in normal rats and decreased as a negative exponential function of injury force ($r=-.81$; $p<0.0001$). Furthermore, inclined plane scores varied as a logarithmic function of axons at the injury site ($r=0.85$; $p<0.0001$). Additionally, spinal cord injury resulted in significant demyelination, particularly of large axons and caused preferential destruction of large calibre axons as reflected by the change in mean axon diameter from 1.74±0.06 um in normal cord to 1.46±0.04 um in injured cord (pooled mean for all injuries). In summary, these data quantify the anatomical basis for neurological dysfunction after cord injury, and for the first time demonstrate the critical number of myelinated axons required for recovery of motor function.

P92.

Post-Traumatic Syringomyelia

R. FIEBEL, R. HAMDY, N.A. RUSSELL and B.G. BENOIT (Ottawa, Ontario)

Eight patients with symptomatic post-traumatic syringomyelia (PTS), diagnosed by magnetic resonance (MR) imaging were treated by a variety of syrinx drainage procedures. These included laser fenestration, syringo-subarachnoid and syringo-peritoneal shunting, and in one case a syringo-pleural shunt. One patient was completely relieved and three were improved. Four did not improve, but their symptoms did not progress.

Difficulty in maintaining patency in syrinx subarachnoid drainage procedures may be due to arachnoidal adhesions associated with PTS. Our experience suggests that unless preservation of the spinal subarachnoid space can be demonstrated by MR imaging, it may be prudent to consider syringo-peritoneal shunting, as the initial surgical procedure in PTS.

P93.

Cervical Spinal Cord Injury in Ankylosing Spondylitis

D.W. ROWED (Toronto, Ontario)

Ankylosing spondylitis (A.S.) (increases the risk of cervical spinal and spinal cord injury as a result of relatively minor trauma. Few comprehensive reviews of this subject exist, and accordingly our experience with 15 consecutive cases from a population of over 1200 cases of spinal and spinal cord injury seemed worth examining.

Mean age of the patients was 62.5 years, mean followup was 48 months, and mean pre-injury duration of A.S. was 23.3 years. Other salient features were a male/female ratio of 13.2 (87%), a cervical injury site in 14 (93%), and causation by falls in 11 (73%).

Patients were initially managed by halo vest immobilization, with 7 (47%) being further subjected to operative decompressive and/or stabilization procedures.

Overall morbidity and mortality were relatively high. Four patients (27%) died from complications of spinal cord injury and 4 (33%) required chronic institutional care. In the operated group, 3 (43%) died and 3 (43%) remained institutionalized.

Additional population characteristics and management strategies will be discussed. A.S. patients are at risk for serious spinal cord injury. Nonoperative management is recommended in patients who are not deteriorating neurologically.

P94.

Spontaneous Atlantoaxial Dislocation of Unknown Etiology

M.G. HAMILTON and M.E. MacRAE (Calgary, Alberta)

Spontaneous atlantoaxial dislocation is well-described and is usually associated with pharyngeal infection or inflammatory joint disease.

A 27-year-old, otherwise healthy female presented with a four month history of neck pain, stiffness and a slight decrease in neck mobility. Two weeks prior to admission she began to experience severe neck pain, a significant decrease in neck mobility, tingling in her fingers, arm heaviness and noted trouble opening jars. There was no history of trauma, throat infection, joint disease, bowel disease or skin lesions.

Physical exam demonstrated a right head tilt, tenderness over the upper posterior neck and a marked decrease in neck range of motion. The remainder of the exam was normal.

Cervical spine x-rays demonstrated atlantoaxial dislocation with an anterior atlanto-dens-interval measuring 9 mm and increasing with flexion. No bone abnormalities were noted. A CT scan and bone scan were unremarkable. A comprehensive lab investigation was remarkable only for an elevated ESR (41 mm/hr) and a marginally elevated alkaline phosphatase (127 U/L). A rheumatologic consultation failed to identify any evidence of arthritis. A Cl-2 posterior fusion was performed.

In summary, we present a 27-year-old female with spontaneous atlantoaxial dislocation with no clinical, radiological or laboratory evidence of infectious or rheumatologic disease. We believe this to be the first such described case.

P95.

Deep Tendon Reflex Characteristics of Spasticity Due to Spinal Cord Injury

P.W. NANCE (Halifax, Nova Scotia)

Although spasticity has been defined partly as hyperreflexia, this term may not be appropriate. A solenoid-driven hammer capable of delivering variable intensity of force from 1-10 was used to evoke deep tendon reflexes (DTR) in six spastic spinal cord injured (SCI) subjects and non-SCI subjects. Electrodes were placed over the mid-point of the calf and 8 cm distal. Force-response curves were generated for each subject. Next, the highest impact force (10) was used to evoke a control DTR, a DTR with Jendressik reinforcement (JR), a DTR during 20 seconds of tibial vibration, and a one minute post-vibration DTR. The data were analysed using an ANOVA with repeated measures. Both groups showed graded responses such that the greater the impact force the larger the DTR amplitude. There was a statistical trend for the mean DTR of the SCI subjects to be below the mean of the control subjects for every impact intensity. Control subjects' DTR was increased with JR. Unlike control subjects, the SCI subjects showed an absence of reflex reinforcement (JR). Vibratory inhibition of the DTR was present for both groups. Thus, a force-response relationship of the DTR exists for both SCI and control subjects. Surprisingly, the DTRs of the SCI group tended to be **less** than the controls with the same intensity of stimulation. Preservation of the inhibitory effects of vibration by SCI subjects suggests that muscle spindle sensitivity and output capacity are preserved in these subjects. These results indicate that hyperreflexia is not a general characteristic of spasticity due to SCI. Spasticity may be best characterized by a velocity associated increase of muscle tone.
(Support by the Canadian Paraplegic Association)

P96.

Extradural Spinal Meningiomas

D. IZUKAWA, N.A. RUSSELL, S. CURUVIJA, B.G. BENOIT and M.R. RICHARD (Ottawa, Ontario)

Spinal meningiomas are well recognized as intradural, extramedullary tumors. In 15% of cases, there may be dural invasion and neoplastic growth in the extra- and intradural space. Purely epidural lesions are rare.

We present 4 patients with spinal meningiomas confined to the extradural space. Three were female, 1 was male and the mean age was 55. Two tumors arose in the mid-thoracic region while 2 were cervicothoracic. Myelopathy was present in all cases. The 2 cervico-thoracic meningiomas also caused radiculopathy and 1 had a Horner's syndrome. Although plain films and computerized tomographic myelography were also used, the most useful investigation was magnetic resonance imaging.

Gross total resection was achieved in each case. In 1 patient, a thoracic root and its dural covering was sacrificed. All tumors were adherent to nerve root dura just proximal to the intervertebral foramina in a "dumbell" pattern. Microscopy revealed moderately cellular, benign meningiomas without nuclear atypia, mytotic figures or invasion of neural structures. All 4 patients improved postoperatively.

Spinal arachnoid villi have 2 patterns of distribution. Usually, they occur within the dura abutting on the dural veins and it is their arachnoid cells that probably give rise to the more common intradural meningioma. The second group is pedunculated and portrudes into the epidural veins and may account for the purely extradural spinal meningioma.

P97.

Cervical Spondylotic Myelopathy: Factors Influencing Surgical Decompression

G. GOPLEN, M. KHAN, K. LEFEVRE, R. GRIEBEL and M. SUNDARAM (Saskatoon, Saskatchewan)

This paper is a detailed retrospective analysis of 10 patients with cervical spondylotic myelopathy who have been investigated and treated at University Hospital over the past 8 years. They have presented with the classical features of cervical spondylotic myelopathy including sensory and motor long tract signs. Five males and 5 females with ages ranging from 44 to 82 (mean 71) are included. All patients had evidence of multilevel involvement by myelography and/or CT investigations. Five patients had symptoms or signs of cervical radiculopathy. Surgical decompression was performed on each patient. Eight patients improved neurologically, one patient remained unchanged and one deteriorated in the follow up period which ranged from 1 to 8 years. Factors which influence prognosis following surgical decompression include: 1) age, 2) duration of symptoms, 3) severity of involvement of long tract signs — sensory and motor, and 5) diameter of spinal canal as measured by CT. These factors will be discussed in detail.

P98.

Beneficial Effects of the "Gliotoxin" 6-Amino-nicotinamide After Spinal Cord Injury

M. KHAN, M. POLITIS, K. LEVEVRE, R. GRIEBEL, G. GOPLEN and K. KHAN (Saskatoon, Saskatchewan)

6-aminonicotinamide (6-AN) is a nicotinamide antimetabolite that inhibits glucose metabolism. A single injection of 6-AN in unoperated rats at doses of 10mg/kg intraperitoneally several days after unilateral optic nerve crush causes widespread degeneration of reactive astrocytes in crushed nerves, but no changes in unoperated nerves. In the present study 6-AN was administered in doses of 5 mg/kg at 4 days after a 400 gm/cm contusion lesion in rat spinal cord, saline being injected into control rats. Behavioral assessment performed at 2 and 3 weeks postoperatively revealed improved performance on the inclined plane test in drug-treated animals. This was accompanied by the presence or axonal profiles in the dorsal columns rostral to the lesion site in "holes" which may have been formed by vacuolization of reactive astrocytes. Studies are in progress to determine if 6-AN administration can facilitate the effects of other treatments known to promote beneficial effects after spinal cord injury. Some of these include: a) DC electric current, b) exogenous laminin and, c) suspensions of fetal tissue or schwann cells.

P99.

The Effect of Electrical Stimulation and Laminin On Experimental Spinal Cord Injury

M.I. KHAN, M. POLITIS, K. LEFEVRE, R. GRIEBEL, G. GOPLEN, and K. KHAN (Saskatoon, Saskatchewan)

The present study was conducted to determine the effectiveness of exogenous electric current and laminin on spinal cord injury after a sin-

gle hemisection in the midthoracic region of the spinal cord of rats. The preliminary studies have indicated that exogenous electric current administered to a spinal cord after crushing injuries produces enhanced recovery as assessed by the incline plain technique. Laminin is a neuritic growth in vitro and various experiments implicate laminin as a factor in axonal regeneration. In addition, static and dynamic electromagnetic fields are known to influence various cell types. Using microsurgical techniques, 35 Sprague-Dawley rats were subjected to a mid thoracic cord single hemisection. The animals were divided into groups as follows: 1) Elvax pellet with laminin, 2) Elvax pellet with collagen, 3) Control — no current, no substrate, 4) Electrode slab with cathode rostral, 5) Electrode slab with anode rostral. Function was assessed for 4 weeks using the incline plain technique, withdrawl reflexes, toe spread and leg draw. After sacrifice, the number of neurofilament-positive profiles in the right dorsal column was determined in frozen sections at 4 mm rostral to the injury site. Conclusions: 1) performance as assessed by the incline plain technique is enhanced by electrical current and laminin. Significant effects were observed in cathode rostral and laminin groups. 2) Laminin and cathode rostral group showed enhanced recovery of sensory ("withdraw") reflexes in comparison to other groups. Cathode rostral and laminin rats do not seem to have profound effect on tow spread. 3) Morphological basis for above changes not known. However, increased axonal elongation into dorsal columns indicated in cathode rostral rats.

P100.

