XXI Canadian Congress of Neurological Sciences

London, Ontario
June 24 - 28, 1986

TUESDAY, JUNE 24, 1986

CONGRESS SATELLITE SYMPOSIUM #1 (0830-1630 hours)

"First Canadian Symposium on the Organic Dementias"

This Symposium will be held in Auditorium "A", University Hospital. Registration forms are available from Continuing Medical Education, Faculty of Medicine, London, Ontario N6A 5C1

Platform and Poster Presentations on:

- Clinical and therapeutic issues
- Neuropsychological challenges
- Cellular clues to pathogenesis
- Biochemical studies
- Imaging of demented subjects

CONGRESS SATELLITE SYMPOSIUM #2 (0830-1200 hours)

"The Molecular Mechanisms of Antiparkinsonian Drugs"

Contact: Dr. H. Robertson
Faculty of Medicine
Dalhousie University
Halifax, Nova Scotia (902) 424-2563

Introduction: "Synergic actions of D_1 and D_2 dopamine agonists"	*H. Robertson*
"Bromocriptine and L-dopa combination therapy: Clinical implications"	*D. Calne*
"Interactions between D_1 and D_2 agonists: Receptor binding studies"	*A. Dunbrille-Ross*
"Studies on the physiological roles of D_1 and D_2 receptors"	*J. Kebabian*
"A possible molecular mechanism for the antiparkinsonian action of bromocriptine in connection with L-dopa"	*M. Goldstein*
"Agonist-induced supersensitivity in rats and MPTP treated monkeys"	*P. Bedard*

This Symposium was made possible by generous support from Sandoz (Canada) Ltd. and Merck Frosst Canada Inc.

TUESDAY, JUNE 24, 1986

CONGRESS SATELLITE SYMPOSIUM #3 (0830-1630 hours)

"Festschrift" for C.G. Drake and H.J.M. Barnett

Contact: Dr. T. Feasby
Dept. of Clinical Neurological Sciences
University Hospital
London, Ontario (519) 663-3000

A day of scientific papers presented by the former residents of C.G. Drake and H.J.M. Barnett, the founders of the Department of Clinical Neurological Sciences at the University of Western Ontario.

All registrants for the Canadian Congress are welcome to attend this event.

ANNUAL SCIENTIFIC MEETING OF THE CANADIAN ASSOCIATION FOR CHILD NEUROLOGY (0900-1600 hours)

Contact: Dr. G. Hinton
Paediatric Neurology
The Children's Hospital of Western Ontario
London, Ontario

"Aspects of non-neurological neonatal disorders of importance for neurologists"	*G. Chance*
"Neonatal seizures: Some basic mechanisms"	*D. Howse*
"Neonatal seizures: Management"	*J. Kronick*
"Muscle disease in the neonate"	*P. Jacob*
"Neonatal clinical-pathological conference" discussant	*S. Seshia*
"Neonatal clinical-pathological conference" presentor	*H. Alcala*
"Follow-up of high risk newborns"	*M. Fox*

WEDNESDAY, JUNE 25, 1986

COURSE #1 - Practical Management of Cerebrovascular Disease
Organizer - V.C. Hachinski

(A) Morning Session (0830-1200)

Cerebrovascular disease: an overview	*V. Hachinski*
Major stroke	*A. Hakim*
The deteriorating stroke	*W. McCormick*
The young stroke	*D. Spence*
TIA and minor stroke	*H. Barnett*
The asymptomatic bruit	*J. Norris*
Subarachnoid hemorrhage: diagnosis and general management	*S. Peerless*

(B) Afternoon Session (1330-1700 hours)

Arteriovenous malformations	*C. Drake*
Aneurysms	*G. Ferguson*
Therapeutic Neuroradiology	*A. Fox*
Issues and answers	*G. Ferguson* *V. Hachinski*

COURSE #2 - Behavioural Neurology (0830-1200 hours)
Organizer - A. Kertesz

Apraxia - disorders of skilled movements	*S. Black*
Neurobehavioural approaches to Alzheimer's disease	*M. Freedman*
Frontal lobe syndromes and deficits	*D. Stuss*
Neuropsychological deficits in childhood vascular syndromes	*M. Dennis*
Visual agnosia - disorders of visual processing	*A. Kertesz*
Neglect and hemiattention	*K. Heilman*

COURSE #3 - Practical Neuro-oncology (0830-1200) hours
Organizer - J.G. Cairncross

Management of brain metastases	*D. MacDonald*
Cancer pain syndromes	*D. Moulin*
Deafferentation pain	*R. Tasker*
Spinal epidural metastases: surgical approaches	*N. Sundaresan*

COURSE #4 - Multiple Sclerosis: An Overview (1330-1700 hours)
Organizer - G. Rice

Introduction - clinical phenomenology	*G. Ebers*
Differential diagnosis and unusual symptoms and signs	*J. Noseworthy*
Neuroimaging and MS	*D. Paty*
Natural history	*B. Weinshenker*
Treatment of the disease	*J. Noseworthy*
Treatment of the complications	*G. Rice*
The cause of MS: a role for lymphocytes	*G. Francis*
The cause of MS: a role for viruses	*G. Rice*
The cause of MS: a role for genes	*G. Ebers*

THURSDAY, JUNE 26, 1986

Morning

Plenary Session

- Presidential Address
  "Acoustic Neuromas: The Importance of Modern Neuroscience in Diagnosis and Treatment since the McKenzie era"

  Dr. Charles H. Tator, president, Canadian Neurosurgical Society

- Platform Presentations - The nine papers to be presented were chosen by the Scientific Program Committee because of their apparent scientific merit and interest to the membership.

- Poster Viewing Session

- Canadian League Against Epilepsy Lecture

Afternoon

- Simultaneous Platform Sessions

  General Neurology
  Cerebrovascular Disease
  Child Neurology
  Multiple Sclerosis
  Neuro-oncology
  Epilepsy

- Poster Viewing Session

FRIDAY, JUNE 27, 1986

Morning

- Simultaneous Platform Sessions

  General Neurology
  General Neurosurgery
  Basic Neuroscience

- Poster Viewing Session

- Prize Lectures (McKenzie, McNaughton)

FRIDAY, JUNE 27, 1986

Afternoon

SPECIAL CONGRESS SYMPOSIUM

"Perspectives in the Clinical Neurosciences"

This Symposium is dedicated to Dr. H. J. M. Barnett and Dr. C.G. Drake in recognition of their contributions to Neurology and Neurosurgery, and is presented by the Honoured Guests of the Congress.

Prof. Raymond D. Adams	- Boston, U.S.A.
Prof. Hajime Handa	- Koyoto, Japan
Prof. Albert J. Aguayo	- Montreal, Canada
Prof. Bryan Jennett	- Glasgow, Scotland
Prof. Joseph B. Martin	- Boston, U.S.A.
Prof. Leonard I. Malis	- New York, U.S.A.
Prof. Fred Plum	- New York, U.S.A.
Prof. Theodore B. Rasmussen	- Montreal, Canada
Prof. Sir John Walton	- Oxford, England

SATURDAY, JUNE 28, 1986

Morning

Continuation of the Symposium on "Perspectives in the Clinical Neurosciences" with keynote Addresses by Drs. H.J.M. Barnett and C.G. Drake.

XXIst Canadian Congress of Neurological Sciences Abstracts of the Scientific Program

Platform Presentations

1.

Use of Detachable Balloons for Proximal Artery Occlusion in the Treatment of Unclippable Cerebral Aneurysms.

A.J. FOX, F. VINUELA, D.M. PELZ, S.J. PEERLESS, G.G. FERGUSON, C.G. DRAKE and G. DEBRUN (London, Ontario; Baltimore, Maryland)

67 aneurysms have been approached for proximal artery occlusion using detachable balloons. 60 of these unclippable aneurysms involved the carotid artery, about two/thirds in the petrous and cavernous portions and one/third in the supraclinoid portion. 7 involved the vertebral or basilar arteries. The ultimate test for tolerance of occlusion is the preliminary occlusion done under systemic heparinization prior to detachment. Following embolization 10% have subsequently had some ischemic episodes, mostly transient. One case (1.5%) has permanent leg weakness. Proximal balloon occlusion has led to complete aneurysm obliteration in most cases including about half of those in the supraclinoid portion. The continued simplicity and acceptable safety of this approach has influenced us to continue proximal occlusion rather than begin again attempt of intraaneurysm placement of balloons with preservation of the parent artery, an approach that led to an unacceptable number of complications in our hands in the early years of using detachable balloons for aneurysm treatment.

2.

Experimental and PET Evaluation of Calcium Channel Blockers in Cerebral Ischemia

A.M. HAKIM, G. MARCHAL, M. DIKSIC, A. EVANS, J. TYLER and E. MEYER (Montreal, Quebec)

Calcium channel blockers, and particularly nimodipine, have been shown in large clinical trials to improve morbidity and mortality following stroke. This effect is usually attributed to their vasodilating properties. We have shown by positron emission tomography (PET) that up to 40% of stroke patients "naturally" reperfuse their ischemic brain regions with 48 hours from the CVA. Thus, we felt it unlikely that these agents exert their beneficial effects through vasodilation. We now report metabolic effects of calcium channel blockers that are more likely to explain their therapeutic values.

The middle cerebral artery was occluded in rats. Local cerebral pH (LCpH) and local cerebral blood flow (LCBF) were determined 4 hours after the occlusion autoradiographically by a double-label technique we developed. At least 4 rats in each of the following groups were studied: controls, nimodipine, verapamil, prostacyclin or carrier given IV starting 15 minutes following occlusion. Our data show that while in the controls and in animals receiving carrier or prostacyclin, LCpH fell in the ischemic regions to as low as 6.72 ± 0.05 (mean ± SEM), LCpH was indistinguishable from normal (7.06 ± 0.06) in those rats receiving nimodipine or verapamil. There was no significant effect of any of these drugs on LCBF. We conclude that calcium channel blockers may exert their beneficial effect by allowing cerebral regions of ischemia to regulate their pH towards normal, thus avoiding the deleterious consequences of acidosis described in the literature.

The evaluation of the metabolic and perfusion effects of nimodipine by PET in a small group of stroke patients will be presented.

Supported by the Medical Research Council of Canada, the Canadian and Quebec Heart Foundations and the Montreal Neurological Institute.

3.

Dopamine Pathways in the Dystonias — Studies with Positron Emission Topography

A.J. STOESSL, W.R.W. MARTIN, M.J. ADAM, T.J. RUTH, B.D. PATE, M.D. MUENTER, R.C. DUVOISIN and D.B. CALNE (Vancouver, British Columbia; Rochester, Minnesota; New Brunswick, New Jersey)

The pathophysiology of the dystonias is poorly understood. Findings in cases of secondary dystonia suggest that the underlying disorder is in the basal ganglia, but in primary dystonia, identifiable pathology is lacking. Pharmacological and biochemical studies have failed to reveal a consistent pattern of abnormalities. Positron emission tomography allows the non-invasive in-vivo assessment of brain function and is thus ideally suited to the study of such disorders. We have examined dopamine pathways in patients with dystonia using the positron-emitting dopa-analogue ^{18}F-6-fluorodopa (6-FD). Eight patients were scanned for two hours following the intravenous administration of 6-FD. The ratio of striatal:cerebellar activity during the second hour following isotope administration was assessed as a measure of the accumulation of 6-fluorodopamine and its metabolites within the basal ganglia. Of four patients with idiopathic generalized dystonia, one had evidence of significantly depressed striatal activity, one had borderline elevated activity and two were normal. Four patients with L-Dopa responsive dystonia were studied; three of these had normal scans. One had diminished activity throughout the striatum bilaterally, but most marked in the putamen contralateral to the side of maximal motor disability, a pattern similar to that seen in idiopathic Parkinson's disease. This study supports the view that dopamine pathways may be affected in some patients with dystonia.

4.

A Method for Anatomical Cross Correlation Between PET, MRI and DSA

A. OLIVIER, E.P. MARCHAND, T.E. PETERS, J. CLARK, G. MAWKO, J. TYLER and G. BERTRAND (Montreal, Quebec)

Positron Emission Tomography (PET) provides metabolic data on cerebral functions. However its poor anatomical resolution with most

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of the available cameras has significantly lessened its application in terms of data for local anatomical structures. By contrast, magnetic resonance imaging (MRI) provides outstanding anatomical resolution which reveals clearly the configuration and extent of most human cerebral structures. Cerebral vascular anatomy can also be elegantly displayed by digital subtraction angiography (DSA). Obviously a combination or integration of these methods is highly desirable to extract the maximum functional and anatomical information in normal and pathological conditions. Such an approach has proven to be very difficult technically, for several reasons, one of them being the lack of common landmarks between these various modalities of imaging. By using the corpus callosum as the basis of an anatomical reference system, various anatomical planes can be established and cross correlation can be made between MRI and DSA. By using a stereotaxic frame, these internal landmarks and planes can be transferred to external markers and planes visible on the skull and on the scalp. PET images can then be generated, which correspond exactly in thickness and orientation to any pre-selected plane previously identified on MRI or DSA.

This approach is most useful for anatomical studies, placement of depth electrodes in epilepsy and evaluation of brain tumours.

5.

Management of Hydrosyringomyelia in Childhood

H.J. HOFFMAN, K.R. CRONE, J. NEILL, E.B. HENDRICK and R.P. HUMPHREYS (Toronto, Ontario)

The authors review their experience in the management of 47 children with hydrosyringomyelia during the past decade. Thirty of these patients had undergone repair of a myelomeningocele in infancy, 12 patients had a Chiari I malformation and secondary hydrosyringomyelia and five patients had an acquired hindbrain malformation secondary to lumboperitoneal shunting for hydrocephalus.

All 47 patients were investigated by CT metrizamide myelography and/or MRI scan. Thirty-one of these 47 patients underwent decompression of their hindbrain malformation and plugging of their obex as the initial procedure for their hydrosyringomyelia. A further six patients underwent posterior fossa decompression without plugging of the obex. Ten patients were treated with a shunt from their syrinx into subarachnoid space, pleural cavity or peritoneal cavity.

The classic signs of a dissociated sensory loss were relatively uncommon in this group of patients. Several of the Chiari I patients were referred by our orthopedic colleagues because of a progressive scoliosis. The myelodysplastic patients presented with deteriorating gait, increasing scoliosis and upper limb weakness despite a well-functioning diversionary ventriculo-peritoneal shunt.

The Gardner operation of decompression of the hindbrain anomaly and plugging of the obex was the most effective form of therapy in our patients with hydrosyringomyelia, no matter what the cause.

6.