Spinal Cord Injuries in An Agricultural Community in Canada — A 10 Year Study

M. KHAN, K. LEVEVRE, C. EKONG, R. GRIEBEL, K. KHAN and G. GOPLEN (Saskatoon, Saskatchewan)

This is a 10 year (1978-1988) retrospective study of spinal cord injuries in an agricultural community of 1 million population in the province of Saskatchewan in Canada. There were 400 patients ranging in age from 15 to 85 years. Almost 80% of patients were male. About 25% of patients were under age 20 years while over 50% were under age 30 years. Only 20% of patients were over age 60 years. Motor vehicle accidents accounted for about 50% of all injuries, work related 15%, falls at home 10%, sports and recreation 10% and others including gunshot injuries, stabbing and suicide attempts 15%. Interestingly, 90% of all patients sustained their injuries over an 8 month period (April - Nov.). Construction accidents were responsible for most work related injuries while diving was responsible for over 90% of sports related injuries. About 75% of all spinal cord injuries were localized to the cervical spinal cord, 20% to the thoracic and 5% to the thoracolumbar segments. Seventy percent of patients suffered from complete cord injury without any significant recovery in neurological function. Eighty percent of patients with partial cord lesions improved in neurological function over a period of time. Within 1 month of admission, 10% of patients died as a result of multiple and complete cord injury. Follow up studies of 1-9 years revealed that about 12% of patients died and these deaths were related to complete cervical cord injuries, chronic renal disease and being over 60 years of age. Approximately 25% of all spinal cord injured patients sustained serious head and/or multiple injuries. The results of this study strongly suggest that certain simple preventative measures may reduce the number of patients suffering from such devastating injuries. These measures will be presented.

P101.

Beneficial Effects of Dexamethazone Administration After Spinal Cord Injury

K. LEFEVRE, M. KHAN, M. POLITIS, R. GRIEBEL and G. GOPLEN (Saskatoon, Saskatchewan)

Exogenous steroid administration was tested for its ability to improve function and inhibit degenerative changes after spinal cord inujury in the rat. Spinal cords were exposed at the T8 level and subjected to a contusion lesion by dropping a 400 gram weight a distance of 1 cm in 200 gm animals. Steroid dexamethazone .25 mg intraperitoneally was injected at either 1 or 24 hours after injury, saline being injected into control groups. Behavioral assessment was performed blindly at 7, 10 and 14 days after surgery using the inclined plane test. Results indicated significantly greater improvement relative to controls at the 10 and 14 day time points in animals receiving steroid at 24 hours post-injury. Morphometeric analysis was assessed 3 mm rostral and caudal to the lesion at 14 days after surgery. Results to date indicate a nearly two fold increase in the number of motor horn neurons caudal to the lesion site in cases were dexamethazone (vs saline) was injected 24 hours after injury. Similarly, a drug-related inhibition of reactive glial hyperplasia is evident in the dorsal columns rostral to the lesion site. In contrast to the beneficial results of drug treatment 24 hours post-operatively, no significant changes are induced by administering steroid 1 hour after spinal cord injury. Results indicate some beneficial effects of steroid administration after spinal cord injury which is related to the time at which drug is administered. Subsequent studies are in progress to determine if steroid related beneficial effects are correlated to changes in blood flow or axonal elongation/sprouting in damaged spinal cord.

P102.

Neurogenic Claudication Secondary to Lumbar Spondylosis

K. LEFEVRE, M. KHAN, G. GOPLEN, K. CHANDLER, M. SUNDARAM and R. GRIEBEL (Saskatoon, Saskatchewan)

This is a retrospective analysis of 40 patients admitted to University Hospital with the clinical syndrome of intermittent neurogenic claudication of the cauda equina in association with lumbar spondylosis. Criteria for inclusion in this study were symptoms precipitated by walking or other activity and relieved by rest, in the absence of vascular pathology (documented by physical examination). All patients had radiological evidence of moderate to severe lumbar spondylosis as confirmed by myelogram with or without CT scan. There were 15 females and 25 males ranging in age from 51-80 with a mean age of 66 years. Occupationally most patients were involved in farming. Average duration of symptoms was 4.4 years. Thirty-four patients presented with bilateral signs of cauda equina nerve root dysfunction. Ninety percent of patients had involvement at multiple levels radiologically. Follow up ranged from 1 to 5 years. Fifty percent of patients were asymptomatic while 50% had occasional symptoms but were able to carry on with normal activities. Factors which significantly contributed towards an adverse prognosis include advanced age, duration of symptoms, multiple levels of involvement and incomplete decompression.

P103.

Enterogenous Cyst Associated with Spinal Cord Duplication

P. MARCOTTE and B. LACH (Ottawa, Ontario)

Autopsy of a 60 year old woman, with no history of neurological symptoms, and dying of non-neurological disease revealed a complete duplication of the spinal cord, extending from the low thoracic level downwards. Both cords were slightly smaller than normal, lying side-by-side, within a single dural sac. The left-sided spinal cord contained an intraparenchymal cyst, measuring approximately 1 cm in diameter and filled with transparent fluid. The cyst was located on the paramedian side of this cord, 3 cm below the cord division. Approximately 2 cm below the cyst, there was a dural sleeve traversing the intradural space in the sagittal plane between the two cords; there was no associated bone spur. On retrospective review of the chest X-rays during the last admission, a thoraco-lumbar scoliosis and abnormalities suggestive of hemivertebrae and increased interpedicular distance were found. No congenital abnormalities of the visceral organs or limbs were noted.

On microscopic examination, both cords show slightly asymmetric but otherwise well-developed gray and white matter. The anterior and posterior horns and roots along the "lateral" aspects of each spinal cord were of a normal size, while the "paramedian" horns and nerve roots were hypoplastic. The leptomeninges at the level of the cord division, contained a few foci of glial heterotopia and rudimentary spinal root ganglia.

Microscopic examination of the cyst, revealed a single layer of flattened and cuboidal epithelial cells lying on a thin connective tissue capsule. The peroxidase anti-peroxidase method revealed positive reactions for cytokeratin, epithelial membrane antigen and Ulex Europeus lectin, compatible with a diagnosis of neuroenteric cyst.

The occurrence of diplomyelia and neuroenteric cyst of the spinal cord is very rare. The coincidence of these two lesions, suggests that both of them resulted from abnormal early embryogenesis of endodermal and neuroectodermal tissues in the region of the neuroenteric canal.

P104.

Mesencephalic Cavernous Angioma Presenting as Aqueductal Stenosis

P. MARCOTTE, B. LACH, N. RUSSELL, D. PRESTON and D. ATACK (Ottawa, Canada)

A 41 year old man was admitted to the hospital with signs of obstructive hydrocephalus due to aqueductal stenosis. Extensive investigation revealed no evidence of an underlying lesion in the CNS. VP-shunt alleviated all his symptoms. Over the subsequent 8 years, his clinical course was punctuated by episodes of transient neurological dysfunction, consisting of headache, nausea and vomiting, ataxia, somnolence, dysarthria and diplopia occurring in various combinations. Initial and repeat angiograms as well as multiple CT scans did not delineate the cause of symptoms. His last admission to hospital was prompted by onset of partial paralysis of upward gaze, impaired mentation and dysarthria. His neurological status progressively declined during the subsequent two months. Extensive testing excluded shunt malfunction as the cause of neurologic deterioration. Deep vein thrombosis with extension to the inferior vena cava and acute renal failure led to his demise. An MRI scan done during the last admission demonstrated a vascular midbrain lesion impinging on the aqueduct.

Post-mortem examination revealed a periaqueductal cavernous angioma measuring approximately 5 mm in greatest diameter. The aqueduct was partially incorporated in the lesion, narrowed, focally displaced and distorted. The lumen of the aqueduct within the tumor was slit-like and not exceeding 0.5 mm in largest diameter. Several cavernous vessels traversed the quadrigeminal plate and extended to the overlying leptomeninges. The adjacent parenchymal tissues showed foci of old hemorrhages, gliosis and scattered dystrophic axons. The third nerve nucleus displayed minimal neuronal loss. Ventriculomegaly and axonal loss in the corpus callosum were the only other pathologic abnormalities detected in the CNS.

This case illustrates a very unusual location and a challenging clinical presentation for a solitary hemangioma of the CNS. Moreover, it reinforces the role of MRI scanning in detection and characterization of brainstem lesions.

P105.

Intrathoracic Cerebrospinal Fluid Leak Post Sympathectomy — A Case Report

D.R. McLEAN, J.D.S. McKEAN, P.J. LEWIS and J.F. MEGYESI (Edmonton, Alberta)

Persistent cerebrospinal fluid (CSF) leakage into the pleural cavity is a rare but documented complication of transthoracic sympathectomy. A case of such a complication, and its successful management, is reviewed here. A 38 year old female presented with a two year history of daily headaches. She had previously suffered from longstanding left arm causalgia. This had been treated with three sympathectomies via 1) a costotransversectomy approach, 2) a left first rib resection, and 3) a transthoracic approach. These operations were performed twelve, eight and two years prior to this admission, respectively. Here causalgia only completely resolved after the last operation. However, during the last procedure a tear in the T_2 dural sleeve was noted, with leakage of CSF. This was treated intra-operatively with a gelfoam patch. On this admission the patient underwent isotope cisternography which demonstrated a CSF leak into the left hemithorax. A CT/myelogram of the cervical and thoracic regions demonstrated a leakage of contrast into the paraspinal soft tissue adjacent to the left neural foramen between T_2 and T_3. Subsequently the patient underwent a left T_2/T_3 hemilaminectomy with identification of an atrophic dural sleeve of T_2 and a pseudomeningocele in the left inter-vertebral foramen. The pseudomeningocele was punctured and CSF released. The CSF fistula was occluded with metal clips placed across the atrophic dural sleeve of T_2. Postoperatively the patient has remained free of headaches.

P106.

Percutaneous Cordotomy for Unilateral Pain of Malignant Origin: Efficacy and Safety

D.E. MOULIN and H.W.K. BARR (London, Ontario)

We assessed the efficacy of C1-C2 percutaneous cordotomy in 19 consecutive patients (14 female, 5 male) with unilateral cancer pain syndromes who failed standard pharmacological therapy. Eleven patients had a lumbosacral plexopathy, 4 had tumor infiltration of the chest wall or abdomen, 3 presented with bone metastases and 1 patient had a brachial plexopathy. CT scans of the chest, abdomen or pelvis were done in all but 2 patients. The mean duration of follow-up post-cordotomy was 4.9 months. All patients had dramatic pain relief for the first 2 days post-cordotomy. However contralateral pain was subsequently unmasked in 9/10 patients with midline or bilateral disease and two-thirds required epidural narcotics or continuous subcutaneous infusion to provide adequate pain control. Eight of nine patients with unilateral disease had sustained pain relief until death with reduced opioid requirements. The procedures were uncomplicated except for transient ipsilateral leg weakness in 6 patients. Percutaneous cordotomy is a safe effective technique for unilateral malignant pain syndromes but does not provide sustained relief in the presence of midline or bilateral disease.

P107.

Effect of Hemoglobin on Isolated Cerebrovascular Smooth Muscle Cells

J.A. STEELE, N. STOCKBRIDGE, G. MALIJKOVIC and B. WEIR (Edmonton, Alberta)

Hemoglobin has been suggested as a causative agent in cerebral vasospasm following subarachnoid hemorrhage. We are employing a voltage clamp technique to investigate the effects of putative spasmogens on the membrane properties of cerebrovascular smooth muscle cells Because of the technical difficulties inherent in the application of voltage clamp techniques to electrically coupled cells in intact arteries, we have chosen to study single cells isolated by the use of enzymes. Basilar arteries from rats were cut into rings and incubated in a low calcium (0.2 mM) physiological saline containing collagenase (0.5 mg/ml) and elastase (0.5 mg/ml) for 1 hr at 21°C. Single cells were released by trituration with a Pasteur pipette. The cells contracted in response to a variety of agonists: serotonin (10^{-7} M), angiotensin II 10^{-5} M), $PGF_{2\alpha}$ (10^{-5} M), PGE_1 (6×10^{-4} M) and caffeine (10^{-2} M), demonstrating that the "excitation-contraction" coupling mechanism was not harmed by

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the isolation procedure. The surface membrane of single, isolated cells was voltage clamped by the use of a single patch clamp pipette in the whole-cell recording configuration. Oxyhemoglobin was prepared from dog or rat hemoglobin (Sigma) by reduction with sodium dithionite. Methamoglobin was prepared by oxidation with potassium ferricyanide. These agents were subsequently removed by dialysis.

Oxyhemoglobin (10^{-5} M) produced contraction and decreased the input resistance of the cells from 8.5±2.5 ($\bar{x}$±S.D.) GΩ to 0.19±0.16 GΩ (n=8), indicating a large increase in membrane permeability to ions. A concomitant increase in the calcium-dependent potassium current suggested a substantial rise in intracellular calcium. The increase in membrane permeability was reversible upon removal of hemoglobin from the medium. Methemoglobin (10^{-3} M), Fe^{++} (10^{-3} M), Fe^{+++} (10^{-3} M) and sodium dithionite (10^{-3} M) had no such effects.

These studies suggest a mechanism whereby oxyhemoglobin produces cerebral vasospasm.

P108.

Cerebrospinal Fluid Infection Associated with External Ventricular Drainage

D.S. MALLOY and K. McEWEN (Halifax, Nova Scotia)

External ventricular drainage and the use of ventriculostomy for intracranial pressure monitoring are common procedures in the modern Neurosurgical Intensive Care Unit (ICU). One of the drawbacks, however, has been the risk of ventricular infection. We report our recent experience in a group of patients studied prospectively. A number of variables were examined to assess their risk for the development of infection.

Fourty-seven patients undergoing a total of 65 ventriculostomies were reviewed. The observed infection rate was 7.7%. Several factors were noted to be of little significance with respect to the risk of infection. These included patient age and diagnosis as well as the place of insertion of the drain (OR vs. ICU). The likelihood of ventricular infection was significantly increased in the presence of prior ventriculostomy ($p<0.0001$), multiple ventriculostomies ($p<0.001$) or when the drainage system was violated ($p<0.0001$). Duration of drainage did not appear to be a factor in the development of infection.

Based upon this study the authors believe that ventriculostomy is a safe procedure which can be performed in the ICU. Meticulous attention to sterile technique and system integrity are vital in reducing infection risk. We recommend avoidance of multiple ventriculostomies. We do not advocate routine removal of drains at an arbitrarily specified time interval.

P109.

Regional Cerebral Blood Flow in Patients with Remote Closed Head Injuries

M. KRELINA, R. REID and J. BALLINGER (Ottawa, Ontario)

We hypothesize that Regional Cerebral Blood Flow (rCBF) is a more sensitive measure of mild cerebral dysfunction than conventional clinical techniques.

Local activity of neuronal populations is reflected in local cerebral metabolism and in turn rCBF. We used the technique of Single Photon Emission Computed Tomography (SPECT) and Tc-99m HMPAO radiopharmaceutical agent to investigate rCBF. The Tc-99m HMPAO is highly lipophilic and crosses the blood brain barrier (in proportion to rCBF) on first pass through cerebral capillaries.

Twelve patients were referred to us for psychiatric and neurological assessment of affective instability, recurrent outbursts of aggression and impaired social judgment 1-9 years after their mild to moderate closed head injuries. All were psychiatrically diagnosed as Organic Personality Syndrome, DSM-III-R. All patients were neurologically examined, had CAT scans, EEG's and SPECT studies.

SPECT showed localized perfusion deficits in 10 cases with activity differences between homologous brain regions in excess of 10% while 7 normal controls showed differences of less than 10%. The Neurological Examination showed lateralized findings in 3 and non-lateralized soft findings in 5 patients. CAT scan showed lesions (usually frontal or temporal contusions) in 6 and EEG showed localized abnormalities in 3 cases.

All techniques agreed on the laterality of abnormalities; the differences in specific localization were small. Generally SPECT showed more extensive involvement, and was abnormal in more cases than other methods.

SPECT using Tc-99m HMPAO is more sensitive than traditional clinical techniques and is likely to be helpful in understanding the pathophysiology of behavioral disturbances in these patients.

P110.

From Coma to Community — A Continuity of Care

N.C. HILL, M. STAMBROOK, G. HAWRYLUK, G. SONES, C. ENGEL and W. McDIARMID (Winnipeg, Manitoba)

We have designed a program for the care of the severely head injured on the premise that these patients will require treatment from the time of injury for the rest of their lives and that because of the enormous numbers of factors which affect outcome, each patient will follow a different pathway to partial recovery. We have noted that in the past, many patients become stalled in inappropriate facilities receiving no or inappropriate treatment because of lack of a clear visualization by physicians and relatives of the overall program, and its concept of a continuous flow of care.

To explain this program, a flow sheet has been designed which shows in an easily understood manner, the progress which the patient with severe head injury should make along appropriate pathways of care, based on early assessment of whether return to the community is likely. The pathway of the patient with a likely recoverable injury is tracked through rehabilitation hospital, transitional facility and group home to the community. The pathway of the patient unlikely to recover is tracked from acute care ward, to a sustained development ward, to care and comfort facilities. Transfer from one to another pathway can be illustrated as can the timing of the appointment of a case manager, and of the assessments of the Head Injury Group.

This concept of continuous care, visualized on flow sheet, has also been used effectively to demonstrate to government and private funding agencies where partial or complete blocks exist in the progress of the patient towards an appropriate final disposition.

P111

The Influence of Patient Demographics on Head Injury Mortality

R. MOULTON, G. HOTZ, W. TUCKER, P. MULLER and A. HUDSON (Toronto, Ontario)

The purpose of this paper is to examine the impact of patient population variables on head injury mortality rates.

Data was collected prospectively on 400 consecutive head injury patients from Jan. 1986 to Dec. 1987. The mortality for the severely injured subgroup (GCS 8) was 46% which is considerably greater than that reported in many recent series employing similar patient management protocols. We hypothesized that patient and injury factors unrelated to medical management may be responsible for the difference in mortality statistics. Logistic analysis was used to establish the most significant determinants of patient mortality among a number of patient and injury characteristics. The most significant factors were GCS, age, presence of a mass lesion, presence of multiple injuries, and etiology ($p=.0000$, .0000, .0000, .0021, and .0115). Sex, alcohol intoxication, and delay in treatment were not significant.

The mortality rates from several head injury series from the past decade were correlated with the mean age and the incidence of mass

lesions in those series. Variation among the latter factors accounted for 83% of the variability in mortality rates in those series (p=.0009).

We conclude that the reduction in head injury mortality described in the last decade may not be as significant as initially thought. Our data indicate the overwhelming importance of injury severity, patient age, and intracranial mass lesions, rather than particular management protocols, in determining patient mortality.

P112.

Evolution of Continuously Monitored Somatosensory Evoked Potentials Following Acute Head Injury

R. MOULTON, P. KRESTA and M. RAMIREZ (Toronto, Ontario)

The purpose of this paper is to present the preliminary results of continuous automated monitoring of somatosensory evoked potentials (SSEPs) in acute head injury.

Using a micro-computer driven system, SSEPs were collected at 1-2 hourly intervals on 16 patients for periods of 3-7 days, with monitoring usually beginning within 12-24 hours of injury. The admission Glasgow Coma Score (GCS) of these patients ranged from 3-12. There were 4 deaths. All patients were ventilated and 15 required continuous pharmacologic paralysis for ICP control. Continuous high quality recordings were obtained in all of the patients receiving muscle relaxants and in one of the patients who did not. Intermittent recordings were obtained from the remaining patient.

All four patients who died showed progressive attenuation and loss of activity subsequent to the P15. In one patient who died of uncontrollable ICP the deterioration in SSEPs preceded the refractory increase in ICP. Deterioration in SSEPs began within the first 24 hours of monitoring in all the patients who died. In one patient who survived in a persistent vegetative state, no recovery of activity beyond the P_{15}-N20 complex took place. In contradistinction, those patients who survived and regained consciousness showed preservation or recovery of activity subsequent to N20 in at least one hemisphere. This occurred in spite of difficult of ICP problems in many of the patients.

We conclude that continuously measured SSEPs may be a useful monitor of neurologic function in the intensive care unit. This is especially true in pharmacologically paralyzed patients. The technique may also allow better characterization of neurologic function in the acute period after head injury and its relationship to intracranial pressure.

P113.

Acute-On-Chronic Subdural Hematoma

K. CHANDLER, M. KHAN, K. LEFEVRE, G. GOPLEN and R. GRIEBEL (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 liquefied 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 20 patients with 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 subdural hematoma. However, several other factors will be considered and discussed. Recommendations for further studies to verify the exact etiology and pathophysiology of AC-SDHS will be made.

P114.

Rheology of Cerebral Arteriovenous Malformations

R. LEBLANC (Montreal, Quebec)

Thirty-three patients underwent intraoperative fluorescein angiography and/or Positron Emission Tomography (PET) to study the rheological, perfusional and metabolic effects of supratentorial AVMs. The 13 males and 20 females were aged 18 to 62 years (mean 34) and had a remote cerebral hemorrhage (15 cases) or a seizure disorder (18 cases). Sixteen had a normal neurological examination, 9 had a mild hemi- or monoparesis, 4 were dysphasic and 3 had a hemi anopsia. Four AVMs were <4 cm, 11 were 4-6 cm, 12 were 7-11 cm and 3 were >11 cm in largest diameter.

Fluorescein angiography demonstrated preferential flow to the AVM in all cases which was seen as very rapid filling of the major feeding arteries, rapid filling of the finer vessels of the nidus, and shunt flow through large draining veins. Combined with cortical brain mapping and using videotaped replay and magnified color photography, the rheological effects of the AVMs on surrounding sensory-motor and language areas could be ascertained: diminished flow restricted to the immediate area surrounding the AVM was seen with smaller lesions (peri-angiomatous stealing) and more widespread filling delays (intrahemispheric stealing) was seen with larger ones. PET scanning demonstrated diminished perfusional reserve and glucose hypometabolism in the hemisphere ipsilateral to AVMs >6 cm. Similar perfusional and metabolic changes were seen contralaterally with the largest lesions.

Cerebral AVMs produce rheological alterations in a fashion proportional to their size. Smaller AVMs produce peri-angiomatous stealing, larger ones produce intrahemispheric stealing, and the largest AVMs produce interhemispheric stealing. These rheological effects are well compensated with lesions <6 cm but larger ones produce diminished perfusional reserve and glucose hypometabolism in a stepwise fashion in proportion to their size.

P115.

Vertebro-PICA Aneurysms: Midline Suboccipital Approach and C1-laminectomy

G. MOHR, A. ROUX and J. HARDY (Montreal, Quebec)

Vertebro-PICA aneurysms represent a particular technical challenge due to an extremely narrow operative field and numerous vital neural and vascular structures. Fenestrated clips of various shapes have been developed and are useful in certain conditions, but the lack of exposure still remains the limiting factor in most cases.

During the nine year period from January 1980 through January 1989, 178 intracranial aneurysms have been treated microsurgically, including 16 aneurysms of the posterior circulation (8 basilar-apex aneurysms and 8 vertebro-PICA aneurysms).

From the eight vertebro-PICA aneurysms (5% of the entire series), 6 underwent a midline suboccipital approach with deliberate removal of the arch of the atlas in park bench position, while 2 underwent a pure suboccipital approach. Complications included one case of symptomatic IVth-ventricular dilatation which was successfully treated by ventrical cisternostomy, and one fatality related to ischemic brainstem damage.