Nuclear Magnetic Resonance (NMR) Changes in Experimental Allergic Encephalomyelitis (EAE) Precede Clinical and Pathological Events

J.H. NOSEWORTHY, J.T. O'BRIEN, J.J. GILBERT and S.J. KARLIK (London, Ontario; Oxford, England)

In order to define the histological and biochemical nature of the MRI-detected lesions in multiple sclerosis (MS) we have previously described the changes in NMR relaxation parameters T1 and T2 during the acute phase of the myelin basic protein (MBP) and CNS induced acute EAE animal models of MS in the guinea pig. This current study characterizes the NMR properties of CNS prior to the onset of clinical signs of EAE at a time (Day 7-9) when blood-brain barrier (BBB) disruption is anticipated and examines the effects of the paramagnetic contrast agents Gadolinium-DTPA (Gd-DTPA) and Gd-deferoxamine (Gd-Df) on the MBP-induced acute EAE model.

We found: 1. T1 and T2 are prolonged in cord and brain prior to the onset of clinical and pathological changes suggesting increased tissue water content due to BBB disruption. 2. The largest change was in thoracolumbar spinal cord T2 prolongation (21.9%). 3. Gd-DTPA produced a moderate (5-11%) or marked (9-19%) decrease in control and MBP-injected animals respectively such that NMR parameters were similar for control and MBP-injected animals following contrast administration. 4. Gd-Df was exceedingly toxic to all animals. 5. The change in T2 in cord and cerebellum was of a magnitude ($\geq$ 10%) that should permit detection by NMR techniques.

NMR detects early changes in tissue water content in EAE and these early changes are maximal in the caudal spinal cord and cerebellum. In that control and MBP-injected CNS tissue may assume nearly identical NMR relaxation times after Gd-DTPA administration, it may be that identification of CNS lesions may need to be made on the relative changes in T1 and T2 values with contrast and on the MRI appearance of the tissue rather than the absolute T1 and T2 values after contrast administration.

7.

Partial Characterization of Neurotrophic Factors from Peripheral Nerve Tumours

R.J. RIOPELLE, S. DOSTALER and P.M. RICHARDSON (Kingston, Ontario; Montreal, Quebec)

Explants of normal rodent peripheral nerve (Riopelle et al., 1981 Neurosci. Lett. 25: 311; Richardson and Ebendal, 1982 Br. Res. 246: 57) and human neurofibromas (Riopelle and Riccardi, 1984 Neurology 34, Supp. 291) release at least two neurotrophic factors, one of which is immunologically cross-reactive with mouse nerve growth factor (NGF).

A neurite-promoting factor for embryonic sensory and ciliary neurons with an apparent MW of 7000 Da has been detected in extracts of neurofibrosarcomas from patients with Von Recklinghausen disease. The factor, designated NFNTF, promotes neurite outgrowth from ciliary neurons on a laminin substrate and from sensory neurons on poly-D-lysine in the presence of antibody to NGF. NFNTF was purified by ion exchange and gel filtration chromotography, followed by reverse phase high performance liquid chromotography (RPLC) on uBondapak C18 in a mobile phase of acetonitrile in trifluoroacetic acid. On RPLC, at least one biologically active fraction with retention time differing from that of NFNTF was detected. The neurite-promoting activity of this latter fraction was completely inhibited by antibody to NGF.

Sheath cell tumour tissue may prove to be a rich source of neurotrophic material found in limiting concentrations in normal peripheral nerve. These findings will facilitate studies to further explore the molecular basis of promotion of central and peripheral axon regeneration by peripheral nerve. Characterization of neurotrophic factors from neurofibroma tumours could have potential for development of diagnostic probes for neurofibromatosis. (Supported by MRC Canada, Clare Nelson Bequest of Kingston General Hospital and PSI Foundation of Ontario).

8.

Control of Neoplastic Development in the Brain by Angiosuppression with Copper Depletion

S. BREM, D. ZAGZAG, H. ALPERN-ELRAN and Y. TANAKA (Montreal, Quebec)

In previous experiments, we demonstrated that angiogenesis induced by a spectrum of human brain tumours could be prevented or inhibited by depletion of copper. Using the experimental model of Zagzag et al., we tested copper depletion (CD) upon the development of the intracerebral tumours and neovascularization in the rabbit brain. Control animals with normal levels of serum copper developed large spheroidal tumours with cortical and tumour neovascularization resembling that of malignant human brain tumours. By contrast, nine rabbits fed a low-copper diet with penicillamine developed tumours that were pale and relatively avascular.

The ratio of capillaries/HPF between the control and treated rabbits was approximately 7:1. Capillary density in the treated animals was equivalent to normal brain. The avascular tumours were small, 5-10% of the volume of the control tumours $p \leq 0.001$. They grew in a laminar, "en plaque" shape rather than as a spheroid. Two other groups were tested; a pair-fed group with restricted intake to match the low-copper diet, and a fourth group that was started on CD after implantation of the tumour. These rabbits had levels of serum copper, tumour size, and vasculature close to the controls.

Despite the dramatic reduction in volume, survival curves of all groups were similar. The group that started CD immediately after implantation showed delayed neurologic signs and the longest survival. The rabbits died from the effects of peritumoural brain swelling.

The experiments illustrate the close interdependence between vascular and neoplastic growth. It is possible to prevent the growth of intracerebral tumours and tumour neovascularization by depletion of copper. The combination of anti-edema drugs with angio-suppressant therapy could become an important new approach to control the growth of brain tumours.

9.

Photo-Dynamic Therapy: Cavitary Photo-Illumination of Malignant Cerebral Tumours Using a Laser Coupled Inflatable Balloon. A Phase I Trial

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

Photo-dynamic therapy (PDT) consists of the exposure of neoplastic tissue to visible light of an appropriate wavelength in order to activate a photosensitizer, administered prior to the light administration. Hematoporphyrin deriviative (HPD), an acidification product of hematoporphyrin (HP), has been the most studied photosensitizer. Recently, dihematoporphyrin ether (Photofrin II), a more active derivative of HPD, has become available for clinical testing.

We are reporting our experience with intraoperative PCT in 16 patients with malignant supratentorial gliomas. A photo-illuminating device which consisted of an inflatable balloon coupled to an argon dye pump laser was used to deliver light at 630 meters to a tumour cavity created by radical subtotal tumour resection and/or tumour cyst drainage.

The first 9 patients in this series received HPD (Photofrin I) and the next 7 received DHE (Photofrin II). The total light energy delivered ranged from 439 to 3888 Joules and the light dose ranged from 8 to 68 J/cm^2. All patients were kept in low light intensity environment for 7 post-operative days and were advised to avoid direct or indirect sunlight for one post-operative month.

There was one post-operative death; this occurred as the consequence of hematoma accumulation in an extensive tumour resection cavity. In 2 patients neurological function was worse post-operatively and did not recover. In both of these patients a pre-operative hemiparesis was made worse as the consequence of radical subtotal resection of a large recurrent tumour mass. Two patients developed wound infections; one of these required surgical drainage and removal of the infected bone flap and the second, whose infection was superficial, required only antibiotic therapy. Three patients, two of whom were hemiparetic, developed deep vein thrombosis and required anticoagulant therapy.

There were no adverse systemic reactions to the administration of either photosensitizer and no adverse skin photo-sensitivity reactions. Follow up has ranged from 1 to 14 months at the time of writing; 11 of 16 are alive.

Photodynamic therapy of malignant brain tumours using surface or cavitary photo-illumination can be carried out with acceptable risk.

10.

Magnetic Resonance Imaging in Benign Intracranial Hypertension

K. FARRELL, O. FLODMARK, A.Q. McCORMICK, E.H. ROLAND and A. HILL (Vancouver, British Columbia)

The pathophysiological mechanisms of benign intracranial hypertension (BIH) are unclear. Any hypothesis must be consonant with the rapid therapeutic response to shunting of CSF via lumbar-peritoneal shunt. Increased resistance to cerebrospinal fluid (CSF) reabsorption, increased cerebral blood volume and diffuse cerebral edema have been demonstrated in patients with BIH. The absence of ventricular dilatation in the presence of increased resistance to CSF reabsorption has been attributed to either increased cerebral blood volume or to cerebral edema. Magnetic resonance imaging (MRI) is a sensitive technique with which to demonstrate cerebral edema. MR imaging in children with obstructive hydrocephalus shows decreased signal intensity in the periventricular region. We have used this technique to establish whether or not cerebral edema occurs in children with BIH.

Six children, 7 to 13 years of age, presented with headache and bilateral papilledema. The CSF pressure at lumbar puncture was elevated in all patients (194-460 mm of CSF). CT scans of the head were normal. MR images of the brain were obtained with a superconducting magnet of field strength 0.15 tesla. Inversion recovery and spin echo pulse sequences were normal in each case.

The absence of decreased signal intensity in the periventricular region in the MR images suggests that significant periventricular edema was not present. These data are consistent with the hypothesis that increased cerebral blood volume is the most probable mechanism to account for the absence of ventricular dilatation in some children with BIH.

11.

Cerebral Morphometry on MRI

A. KERTESZ, S.E. BLACK, M. POLK and J. HOWELL (London and Toronto, Ontario)

Magnetic Resonance Imaging (MRI) is suitable for studying cerebral morphometry in young adults because it does not use ionizing radiation and it provides superior grey and white matter contrast and brain CSF interface. 104 volunteers, 52 right handers and 52 left handers, average age 29, equally distributed among sexes were recruited for the study. Dichotic listening studies, reaction times to read tachistoscopically presented material and hand performance tasks were done by the volunteers at the time of their MRI scans. These measures of functional lateralization of auditory, visual and motor processing were correlated with measurements of sagittal length, anterior and posterior frontal length, posterior and occipital width and area measurements of the total hemispheres, parietal, frontal, temporal area and the corpus callosum.

Results indicated slightly larger right brain areas but no significant differences between right and left handers. Left cerebral dominance for hand performance was correlated on a regression analysis with right

frontal width and left posterior frontal width. Visual field dominance on the left hemisphere was correlated with left occipital width and right parietal width.

Estimations of a larger opercular demarcation from the parietal cortex on the right side equivalent to a larger planum temporale on the left are positively dichotomized for handedness but not for dichotic listening performance.

Callosal size is not related to handedness but size corrected ratios of callosal area are slightly larger in females. Comparison of splenial area vs. genu of the corpus callosum indicated no sex difference. The splenium was larger in the majority of instances.

12.

Vascular Risk Factors and Leuko-Araiosis

J.F. DIAZ, D. INZITARI, V.C. HACHINSKI, A.J. FOX, K. LAU, A. DONALD, A. STEINGARTand H. MERSKEY for the U.W.O. Dementia Study Group (London, Ontario)

Low density areas of white matter on CT scan, leuko-araiosis (LA), has been associated not only with dementia, but also with hypertension, heart disease and stroke. More recently, LA has also been observed in normal elderly individuals. Most of these observations have come from CT series, and no attempt has been made to assess the relative importance of these conditions as predictors of LA in a group of demented and control subjects.

One hundred forty demented and 110 elderly control subjects underwent an evaluation for LA and a thorough clinical assessment. LA was found in 49 (35.5%) of the demented as compared to 12 (10.9%) of the control subjects. Demented patients with LA had suffered a stroke 4 times as frequently as had those without LA (17.4% and 4.4%, $p < 0.05$). A two-fold increase was found for hypertension (63.3% and 34.1%, $p < 0.01$). In the controls, stroke occurred in 25% of those with LA as compared to only 2% of those without LA ($p < 0.01$), but no difference was found for hypertension. In both demented patients and controls, the average systolic blood pressure was associated with LA ($p < 0.05$). No association was found for diastolic blood pressure, myocardial infarction, angina, diabetes and carotid bruits.

Logistic regression analyses showed that the strong relationship between dementia and LA was mainly due to strokes, which emerged as the most predictors of LA.

These data suggest that there are common factors in the pathophysiology of LA and stroke, but stroke alone does not account for LA.

13.

Dementia-Parkinsonism-Motor Neurone Disease Syndrome: Neurochemical and Neuropathological Correlates

S.J. KISH, J. GILBERT and O. HORNYKIEWICZ (Toronto and London, Ontario; Vienna, Austria)

We measured the neurochemical markers for the major neurotransmitter systems in the autopsied brain of a patient dying with a dementia-Parkinsonism-motor neurone disease (DPMN) syndrome complex. Histological analysis revealed severe neuronal loss in substantia nigra and locus caeruleus, spongiform changes in the frontal cortex, and severe anterior horn cell loss through the spinal cord. A severe nigrostriatal dopamine deficiency provides the basis for the Parkinsonian features observed in our patient. However, whereas in idiopathic Parkinson's disease the striatal dopamine deficiency is more pronounced in the putamen, in our DPMN case all subdivisions of the caudate head nucleus were more affected than the putamen. Activities of the cholinergic marker enzyme cholineacetyltransferase were generally normal throughout the brain. This finding, together with our histological observation of normal cell number in the nucleus basalis, suggests that the dementia in our DPMN patient was unlikely to be the result of a brain cholinergic deficiency as occurs in Alzheimer's disease. More likely explanations for the cognitive impairment include the severe dopamine deficiency in caudate and/or the neuronal dropout in frontal lobe which was accompanied by cortical glutamic acid reduction. (Supported by the Parkinson's Disease Foundation of Canada. S.J.K. is a Career Scientist of the Ontario Ministry of Health.)

14.

The Electroencephalogram (EEG) in Sepsis

G.B. YOUNG, C.F. BOLTON, T.W. AUSTIN and Y. ARCHIBALD (London, Ontario)

In this project, all hospital patients with positive blood culture and fever were studied prospectively. Neurological examinations, EEGs and serum biochemistry were performed within 1 day of the positive blood culture. Patients were classified as non-encephalopathic (NE), mildly encephalopathic (ME) and severely encephalopathic (SE) using standard clinical criteria. Cases with contaminant cultures, active nervous disease of other causes, pre-existing organ failure or drug intoxication were excluded.

The NE group contained 7 males and 3 females aged 51-78 years. EEGs were normal in 5; mild excess theta in 5. The ME group had 4 males and 4 females aged 58-78. EEGs showed intermittent delta in 4 and excess theta in 4 as principal abnormalities. The SE group had 9 males and 3 females aged 43 to 74. EEGs showed triphastic waves in 4, suppression in 2, persistent delta in 1, intermittent delta in 3 and excess theta in 2.

There was no significant difference between Gram positive vs. Gram negative infections among the 3 groups. The SE group had more numerous and marked metabolic abnormalities than the other group, but none were consistent.