The authors recommend the midline suboccipital approach with C1-laminectomy for vertebro-PICA aneurysms in ventrolateral decubitus. The main advantages are:

— Improved exposure of the laterobulbar cisterns, allowing cranial retraction of the cerebellar tonsil.

— Constant access to the proximal vertebral artery.

— Section of the upper two attachments of the dentate ligaments, providing less traumatic mobilization of the lower medulla, thus reducing edema from retraction, particularly in ventrally located aneurysms.

— Improved access to the lateromedullar and tonsillar segments of the PICA, allowing extensive mobilization of this artery and facilitating exposure of the aneurysm.

— Reduced incidence of air embolism.

P116.

Transcranial Doppler Monitoring During Carotid Endarterectomy

A. KRAJEWSKI, J.W. NORRIS, W.S. TUCKER, D.W. ROWED, R. MAGGISANO, M. FAZL and M.L. SCHWARTZ (Toronto, Ontario)

During carotid endarterectomy cerebral blood flow (CBF) may be critically reduced by crossclamping of the carotid artery. Present methods of monitoring CBF such as stump pressure or EEG are time consuming and cumbersome. With transcranial Doppler technique (TCD) the blood flow velocities in middle cerebral artery (MCA-BFV) measured intraoperatively may prove a valuable way of monitoring cerebral perfusion during carotid surgery.

We evaluated MCA-BFV in 29 patients during carotid surgery using a MedaSonic (Transpect) transcranial Doppler machine with a modified flat probe. Technically adequate recordings were obtained in 25 subjects. MCA-BFV was measured before, during and after clamping. MCA-BFV was reduced in 14 patients and unchanged in 11. In one patient MCA-BFV increased when the carotid artery was clamped. There was no relationship between the BFV reduction and the degree of extracranial carotid stenosis. The MCA-BVF dropped from 75.4±27.4 cm/sec. This represents a reduction from 17% to 77% (Mean 50%±20%) of the maximum blood flow velocities and relates closely to cerebral blood flow.

Our preliminary data indicate that TCD is a practical and accurate method of monitoring cerebral blood flow during carotid surgery and may help in deciding on the need for arterial shunting.

FRIDAY, JUNE 16TH

Neuroradiology

P117.

Internuclear Ophthalmoplegia Following Head Injury

D. LADOUCEUR and E. HEON (Sherbrooke, Quebec)

Internuclear ophthalmoplegia (INO) refers to the disturbances in conjugate ocular movements that result from lesions of the medial longitudinal fasciculus (MLF). Multiple sclerosis is usually responsible for bilateral INO, while a vascular lesion is commonly implicated in unilateral cases. Head trauma is a rare cause of INO. A case is described of unilateral INO following head trauma with a periaqueductal pontine lesion demonstrated on Magnetic Resonance Imaging.

P118.

Myelomalacia (Microcystic Degeneration) Simulating Post-Traumatic Syringomyelia

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

Two patients with spinal cord injury developed the delayed onset of symptoms indicating progression of their neurologic deficit. Magnetic resonance (MR) imaging revealed an intramedullary low intensity lesion consistent with post-traumatic syringomyelia (PTS). Exploration, utilizing intraoperative ultrasonography did not reveal a syrinx. Myelotomy revealed softened spinal cord with a "honeycombed" trabeculated appearance. This phenomenon, i.e. late deterioration after spinal cord injury and a false positive imaging study indicating syringomyelia, is strikingly similar to the findings in two cases recently reported by Tator, et al. They referred to it as "microcystic degeneration" and speculated that it might represent the very early stages in the development of a "macrocystic syrinx".

Modern imaging techniques may fail to distinguish between these two lesions, yet post-traumatic syringomyelia causing neurologic deterioration, usually requires surgical exploration. Our experience with these two cases leads us to concur with Tator's suggesion that intraoperative ultrasonography be used and that myelotomy be reserved for those cases in which a cavity is demonstrated.

P119.

Post-traumatic, Subacute CNS Demyelination

I. MENDEZ, G.B. YOUNG, D. LEE, N. MacKENZIE, J.J. GILBERT and K. ELISEVICH (London, Ontario)

We present a unique case of a 19 year old boy who developed progressive neurological deterioration 6 weeks after a motorcycle accident which resulted in immediate blindness of the left eye and an amnestic state. A right frontal lucency was present on initial CT scan.

The patient improved over 6 weeks, but then became blind over 2 days. This was followed by a left hemiparesis a week later. Subsequently he developed quadiplegia and pseudobulbar palsy over 2 weeks. CT and MRI studies showed extensive, confluent progressive white matter disease involving both cerebral hemispheres, corpus callosum, optic nerves and brain stem. A cerebral biopsy revealed a demyelinating process. No abnormalities were found in serum electrolytes or vitamin levels. CSF did not show oligoclonal banding.

Two months after the deterioration, his pseudobulbar palsy and right hemiparesis resolved. Several months later the left hemiparesis resolved. He remains blind with mild mental subnormality. The MRI scan has shown remarkable improvement.

We propose the patient suffered a central nervous system demyelination as a reaction to the severe head injury.

P120.

Proton Magnetic Resonance Spectroscopy Allows Non-invasive Biochemical Study of Diseased Human Brain *In Vivo*

P.M. MATTHEWS, F. COMMODARI, E. SHOUBRIDGE, F. ANDERMANN and D.L. ARNOLD (Montreal, Quebec)

Proton magnetic resonance spectroscopy (MRS) can be used for non-invasive study of brain metabolites. Using a Philips Gyroscan imaging-spectroscopy system operating at 1.5 T, we have found that such examinations can be easily performed within the routine clinical imaging schedule. Resonances from N-acetylaspartate, phosphocreatine/creatine, choline, lactate, and an unassigned resonance at 2.66 ppm (chemical shift relative to TMS) can be clearly observed from the normal human brain. The method is in principle quantitative.

Potential clinical applications have been explored in studies of inflammatory, neoplastic and metabolic diseases. For example, *in vivo* proton MRI with chemical shift imaging of a patient with chronic localized encephalitis demonstrated focal biochemical changes (a massive increase in the 1.3 ppm lipid/lactate resonance and decreased N-acetylaspartate) in the volume of recent inflammation. *In vitro* pathological, biochemical, and spectroscopic studies of specimens obtained after hemispherectomy correlated well with this finding. Comparison with spectra obtained from patients with extensive gliosis secondary to long-standing subacute sclerosing panencephalitis or past history of acute disseminated encephalomyelitis suggest that spectroscopy can be used in some cases to distinguish active from chronic disease where conventional MR imaging fails to show differences.

P121.

Computerized Tomography Density Change in Colloid Cyst

C. CLOUTIER, R. MOUMDJIAN, R. ASHFORTH and J.-G. VILLEMURE (Montreal, Quebec)

The diagnosis of colloid cysts of the third ventricle using different radiologic technics rarely causes a problem. The typical well-rounded mass in the anterior part of the third ventricle is usually well recognized with computed tomography. The common CT characteristics will include: site, volume, density. Colloid cysts have different CT appearances; they can be either hypodense, hyperdense or ring enhancing. This variable appearance on CT is thought to be secondary to different composition of the cyst content. The cyst does not appear to change in size or density over large periods of time, but few authors have reported initially isodense lesion, which later became hyperdense; this hyperdensity is interpreted by many as representing hemorrhage within the cyst. Others attribute the change to non-hemorrhagic chemical change in the lesion. We report a case with changing appearance in a reverse fashion; a colloid cyst intially hyperdense on C.T. which became isodense within an interval of 14 months. The C.T. parameters of window level and width were identical in both studies; the mean Hounsfield units were determined and these changed from 58.5 when the cyst was hyperdense to 45.08 when it became isodense. Review of the MNI series and of the literature do not show any other similar case. We suspect a non-hemorrhagic chemical change within the colloid cyst to explain its change in density on C.T. scan.

General Neurology

P122.

The RED-M Syndrome (Retinopathy, Encephalopathy, Deafness with Microangiography): A Variant of Systemic Lupus Erythematosus or a Distinct Disease

M. NICOLLE and R.S. McLACHLAN (London, Ontario)

Since 1979 there have been occasional reports of a syndrome in previously healthy young women who developed retinopathy, encephalopathy and deafness in association with a microangiography of unknown etiology (called RED-M Syndrome by Mass, et al. Neurology 1988). Although a relationship to SLE has been suggested, these reports have emphasized the differences between the two conditions, mainly an absence of other non-neurological signs and symptoms, lack of serological evidence of lupus and a good prognosis for recovery within one to two years. We report a case of this rare disease in a 24 year old woman who unlike previous patients developed a syndrome with clinical features of seronegative SLE. In addition to retinal infarcts, bilateral sensorineural deafness, bihemispheric TIA's and episodic neuropsychiatric dysfunction, she developed cerebellar ataxia, areflexia, optic atrophy, migraine-like headaches, fatigue, photosensitive malar rash, arthritis and myalgias. Extensive investigations were negative except for elevated CSF protein, elevated serum IgM and MRI's which revealed white matter lesions consistent with micro infarcts. ANA, anti-phospholipid antibodies, cerebral angiograms and a muscle biopsy were all normal. The course of the disease has been one of intermittent exacerbation and remission with residual permanent deficit. Immunosuppression with oral cyclophosphamide and prednisone (but not azathioprine) reduced the frequency and severity of exacerbations but complete remission has not yet occurred four years after onset. Although the signs and symptoms in this patient suggest a vasculitis, the laboratory evidence favours a thrombotic microangiography as the underlying disease process.

P123.

The Distribution and Chronology of Cerebral Pathology in a Case of Juvenile Systemic Lupus Erythematosus

P. HUMPHREYS and A.M. GALABURDA (Boston, U.S.A.)

We report a detailed study of neuropathological change in the cerebrum of a left-handed woman dying at age 26 of juvenile systemic lupus erythematosus (SLE). Joint and cutaneous symptoms developed at age 8, followed by renal and endocardial involvement. She appeared neurologically intact until age 18, at which time there was acute onset of left hemiparesis and aphasia. Further intermittent cerebral ischemic symptoms occurred in the weeks prior to her sudden death.

The formalin-fixed brain was embedded whole in celloidin and serially sectioned at 35μm in the coronal plane. Sections were Nissl and myelin stained, and spare sections underwent routine histological stains. Pathologic change was of two types: (1) Old cystic necrosis of the right caudate, putamen, internal capsule and insular cortex, which correlated with the acute event at age 18; and (2) numerous small cortical scars resembling the lesions of remote thrombotic thrombocytopenic purpura (*Neurology* 8:55, 1958; *Semin. Thromb. Hemost.* 5:184, 1979). The distribution of the scars showed, in both hemispheres, dense clustering in the arterial borderzone regions with variable extension into middle cerebral artery territory. Many scars in deeper cortical layers were myelinated, suggesting that they had formed late *in utero* and/or in infancy.

The borderzone distribution in this case could shed light on the pathogenesis of brain lesions in SLE. Further, this case suggests that SLE patients may exhibit significant CNS pathology well before systemic and hard neurological manifestations appear.

P124.

Regional Cerebral Glucose Utilization in Hepatic Encephalopathy

J-F. GIGUERE, M.R. DEJOSEPH, R.A. HAWKINS and R.F. BUTTERWORTH (Montreal, Quebec and Chicago, U.S.A.)