We conclude the EEG reflects the severity of the septic encephalopathy, showing a diffuse abnormality likely due to metabolic disturbance.

15.

The Medicolegal Whiplash Report

W.J. VANAST (Edmonton, Alberta)

The medico-legal letter has little relevance if only the normal office exam, CT scan and EEG are reported. Based on experience with 200 whiplash cases, our report includes:

1. The make, type and speed of the patient's car. The use of seatbelts and headrest. Angle of the seat and whether it broke. The direction in which the patient was looking. The direction, speed and type of the offending vehicle.
2. Objects struck. Initial stunned or twilight state. Visible injuries. Amnesia. Behaviour in the hours after impact.
3. Pain in the neck, shoulders, interscapular area and lumbar region. Vertigo and tinnitus (often starts weeks later — ENG should always be done). Visual blurring; (loss of taste and smell are extremely rare). Radicular nerve symptoms; Thoracic outlet complaints (occurs in 50%).
4. Long term change in mood, sexual drive, sleep pattern, memory, concentration, drive and ability to absorb new material. Problems

with irritability, explosive anger or other personality changes. Alteration in long-standing conjugal, parental, leisure or business activity. Changes in memory (often of the scratch-pad type).

5. Headache location, severity and associated symptoms such as nausea, vomiting, light and noise phobia and increase by exertion; consequent changes in job or leisure activities.

For all focal symptoms, the number of days per month, length of time per day, and intensity is noted. A hundred point analogue scale is used to compare original to current intensity. Similar data is provided for any previous whiplash injuries (30% of our series).

16.

MELAS Syndrome: A Cause of Stroke in Young Adults

E.H. ROLAND, A. PENN, S.A. HASHIMOTO and T. PERRY (Vancouver, British Columbia)

The "mitochondrial encephalopathies" constitute a heterogeneous group of disorders in which structural and/or functional abnormalities of mitochondria have been demonstrated. MELAS syndrome is a distinct clinical entity which belongs in this category. It is characterized by mitochondrial myopathy, spongiform encephalopathies, lactic acidosis and recurrent stroke-like episodes. We report the metabolic, radiological, histochemical-ultrastructural findings and a 10-year clinical follow-up of 2 sisters with MELAS syndrome.

The presenting features were cortical visual loss, generalized seizures and intellectual deterioration. Muscle weakness was never prominent but exercise caused profound fatigue, systemic acidosis, encephalopathy and seizures. The older sister developed right parietal cerebral infarction at 38 years of age.

CT scan of the head and magnetic resonance imaging in this patient showed cerebral infarction in the right parietal lobe. Positron emission tomography showed diminished glucose metabolism in the right parietal left cerebellar hemispheres. Muscle biopsy demonstrated ragged red fibres. There were no abnormalities of mitochondrial oxidative metabolism. Nuclear magnetic resonance spectroscopic studies of muscle are being undertaken and will be reported. Diminished levels of arginine, orthinine and citrulline were demonstrated in plasma and CSF. Urine amino acid studies were normal. These findings presumably represent impaired mitochondrial membrane function. Preliminary observations suggest that dietary supplementation with citrulline is helpful in seizure control.

This study focuses attention on a cause of stroke in young adults which is seldom appreciated.

17.

Clinical Study of Prostacyclin Infusion after Acute Ischemic Stroke

R. POKRUPA, A. HAKIM, J. VILLANUEVA, G. FRANCIS and L. WOLFE (Montreal, Quebec)

The effect of administration of prostacyclin (PGI_2) on neurological recovery after ischemic cerebral vascular accidents was investigated in a clinical trial. The PGI_2 infusions began within 50 hours of the CVA and were carried out daily over 8 hours for five days. The drug was tapered at beginning and end of the infusion and the peak infusion rate was 10 ng/kg/min. 5 patients were initially studied in an open label group and then 12 placebo and 11 PGI_2 treated patients in the randomized double-blind study group. The majority of the CVA's were middle cerebral artery infarcts. Neurological examinations were performed and scored on admission to hospital, near the end of the infusion period and at intervals up to one month after admission. There was no significant difference in the changes in neurological scores between the infusion and placebo groups either immediately after the infusion period or one month after admission. The initial neurological score was lower and the mean age of the patients was older in the placebo group on the basis of randomization. Final neurological scores were higher and mortality rate was lower in the PGI_2 treated groups. The incidence and nature of complications were similar in the groups with the exception of the occurrence in the PGI_2 group of dose related flushing, headache and nausea and the occurrence in two patients of transient worsening of neurological deficits during PGI_2 infusions. We conclude that PGI_2 alone does not improve clinical deficits after CVA. This conclusion emphasizes the therapeutic limitations of medications primarily intended to reperfuse ischemically injured tissue.

Supported in part by the Upjohn Company of Canada and the Canadian Heart Foundation.

18.

Evaluation of Non-invasive CBF for the Diagnosis of Cerebral Arterial Spasm

J.K. FARRAR and G.G. FERGUSON (London, Ontario)

We have obtained 111 inhalation CBF measurements (Xe-133) in 67 patients with recent subarachnoid hemorrhage. The patients were divided into 3 groups according to their neurological status: Group I — alert; Group II — drowsy but without deficit; and Group III — major deficit or drowsy with minor deficit. The CBF test was considered 'positive' (spasm present) if the hemispheric mean flow value (ISI) was below 40 in Group I, 35 in Group II and 28 in Group III. The test results were compared against angiographic evidence of arterial spasm (>30% narrowing).

The sensitivity of the CBF test was 78%, 57% and 41% (Groups I-III: 60% overall) and the specificity ranged from 86 to 97%. The positive predictive value was approximately 80% and the positive likelihood ratios were 13.0, 4.1 and 13.7 (Groups I-III: 8.6 overall). Assuming a pretest probability of 33% (average prevalence), a positive result would raise the post-test probability to 86% for a Group I patient and to 81% overall.

These results indicate that non-invasive CBF measurements are clinically useful in the diagnosis of cerebral vasospasm.

Supported by: Heart & Stroke Foundation of Ontario.

19.

Subarachnoid Hemorrhage with Normal Initial Angiogram

A. SHUAIB and M.A. LEE (Calgary, Alberta)

Management of subarachnal hemorrhage (SAH) in patients with a normal cerebral angiogram has been a subject of great debate for decades.

Most standard textbooks and some studies suggest a 5-10% incidence of visualizing an aneurysm if such patients have a second angiographic study. In recent years, there has been a trend in the literature to abandon the use of a second study as the prognosis is said to be excellent if the first study is normal.

We reviewed our hospital records of patients with SAH between 1980 and 1984. In this four year period there were 216 patients with a diagnosis of SAH. Diagnosis was made by clinical history and either a positive lumbar puncture or a positive Computerized Axillary Tomography scan. In 181 of these patients, angiographic studies were performed. Of these patients, 25 had a normal initial study. Twenty of these

patients had a second angiogram and on the second study, 15 of 20 were normal. In the other 5 patients (20% of the patients with an initial normal angiogram), an aneurysm was observed on the second study. Aneurysms were evident on the first angiogram however when they were reviewed after the second study in 4 of the 5 patients. Four patients had the aneurysm clipped surgically.

The first angiogram in most of the patients was done within 24 to 48 hours of the ictal event and the second study was done between 7-14 days in all the 20 patients. The initial angiograms were of a good quality in most of the patients.

The location of the initially nonvisualized aneurysms was as follows: Anterior communicating artery (2); Posterior communicating artery (1); Middle cerebral artery (1). In two of the patients, the aneurysms were better defined on the second study despite the presence of arterial spasm.

In order to assess the observer error the initial angiograms of the patients with aneurysms on the second study were shown to a second neuroradiologist unaware of the second positive study. Of the four patients with the positive second study, three were picked up on the initial angiogram by the second observer.

20.

Failure to Detect Free Radical Mitochondrial Lipid Injury After Complete Cerebral Ischemia

R.F. DEL MAESTRO, C. VIERECK and M. CINO (London, Ontario)

The role played by free radical reactions in mitochondrial injury during complete cerebral ischemia has been studied. Cerebral mitochondrial membrane lipids have been quantitatively assessed from a rat decapitation model and a human cortical excision model.

Mitochondrial lipid alterations in these models were characterized by a decrease in cardiolipin (20%) and by increases in selected free fatty acids. Normal rat mitochondria lipid structure was shown to be susceptible to free radical generating system but the changes seen were distinctly different from those seen after complete ischemia. A number of methods were used to detect free radical lipid peroxidation in mitochondria isolated from the rat complete ischemia model (thiobarbituric acid, diene conjugation and lipid soluble fluorescence). No evidence of lipid peroxidation was found using any of these assays.

These results suggest that although cerebral mitochondrial lipids are susceptible to free radical reactions they do not appear to be involved in the mitochondrial lipid alterations seen during complete cerebral ischemia.

21.

Topographic EEG Correlates of Cerebral Blood Flow and Oxygen Metabolism in Brain Ischaemia

S. HIROI, K. NAGATA, K. TAGAWA and F. SHISHIDO (Akita, Japan)

Topographic EEG data were correlated with cerebral blood flow (CBF) and oxygen metabolism in 43 patients with unilateral cerebral infarction. Power ratio index (PRI) which is a ratio of combined delta and theta intensity to the combined alpha and beta intensity was used as a single parameter reflecting slowing of the background EEG activity. The positron emission tomography provided CBF and cerebral metabolic rate of oxygen ($CMRO_2$). On the PET images, local CBF and $CMRO_2$ values were calculated at the cortical sites corresponding to the location of the EEG electrodes. A significant negative correlation was seen between the mean hemispheric PRI (mPRI) and mean hemispheric CBF and between mPRI and mean hemispheric $CMRO_2$. The correlation was tighter on the affected hemisphere than on the unaffected hemisphere. The local PRI was compared with the local CBF and $CMRO_2$. The best correlation was seen at the parietal and temporal regions whereas the correlation was poor at the frontopolar regions which included artifacts from the eye movements and blinks. The correlation was not very close at the occipital regions because there was less slow wave activity although the depression of alpha activity was marked. As a conclusion, the slowing of the EEG activity correlated well with the reduction of the local CBF and $CMRO_2$ at the parietal and temporal regions of the ischaemic brain.

22.

Rabies in Mexican Children: Clinical Analysis of 65 Post-Mortem Cases

H. ALCALA (Calgary, Alberta)

Urban rabies continues to be a major public health problem in Mexico. During a 31 year period (1950-1981) 106 children were admitted to Hospital Infantil de Mexico with the diagnosis of rabies encephalitis. All died and post-mortem examination was performed in 65. There was a male predominance with 43 boys and 22 girls. Forty-nine children had a history of dog bites on various parts of the body. Sixteen had some form of exposure to dogs without bites. Only one child had been exposed to skunks and bats without a history of bites. Incubation period ranged from 2 weeks to 12 months in 52 children; in 10 it could not be determined. Death occurred from 2 to 20 days in 63 children; only 2 survived longer. Rabies vaccination was administered to 12 of these children but did not alter the outcome perhaps because of delayed or incomplete immunization. The most common systemic manifestation was fever (92%). Swelling and pain in the area of the bite was seen in 9 children. Signs of increased intracranial pressure were noted in half of the patients. Seizures occurred in 20% of them. Lumbar puncture was performed in all children. CSF was found clear in 60 children and xanthochromic in 5. Glucose levels ranged from 0.9% to 6.2 g/L; protein from 0.11 to 1.4 g/L; and cells from 1 to 285. Meningeal signs were present in 26% of children. The most common signs of cranial nerve impairment were dysphagia (63%); dysarthria (41%) and poor pupillary response (41%). The most common autonomic dysfunction was sialorrhea (61%). Motor signs such as hypertonia was present in 21%; Babinski was only seen in 3% of the children. Paralysis was a rare finding (only in 2 children). By contrast with European or North American series in which bats, wolves and foxes are the most common vector, canine urban rabies in Mexico usually is not a paralytic form. The most common neurologic manifestations were cerebellar, (60%) and complex psychic and perceptual distortions such as phobias (90%): aerophobia, hydrophobia, sonophobia, and photophobia. These phenomena will be shown on film.

23.

Benign Osteoblastoma of the Spine in Childhood

S.T. MYLES and M.E. MacRAE (Calgary, Alberta)

Osteoblastoma of the spine is a rare but important cause of back pain in children. Nine children with this tumour have been treated at the Alberta Children's and Foothills Hospitals in Calgary, Alberta between 1974 and 1985. There were 6 males and 3 females, and the age at diagnosis ranged from 6 to 16 years, with the median being 13 years. In 8 patients the tumour involved the posterior vertebral elements. The lone cervical lesion was in the vertebral body. Three patients had tumour in the extradural space. The commonest symptom was pain in the back, and scoliosis for 3 to 18 months prior to diagnosis, with the

average duration being 9.3 months. Bone scans were positive in all patients, and CT scans were abnormal in the 7 patients who had this imaging performed.

Eight children were treated with laminectomy and removal of the abnormal pedicle and facet. Two patients required 2 operations each because of incomplete tumour excision at the first operation. Subsequent surgery gave complete relief of symptoms and radiographic studies showed no further tumour. In another 3 patients, tumour removal was incomplete and post-operative radiation therapy was used in 1 patient. Bone grafts were placed in 4 patients. The diagnosis of benign osteoblastoma was confirmed histologically in 8 patients.

The outcome was good in all cases, with excellent pain relief. Follow-up has varied from 7 to 139 months (median 48 months) and there have been no recurrences.

Based on this experience, we recommend complete excision of spinal osteoblastomas whenever possible. However, a satisfactory outcome may occur following incomplete excision and bone grafting.

24.

Infant Botulism: A Rare Entity in Canada?

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

Infant botulism is an age-related neuromuscular disease which differs from botulism in older individuals. The clinical syndrome results from intestinal absorption of toxin produced by ingested *Clostridium botulinum*. We report the rare occurrence of infant botulism in a 4-week-old infant.

The patient was healthy until one month of age, when she became constipated, lethargic and progressively weak over a period of 4 days. There was no exposure to drugs, infectious contacts, home remedies or honey. Initially the infant was considered to be septic and was treated with ampicillin and gentamicin intravenously. Twenty minutes following the initial dose of antibiotics, the patient became apneic and required ventilation. On examination, the infant was drowsy, had sluggish pupillary responses to light, impaired extraocular muscle function, facial diplegia and a weak cry. There was marked hypotonia with absent tendon reflexes and urinary retention. Metabolic investigations, cultures of throat, urine, blood and CSF, electroencephalogram, CT scan of the head, and brainstem auditory evoked responses were normal. The results of edrophonium chloride and neostigmine injection were equivocal. *Clostridium botulinum* type A organisms and toxin were detected in 4 stool specimens. A serum sample contained botulinal toxin, a rare occurrence in infant botulism. Electromyography and nerve conduction studies were consistent with infant botulism. The child recovered slowly over a period of 2 months.

This is only the third case of infant botulism reported in Canada. In contrast, over 500 cases have been reported in the United States since 1976. This disparity raises the possibility that transient hypotonia, a not unusual occurrence in infants who become acutely ill, may represent mild infant botulism. The equivocal results of edrophonium chloride injection initially made exclusion of persistent neonatal myasthenia gravis difficult in this case. Although, the diagnosis of infant botulism may be suspected on the basis of history, physical findings and electromyography it requires confirmation by culture of *Clostridium botulinum* and possibly the demonstration of toxin in stools.

25.

Kinsbourne's Ataxia-Opsoclonus-Myoclonus Syndrome: Clinical and Immunologic Investigations

M. THIBAULT, A.V. PLIOPLYS, G. FORTIN, S. VERRET and J.-P. BOUCHARD (Quebec City, Quebec)

We have studied 5 cases of the ataxia-opsoclonus-myoclonus syndrome first described by Kinsbourne in 1962. The incidence of associated diseases and the evolution of the clinical picture have been delineated. Anticerebellar and anti-CNS serum and CSF antibody investigations have been performed.

The presentation was similar to those reported in the literature, with onset between 12 and 30 months of age, irritability and ataxia in all, opsoclonus in 3 and myoclonus in 4. With a follow-up ranging from 3 to 8 years, 3 still show evidence of mild ataxia and 4 have language problem. None of the 5 have been discovered to have a neuroblastoma. Of the 5, recent viral infections had occurred in 3 (rubeola, upper respiratory infection and gastroenteritis) and one had received a DPT-Sabin immunization.

Serum samples of 4 were screened against SDS-PAGE blots of normal human cerebellum and other areas of the CNS. Two of the 4 were screened both during the acute phase and during convalescence, 2 years later. When screened against cerebellar blots, 2 showed no immunoreactive labelling, one recognized a 210K molecular weight band corresponding to the high molecular weight subunit of neurofilaments, and the fourth recognized a 62K band only during the acute phase. No banding was noted against blots of frontal and occipital cortex and white matter. No banding occurred when CSF was used instead of serum. These results do not support the pathogenetic role of anti-neurofilament antibodies in this syndrome (Ann. Neur. 1985, 18:403) since only one of the 4 had such reactivity. It is intriguing that one child demonstrated a transient anti-62K band during the acute phase.

This work was supported in part by a MRC fellowship to AVP.

26.

Benign Familial Neonatal Seizures: Clinical and Electroencephalographic Characteristics

D.B. SINCLAIR, M. SHEVELL and K. METRAKOS (Montreal, Quebec)

Two families with benign familial neonatal seizures evident over three generations are presented with emphasis on clinical and electroencephalographic features. Benign familial neonatal seizures represents a disorder with the onset of frequent generalized seizures during the first few weeks of life. There is a positive family history with autosomal dominant inheritance reported for this disorder. The neonates are neurologically normal and the outcome is usually benign. In our families, none of the patients had seizures recur after the first ten months of life with long term follow up ranging from 10 months to 56 years. The use of anticonvulsant medication seems to have little effect on the course or eventual outcome. The EEGs, both initially and on follow up, range from normal to epileptiform and did not correlate with risk for further seizures in infancy or subsequent epilepsy. Benign familial neonatal seizures represents a distinct clinical entity whose key features and favourable prognosis should be appreciated by all physicians dealing with neonates. This would result in an earlier diagnosis and conservative treatment.

27.

Perinatal Post-Hemorrhagic Hydrocephalus: Patterns and Associated Lesions

H. ALCALA (Calgary, Alberta)

This study describes the neuropathology and patterns of central nervous system (CNS) damage in 14 premature infants (24-32 weeks

gestational age) who survived subependymal intraventricular hemorrhage (SE-IVH) from 2 weeks to 8 months. Two infants had Grade I-II, and 12 had Grade III-IV SE-IVH. No correlation was found between head circumference (HC) at autopsy and degree of dilatation of lateral ventricles. Four patterns of hydrocephalus were observed: 1. *severe symmetric* supratentorial (ST) and infratentorial (IT) damage; 2. *severe asymmetric* ST damage and IT damage; 3. *moderate symmetric* ST and IT damage; 4. *moderate symmetric* ST damage and severe IT damage. Patterns 1 and 2 correlated with grades III-IV SE-IVH. No such correlation was found in patterns 3 and 4. Hydrocephalus in pattern 1 was severe and affected the 4 ventricles by a combination of ST-IT ex-vacuo mechanisms plus obstruction of the foramina of Luscka and Magendie. Pattern 2 had asymmetric hydrocephalus due to obstruction of the foramina of Monroe and periventricular extension of the IV hemorrhage. Patterns 3 and 4 appeared to be caused more by ex-vacuo than obstructive phenomena. In addition to the hydrocephalus, multiple anoxic/ichemic and hemorrhage lesions were found in the brains of these infants. The cerebral cortex showed neuronal loss or focal necrosis. White matter was affected in all cases by a combination of edema, gliosis, axonal loss, demyelination or periventricular leukomalacia. The basal ganglia and diencephalon showed neuronal loss and iron deposits. The cerebellum exhibited severe atrophy and siderosis. Secondary ponto-olivary degeneration was seen. Siderotic ependymitis of variable degree was found in all cases. Iron deposits throughout the CNS were most severe in pattern 1. Choroid plexi showed atrophy, siderosis and fibrosis, suggesting impaired cerebrospinal fluid secretion. Minute iron deposits also were present in areas distant from sites of bleeding, indicating mobilization of iron particles through the CNS. Severe siderosis and demyelination of cranial nerves was found. The above mentioned lesions might explain the neurologic deficits observed in children surviving grade III-IV SE-IVH.

28.

Magnetic Resonance Imaging (MRI) in Multiple Sclerosis (MS): Quantitative Changes in the Size of Lesions over 6 Months in the Placebo Limb of a Therapeutic Trial

D.W. PATY, M. PALMER, M. BERGSTROM, E. GROCHOWSKI, C. APTED, D. LI and S. HASHIMOTO (Vancouver, British Columbia; Stockholm, Sweden)

MRI may give us an objective way of following the MS process. If progression of MS is marked by new lesions or the enlargement of old ones, MRI should allow quantitation of such changes. We have applied this principle to a double blind placebo controlled clinical trial of alpha interferon (IFN, Welferon) in chronic progressive (CP) MS (N = 55). An interactive computer program and careful repositioning techniques were used to measure the number, size and distribution of lesions. Comparison between clinical severity (mean EDSS 5.82) and MRI severity (mean area 2270 mm^2) gave a correlation coefficient of R = 0.088 at entry into the trial. In the placebo group the mean MRI value was 2335 mm^2 at entry and 2525 at 6 months. Variation was between −70% and +221%. Final quantitative MRI in this study will be 2 years from entry. We expect the magnitude of change at that time to be greater but the wide fluctuations seen may provide problems in statistical analysis. Studies of T_1 and T_2 values in addition to simple area quantitation may help to resolve these problems.

29.

A Comparison of Familial and Sporadic MS

B. WEINSHENKER, H. ARMSTRONG, D. BULMAN and G.C. EBERS (London, Ontario)

Linkage studies in properly ascertained multiple sclerosis (MS) families have not shown the tight linkage to HLA expected from the population association with the HLA-B7, DR2 haplotype. Since the population associations have been demonstrated largely in patients having sporadic MS, one possible explanation for the linkage data is that familial cases differ with respect to genetic susceptibility factors from sporadic ones. We have reviewed 1028 patients with MS followed at the Clinic at University Hospital in London, Ontario, and have verified that 122 patients have an affected family member (of which 61 were first degree relatives). These figures do not include additional patients in whom corroborating evidence for familial involvement was not obtainable. The 2 groups were compared for clinical features, including age of onset, sites of involvement, type of disease (relapsing remitting vs. chronic progressive), frequency of oligoclonal banding and abnormalities on evoked potentials, and for prognosis assessed by the number of years taken to reach successive levels of disability measured by the Kurtzke Disability Scale. Clinical features and typing results do not appear to differ between familial and non-familial cases. There does not appear to be a familial/sporadic heterogeneity in MS.

30.

Risk of Multiple Sclerosis Among Relatives of Patients

A.D. SADOVNICK, P.A. BAIRD and R.H. WARD (Vancouver, British Columbia)

Two important features of multiple sclerosis (MS) are familial clustering and a variable age of onset. There is increasing evidence for a genetically determined susceptibility to MS. Therefore, MS patients and their relatives are increasingly requesting information on familial risks for the disease.

The MS clinic in B.C. is *unique* as standardized genetic histories are taken for all patients. These are updated annually. Patients do not attend the clinic specifically to participate in genetic studies, a situation which could lead to over-representation of familial cases.

Family data for 836 unrelated MS patients (index cases) and 19,736 of their relatives were analysed. Age-specific risks for developing MS were calculated for first-, second- and third-degree relatives of MS patients. These risks will be presented according to the sex of the index case and the exact relationship (eg. child, sibling, first cousin) to the patient. These data are directly applicable for counselling MS families. In general, first- and second-degree relatives of index cases have risks for MS which are respectively 30x and 12x greater than that for the general population.

31.

Acute and Chronic Pain Syndromes in Multiple Sclerosis (MS)

D.E. MOULIN, K.M. FOLEY and G.C. EBERS (London, Ontario; New York, New York)

To determine the prevalence and nature of pain in MS, we evaluated by questionnaire and chart review 159 patients residing in Middlesex County and followed in the MS Clinic at University Hospital, London, Ontario. 88 patients (55%) had either an acute or chronic pain syndrome at some time during their disease. 15 patients (9%) with acute pain syndromes had episodes of paroxysmal tic-like pain diagnosed in 7 as trigeminal neuralgia. Chronic pain syndromes, present for a mean duration of 4.9 years, occurred in 76 patients (48%) and included dysesthetic extremity pain (29%), low back pain (14%), painful leg spasms with spasticity (13%), and abdominal pain (2%). MS patients

with pain were similar to the pain free group in mean age of onset (34 vs. 32 years), average duration of disease (13 vs. 12 years), spinal cord involvement (97% for each group) and mean rating on Kurtkze Disability Scale (4.2 vs. 3.5). They differed in sex ratio with a higher female to male ratio in the pain group (3:1 vs. 1.5:1). Chronic pain is a common feature of well-established MS and is usually associated with a myelopathy. A wide variety of pharmacologic and non-pharmacologic approaches are employed with varying success to manage the pain but therapy must be individualized for each specific pain syndrome.

32.

Significance of the Single Band in CSF Protein Electrophoresis

B. BASS, H. ARMSTRONG, G.C. EBERS, J. NOSEWORTHY, B. WEINSHENKER and G.P.A. RICE (London, Ontario)

The usefulness of agarose electrophoresis in the diagnosis of multiple sclerosis (MS) has been clearly defined. Oligoclonal bands are found in 93% of clinically definite and 31% of possible cases, and approximately 8% of those with other neurological diseases.

We have examined the diagnostic significance of the finding of one band in the gammaglobulin region. In the period from January 1983 to December 1985, 855 serial electrophoreses were performed. A blinded observer identified one band in the gamma region in 69 cases (8.1%). In 24 patients the clinical features were thought to be suggestive of possible MS. In 2 of these, the single band was shown to resolve into multiple bands by isoelectric focusing. The majority of patients (45) with a single oligoclonal band had another neurological diagnosis or were normal. Many of the other neurological disorders in which a single band was found, were not disorders in which an increased synthesis of immunoglobulin would have been expected.

Immunofixation techniques have shown that the "single band" is sometimes not IgG. The MS suspects in whom a single band has been demonstrated are being followed prospectively to study the evolution in their clinical syndrome and in the electrophoretic mobility of their CSF IgG band.

The majority of patients with a single band in their spinal fluid immunoglobulin do not have a demyelinating disorder.

33.

Chronic Progressive Central and Peripheral Demyelinating Disease

M. RUBIN, G. KARPATI and S. CARPENTER (Montreal, Quebec)

Symptomatic chronic demyelinating-hypertrophic neuropathy (CDHN) is exceedingly rare in patients with multiple sclerosis (MS) although peripheral nerve and spinal root abnormalities have been shown electrographically and pathologically. We report 2 patients with severe CDHN and central demyelinating disease. Patient 1 presented at age 19 with progressive peripheral neuropathy over 1 year. Nerve biopsy showed segmental demyelination and extensive onion bulb formation. By age 30 he showed areflexic, flaccid, atrophic quadriparesis, glove-stocking sensory loss, extreme optic atrophy, bilateral internuclear ophthalmoplegia and cerebellar dysarthria and dysmetria. CSF protein was 3600 mg%. Magnetic resonance imaging showed multiple periventricular lesions. Patient 2 developed incoordination and progressive muscle wasting during the third decade. Examination at age 30 revealed muscle atrophy, hyperreflexia, Babinski signs, cerebellar dysmetria and gait ataxia. Motor nerve conduction velocities were markedly slowed; nerve biopsy showed segmental demyelination and onion bulbs. Since investigation of our patients excluded known metabolic causes of combined central and peripheral myelinopathy, their disease may be explained by: A. Rare occurrence of both central and peripheral demyelination in MS; B. Chance co-existence of MS and unrelated CDHN; C. A new type of central-peripheral myelinopathy.

34.

Intracerebral Growth of Tumours and Vascular Proliferation: An Experimental Model Using the Rabbit Brain

D. ZAGZAG, H. ALPERN-ELRAN, F. ROBERT and S. BREM (Montreal, Quebec)

The development of a blood supply, angiogenesis, is a crucial step for the continued growth of tumours. Current models for *in vivo* experiments include the rabbit cornea and the chick CAM. Because of the special properties of cerebral capillaries, e.g. the blood-brain barrier, the prominent vascularization of CNS tumours, we studied tumour angiogenesis in the rabbit brain. The V-2 carcinoma grows easily in the rabbit; the angiogenic capacity in the cornea (Gimbrone et al, *JNCI*, 1974) and its suitability for cerebral angiography (Carson et al, *Neurosurgery*, 1982) have been demonstrated.

We prepared a cell suspension, containing 1×10^6 cells, injected through a burr hole 5 mm into the right fronto-parietal lobe of 36 rabbits. All (100% take rate) developed neurological signs and then were sacrificed on day 16-30 after implantation.