Patients with hepatic dysfunction or portacaval shunts (PCS) are sensitive to ammonia load which may cause coma. In the brain, glucose provides energy as well as the hydrocarbon skeleton for glutamine synthesis, the cerebral mechanism for ammonia detoxification. It has been demonstrated that experimental animals and humans with PCS manifest reduced regional cerebral glucose use (rCMRglu). The aim of our study was to study the effect of a coma-inducing dose of ammonium acetate (5.2 mmol/kg) on rCMRglu. Four groups of rats were used: sham and shunt (four weeks after surgery), injected with NaCl (control) or 5.2 mmol/kg ammonium acetate. In the last group, coma (defined as loss of corneal reflex) was reached in 13 to 15 minutes. rCMRglu was determined with [6-^{14}C] -glucose and autoradiography. The PCS-NaCl rats showed, as expected, a depression of rCMRglu compared to sham-NaCl rats. In comatose PCS-NH_4 rats we observed two responses: a further depression mainly in forebrain and reticular formation, and a paradoxical stimulation particularly in caudal parts of the brain. The further depression may be explained by a decreased metabolism resulting from coma. The stimulation of rCMRglu could be the expression of an enhanced glutamine synthesis for ammonia detoxification. (Supported by NS16389, MRC Canada and FRSQ)

P125.

Ammonia in the Pathogenesis of Brain Edema in Hepatic Failure

M.S. SWAIN, R. GANZ, A.T. BLEI and R.F. BUTTERWORTH (Montreal, Quebec and Chicago, U.S.A.)

Brain edema is a leading cause of death in fulminant hepatic failure (FHF). However, the etiology underlying the pathogenesis of this disor-

der is not yet understood. Ammonia, a key toxin involved in the pathogenesis of hepatic encephalopathy is increased 10 fold in rat brain following hepatic devascularization. Using a model of FHF (the portacaval shunted rat (SHUNT) combined with hepatic artery ligation (HAL), we measured cortical brain water by determining tissue specific gravity after flotation of tissue samples in a bromobenzene-kerosene gradient (Marmarou et al., *J. Neurosurg.* 1978; 49: 530). Animals were divided into 4 groups: SHUNT+HAL; SHUNT+SHAM; SHAM+HAL; and SHAM+SHAM. The animals in the SHUNT+HAL group were further divided into 3 classifications based upon neurological status: Advanced Encephalopathy — loss of righting relfex; Early Coma — loss of corneal reflex and Late Coma. Body temperatures of the SHUNT+HAL group were maintained at 37±1°C. The water content of cortical grey matter was found to be increased by 2.0±0.5% ($p<0.01$) in HAL (Early Coma) animals, and by 2.9±0.5% ($p<0.01$) in the HAL (Late Coma) animals, when compared to controls by analysis of variance. In a separate series of experiments, we examined the effect of pathophysiological amounts of ammonia on rat cerebral cortical brain slices. Water content was evaluated using the wet weight/dry weight method. Ammonia, at a concentration of 5 mM resulted in significant increases in water content (3.1±0.2% control vs 4.1±0.4% NH_4Cl; $p<0.05$). This data provides evidence for a role of ammonia in the pathogenesis of cerebral edema resulting from hepatic failure. (Funded by NIH and MRC Canada)

P126.

Familial Paroxysmal Ataxia — Metabolic Changes and Acetazolamide Treatment

A.F. HAHN, A.A. BRIEDGER, B.A. GORDON, W.J. KOOPMAN and G. MARSH (London, Ontario)

The biochemical abnormalities and cellular defects in this rare inherited disorder remain unknown. We previously reported our observations in a man and his 2 sons, who suffered from repeated episodes of mild confusion, headache and florid cerebellar ataxia. An unusual and unique observation was the association with a peripheral neuropathy (Hahn et al., Ann Neurol 22:168, 1987).

We have extended our observations to 20 family members in 3 generations. This shows an autosomal dominant inheritance with considerable variability in the onset and severity of clinical symptoms. The attacks are stereotyped and are heralded by a feeling of lightheadedness. This is quickly followed by a sense of leg weakness, progressive truncal ataxia with inability to sit or stand unaided, striking titubations and large-amplitude dysmetric appendicular movements. Speech is markedly dysarthric and ocular movements are impaired. The episodes are precipitated by physical or emotional stress and last 1-6 hours. They are fully controlled with Acetazolamide.

Between and during attacks, plasma and urinary amino acids, urinary organic acids, serum ammonia, serum and CSF lactate, alanine and pH are normal. Pyruvate was slightly elevated in serum and CSF during an attack. Pyruvate dehydrogenase complex activity in cultured skin fibroblasts was normal. The remarkable finding on $P^{31}NMR$ spectroscopy was a drop in intracellular pH during and most marked after cessation of exercise followed by slow recovery. This abnormality was normalized with Acetazolamide treatment.

These results suggest that there is a direct or indirect effect of Acetazolamide on glycolysis, although the mechanism is unknown.

P127.

Tuberculous Meningoencephalitis: CT and MRI Findings

W-C. YEE and W.L. GORDON (Winnipeg, Manitoba)

The entity of tuberculous meningoencephalitis with concomitant cerebral involvement is well accepted. However, it has not been well characterized radiographically. We present a patient with this entity who demonstrated striking changes on CT and MRI.

A 28 year old, right handed Filipino man developed increasing headache and diplopia over 2 weeks. Examination showed mild dysphasia, right arm drift and bilateral 6th nerve palsies without neck stiffness. Plain CT scan of the brain showed *increased* density of the left hemisphere, involving both cortical and subcortical regions. Sulcal patterns over the hemisphere were less prominent compared to the right side. Infusion of contrast showed unusual meningeal or superficial cortical enhancement with complex vascular patterns. MRI of the brain likewise showed increased signal over the left hemisphere. Following infusion of contrast, meningeal and superficial cortical enhancement was also seen.

Repeated CSF examinations showed lymphocytosis but negative smears for acid fast bacilli (AFB). Prior to confirmation of positive CSF cultures for mycobacterium tuberculosis, a diagnostic brain biopsy revealed granulomas with AFB in the meninges and reactive gliosis in the superficial cortical layer. Institution of anti-tuberculous therapy was followed by recurrent episodes of severe drowsiness and marked worsening of dysphasia and right hemiparesis. Repeat CT scans showed fleeting, multiple small lucencies in the left internal and external capsular regions.

CT and MRI findings in this patient may be correlated with inflammatory and hyperemic changes in the meninges and underlying cortical and subcortical regions. Recognition of these radiographic changes is helpful in the diagnosis of this potentially treatable condition.

P128.

Utilite du Reflexe Bulbo-caverneux Dans l'Investigation d'Une Impuissance

F. DELISLE, P. ALARIE, L. VALIQUETTE and M.L. D'AMOUR (Montréal, Québec)

Dans l'évaluation de l'impuissance chez l'homme, les causes neurologiques sont peu fréquentes. Nous avons essayé de déterminer la validité du réflexe bulbo-caverneux et de la comparer à l'examen neurologique.

L'ors d'une évaluation multidisciplinaire, 51 malades ont eu un questionnaire et un examen neurologique complet et une étude du réflexe bulbo-caverneux par méthode de surface. La latence du réflexe a été mesurée.

Quatorze sur 51 malades (groupe 1) ont eu des latences prolongées (moyenne 55 msec.) dont 7 avec une évidence clinique de polynévrite diabétique, 2 de polynévrite alcoolo-nutritionnelle, 1 patient avec une fracture du bassin ancienne, 2 avec une chirurgie lombaire basse et 1 malade avec une sclérose en plaques. Deux malades diabétiques et 1 traumatisé du bassin avaient un examen neurologique normal.

Trente-sept malades (groupe 2) ont eu des latences normales (moyenne 38 msec): 16 diabétiques dont 7 avaient un examen neurologique suggérant une polynévrite, 4 cas de SEP possible, 2 cas de vessie spastique, 1 cas de chirurgie discale, 1 cas de trouble d'éjaculation primaire et 1 cas d'origine vasculaire. Dans les autres cas, l'étiologie n'a pu être identifiée.

Donc, les patients référés pour une évaluation d'impuissance en neurophysiologie, ont dans 27,4% des cas un réflexe bulbo-caverneux anormal et les causes que nous avons rencontrées sont la polynévrite, les traumatismes sacrés ou la SEP.

Par ailleurs, 3 malades sur ces 14, malgré un examen neurologique normal, avaient une latence prolongée du réflexe bulbo-baverneux, montrant la valeur de cet examen dans un bilan d'impuissance.

P129.

Coordination of Distal and Proximal Arm Muscles During a Rapid Multi-joint Movement in Patients With Cerebellar Dysfunction

W.J. BECKER, E. KUNESCH and H.J. FREUND (Calgary, Alberta and Düsseldorf, Germany)

Coordination between distal and proximal arm muscles was studied in 3 normal subjects and in 3 patients with diffuse degeneration of the cerebellar cortex, using a rapid overhand ball throwing movement as a model of a multi-joint movement.

While subjects threw the ball repeatedly at a target, the positions of the thumb, index finger, second MCP joint, and distal forearm were monitored with a SELSPOT II 3 dimensional position analysis system. The onset of hand opening was used as a measure of distal arm muscle activation. The velocity curve of the distal forearm was used as an index of proximal arm muscle (primarily triceps) function.

The time interval by which the onset of hand opening preceded the attainment of distal forearm peak velocity was relatively constant from trial to trial in any given subject. This interval was not more variable in individual patients as compared to individual control subjects.

Normal function of the cerebellar cortex does not appear essential for coordination of the onset of hand opening with proximal arm muscle activations. Patients did not throw as accurately as control subjects, however, and were unable to consistently produce the same hand direction while throwing to the same target.

P130.

Postherpetic Neuralgia: Postmortem. Two further cases

C.P.N. WATSON, J. DECK, D. VAN DER KOOY, C. MORSHEAD, S. RAMJOHN and R. EVANS (Toronto, Ontario)

This presentation reports two further autopsies of patients with postherpetic neuralgia (PHN) of 2 and 20 years duration in the 6th, 8th and 9th thoracic dermatomes. The affected roots were visibly atrophic. We have confirmed in both, atrophy of the ipsilateral dorsal horn and fibrosis of one dorsal root ganglion only. Peripheral nerve and nerve root showed a marked loss of myelinated fibres with preserved axones. Nerve fibre spectra showed excess small myelinated fibres and loss of large myelinated fibres compared with controls. Serotonin, noradrenaline and substance P staining of the affected dorsal horn appeared the same as controls.

Postherpetic neuralgia may result from an imbalance in peripheral input to a damaged dorsal horn containing hypersensitive deafferented neurones.

P131.

Postmastectomy Pain Syndrome and the Effect of Topical *Capsaicin*

C.P.N. WATSON, R.J. EVANS and L. ROBINSON (Toronto, Ontario)

Eighteen patients with the postmastectomy pain syndrome (PMPS) form the basis of this study. PMPS probably occurs in a minority of women after mastectomy. The onset of pain was most usual immediately or very shortly after the operation. The pain and sensory findings implied involvement of other cutaneous branches of the intercostal nerves as well as the intercostobrachial nerve. A variety of treatment approaches were unsatisfactory. Twelve of 14 patients treated with topical .025% capsaicin showed improvement after 4 weeks and 8 (57%) were judged to be good or excellent responses. This therapy should now be subjected to a randomized, double-blind, placebo-controlled trial.

P132.

Causes of Persistent Dizziness

T.R. WINDER and R.W. BALOH (Los Angeles, U.S.A.)