The cortical surface characteristically revealed multiple, hypertrophied, tortuous new vessels with feeding arteries directed towards the tumour with hemorrhages and large draining veins resembling the vascular patterns of malignant human brain tumours. The new vessels on the surface were obvious. Intratumoural vessels could be delineated by carotid angiography or perfusion with colloidal carbon. Post-mortem coronal sections revealed discrete, nodular, vascularized tumours with hemorrhages, central necrosis, peritumoural edema, and midline shift. Injections into CSF were avoided as this led to "seeding" with diffuse multiple implants, and penetration of the basal ganglia and spinal cord through perivascular channels.

The microvasculature showed a marked, uniform, increase in the capillary density throughout the viable tumour. Hyperplastic endothelial cells with primitive cytologic features, as seen in certain malignant human tumours, were only rarely encountered.

This reproducible model of three-dimensional tumour growth and neovascularization will be valuable to study the interrelation of a brain tumour and its vasculature, and to develop angiosuppressant therapy.

35.

The Influence of Nonsteroidal Anti-inflammatory Drugs on Rat Peritumoural Cerebral Edema

H. REICHMAN, C.L. FARRELL and R.F. DEL MAESTRO (London, Ontario)

Peritumoural cerebral edema is experimentally and clinically decreased by the use of corticosteroids. A number of systemic inflammatory conditions are treated with nonsteroidal anti-inflammatory drugs (NSAIDs) but the influence of these compounds on peritumoural cerebral edema has not been evaluated.

The corticosteroids, methylprednisolone and dexamethasone, and two NSAIDs, indomethacin and ibuprofen, have been compared for their ability to decrease protein extravasation in a rat C6 astrocytoma spheroid implantation model. Serum albumin extravasation was quanti-

tated using Evans Blue as a marker. The concentration of Evans Blue was measured in tumour, peritumoural and contralateral brain tissue one hour after intravenous injection.

The extravasation of the Evans Blue albumin complex was decreased in all treatment groups when compared to controls. The differences between the control group and the dexamethasone, methylprednisolone and indomethacin groups were highly significant ($P < .005$). Evans Blue extravasation was also decreased in peritumoural and contralateral brain specimens.

The results suggested that NSAIDs compare favourably with steroids in reducing tumour associated protein extravasation in a rat C6 astrocytoma tumour model. Nonsteroidal anti-inflammatory drug may be beneficial in clinical instances either used alone or in conjunction with steroid therapy.

36.

Rat Intracranial Tumour pH Modification in Vivo by Hyperglycemia

E. DOLAN, G. MIES, S. KRAJENSKI, W. WECHSLER and K.A. HOSSMAN (Toronto, Ontario; Cologne, West Germany)

Glucose feeding can substantially affect both responsiveness to chemotherapy and hyperthermia treatment in vitro by lowering tumour pH. We report preliminary results of the effects of hyperglycemia on brain tumour pH in vivo.

Intracranial F98 (gliosarcoma) tumours were stereotactically induced by cell suspension injection into the right caudate nucleus of rats. When symptomatic, the animals were anaesthetized and randomly assigned into the control or treatment group. Controls were monitored while the treatment group received a bolus of 0.5 ml of 20% glucose over 45 seconds, followed by a continuous infusion to maintain plasma glucose over 30 mM. Arterial blood gases were frequently monitored for both groups and 3 hours after the start of the infusion (or the monitoring), the brains were frozen in situ. After removal, 20μ frozen sections were placed on umbelliferone paper and illuminated at 340 nm and 370 nm, and the resultant fluorescence recorded. Regional brain pH could then be obtained as described by Csiba et al (Brain Res. 289: 334-337, 1983).

The 5 controls developed 3 intracerebral and 3 subarachnoid tumours, while the 9 hyperglycemic animals developed 8 intracerebral and 4 subarachnoid tumours. Intracerebral tumours had alkaline pH's and no significant difference existed between controls ($pH = 7.315 \pm 0.074$ SEM: $N = 3$) and hyperglycemics ($pH = 7.281 \pm 0.056$ SEM: $N = 8$). In the subarachnoid tumour in controls 2.4%, 6.1%, and 4.1% of the tumour had pH of 6.0 or less, while in the hyperglycemic animals 19.5%, 27.2%, 38.6%, and 74.2% ($p < 0.05$) of the tumour had $pH < 6.0$.

Our study has shown that subarachnoid tumour pH can be substantially lowered in a significant portion of the tumour. The factors influencing this effect are presently under investigation, and it remains to be determined if agents other than glucose can more effectively lower tumour pH, particularly in intracerebral tumours.

37.

Metabolic and Hemodynamic Studies of Gliomas Using Positron Emission Tomography (PET)

J.L. TYLER, M. DIKSIC, J-G. VILLEMURE, A.C. EVANS, Y.L. YAMAMOTO and W. FEINDEL (Montreal, Quebec)

PET was used to evaluate 15 patients suspected of having high grade cerebral gliomas. All patients were studied before any intervention was undertaken. Measurements of cerebral glucose and oxygen metabolism, oxygen extraction, and blood flow and volume were done in all patients. In addition, pH values were obtained in 6 cases. These patients were later proven by biopsy to have gliomas; 3 were Grade II, one was Grade III, and 12 were Grade IV.

Compared to homologous regions in the contralateral hemisphere, tumour tissue demonstrated decreased oxygen extraction and oxygen metabolism, and increased blood volume. Compared to Grade II tumours, Grade IV tumours demonstrated higher relative oxygen extraction and utilization, and higher blood volumes. Tumour blood flow was variable, but tended to be higher in the higher grade tumours. Rates of glucose utilization in tumour, using individually calculated rate constants, were variable, and did not correlate with tumour size or tumour grade. These findings differ from results obtained from studies of gliomas after radiation and/or chemotherapy. Parietal tumours ($N = 6$) tended to have higher relative glucose utilization and blood flow, and lower relative oxygen extraction, when compared to frontal tumours ($N = 4$). Tumour pH differed significantly from the pH in contralateral brain ($p < .005$); despite uncoupling of oxygen and glucose metabolism consistent with anaerobic glycolysis, alkalotic pH values were consistently seen. Primary cerebral gliomas and surrounding cerebral tissue studied before intervention are different metabolically and hemodynamically from similar tissues after exposure to radiation or chemotherapy.

This research is supported by NIH and MRC grants.

38.

Radiologic Manifestations of Spinal Metastasis

B.W. KRUSHELNYCKY and R.G. PERRIN (Toronto, Ontario)

Symptomatic spinal metastasis represent an important complication of systemic cancer. Radiographic investigation plays an important role in assessing the tumour burden and in characterizing the symptomatic spinal metastasis to help determine the most appropriate treatment strategy.

This study catalogues the radiographic findings in a consecutive series of 101 neurosurgical patients with symptomatic spinal metastasis. The most common plain film finding was pedicle erosion ("winking owl sign") seen in 76 (76%) patients. More advanced vertebral destruction displayed as wedge compression fracture was identified in 55% and frank pathological fracture dislocation was identified in 7% of patients. Paraspinal soft tissue shadow was noted in 23%.

Radiographic abnormality in symptomatic spinal metastasis was most frequently localized to the thoracic spine — with particular predilection to the levels about T4 and T11. Pedicle erosion occurred most commonly at T3-5 (21%), T11-L1 (21%), and L3-5 (20%). Wedge compression fracture was most frequently seen about T7-8 (22%) and L1-2 (18%). Pathological fracture dislocation occurred most frequently at the cervical segments. Paraspinal soft tissue shadows were most often seen at segments about T5 and T11.

Complete myelographic block was found in 75% of patients with partial block recorded in 15%. Multiple blocks were documented in 12% of patients. Lumbar myelography, followed by cisternal myelography, was of particular benefit to identify multiple levels of spinal canal encroachment and the extent of involvement.

Bone scan appears to be of no greater benefit than skeletal survey in the evaluation of skeletal disease preoperatively.

Thorough radiographic evaluation preoperatively was essential not only in determining a patient's suitability for surgery, but also in determining the most appropriate approach (anterior vs. posterior) in the neurosurgical treatment of symptomatic spinal metastasis.

39.

Prognostic Factors in Patients with Symptomatic Spinal Metastasis

R.G. PERRIN (Toronto, Ontario)

Symptomatic spinal metastasis is an ominous complication of systemic cancer. Treatment is palliative. The management of symptomatic

spinal metastasis is undertaken to relieve pain and improve neurologic function. Cancer patients do not die from spinal metastasis, nevertheless, satisfactory relief of spinal cord (and nerve root) compression contributes immeasurably to the quality of remaining life.

The outcome following treatment for symptomatic spinal metastasis depends upon a number of factors.

1. Speed of onset
2. Degree of deficit
3. Culpable primary
4. Advanced disease
5. Location of tumour
6. Surgical technique

The overall outlook for patients with symptomatic spinal metastasis is related to the evolution and course of metastasis elsewhere in the body.

Our experience with 200 consecutive patients requiring neurosurgical decompression of symptomatic spinal metastasis has produced results superior to those generally reflected in the literature. Optimal management of patients with symptomatic spinal metastisis requires a multidisciplinary approach with cooperation among oncologist, neurosurgeon and orthopaedic surgeon.

40.

Nuclear Magnetic Resonance Spectroscopy in an Experimental Model of Epilepsy

R.S. McLACHLAN, V.J. MYLES and S.J. KARLIK (London, Ontario)

Recently, we observed that magnetic resonance imaging of some patients with temporal lobe epilepsy reveals focal increases in T1 and T2 which appear to correlate with the electrophysiologically determined seizure focus (McLachlan et al., Epilepsia 26:555-562, 1985). In an attempt to elucidate the nature of these changes, we used a Praxis II spectrometer to study the proton NMR of cortex of urethane anaesthetized rats in which interictal and ictal epileptiform activity was induced with topical penicillin G. T1, T2, specific gravity, and wet to dry ratios were determined and compared to values from surrounding tissue and also from non-seizing controls. T1, but none of the other parameters, was found to be increased at the seizure focus, as well as at the "mirror focus" in the opposite hemisphere, suggesting that the change was related to on-going seizure activity rather than the penicillin itself. These results provide only mild support for the hypothesis that focal increases in T1 and T2 seen with magnetic resonance imaging at a seizure focus may reflect abnormal EEG activity possibly related to slight increased water content or edema in the area of the focus.

41.

Stimulation of the Substantia Nigra Inhibits Interictal Focal Penicillin Spikes in Rats

D. WHITNEY and R.S. McLACHLAN (London, Ontario)

Recent evidence suggests that the substantia nigra (SN) facilitates seizure generalization and that some anticonvulsants may exert their effect by inhibition of the SN. Lesions of the SN also may have an anticonvulsant effect on experimentally induced seizures. We examined the effect of electrical stimulation of the SN on penicillin induced focal cortical spike activity in urethane anaesthetized rats. Penicillin G 100,000 IU/ml applied topically to the cortex using a one millimeter square pledget of filter paper induces after a few minutes, focal spikes with some homologous spread to the other hemisphere which can be maintained for several hours. Low frequency bipolar stimulation of the SN on the side of the focus (0.5 ma, 5 ms, 10 hz) either inhibits or has no effect on spike frequency during and for a brief period after stimulation. The more active the focal spiking, the greater the inhibitory effect. Release of GABA from striato nigral nerve terminals in the SN, excitation of dopaminergic nigral cortical efferents, inhibition of the cortex via excitation of the caudate or some other mechanism may account for the inhibitory effect of SN stimulation on focal cortical spike activity.

42.

Primary Reading Epilepsy: Intensive Monitoring and Investigation of Critical Stimuli in 3 Cases

S. CHRISTIE, A. GUBERMAN, B. TANSLEY, R. NELSON and M. COUTURE (Ottawa, Ontario)

Three cases of primary reading epilepsy (onset at ages 14, 18, 20) were investigated by EEG and video monitoring (2 cases) while reading under various conditions. EEG showed brief paroxysmal frontal-central-temporal epileptiform bursts provoked by reading which were bilateral in 2 cases and over the right hemisphere in one (left-handed) case.

In one case we presented computer-generated reading material on a screen in a controlled manner. Utilizing a factorial design, we systematically examined the relative contribution of the following variables in precipitating seizures: eye movements, proprioceptive input from jaw and pharyngeal muscles, reading aloud versus silently, linguistic complexity and concentration. Within the framework of our design none of these factors in isolation appeared to serve as a critical stimulus.

Videotapes of seizures in 2 cases will be shown.

43.

Severe Carbamazepine Intoxication Due to Coadministration of Erythromycin

K. GOULDEN, P.R. CAMFIELD, J.M. DOOLEY, A.D. FRASER, D.C. MEEK, K.W. RENTON and J.A.R. TIBBLES (Halifax, Nova Scotia; Saint John, New Brunswick)

The commonly used antibiotic erythromycin can interact with carbamazepine (CBZ) to cause toxicity with somnolence, ataxia, dysarthria and nystagmus. We report seven children receiving CBZ for epilepsy who became severely intoxicated when they received erythromycin. The intoxication begins within hours of the first erythromycin dose. One patient had two documented courses of erythromycin, once with clinical toxicity and one without it. One patient showed a clear clinical dose-response relationship, with toxicity only after an increase in erythromycin dose from 27 mg/kg/d to 55 mg/kg/d. One child became semi-comatose with a CBZ level of 65 uMol/L (Ther 13-40), yet his plasma CBZ half-life was determined to be 8.3 hours starting eight hours after the last dose of erythromycin. Two months later with a return to steady state (peak level 28 uMol/L), the plasma half-life was 9.0 hours. The "normal" half-life while this patient was still toxic (i.e. the rapid recovery of metabolic function) is strong evidence that erythromycin interacts with the metabolism of carbamazepine through a mechanism which has not been previously described. This mechanism almost certainly involves a competitive inhibition by erythromycin of the active site of the hepative mixed function oxidase enzyme which metabolizes CBZ to CBZ -10,11-epoxide. The clinical dose-response relationship seen in one patient further supports this hypothesis.

Patients on chronic CBZ therapy should not receive erythromycin or other macrolide antibiotics unless they can be very carefully monitored.

44.

Temporal Lobe Neuron Activity During Epilepsy Surgery

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

The cellular pathophysiology of focal seizure disorders has been elucidated in both acute and chronic experimental models of epilepsy in animals. The value of these findings would be enhanced if similar mechanisms could be shown to exist in the human condition. We have recently begun intraoperative recording of extracellular neuron activity from temporal lobe neocortex and hippocampus in patients undergoing surgery for intractable seizures. Local anaesthesia is used in most cases. Simultaneous unit activity and ECoGs are recorded from glass or tungsten microelectrodes and the cortical surface. Bi or triphasic action potentials from 100 to 1000 microvolts in amplitude and 0.8 to 1.5 milliseconds in duration can be recorded in most patients. Neurons tend to fire in bursts of action potentials particularly in the deeper cortical layers. The more frequent the EEG epileptiform activity, the more likely the bursts are to be associated with surface waves and the more synchronous the burst firing of different neurons. These early observations support the findings from experimental models of epilepsy that paroxysmal interictal EEG events are associated with increased intensity and synchrony of underlying neuronal activity.

45.

Multilobar and Plurilobar Resections for Epilepsy

F.E. LeBLANC and F.B. MAROUN (Calgary, Alberta; St. John's, Newfoundland)

Seizure disorders resulting from non-progressive pathological lesions involving more than one lobe of the brain are rarely controlled by anticonvulsant medications. Plurilobar (two lobes or parts thereof) resections in one hemisphere constitute the surgical treatment in such patients. A review of the magnitude and outcomes of such surgical treatments from two university centres is combined for this presentation.

Thirty-four patients underwent cortical resections for epilepsy the extent of which was determined by preoperative EEG and/or intraoperative ECOG patterns of paroxysmal discharge and observed gross deformity of the brain at operation. Seventeen patients underwent plurilobar resections and seventeen multilobar resections of which three were complete extrathalamic hemispherectomies and fourteen were anatomical sub-total hemispherectomies.

In follow-up from one to fifteen years; seventeen patients (50%) are seizure-free, nine patients (26.5%) were "improved" with marked reduction in seizure frequency and a definite positive effect on quality of life, seven patients (20.5%) were not improved enough to affect quality of life, and one patient (3%) died two months post-subtotal hemispherectomy of acute obstructive hydrocephalus. Expanding the cortical resection to plurilobar and multilobar removals based on the pre and intra-operative electrophysiological indications and evidence of gross pathology has resulted in a good outcome in 76.5% of patients so treated.

46.

Evaluation of Spinocerebellar Degeneration with Positron Emission Tomography

K. NAGATA, K. TAGAWA and E. SHISHIDO (Akita, Japan)

To evaluate the effects of thyrotropin-releasing hormone (TRH) on cerebral circulation and metabolism in spinocerebellar degeneration (SCD), cerebral blood flow (CBF), cerebral metabolic rate of oxygen (CMRO2) and oxygen extraction fraction (OEF) were measured using positron emission tomography (PET) in 3 patients with SCD. The control data were obtained from 7 normal volunteers. Intravenous administration of TRH at 2-4 mg/day had been continued for 28 days and the PET study was performed on the last day of the treatment. The first baseline was measured before the initiation of the treatment and the second baseline was measured 28-42 days after the termination of the treatment. In the first baseline, both CBF and CMRO2 were reduced specifically at the cerebellar hemisphere, vermis, pons and thalamus in 3 patients. With the treatment all patients showed clinical improvements. In 2 patients, there was a generalized increase of CBF and CMRO2. The increase of CMRO2 was relatively greater than that of CBF and there was a significant increase of OEF. Another patient showed no significant change on the PET data. At the second baseline, the patients showed clinical deterioration and the CBF and CMRO2 were reduced to the level of the first baseline. It was suggested that TRH can activate the oxygen metabolism and blood flow of the brain in SCD.

47.

Amyotrophic Lateral Sclerosis/Parkinsonism-Dementia: The Alzheimer-related Disease of Guam

J. STEELE, D. McLACHLAN, D. PERL, B. SCHOENBERG, K-M. CHEN and T. GUZMAN (Guam; Toronto, Ontario; Burlington, Vermont; Washington)

On Guam unidentified factors of the island environment and native life style cause an Alzheimer-related, aluminum-associated disease of indigenous Chamorros termed amyotrophic lateral sclerosis/Parkinsonism-dementia (ALS/PD).

The hallmark of the disease is neurofibrillary degeneration of nerve cells (NFD) which is similar to that of Alzheimers disease and in the aged brain. In Chamorros NFD is more widespread, it occurs earlier in life and it is not accompanied by senile plaques.

Most Chamorros are asymptomatic but some develop a fatal syndrome of amyotrophy, spasticity, parkinsonism, and/or dementia because of severe nerve cell loss. The clinical illness usually begins in middle life and causes death in 4 to 5 years. Some patients have had symptoms in their early twenties and in some patients survival has been for more than 24 years. From migrant studies we know it requires prolonged exposure to the Guam environment of more than 17 years to be at risk of developing the disease. There may be a very long latency of up to 50 years between the environmental exposure and the occurrence of symptoms.

Because the disease is common in some families it was at first thought to be inherited. Subsequent studies show that although there may be a genetic predisposition, the cause of ALS/PD is environmental and likely relates to the native diet and subsistence foods.

This report reviews the clinical and pathological features of ALS/PD and its epidemiology. We describe our present investigations of environmental aluminum in the pathogenesis of the disease. We discuss our search for markers of the disease in its latent stage and propose a treatment trial of aluminum chelation by desferrioxamine.

Guam offers a unique opportunity to study this unusual disease and to continue the search for the cause of the neurofibrillary degeneration which occasions it.

48.

Lisuride Infusion Therapy in Advanced Parkinson's Disease

M.N. HASSAN, J.D. GRIMES, J. ROBERTS, J.H. THAKAR and L. PAYNE (Ottawa, Ontario)

Severe daily mobility fluctuations may still occur despite optimum oral antiparkinson therapy. Lisuride (0.025-0.15 mg/cc), a water solu-

ble dopamine agonist was given to three patients via a portable, subcutaneous pump (AS2C) infusion system. Levodopa was continued, and trials were done both on and off oral dopamine agonists. Bolus doses of Lisuride varying from 0.05 mg to 0.4 mg were given before, at the onset of, and during "off" spells. Lisuride blood levels were obtained frequently.

Sixty-six percent of the pretimed and demand infusions resulted in improved mobility. Antiparkinsonian effects were seen quickly (5-15 minutes) and doses given just preceding or during a slow period were the most effective. Mild drowsiness was the only adverse effect. Studies are continuing with the more recently available higher concentrations of Lisuride and larger single doses will be given.

With the availability of versatile portable pumps, this type of treatment approach is technically quite feasible and has been found highly acceptable by the patients. Lisuride by demand or pretimed subcutaneous bolus injection may give improved mobility to Parkinsonian patients with uncontrolled mobility fluctuations.

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49.

The Early Use of Bromocriptine in de novo Parkinson's Patients

M.J. GAWEL, I. LIBMAN, R.J. RIOPELLE and S. BOUCHARD (Toronto, Ontario; Montreal, Quebec; Kingston, Ontario; Dorval, Quebec)

Fifty-one patients with de novo Parkinson's disease were enrolled in a double blinded, parallel group, multicentre study to assess the short-term efficacy and tolerance of bromocriptine or L-dopa/carbidopa at the lowest effective dose. Following initial and 2-week baseline assessments, patients were reviewed every 3 weeks for 21 weeks. Medication dosage of each agent was increased gradually until a stable or maximal improvement, or a maximum dose of 30 mg bromocriptine or 300/75 mg L-dopa/carbidopa was achieved. This dose was maintained for the next 6 weeks. Seventy-five percent of patients in each group responded to therapy; the mean daily dose of medication used by responding patients was 21 mg bromocriptine or 223 mg L-dopa/carbidopa.

Significant improvement was observed in clinical status and disability assessments with both agents, with no differences between them.

These results are relevant to the management of Parkinsonism, since recent studies suggest that initial treatment with bromocriptine may protect against later side effects from L-dopa treatment (Rinne UK, *J Neurol* 232 (suppl): 185, 1985).

50.

Sex-linked Recessive Ocular Myopathy in a Newfoundland Kinship

W. PRYSE-PHILLIPS (St. John's, Newfoundland)

In a kinship with ocular myopathy/oculopharyngeal dystrophy detected in 6 members over 3 generations, a sex-linked recessive mode of transmission appears probable. Study of the natural history of the disease in this family demonstrates that ptosis, external ophthalmoplegia, bulbar involvement and girdle weakness occur sequentially and progressively over 20 to 30 years with onset in the third or fourth decades. The features allowing a diagnosis of Kearns-Sayre syndrome are not present.

Ocular myopathy is said to differ from oculopharyngeal dystrophy on the basis of its earlier age of onset, the absence of dysphagia and associated muscle weakness in other areas, and possibly other parameters. In this kinship, "pure" ocular involvement exists for years before involvement of other muscle groups. The clinical features are compared with those of the reported cases in the world literature. On the basis of these data and the usual tendency to phenotypic variability in autosomal dominant disorders, the concept that ocular myopathy and oculopharyngeal dystrophy are distinct entities is critically discussed.

51.

Topical ^{31}P NMR Spectroscopy Exercise Studies in Mild Human Forearm Denervation

D.W. ZOCHODNE, R.T. THOMPSON, A.A. DRIEDGER, C.F. BOLTON, M.J. STRONG and A.J. HUDSON (London, Ontario)

In the animal model, denervation alters the activity of several enzymes responsible for intracellular energy production. Topical ^{31}P NMRS (31-phosphorus nuclear magnetic resonance spectroscopy) permitted us to study in vivo energy metabolism during exercise in human subjects with mild forearm denervation. Rest, exercise and recovery spectra in 7 patients were obtained using a 1.89 Tesla TMR-32 (Oxford Systems) 26 cm. bore magnet: motor neuron disease (5), polyneuropathy (1) and "post-polio syndrome" (1). The exercise protocol, as employed by other investigators (Arnold et al, 1985), required the patient to repetitively squeeze a hand bulb connected to a manometer. All patients attempted exercise but performance often declined due to fatigue in later exercise.

At rest, the ratio PCr/ (Pcr + Pi)*, a measure of intracellular high energy reserve, was normal in 3 patients (0.874 ± 0.019) and reduced in 4 patients (0.780 ± 0.031) compared to controls (0.851 ±0.020; $n = 10$; $p < .05$). Patients with normal resting reserves experienced an early decline with exercise of the PCr/ (Pcr + Pi) ratio that was greater than in controls ($p < .05$). Patients with low resting reserves experienced a more gradual decline of PCr/ (Pcr + Pi) in early exercise. The ratio values were similar to controls in all 7 patients in later exercise and recovery. In contrast, pH values did not significantly differ between patients and controls throughout the protocol.

The results suggest that PCr reserves may be reduced at rest or inappropriately depleted during early exercise in patients with mild forearm denervation. Further PCr depletion in exercise is likely limited by patient fatigue. The cause of these abnormalities may include loss of conditioning, altered blood flow or loss of neurotrophic influence. (Supported by O.M.H.).

*PCr = phosphocreatine; Pi = inorganic phosphate

52.

Muscle Properties Following Neurapraxia

A.J. McCOMAS and N. KOWALCHUK (Hamilton, Ontario; Oxford, England)

The study of paralysed muscle is of interest for two reasons: it demonstrates the degree of muscle fibre atrophy which may be anticipated unless there is a therapeutic intervention and it sheds light on the nature of the trophic influence exerted by motoneurones on muscle fibres. We have developed an animal model of disuse which avoids major trauma and, unlike other methods, is capable of inducing total paralysis rather than lessened muscle activity. The model involves transient compression of the sciatic nerve in an anaesthetized rat so as to produce impulse blockade (neurapraxia). After 1 week of paralysis the plantaris and soleus muscles exhibit striking atrophy of both type I

and type II fibres. In keeping with this atrophy there is a marked reduction in tetanic tension; in contrast the twitch is well preserved although somewhat prolonged in the plantaris. The paralysed muscles also become more susceptible to fatigue. Comparison of these results with those obtained by Finol *et al* (*J. Physiol.*, 319: 81-92, 1981) following surgical denervation indicates that it is activity, rather than axoplasmic transport, which is the prime determinant of myofibrillar properties, at least in the rat hind limb. In conjunction with our earlier study of muscle disuse involving rear-end suspension (Corley *et al, Exp. Neurol.*, 85: 30-40, 1985), the present investigation further suggests that the contractile properties characteristic of fast-twitch muscles may be maintained by small amounts of activity.

53.

Studies of the Sympathetic Skin Response and the Galvanic Skin Response

A.D. RAE-GRANT, T. PARKES and C.F. BOLTON (London, Ontario)

The above responses reflect conduction in small or unmyelinated fibers. Both may be evoked by electrical stimulation of the median nerve at the wrist or by a variety of nonspecific stimuli, with recordings from either the opposite hand or foot. The sympathetic skin response (SSR) measures a voltage change and the galvanic skin response (GSR) a skin impedance change. The inconsistency of the responses and concerns about their underlying mechanisms have limited their application. Thus 16 healthy controls and 18 polyneuropathy patients were studied to compare and delineate several aspects of the electrically evoked responses.

In controls, the sympathetic skin response was quickly abolished by habituation and by low temperature at the recording site, explaining some of the inconsistency that had been noted previously. Other factors, such as degree of anxiety, also influenced the responses. Nonetheless, under controlled conditions, all healthy subjects demonstrated both responses. While the amplitudes of both responses were highly variable, the latencies were not. The SSR latency to the opposite hand was 1.4 ± 0.1 (mean $\pm$ S.D.) seconds and it preceded the GSR by approximately 0.5 seconds. This suggests that the sympathetic skin responses arise from neural input to sweat glands in the skin. In 12 of 18 polyneuropathy patients, both responses were absent, including 2 patients in whom nerve condition studies were entirely normal.

Thus, when variability is controlled, we believe these tests may play a role in investigating small fiber conduction in polyneuropathy patients and the above results encourage further, more extensive investigation.

54.

Non-Operative Management of Simple Depressed Skull Fractures in Children

P. STEINBOK, O. FLODMARK and D. MARTENS (Vancouver, British Columbia)

Surgical elevation is usually recommended for a simple depressed skull fracture if the depression is more than the full thickness of the adjacent skull, but there is no scientific evidence to support this line of management. We have adopted a progressively more conservative approach to this condition, especially in young children, and we reviewed our experience over the period 1972-1984. Of 111 patients less than 16 years old with depressed skull fractures, 64 were simple and 47 compound. Simple depressed skull fractures occurred in a younger age group after less significant trauma than compound fractures. In those patients who were treated surgically there was a 11% incidence of dural laceration in patients with simple depressed fractures versus 67% for the patients with compound depressed fractures. There was no difference in outcome between surgically and non-surgically treated patients with simple depressed fractures with respect to seizures, neurologic dysfunction or cosmetic appearance. Surgical treatment prolonged hospitalization and resulted in the only mortality in the group. We suggest that the standard treatment of pediatric simple depressed skull fractures should be non-operative. Surgery is indicated when there is definite evidence of dural penetration and in the older child with an unacceptable cosmetic abnormality.