We reviewed the records of 108 patients referred to our neurotology clinic in a 1-year priod complaining of persistent disabling dizziness. The 2 most common diagnoses were: psychophysiologic dizziness (30) and migraine (18). The former was characterized by long-standing recurrent dizziness associated with symptoms of acute and chronic anxiety. Illusions of body movement were common but no one reported vertigo. Associated complaints included tension headaches, paresthesias, palpitations, and gastric distress. Dizziness was often provoked by specific situations (e.g., driving on a freeway). Three patients had panic attacks with the dizziness and 3 others had associated agoraphobia. Diagnostic studies including ENG were consistently normal. Fourteen of 18 patients with migraine reported vertigo. The dizziness was accompanied by headache in 15 but occurred in episodes separate from headache in 3. Thirteen had a family history of migraine. Nonspecific abnormalities were found on ENG in 8 patients.

We conclude that the history alone provided the key diagnostic information in about half of all patients presenting to our clinic with persistent dizziness.

P133.

Effects of Mechanical Loading on Manual Tracking Performance in Patients With Cerebellar Incoordination

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

Increasing inertial load by adding weights to the extremity is a technique sometimes used in rehabilitation units to suppress oscillation and improve motor performance in patients with cerebellar incoordination. We studied the effects of various types of mechanical loading on manual tracking performance in 5 patients with unilateral cerebellar lesions. Subjects moved a cursor controlled by flexion-extension movements at the wrist to track a target moving back and forth across an oscilloscope screen in a pseudo-random pattern. The integrated difference between target and cursor position during 20 second tracking trials was used as an index of tracking accuracy. EMG activity was recorded from the wrist flexors and extensors to determine the relative amounts of co-activation and reciprocal activation of opposing muscle groups.

In comparison to normal subjects the cerebellar patients demonstrated irregular tracking patterns with inappropriate acceleration and deceleration and numerous high velocity peaks.

A viscous resistance was provided by feeding back wrist velocity to a torque motor coupled to the apparatus. This resulted in significant improvement in tracking performance in the cerebellar patients and suppression of the high velocity peaks. Tracking performance was not consistently improved by adding elastic stiffness (by feedback of wrist position). No patients benefited from the addition of weights to the hand to increase the inertial load and performance deteriorated in some. It is proposed that a hypotonic cerebellar limb behaves like an underdamped mechanical system. The addition of a viscous load restores some of the damping which, in normal subjects, may be generated internally by precisely controlling co-activation of agonist and antagonist muscle groups.

P134.

The Neurologic Exam in Early Schizophrenia

R.S. McLACHLAN and E.M. WARING (London, Ontario)

Kraepelin in the early 1900's was convinced that schizophrenia was a structural disease of the central nervous system involving primarily the frontal lobes. This idea fell into disfavour as theories of a psychological

basis for the disorder emerged but recently there has been a resurgence of interest in schizophrenia as an organic disease of the CNS. One argument said to favour this is the presence of various neurologic signs in up to 80% of schizophrenia patients. However, these data were acquired from heterogeneous populations including chronic medicated patients and patients recently taken off medication. As part of a larger study of a selected cohort of young recently diagnosed schizophrenia patients, one of us (RM) carried out a detailed neurological examination before neuroleptic treatment had been established. Cognitive function, cranial nerves and sensory and motor systems were examined with particular attention to potential findings which had been described previously. Eleven patients with a mean age of 24 years were examined. Nine of these had a striking defect in abstract thinking as indicated by a virtually complete inability to interpret proverbs such as "a rolling stone gathers no moss". This was in contrast to other cognitive functions such as memory and mathematical ability which were normal. A mild attention deficit was found in nine patients. Minor "soft" signs occurred on examination of the motor system in eight patients, the most common of which was a sustained glabellar response in six. In contrast, two patients aged 21 and 17 years who were re-examined two and three years after starting anti-psychotic medication and benztropine had numerous prominent motor abnormalities. The findings of this preliminary study support the hypothesis that frontal lobe function is abnormal in schizophrenia. However, many of the motor abnormalities which have been implicated in the disease likely appear as a result of treatment.

P135.

Downbeat Nystagmus with Waldenstrom's Macroglobulinemia

D. RANKINE and W. PRYSE-PHILLIPS (St. John's, Newfoundland)

Downbeating nystagmus is associated with craniocervical junction pathology in 30% of reported cases. Other etiologic causes are drug intoxication (alcohol, phenytoin, lithium, toluene), multiple sclerosis, vascular disease, alcoholic cerebellar degeneration, brainstem tumors, hematomas, encephalitis, magnesium depletion and communicating hydrocephalus.

We report a case of a patient who presents with downbeating nystagmus, and a peripheral meuropathy, in association with Waldenstrom's macroglobulinemia. We discuss this case and review the literature. The proposed mechanisms of downbeating nystagmus will also be discussed.

P136.

Cerebral Aneurysms Secondary to Lymphomatoid Granulomatosis

S. GOSSELIN, D. LADOUCEUR and E. FRENETTE (Sherbrooke, Quebec)

CNS complications of lymphomatoid granulomatosis (LYG) occur in 20 to 30% of patients. Pathologic findings include antiitis, necrosis and lymphoreticular infiltration. To our knowledge, there is no pathologic nor angiographic report of cerebral aneurysm in this condition. We report one patient with multiple cerebral aneurysms secondary to LYG.

A 30 year old male diagnosed with LYG on a lung biopsy one month earlier and treated with Prednisone 80 mg and cyclophosphamide 100 mg daily, presented with focal seizure. Neurologic examination was normal. A brain CT Scan showed left frontal and right parieto-occipital hemorrhagic infarcts. Cerebral arteriogram revealed two saccular aneurysms on distal branches of the right middle cerebral artery and multifocal arterial narrowing. Multiple blood cultures were sterile and an echocardiogram normal.

Cyclophosphamide was increased to 150 mg and Prednisone to 90 mg daily. On control angiogram one month later there was significant decrease in size of the aneurysms and disappearance of multifocal arterial narrowing.

Cerebral aneurysms are very uncommon in non-infectious vasculitis. In our patient, the absence of infection at the time of initial angiogram and the improvement of angiographic findings with chemotherapy alone suggest the aneurysms were secondary to the vasculitic process associated with LYG.

Multiple Sclerosis

P137.

Influence of Pregnancy on Disability From Multiple Sclerosis: A Population Based Study in Middlesex County, Ontario

B.G. WEINSHENKER, W. HADER, J. BASKERVILLE and G.C. EBERS (Ottawa and London, Ontario; Saskatoon, Saskatchewan)

Retrospective studies report an increase in the frequency of attacks of multiple sclerosis (MS) in the post partum period. Yet the limited information from 2 studies that addressed the issue of long-term disability fails to document an association of disability with total number of pregnancies or with those specifically occurring following the onset of MS. These studies may be lacking in power to demonstrate an association due to biases of ascertainment which may limit the value of comparison of mean disability in patients in clinic based studies stratified according to their reproductive history.

We analyzed the effect of pregnancy on long-term disability resulting from MS in 185 female patients ascertained through a population based survey of MS in Middlesex County, Ontario. No association was found between disability and (1) total number of term pregnancies, (2) timing of pregnancy relative to onset of MS or (3) either onset or worsening of MS in relation to pregnancies both before and after onset of MS was no different among groups stratified according to disability. This study addressees the difficulties inherent in studying the effect of pregnancy on disability resulting from MS.

P138.

Demyelinating Disease Presenting as a Partial Oculomotor Nerve Paresis

A. ABDOLLAH and G. FRANCIS (Montreal, Quebec)

Oculomotor nerve paresis with pupillary involvement has not been described in demyelinating disease. A 23 year old female presented with blurred vision and diplopia. Examination revealed a left efferent pupillary defect and impaired left medial and inferior recti function. In addition, there were mild left cerebellar and right corticospinal tract signs. No structural lesions were found on CT and angiography. CSF protein was elevated (0.89g/l); oligoclonal banding was positive. T2-weighted MRI of the brain revealed areas of increased signal intensity in the periventricular white matter and corona radiata. No abnormal signal was detected in the midbrain. Symptoms and signs resolved over two weeks. A small plaque in the left midbrain was postulated to account for this presentation.

The site of the lesion cannot be nuclear (Daroff RB, Neuro-ophthalmology V, 1970. 104-118). The lesion therefore involves the fascicles of the third cranial nerve.

This case illustrates the topographic arrangement of the fascicular fibers indicating the parasympathetic fibers are adjacent to oculomotor fibers innervating the medial and inferior recti muscles.

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P139.

MRI in MS: The Extent of Pathology Present in Multiple Sclerosis Shortly after Clinical Onset in Patients Who Later Developed Definite MS

R.A. KOOPMANS, D.K.B. LI, K. REDEKOP, R. FARQUHAR and D.W. PATY (Vancouver, British Columbia)

Little is known about the extent of pathology present early in the course of MS.

We studied 69 suspected MS patients with MRI shortly after disease onset (mean 5 months) to determine the extent and variability of lesions present at that time. During subsequent 3 year follow-up, 26 of these patients (mean age 33 yrs, EDSS 1.8) converted to laboratory supported or clinically definite MS. Twenty-three out of these 26 (89%) definite MS patients had MS lesions on MRI when originally studied. All had cerebral lesions, 35% had brainstem and 24% had cerebellar lesions. Most patients (78%) had larger (>1 cm), often extensive confluent, periventricular lesions; 22% had smaller lesions only. Mean lesion number per patient was 9. Most (57%) lesions were periventricular, 21% were in the cerebral deep white matter, 9% in the grey white matter junction and 13% infratentorial. More than half (52%) of the patients had both cerebral and infratentorial lesions; many (58%) of these cases also had confluent periventricular lesions. Only 1 of 11 cases with lesions limited to the cerebrum had confluent periventricular lesions. No cases had lesion limited to brainstem or cerebellum without simultaneous cerebral involvement. Of the 43 patients whose diagnosis remains probable or possible MS, 19 (44%) had abnormal MRI with lesion extent and distribution similar to those who had become definite MS.

This study demonstrates that many cases already have extensive pathology early after onset of symptoms and prior to development of a definite diagnosis of MS based on clinical criteria. This cohort will be further investigated to determine if these early MRI findings are of any prognostic significance.

P140.

MRI in the Diagnosis of MS: A Prospective 3-year Follow Up with Comparison of Clinical Evaluation, Evoked Potentials, Oligoclonal Banding, and CT

K.H. LEE, S.A. HASHIMOTO, J. HOOGE, L.F. KASTRUKOFF, J. OGER, D. LI and D.W. PATY (Vancouver, British Columbia)

We compared the diagnostic capabilities of head MRI to CT, evoked potentials (EP) and CSF oligoclonal banding analysis in a prospective evaluation of 200 patients with suspected MS (Neurology 38: 180-185, 1988). Laboratory-supported definite MS (LSDMS) could be diagnosed in 85 patients by using these paraclinical tests.

In order to examine the accuracy for predicting the diagnosis of clinically definite MS (CDMS) we did a three year follow-up. We discarded one patient diagnosed as LSDMS who was considered to have had CDMS at entry and 14 patients who were eventually diagnosed as having other diseases.

Out of the remaining 185 patients, 55 (30%) had developed CDMS. Thirty-eight out of 84 patients with LSDMS (45%), and 17 out of the remaining 101 patients with suspected MS (17%) had become CDMS. In 46 of the 55 patients with CDMS (84%), that diagnosis was predicted by a scan "MRI strongly suggestive of MS" (3 or more MS-like lesions). Fifty-two out of the 55 CDMS patients (95%) had shown at least one MS-like abnormality on MRI when originally studied. Only 3 of the 55 had a completely normal head MRI when first studied. In contrast, only 38 of the 55 (69%) had CSF oligoclonal bands, 38 of the 55 (69%) had abnormal visual EP, 35 of the 55 (64%) had abnormal somatosensory EP, and 23 of the 55 (42%) had abnormal CT scans.