55.

Stereotaxic Surgery Planning using C.T., MRI and DSA

T.M. PETERS, A. OLIVIER, J. CLARK, E. MARCHAND, G. MAWKO and R. ETHIER (Montreal, Quebec)

Stereotaxic surgery is used to perform certain operations and biopsies via burrholes in the skull. To achieve this, the surgeon must have detailed knowledge of the spatial location of the lesion. This information is obtained by using a rigid frame fixed to the head with accurately engraved markers establishing a coordinate system for all three dimensions. The frame is used both during the imaging procedure to establish the location of the lesion and also during the operative procedure to support the instruments for the operation.

In order to accurately establish coordinates during the imaging sessions, a set of fiducial markers appropriate to the specific imaging modality is affixed in the reconstructed image to the frame. These show up as spots which can be recognized by computer software.

From this information, the three dimensional coordinates of structures and lesions in the brain are determined. We have developed a stereotaxic frame which is compatible with each modality (C.T., MRI and DSA) and have designed appropriate software to analyse images made by each system. We present examples relating to the location of lesions requiring stereotaxic operative approach, and also to the implantation of depth electrodes within the brain.

56.

Periaqueductal Tumour as a Cause of Late Onset Aqueductal Stenosis

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

Congenital aqueductal stenosis of late onset is a well documented cause of hydrocephalus in children and young adults. In a number of these patients, obstruction of the aqueduct of Sylvius has been shown to be caused by a localized periaqueductal tumour which has often been unrecognized because of the small size of the tumour and the lack of localizing neurologic abnormalities.

In the past, radiologic investigations including pneumoencephalography, positive contrast ventriculography, and more recently contrast CT scanning, have frequently failed to show tumours in this region in the early stages. However, recent experience using MRI on patients with unexplained late onset aqueductal stenosis has in some instances shown the presence of a tumour as the cause of obstruction of the aqueduct of Sylvius.

We discuss four patients who presented with hydrocephalus secondary to presumed late onset congenital aqueductal stenosis, all of whom were shown to have a periaqueductal tumour. One patient had been investigated with a pneumoencephalogram and positive contrast ventriculogram and a CT scan with an early generation scanner, but the tumour was diagnosed only at the time of autopsy. In a second patient,

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the tumour was diagnosed by CT scan and also confirmed with an MRI scan, but no histologic diagnosis has been obtained up to this time. In two other patients, CT scans with and without contrast enhancement were negative and in one of these patients, a positive contrast ventriculogram was also felt to be negative, but the tumour was easily identified on MRI scans. In one of these patients, a histologic diagnosis was obtained initially by biopsy and later at autopsy but the second patient has had no biopsy up to the present time.

It is important to recognize that periaqueductal tumours usually present like congenital aqueductal stenosis of late onset. Based on our experience, we recommend that where possible, all patients who present with late onset aqueductal stenosis be investigated with an MRI scan to rule out the presence of a periaqueductal tumour.

57.

Adult Medulloblastoma: Analysis of Ten Cases

R.N. GOYAL, N.A. RUSSELL, R. Del CARPIO-O'DONOVAN, B.G. BENOIT and V.F. DA SILVA (Ottawa, Ontario)

Medulloblastomas are generally considered to be uncommon in older age groups, an often quoted figure being twenty percent in patients older than fifteen years.

In 1985, five adult patients with medulloblastoma were managed at the Ottawa Civic Hospital. A review of hospital records revealed that five similar patients had been admitted in the preceding eight years. In the total of ten patients there were four females and six males. The age ranged from eighteen to forty-five, the average being thirty. The clinical features at presentation were those of posterior fossa mass lesions. Six had associated hydrocephalus and one of these needed emergency ventriculoperitoneal shunt. One woman was four months pregnant at presentation. All patients were investigated by computerized tomographic (CT) scanning in addition to more conventional methods. Four were located in a cerebellar hemisphere, five in the midline and one in both sites. All patients were treated by radical excision followed by craniospinal axis irradiation.

The results of treatment are discussed and the features of these cases compared with those of childhood medulloblastomas.

58.

Choroid Plexus Tumours

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

Choroid plexus tumours are uncommon but well documented neoplasms of the CNS. We review a series of 12 cases from the Vancouver General and British Columbia Children's Hospitals during the last 12 years. Some of the management problems commonly associated with tumours are discussed.

Due to several factors many of these tumours are associated with a massive degree of hydrocephalus at the time of diagnosis. The perioperative management of this hydrocephalus remains a matter of some debate. The timing or necessity of shunting is the major consideration.

Often large subdural fluid collections are discovered in the post operative period and on occasion cause symptoms of increased intracranial pressure. The appropriate treatment of this problem is also in question.

The similarity between papillary ependymomas and choroid plexus papillomas has on occasion caused some difficulty in pathological diagnosis. Choroid plexus carcinomas, of which there were two in this series, also present a challenge for diagnosis. The implication of this problem becomes evident when considering the further treatment and prognosis for the patient.

59.

Cavernous Sinus Venography and Selective Venous Blood Sampling in the Management of Sella and Parasellar Lesions

F.B. MAROUN, M. MANGAN, E.R. REDDY, J.C. JACOB, T. CUMMINGS, J. HARDJASUDARMA and W. MALONEY (St. John's, Newfoundland)

Cavernous sinus venography is an adjunct in the diagnosis and management of sellar and parasellar lesions. Examples from our series of 52 patients who underwent the procedure will be presented to illustrate:

(a) Normal and abnormal radiographic anatomy.
(b) The value of hormonal assay in samples of venous blood obtained from peripheral systemic vein, jugular vein and petrosal sinus.

60.

"Failed Back" Surgery: Review of 53 Cases

H.J. ROSEN (Montreal, Quebec)

53 patients who presented with disabling lumbosciatica after previous surgery on the lumbosacral spine, and who underwent repeat spinal extradural surgery after careful clinical and radiological assessment, were submitted to a detailed review. The review was completed after a post-operative interval of at least one year in all cases.

The patient population consisted of 36 males and 17 females; 20 of the patients (all males) had some form of third party coverage. In 20 cases the clinical presentation was chiefly a mechanical disability; in 4 the deficits were exclusively neurological; in 29 the deficits were both mechanical and neurological.

In 17 patients the pathology was new; in 15 it was recurrent; and in 21 it was concluded to be persistent since the initial surgery. The new and recurrent lesions were almost always "fresh" disc protrusions. The major pathology in the persistent cases was an extradural fibrosis, either exclusively, or associated with other abnormalities. Patients presenting with the clinical and radiological findings of a lumbar arachnoiditis were not treated surgically, and are therefore not included in this study.

The results of the repeat surgery were uniformly good when the pathology was new or recurrent. However, in the 21 patients with persistent pathology the results were good in only 7, fair in 6 and poor in 8. Yet, if the persistent pathology was a lesion missed at the previous surgery, the results were reasonable; whereas, if the major persistent lesion was an extradural fibrosis involving one or more specific nerve roots, they were generally unsatisfactory, and especially so when the patient had some form of third party coverage.

In summary, this study suggests that the problem presented by a patient who has third party coverage, and whose persistent post-operative lumbosciatica is chiefly due to extradural fibrosis, cannot be solved by repeat lumbar extradural surgery.

61.

Trigeminal Neuralgia: Comparison of Long-Term Results with Percutaneous Trigeminal Rhizotomy and Posterior Fossa Exploration

H.R. REICHMAN and G.G. FERGUSON (London, Ontario)

This study compares the long-term results of percutaneous trigeminal rhizotomy (PTR) and posterior fossa exploration (PFE) in 142 patients with classical trigeminal neuralgia treated between 1976 and 1985.

Seventy-two patients underwent PTR. The average follow-up is 61 months. Six patients (8%) were immediate failures, while 42 (58%) have had a recurrence of pain (10 mild, 10 moderate, 20 severe). Thirty (42%) remain totally free of pain. Complications included corneal anesthesia (12%), anesthesia dolorosa (3%) and keratitis (1%).

PFE was performed on 72 occasions in 70 patients (2 patients had bilateral symptoms). The average follow-up is 46 months. In 63 procedures (88%) compression of the trigeminal nerve was found (62 vascular, 1 tumour). These patients were treated by microvascular decompression (MVD). The recurrence rate is 29% (5 mild, 5 moderate, 8 severe). In 9 cases (14%) neural compression was not found and a partial sensory rhizotomy (PSR) (7 cases) or nerve massage (2 cases) were performed. One patient has had recurrent pain following PSR. Altogether, 53 procedures (74%) have resulted in total pain relief, while in 19 procedures (26%) there has been a recurrence of pain. There were no deaths and there has been no serious long-term disability in these 70 patients.

PTR is well suited to high risk and elderly patients in spite of the high recurrence rate, as it is safe in such patients and easily repeated. MVD is the procedure of choice in younger and low risk patients as there appears to be a significant potential for cure. Complications have been minor in our experience. PSR is a reasonable alternative to MVD when neural compression is not found.

62.

Bridge Implantation in Transected Rat Spinal Cord

J. DE LA TORRE, L.P. IVAN and M. RICHARD (Ottawa, Ontario)

As part of our project SCoRR (spinal cord repair & reconstruction), we examined various tissue and non-tissue bioimplants in experimentally damaged/transected spinal cords.

Rats were subjected to a severe impact injury using the weight-drop method, then allowed to stabilize for 3 weeks before complete transection of the cord at the lesion site.

The cord was transected in all rats using a Codman CO_2 laser. Five groups of rats were randomly chosen: controls (C) transection only, cord apposed; in the remaining four groups, all rats had the proximal-distal cord stumps trimmed between 0.8-1.0 mm using the laser. A gap was thus created measuring between 1.6-2.0 mm. A well-fitted section of skeletal muscle (M), sciatic nerve (SC), gelfoam (G) or collagen matrix (CM) was used to fill the gap. All rats were killed 5 weeks after the initial injury. Microscopic examination, SPG catecholamine histofluorescence, somatosensory evoked potentials (SEP) and neurological evaluation showed the following:

CM and to a lesser extent M, showed catecholamine-containing varicosities (CCV) at the proximal interphase and within the implant. One rat in CM, showed CCV distal to be cord injury.

CCV were also evident in the proximal stump close to the implant in SC and G but *not* within the implant or distal to it. No SEP were seen in any rat and as expected, neurological evaluation was negative at the time of sacrifice in all groups.

It is concluded from this acute study that CM is superior as a bioimplant to M, SC, G or no implant with respect to CCV support and proliferation.

63.

Nerve Reconnection using Collagen Matrix.

R.N. GOYAL, M. KARACA, B. LACH, B.G. BENOIT, N.A. RUSSELL, V.F. DA SILVA and J.C. DE LA TORRE (Ottawa, Ontario; Turkey)

The use of a bioimplant as a substitute for nerve grafting in peripheral nerve injuries has important therapeutic implication. It has been previously shown that a cell free collagen matrix (CM) can support the growth of catecholaminergic axons and microvessels in transected rat spinal cord (de la Torre JC Brain Res. Bull. 9: 545, 1982). This study examines the effectiveness of CM in bridging a traumatic peripheral nerve gap.

16 adult male Long Evans hooded rats weighing 350-400 grams were used. Both sciatic nerves were exposed at mid thigh. A 1 cm polyethylene tubing was divided longitudinally into two halves. The nerve was sutured to each end of one half of the tubing to relieve tension at the center of the preparation. Transection of the nerve was then done at mid point of the tubing using microscissors. This created a gap of 3 mm. The gap was either left empty (control) or filled with CM. The top half of the tubing was replaced to enclose the nerve. Serial neurological examination was done until the animals were killed at 9-12 weeks. Horse radish peroxidase (HRP) was injected distal to the lesion 24 hours prior to, and somatosensory evoked potentials (SEP) were performed on the day of sacrifice. Specimens were examined using light microscopy (LM), electron microscopy (EM) and fluorescent microscopy for Sucrose Phosphate Glyoxylic acid (SPG) histo fluoresence for catecholamine containing varicosities (CCV).

Our results show partial sensori-motor recovery in the two groups. HRP labelling was found proximal to the lesion site equally and LM revealed reconnection in both groups. SEP findings were comparable in the two groups. SPG demonstrated a greater density of CCV in CM group than the control distal to transection. This was supported by LM and EM findings of increased number of myelinated axons in the distal side in CM group.

We conclude from these preliminary findings that CM has potential as a bioimplant and further study is required.

64.

Mechanisms of Regeneration of Primary Sensory Neurons

P.M. RICHARDSON (Montreal, Quebec)

Regeneration of axons in dorsal spinal roots or the dorsal columns can be enhanced by peripheral axonal injury to the appropriate neurons.

Sciatic nerve transection increases one hundred-fold the probability that the central axons of lumbar sensory neurons will regenerate from the spinal cord into a peripheral nerve graft (Nature (1984) 309: 791-793). Further studies with alternative or additional sciatic nerve injuries suggest that dorsal root ganglion neurons are stimulated to regenerate when deprived of normal retrograde influences from peripheral sheath cells (Schwann cells and endoneurial fibroblasts).

A second transganglionic effect of peripheral axonal injury is to accelerate regeneration in crushed dorsal roots. Without sciatic nerve injury, axons in lumbar dorsal roots regenerate at approximately 1mm/day: this rate is doubled if the sciatic nerve is transected one week before crushing of the root.

Both experimental preparations serve to assay the growth state of primary sensory neurons. The results indicate two mechanisms of action for peripheral sheath cells during regeneration. Such cells provide a favorable local environment for axonal growth and are a source of retrograde signals that activate the nerve cell body.

65.

Receptors for Nerve Growth Factor in the Rat Brain: Radioautography and Binding Studies

V. VERGE, R.J. RIOPELLE and P.M. RICHARDSON (Montreal, Quebec; Kingston, Ontario)

Several lines of evidence now suggest that nerve growth factor (NGF) acts on neurons in the mammalian brain as well as peripheral

neurons. NGF receptors in the rat brain have been investigated by radioautography of tissue sections or biochemical studies of brain extracts following incubation with radioiodinated NGF.

In radioautographs of the forebrain, neurons with NGF receptors were seen in the neostriatum, medial septal region, diagonal band of Broca, lateral preoptic area and globus pallidus (homologous to the basal nucleus of Meynert in the rat). Neurons in the medullary reticular formation and other discrete regions of the brainstem were also specifically labelled by radioiodinated NGF. The distribution of neurons with NGF receptors matches the known distribution of cholinergic neurons in the basal forebrain and caudatoputamen but not in the brainstem.