Autopsy was done in 3 out of 8 patients who had died during follow up. All three had demyelination at autopsy. One (with a N MRI) had demyelination restricted to the spinal cord. The other two (one with "MRI strongly suggestive of MS" and one with only 1 MRI lesion) had MS.

These results confirm our previous observation that MRI is the best diagnostic study for detecting dissemination in space and for predicting the diagnosis of CDMS.

P141.

Chronic Progressive Multiple Sclerosis: Abnormal enumeration and reduced function of T Helper Subsets

J. OGER, T. AZIZ and M. O'GORMAN (Vancouver, British Columbia)

In chronic progressive multiple sclerosis patients (CPMS) immunoglobulin secretion abnormalities both in vivo and in vitro have been consistently observed. We measured Pokeweed mitogen (PWM) induced IgG secretion, Concanavalin A induced suppression IgG secretion and enumerated the T helper cell subsets (i.e. CD45R and CDw29) using the ratio of CD3+2H4+/CD3+4B4+ in healthy controls, CPMS and other neurological disease controls (OND).

PWM induced IgG secretion was increased in CPMS (2791±652 ng, n=14) compared to healthy control subjects (1483±323 ng, n=21, $p<.025$), OND were not different from controls (1995±499 ng, n=14). Suppression of PWM induced IgG secretion by Concanavalin A activated cells was reduced when CPMS (81.3±3.4%, n=6) were compared to both the healthy controls (89.2±2.5%, $p<.025$, n=6) and the OND group (89.0±2.5%, $p<.05$, n=6). The CD3+2H4+/CD3+4B4+ ratio in the chronic progressive MS group (0.5±.1, n=6) was significantly lower than both the healthy control group (1.1±.1, $p<.025$, n=14) and the other neurological disease control group (1.2±2, $p<.005$, n=8).

It is possible that immunological abnormalities observed in vitro contribute to the immunoglobulin secretion abnormalities observed in vivo in chronic progressive multiple sclerosis patients.

P142.

Demyelinating Plaques in a Patient with Sjogren's Syndrome

L.M. METZ, J.P. RYAN and B. CURRY (Calgary, Alberta)

Sjogren's Syndrome (SS) is a common autoimmune disease with neurologic manifestations in up to 20% of patients. CT and MRI have detected CNS lesions in SS patients with active neuropsychiatric disease which have predominantly involved white matter and were frequently periventricular. Neuropathologic findings have included inflammatory meningeal infiltrates and vascular lesions. Demyelination has not been reported. We report a patient with primary SS and CNS demyelinating plaques indistinguishable from plaques seen in MS. A 75 year old male with a ten day history of poor recent memory and episodes of confusion was found to have bilateral enhancing periventricular lesions on CT. One month later he was much improved and the CT lesions had resolved. One year later he was found to have primary SS. At age 77 he died of complications of a liver abscess. A history of intermittently failing memory was noted at this final admission. Neuropathologic examination revealed several focal demyelinating plaques, predominantly periventricular, with a histological appearance similar to that of MS. Some corresponded to the sites of the CT lesions identified two years earlier.

The cognitive deficits and CT lesions are consistent with similar abnormalities reported in other patients with SS. Their temporal association and the similar location of the plaques and CT lesions suggest an acute demyelinating process caused both the clinical syndrome and the CT lesions. The coexistence of SS and demyelinating plaques, in the absence of another condition known to cause demyelination, suggests that SS may be a cause of CNS demyelination. We cannot rule out late onset MS in this patient but if SS does cause demyelination more cases with similar lesions should soon be found as awareness of SS and its neurologic manifestations is increasing. Proving that SS can cause

demyelinating plaques may shed some light on the role of the immune system in MS as well as the pathophysiology of CNS dysfunction in SS.

P143.

HTLV-1 Myelopathy in Canada

C. POWER, B.G. WEINSHENKER, G.A. DEKABAN and G.P.A. RICE (London, Ontario)

We report the clinical and laboratory findings of 3 Canadian patients with a progressive myelopathy compatible with Tropical Spastic Paraparesis (TSP) and associated with HTLV-1 infection. All patients (2 females, 1 male) are of Caribbean descent with a mean age of 39 years and a duration of symptoms of 10.5 years. Symptoms include leg weakness, muscle spasms, urinary incontinence and low back pain while signs revealed distal muscle wasting, spasticity, weakness, Babinski reflexes, hypereflexia and sensory changes. MRI scans show periventricular lesions suggesting demyelination in 2 patients. Electrophysiological studies demonstrate central conduction delays on motor and sensory evoked potential in 2 patients while EMG shows chronic denervation in 2 patients. Sera from all patients reveals IgG antibodies to HTLV-1. CSF shows oligoclonal banding in all patients. Polymerase chain reaction technique yields expected fragments of the tax/rex gene of HTLV-1 from all patients. Each patient was treated with corticosteroids with no observed benefit. The pathogenesis of this condition and the serological and molecular means by which this diagnosis can be made are reviewed.

Cerebrovascular

P144.

The Darwinian Brain — "Survival of the Fittest" in Unilateral Carotid Occlusion

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

To determine the pattern of intracranial circulation responsible for cerebral survival in unilateral carotid occlusion, we investigated 46 patients using Transcranial Doppler. Middle cerebral artery blood flow velocities (MCA-BFV) were evaluated during carotid compression and the dependency of each hemisphere on the contralateral (patent) carotid was determined. MCA reactivity to CO-2 in each hemisphere was also recorded to establish the capacity of collateral circulation.

Cerebral hemispheres were totally dependent in 91% cases where the patent control artery showed minimal stenosis. When the patent carotids had severe stenosis (>85%) most (80%) were totally independent.

CO-2 reactivity index did not differ significantly between the "occluded" (3.86±4.23) or "patent" (3.87±1.89) hemispheres nor between control values (3.36±2.45) in 23 volunteers. In hemispheres ipsilateral to the patent artery, CO-2 reactivity was inversely related ($r=-0.8$, $p<0.001$) to the percent stenosis of the patent artery in totally dependent hemispheres only.

Patients survive carotid occlusion without death or stroke only if their cerebral hemispheres are mainly independent of the occluded artery. Their outcome can be predicted if the CO-2 reactivity and degree of stenosis of the patent carotid artery are monitored.

P145.

Significance of Hemorrhage in Carotid Plaque

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

The significance of hemorrhages in carotid plaques is controverisal; they may contribute to ischemic cerebral events by sudden narrowing of the lumen, or by disrupting plaque to produce intraluminal thrombus and distal embolism.

We evaluated 77 consecutive symptomatic carotid plaques at surgery and then microscopically. Intraluminal clot was infrequent and microscopic (15/77). Intraplaque hemorrhage was seen in 66/77 (86%) of the plaques. They were deeply located in 52/83 (63%) and subintimal in the remaining 31 (37%). Of those, only 11/83 (13%) were connected to the lumen. Intraplaque hemorrhages occurred mostly in highly stenotic arteries. Time delay between TIAs and stroke correlated poorly with the age of the hemorrhages and often the hemorrhages apparently preceded clinical events by weeks.

Our data suggest that intraplaque hemorrhage is a marker of severely stenosing plaque and may contribute instability of the plaque producing secondary embolic or ischemic stroke.

P146.

Intracranial Circulation in Takayasu's Disease

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

Takayasu's disease is an arteritis of large vessels, but occasionally medium sized vessels are also involved. Stroke is one complication of this disease. We report here a case of involvement of intracranial vessels which is unique and indicates much more widespread involvement than generally believed.

A 42 year old, previously well, woman had a sudden severe right hemiparesis with aphasia, which resolved over the ensuring 6 weeks. Duplex scanning of the neck indicated severe stenotic lesions of right common carotid and subclavian arteries with involvement of the internal carotid arteries. Whole body angiography confirmed those findings and fulfilled the criteria for the diagnosis of Takayasu's disease.

Transcranial Doppler (TCD) using the EME TCD-64 showed the following velocitites in the middle and anterior cerebral arteries (MCA and ACA):

	Left Side		Right Side	
	MCA	ACA	MCA	ACA
Normal Values	(33-90)	(30-74)	(33-90)	(30-74)
Oct. '86	56	58	70	40
Jun. '88	230	210	106	118
Sep. '88	106	162	113	76

The increased velocities in the left MCA and ACA suggesting arterial stenosis resolved following cyclophosphamide therapy.

We conclude that TCD is a valuable method of confirming intracranial involvement in this condition and monitoring progress of the disease.

P147.

Changes in CO_2 Reactivity of Intracranial Vessels in Cluster Headache

A. KRAJEWSKI, Y.M. LUO and M.J. GAWEL (Toronto, Ontario)

Cluster headaches occur in bouts which come at regular intervals and are characterised by severe, unilateral, retro-orbital pain with associated

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autonomic symptoms. Our previous study demonstrated an asymmetry in maximum blood flow velocities in the middle cerebral arteries (MCA), the headache side recording the higher indices.

In this study we assessed CO-2 reactivity in the MCA and anterior cerebral artery (ACA) in 21 patients with cluster headache (12 active, 9 in remission), and in 12 controls, using the transcranial Doppler technique. MCA and ACA velocities were measured at rest and following a period of inhalation of 5% CO-2 until stable levels of expired CO-2 wer reached. Percent changes of the velocity per 1 mm pa CO-2 were expressed as the reactivity index.

We found a decreased reactivity in the ACA on the headache side during the cluster period (out of an attack) — 3.26±0.77 (mean ± standard error) and an increased reactivity in ACA on the side of the headache outside the cluster period — 6.68±1.01. This difference was significant ($p<0.05$). The control value was 4.62±0.83.

Although preliminary, these results suggest a cyclic change in reactivity in the ACA on the headache side. The mechanism of such changes could be explained on the basis of an alternating neural input into the artery.

P148.

A Prospective Study on the Usefulness of Echocardiography in the Management of Patients with Cerebrovascular Disease

W.J. OCZKOWSKI and V.H. HACHINSKI (Hamilton and London, Ontario)

In order to directly answer the controversial question of "How useful is echocardiography in the care and treatment of patients with cerebrovascular disease?" we carried out a prospective study involving 176 patients with TIA (72) or stroke (104) recruited among inpatients and outpatients over a consecutive six month period.

Pre- and post-echocardiogram questionnaires were administered to the physician most directly involved in the patient's care. The results of the M-mode and two-dimensional echocardiogram changed management directly in 32 (18.2%) patients. Twelve were anticoagulated for a cardiac source, seven had their anticoagulants altered, six patients with a high pre-test probability for anticoagulation with normal or non-specific echocardiographic findings were not anticoagulated. Seven patients were further investigated because of the results of echocardiography.

Patients who had their management altered by the echocardiographic result were felt more likely to have had a cardio-embolic stroke ($p<0.01$). These patients were younger (mean age 54.5 years compared to a mean age of 62.2 years, $p<0.01$, of those who did not have their management changed) but no other factors including gender, history of cardiovascular disease, the physical examination, the electrocardiogram, and combinations thereof were predictive of a change in management.

The results of echocardiography change the management of one in every five patients with cerebrovascular disease.

P149.

Stroke Risk and Critical Carotid Stenosis

C.Z. ZHU, S. BHIMJI and J.W. NORRIS (Toronto, Ontario)

The hierarchy of stroke risk associated with carotid stenosis indicates a significant risk only at stenoses >75%, yet this risk appears to decrease suddenly when the artery occludes. To investigate this relationship further, we compared the outcome in three groups of patients: 500 with asymptomatic neck bruits, 901 with TIAs (with and without bruits), and 261 with stroke (with and without bruits), to a group of 500 controls.

Only 4% of the control arteries had Doppler-detectable carotid stenosis, while 40% of the asymptomatic group had carotid stenosis, with a bi-modal distribution. Ischemic cerebral events related to the severity of carotid stenosis, especially >75%. The extent and severity of carotid stenosis increased in all symptomatic groups when neck bruits were present (shift to the right). This distribution was not explained by age and sex. In all groups (except controls), there was a consistent bi-modal distribution of carotid stenosis, with the junction between the two groups always about 85%.

This appears to be a point of critical stenosis carrying maximal stroke risk.

P150.

"Silent" Strokes and Carotid Stenosis

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

Data concerning "silent" (asymptomatic) strokes in the vascular territory of carotid artery stenosis (CAS) may affect surgical or medical management. Using CT scanning we compared the prevalence of cerebral infarction in 24 patients with CAS + TIAs to 50 with asymptomatic CAS, and 38 with TIAs and normal carotid arteries. Vertebrobasilar TIA patients were excluded.

In the total patient population (112) there were 33 infarcts and 16 (46%) of these were lacunar. In the TIA+CAS group, 9/24 (38%) had cerebral infarcts, almost identical to the group with TIAs and normal carotids (12/38, 32%). However, in the asymptomatic group there were significantly fewer ($p<0.05$) infarcts (10/50, 20%). CAS was significantly more severe in the symptomatic group (28%) than the asymptomatic group (10%). Cerebral infarctions were ipsilateral to the most stenosed artery in 80%.

20%-30% of patients with carotid stenosis but with no, or minimal symptoms, sustain cerebral infarction. However, only further prospective follow-up can determine whether those "silent" strokes have the same prognostic implications as clinically overt strokes or TIAs.

P151.

Cerebral Thomboangiitis Obliterans

D. ROBINSON, N. CAHSMAN, D. MELANSON and S. CARPENTER (Montreal, Quebec)

Involvement of the cerebral circulation by thromboangiitis obliterans has been questioned.

We report a thirty-one year old male smoker who presented in 1982 with dysphasia, right hemiparesis and hemianesthesia. Cerebral angiography revealed focal narrowing of the left internal carotid artery and complete occlusion of the middle cerebral artery suggestive of a vasculitic process. Complete blood count, biochemistry, reagin test for syphilis, serum protein electrophoresis, rheumatoid factor and complement were normal or negative.

In 1983 he presented with right leg deep venous thrombosis. In 1984 recurrent right leg ulcerations progressed to gangrene necessitating amputation. Pathology demonstrated organized, concentric arterial thrombotic occlusion with lymphocytic infiltration. In 1988 he underwent surgical resection of ischemic bowel and left leg amputation.

We suggest that the various peripheral and cerebral vascular occlusions are etiologically related under the diagnosis of thromboangiitis obliterans.

P152.

Migraine-Stroke: An Autopsy Report of Two Cases

A. SHUAIB and R. AUER (Durham, U.S.A. and Calgary, Alberta)

Patients with migraine-stroke make an almost complete recovery and thus rarely come to autopsy. The mechanism leading to the cerebral infarction (CI) is not understood but is commonly considered to be secondary to vasospasm. Other conditions that have been reported to cause

migraine-stroke, with only isolated case reports, include vascular dissection, hyperplasia and endarteritis, cerebral edema and cerebral aneurysm. It is also possible that migraine headache may be precipitated by the stress associated with the ictal event and not directly the cause of the CI.

We wish to report two cases where migraine-stroke was suspected as the clinical diagnosis and the patients died. Autopsy in both cases showed unexpected findings. One patient a 46 year old female develop an increase in severity of migraine headaches and a right hemiplegia and aphasia developed during a headache. Extensive investigations including two cardiac echos failed to show a specific cause. The patient died after a second CI, and autopsy showed marandic endocarditis and an unsuspected carcinoma of the cervix. In the second case, the patient presented with a rapid onset of coma several hours after a severe migraine headache. The patient died several weeks later and at autopsy there was dissection of the basilar artery.

Our experience suggests that migraine may incidentally occur in association with stroke without being necessarily related to it. Migraine-stroke should thus be considered a heterogeneous condition and not a single entity. Every effort should be made to rule out other causes of stroke, which unfortunately may not always be apparent during life.

P153.

Pontine-Medullary Hemorrhage and Central Hypoventilation: A Case Report

A. SHUAIB, H. ALAZZUNI and S. MUKERJEE (Durham, U.S.A. and Calgary, Alberta)

Medullary lesions can cause central hypoventilation (CHV) and sleep apnea and has been reported with lateral medullary infarction, poliomyelitis, multiple sclerosis and neoplasms. We report a patient who developed acute respiratory arrest with a medullary hemorrhage.

A 61 year old male was seen with right sided hemiparesis, nausea/vomiting, and unsteadiness developing after a brief episode of loss of consciousness. Examination revealed a normal mental status, conjugate gaze paralysis towards the left, left facial weakness, decrease sensation in the right trigeminal nerve distribution, and an absent gag and cough reflex. In addition, he had a 4/5 motor weakness and sensory deficit involving the right arm and leg. Cranial CT scan showed a small hemorrhage in the pontine-medullary region.

Five days later acute respiratory arrest developed that required intubation. During the next 2-3 days any attempt at extubation would result in apnea. Prolonged support with tracheostomy and assisted ventilation over three weeks was followed by gradual return of respiratory function.

Outcome with previously reported cases of CHV have been poor, reflecting the prognosis of the underlying condition. The better outcome in our patient reflects return of function with resorption of the hematoma.

P154.

Mitral Valve Prolapse and Recurrent Cerebral Infarction in Anticoagulated Patients

A. SHUAIB and W. MURPHY (Durham, U.S.A. and Calgary, Alberta)

Patients with mitral valve prolapse (MVP) are at an increased risk to develop ischemic cerebral infarction that probably results from cardioembolic disease. Most patients develop transient ischemic attacks or minor strokes and respond well to anti-platelet agent or anticoagulants. Recurrent strokes after the patient is anti-coagulated have not been reported. We wish to report two patients who developed recurrent cerebral infarctions despite anticoagulation. One patient developed three hemorrhagic infarcts and MVP was the only identifiable risk factor. In the second case, the patient sufferer large bilateral cerebral infarction that resulted in a chronic vegetative state and eventual demise of the patient. Autopsy in this case confirmed the MVP and did not disclose any other cause for the cerebral infarction.

Mitral valve prolapse is a common condition and associated cerebral events are usually benign. These may on occasion however lead to serious disability and even death. We discuss the clinical course of our patients and based on our experience and a review of the literature suggest treatment recommendations.

P155.

Does Temporal Artery Biopsy Help in the Management of Giant Cell Arteritis?

C. GRAFFAGNINO and T.E. FEASBY (London, Ontario)

Temporal artery biopsy is the established method of confirming the diagnosis of temporal arteritis (TA) but does it help in the subsequent management of this condition?

We reviewed the charts of 62 patients seen at University Hospital, London between 1973 and 1986. These patients either had a clinical diagnosis of TA or were biopsied for suspicion of TA.

A clinical diagnosis of TA was made in 22 patients of whom 14 had a positive biopsy, 4 had a negative biopsy and 4 had no biopsy. Forty others had negative biopsies, of whom 15 were diagnosed as having polymyalgia rheumatica and 25 with other diseases. In the TA group, there was no difference in the initial dose of steroids used in those with positive biopsies and those with negative or no biopsies nor was there a significant difference in the duration of treatment. The biopsy results seemed to have no influence on the management decisions which were made more in response to fluctuations in the clinical symptoms and the ESR.

We conclude that temporal artery biopsy is not very useful in the management of patients with suspected temporal arteritis.

P156.

Symptomatic Treatment of Cluster Headache with Intranasal Instillation of Lidocaine

B. RABY, C. ROBERGE, S. TENNINA and J. BRISSON (Quebec City, Québec)

The treatment of the severe pain of cluster headache is difficult, with often only partial relief despite powerful drugs; a better symptomatic treatment without important side effects, acting rapidly, would be a welcome addition to therapy.

We tested the effect of intranasal instillation of lidocaine in the symptomatic treatment of spontaneous cluster headache attacks, in a randomized, double-blind, placebo-controlled crossover study. The patients were instructed to instill 1 ml of a 4% solutionof lidocaine in the ipsilateral nostril as soon as possible after the onset of an attack. During the first week, the patients received only their usual prophylactic and analgesic treatments, and made a careful recording of the attacks and their characteristics. They were then randomized to treatment with either lidocaine or placebo, for one week; during the third week, they crossed over to the other medication. Fifteen patients (12 cluster form, 3 chronic form) completed the study.

Lidocaine reduced significantly the duration of the attacks. The mean (±SD) duration of the attacks was 35.9±5.8 minutes with lidocaine and 53.4±6.7 minutes with placebo ($p=0.0115$). The peak severity of pain, however, was usually attained early in the attacks and was not reduced by lidocaine. The perceived effect, scored 0 to 5, was much greater for lidocaine (2.58±0.42) than for placebo (0.77±0.35) ($p=0.0011$). Tearing of the eye and nose congestion, frequent accompaniments of the attacks, were not modified by lidocaine, suggesting that their mediating pathways may be different from those for pain.

In conclusion, we feel that the addition of symptomatic treatment with intranasal lidocaine may be useful to reduce the duration of the attacks in patients with cluster headache.

P157.

Response of Non-migrainous Headaches to Chlorpromazine

C.L. BARCLAY, A. SHUAIB, D. MONTOYA, T.P. SELAND and H.G. THOMAS (Calgary, Alberta and Durham, U.S.A.)

Chlorpromazine, given intravenously, is a useful agent in the treatment of acute migraine headache. Patients with more serious conditions, however, may also respond to this medication.

In this paper, we report two patients who were initially diagnosed as having migraine headaches and treated with chlorpromazine. Both experienced temporary pain relief and it was only after repeated presentations to Emergency that their conditions — a subarachnoid hemorrhage and a subdural hematoma were accurately diagnosed.

Because of this, caution must be exercised before retreating within a short period of time, a patient with a recurrent headache. Strong consideration must be given to an alternate diagnosis and such a diagnosis should be actively sought should there be any suspicion of a non-migrainous cause for the headache. It is only by doing so that we may avoid missing a more serious and life-threatening condition, such as those with which our patients presented.

P158.

Recurrent Spinal Cord Ischemia Due to Abdominal Aortic Aneurysm

H.B. DESAI, A.H. RAJPUT, D. MUNOZ and R.J. UITTI (Saskatoon, Saskatchewan)

Ischemic spinal cord lesions with abdominal aortic aneurysm are rare and are usually characterized by a single catastrophic event. We are reporting a 75 year old woman who, over a period of 3 years, had 3 attacks of acute neurologic deficit, characterized by bladder incontinence, lower limb motor deficit (upper and lower motor neuron), and patchy sensory loss with a sensory level at T10-T12. Investigations revealed a large abdominal aortic aneurysm which enlarged progressively and eventually ruptured leading to death.

Autopsy showed marked atherosclerosis of the entire aorta with destruction of the intima and a large abdominal aortic aneurysm with a thin posterior wall. Most of the ostia of the spinal radicular arteries were either blocked or buried under the atherosclerotic plaques. X-ray study after injection of barium into the visible ostia showed occlusion of all the spinal radicular arteries in the thoraco-lumbar region except the Artery of Adamkiewicz. Sections of the spinal cord revealed multiple infarcts below T7 levels. Occlusion of many epidural vessels including the posterior spinal arteries was seen at multiple levels. The anterior spinal artery was occluded and recanalised at T10 level.

Atherosclerotic aortic aneurysm and spinal cord ischemia should be considered in elderly patients with spinal cord and cauda equina dysfunction as well as in poorly understood gait and lower limb dysfunction.

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