For biochemical studies, extracts of the basal forebrain, enriched for plasma membranes were incubated with radioiodinated NGF. The receptorligand complex was stabilized by cross-linking, solubilized with detergent and submitted to SDS-polyacrylamide gel electrophoresis and radioautography. The rat basal forebrain contains NGF receptors of high affinity (16 pM) and also of lower affinity, one of which has an apparent molecular weight of 150-200 kilodaltons. In these regards, NGF receptors in the mammalian brain bear some resemblance to receptors on cultured neurons or neoplastic cells from the neural crest.

These and other studies indicate that NGF may be implicated in the development, normal function, or disease of cholinergic neurons in the basal forebrain.

66.

A Study of Calcium Induced Myelopathy in Rats

D. MORASSUTTI, J.C. DeLa TORRE, Z. MERALI and M.T. RICHARD (Ottawa, Ontario)

Calcium has previously been proposed as a mediator of nerve fibre degeneration following spinal cord trauma.

This study used a rat model developed in our laboratory to investigate the effects of Ca^{++}-induced myelopathy in neurologically intact, alert rats. Long Evans hooded rats had a drug-delivery catheter system implanted following a one-level thoracic laminectomy. Subsequent to recovery from anaesthesia, to ascertain that no sensory-motor deficits were present, the rats had their cords infused with either 7%NaCl or 10%$CaCl_2$ solution. Evan's Blue dye was used to confirm drug delivery to the spinal cord. A neurological assessment scale ranging from 0 (complete hind limb paraplegia) to 4 (normal) was used.

RESULTS

	10%$CaCl_2$	7%$NaCl_2$	Evan's Blue
Total # rats	11	8	3
# without deficit	0	8(100%)	3(100%)
# deficit (3)	1 (9%)	0	0
# deficit (0-2)	10 (91%)	0	0

Rats with post-surgical deficits were not included nor infused. All rats allowed to survive 2 weeks had complete neurological recovery. Histochemical fluorescence studies showed a significant decrease in catecholamine levels distal to the lesion. High performance liquid chromatography studies are being conducted to elucidate the type of catecholamine involved. We feel these results support the hypothesis of a Ca^{++}-mediated transport block which may occur in cord trauma.

67.

Comparison of Bchavioral and Biochemical Effects Induced by the Injection of Neurotoxic Substances in the Substantia Nigra of Rats.

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

The neurotoxic substances manganese (Mn^{2+}) and 1-methyl-4-phenyl-1, 2, 5, 6-tetrahydropyridine (MPTP) induce parkinsonism in man. MPTP and 6-hydroxydopamine (6-OHDA) have both been successfully used to produce animal models of parkinsonism in several animal species. We have compared these three compounds with regard to their potential in producing the rotating rat model (Ungerstedt), and their influence on striatal dopamine (DA) metabolism.

Grops (n = 12) of male Sprague-Dawley rats (150-175g) were subjected to stereotaxic unilteral injection of 6-OHDA (8 μg), MPTP (80 μg) and Mn^{2+} (10-80 μg, as $McCl_2$) in 4 μl of saline containing ascorbic acid. Control animals were injected with vehicle. Three weeks later, animals were injected with apomorphine (1mg/kg) and tested once for circling behavior in rotometers. One week later, all animals were sacrificed and the striata dissected, frozen and homogenized. The striata were individually analysed for DA and its metabolites, dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) by high pressure liquid chromatography.

Injection of vehicle, 6-OHDA and MPTP resulted in a mortality of 10-20%, whereas the highest dose of $MnCl_2$ (80 μg) had a mortality of 75-80%. 6-OHDA lesioned animals exhibited marked contralateral rotational activity to apomorphine, in contrast to vehicle, MPTP and $MnCl_2$ -treated animals. DA, DOPAC and HVA were signficantly decreased in the striata ipsilateral to the lesion, as compared to the striata on the non-lesioned side, in all animals treated with the neurotoxins. In vehicle-treated rats, there was no difference in the concentrations of DA and its metabolites between the striata of the two sides.

These preliminary data indicate that the various neurotoxic substances induce qualitatively similar changes in DA metabolism. However, only 6-OHDA lesioned animals produce significant circling activity to apomorphine. These results will be presented and discussed with regard to the possible differences in the mechanism of action of these neurotoxins.

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68.

Functional Microcircuitry of Motor Cortex

J.T. MURPHY, H.C. KWAN and Y.C. WONG (Toronto, Ontario)

Previous work in our laboratory has demonstrated that columns of cells orthogonal to the surface of precentral cortex control movement of forelimb parts about single joints. In the present study we examine functional interaction between single neurons within such columns during voluntary forelimb movement in awake primates (M. speciosa). Two types of cells are observed: output cells and local interneurons, excitatory and inhibitory. We find by cross correlation technique that these two cell classes synaptically interact with each other during limb movement. Interacting cells are present with the same column, and in different columns. The synaptic interactions are plastic, that is their presence depends on the movement context.

69.

Organic Acid Transport Inhibition and CSF Lactate in Hypoxemia

V. MacMILLAN (Toronto, Ontario)

Previous studies from this laboratory have indicated that probenecid, valproic acid and diazepam inhibit the transport of short chain monocarboxylic acids from CSF to blood. Since lactate is transported from brain to blood by this system, and since elevated lactate is believed to play a role in hypoxic-ischemic brain damage, agents which could impede its elimination during or after hypoxia-ischemia could potentiate cellular damage.

Male wistar rats were prepared with a permanent cannula in the cisterna magna which allowed for repeated sampling of CSF in the unanesthetized animal. After an initial CSF sampling, probenecid (200 mg. Kg^{-1}), divalproex Na (100-500 mg. Kg^{-1}) or acetysalyclic acid (50-200 mg. Kg^{-1}) was given i.p. and followed by 0.5h exposure to 5% 0_2. The lactate content of CAS was determined at 0 and 0.5h exposure and 0.5 and 1.5h reoxygenation. At 0.5h exposure CSF lactate was statistically equivalent in all groups (10 $mm.L^{-1}$). At 0.5 and 1.5h reoxygenation CSF lactate was significantly increased in probenecid (170% control) and divalproex Na (130-180% control) animals, whereas ASA was without effect.

The results indicate that certain drugs are capable of retarding the restitution of cerebral hypoxic lactacidosis and thus have the potential of increasing cerebral damage in these states.

By Title Only

70.

Rabies Encephalomyelitis Treated with Interferon

D.A. CAMERON, T.A. HURWITZ, R.C. SAYSON and S.L. SACKS (Vancouver, British Columbia)

It is generally accepted that human rabies once clinically manifest, is invariably fatal. However there are three well documented cases of clinical rabies, who received post exposure prophylactic therapy and survived. The publication of Hatwick et al in 1970 records the first case of recovery in which the application of intensive medical care appeared to play an important role.

We present the case of a 25 year old university student who died from biopsy proven rabies 130 days after being bitten by a bat. The patient had not received post exposure prophylactic rabies vaccine until the syndrome was clinically manifest.

Treatment was designed to maximize the possibility of recovery from rabies. The patient was treated in an intensive care unit and received Rabies Immune Globulin and Interferon systemically and intrathecally. Despite intensive medical therapy, the patient became comatose 10 days following initial symptoms and died 22 days after onset of coma.

In conclusion, this is the first documented case of maximal intensive care treatment in an individual without preclinical, post exposure prophylactic therapy. Treatment did not alter the natural course of the disease.

71.

Experimental models of cerebrospinal fluid shunt obstruction.

M.R. DEL BIGIO and J.E. BRUNI (Winnipeg, Manitoba)

Obstruction of the ventricular end of cerebrospinal fluid (CSF) shunts was investigated in adult rats and rabbits by implanting sterile silicone shunt tubing into the fourth ventricle and frontal horns of the lateral ventricles, respectively. The implants were 5 mm long with 0.4 mm diameter holes. Animals were killed at postoperative intervals of 3 days to 16 weeks by intracardiac perfusion with mixed aldehydes and their brains were processed for correlative scanning and transmission electron microscopy. Reactive changes in the periventricular tissue correlated with the extent and duration of contact with the shunt tubing. In both rats and rabbits ependymal cells underwent progressive loss of cilia and microvilli and became attenuated. A significant subependymal gliosis accompanied these changes and in the most severly affected regions ependyma was denuded exposing glia and neurons to the CSF. In the rabbit, mitotic activity adjacent the implant was increased ($p<.005$) among astrocytes at 3 days and 1 week and among ependymal cells at 1 and 2 weeks post-implantation. Ventricular surfaces adjacent to shunt tubing holes developed tissue evaginations. These outgrowths, partially covered by ependyma, consisted of a core of loosely organized glial and inflammatory cells and, by 4 weeks, a dense array of astrocytes and vascular elements. In the rat, the number of outgrowths from the surface of the vermis and the ventricular floor differed significantly. Choroidal and collagenous tissues were occasionally found near the implants in the rabbit frontal horn. Implants in the rat fourth ventricle, however, were often invaded by choroidal and leptomeningeal tissues. Cellular proliferation and mechanical factors are believed to contribute to the development of these periventricular tissue outgrowths in both experimental models. This type of tissue response may be a factor in the pathogenesis of shunt obstruction in human hydrocephalus.

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72.

Early Surgery for Intracranial Aneurysms.

A. MEDHKOUR, G. LEBLANC, J. FRANCOEUR, M. COPTY, J.M. BOUCHARD, J.F. TURCOTTE and C. PICARD (New York, New York; Quebec City, Quebec)

Subarachnoid hemorrhage (SAH) due to ruptured intracranial aneurysms remains a major neurosurgical problem. The overall outcome of SAH patients is very poor, with a morbidity/mortality of 64%. International cooperative studies report that the highest rate of rebleeding occurs during the first 24h post SAH. Cerebral vasospasm begins around the 2d-4th day and reaches its peak on the 8th day post SAH. Anti-fibrinolytics do not reduce the rebleeding rate significantly, but increase the rate of vasospasm, hydrocephalus and thromboembolic phenomenon.

At Infant Jesus Hospital, Quebec City, we operated on 136 patients during the period Jan 1983 through Dec 1984. Twenty-two patients were operated on acutely, less than 72 hours post bleed. Evaluation of these patients included the Glasgow coma scale (GCS), Botterell classification, CT scan and angiography. Post-operative evaluation included GCS, date of discharge, a follow up of two to six months and a Glasgow outcome scale. Fourteen of the 22 patients were operated on acutely because of the coexistence of the aneurysm and a life threatening hematoma. Eight patients of this group had a significant improvement, 57%. Among the eight patients grade I-II of Botterell without a hematoma, one died of vasospasm, five had a good recovery, two were moderately disabled, a satisfactory outcome for 7 patients of this group or 87%.

Most of the disastrous and major complications post SAH occur during the first fifteen days. The principal causes of death are rebleeding and vasospasm. Early surgery prevents fatal rebleeding and allows more aggressive treatment of vasospasm. Once the aneurysm is clipped,

hypervolemia (the only effective therapeutic modality today) may be used without fear of aneurysm rupture.

The ideal treatment would be the diagnosis and the treatment of intracranial aneurysms before their rupture.

73.

Subarachnoid Pressure Monitoring: Complications and Recommendations for Usage

A.R.T. COLOHAN, W.M. BROADUS, G.A. PENDELTON, D. BOLDING and J.A. JANE (Montreal, Quebec; Charlottesville, Virginia)

The role of intracranial pressure (ICP) monitoring in the treatment of neurological disease is still controversial. We present a study of ICP monitoring in 348 patients in the management of their disease. ICP bolts (Richmond subarachnoid screw) were used on 378 occasions, ventriculostomies on 23, and epidural monitoring only once. Indications for monitoring included: trauma 36.2%, tumour 26.4%, vascular 12.4%, spontaneous intracerebral clot 8.0%, subarachnoid hemorrhage 4.3%, hydrocephalus 3.4%, and other 9.3%. There were 2 intracranial abscesses, 1 intracerebral hematoma and 2 cases of meningitis which could be directly attributed to the use of the bolt, while there were 6 cases of infection (1 abscess, 4 cases of meningitis, and 1 infected craniotomy flap) in the setting of post-craniotomy ICP monitoring. This gives a major complication rate of 1.3% for complications directly attributable to the use of subarachnoid bolts. If one includes the 6 cases mentioned above it gives an absolute complication rate of 3.2%. The overall mortality in the series was 20.4%. However, the mortality was 71.0% in those patients whose highest ICP recording was greater than 40 mm Hg but only 8.6% in those whose highest measured ICP was less than 20 mm Hg. Subarachnoid bolts had to be replaced in only 1.8% of cases due to malfunction. We have performed bilateral frontal subarachnoid ICP monitoring on 65 occasions and found a differential ICP recording frequently. Recommendations on the placement of ICP bolts and the techniques used to assure such a high success rate will be presented.

74.

Factors Influencing Outcome After Mild Head Injury

A.R.T. COLOHAN, W.M. ALVES, R.W. RIMEL, T. O'LEARY and J.A. JANE (Montreal, Quebec; Philadelphia, Pennsylvania; Charlottesville, Virgina)

The staggering social and economic costs of mild head injury are undeniable. We prospectively studied 1,216 consecutive patients admitted to the University of Virginia hospital over a two and one-half year period with mild head injury. Inclusion criteria were: 1) a history of transient loss of consciousness or other neurological function following head injury, such as memory, speech or vision; and 2) an initial Glasgow Coma Score of 13-15 (as assessed by a neurosurgeon). 54.5% of patients had vehicle-related injuries. Only 7% of those involved in automobile accidents were wearing seat belts. Patients were reassessed at 3, 6 and 12 months post-injury. 41.2% of adult patients had resumed work within 7 days post-injury, but 31.3% had still not returned to work by 6 weeks. Associated injuries proved to be a significant cause of delay in return to social activity and work. For a Glascow Coma Score of 15 the average length of stay in hospital was 1.87 ± 0.12 days without associated injuries and 8.13 ± 0.67 days with associated injuries ($P<0.05$). The average return to work was 14.3 ± 1.3 days without associated injuries and 41.3 ± 3.8 days when associated injuries were present ($P<0.05$). Attempts to reduce associated injuries would have profound effects in the reduction of health care costs and lost productivity following minor head injury. Interpretation of the role of associated injuries in the context of minor head injury must be tempered by recognition that most patients (80% in our series) do not present with extracranial trauma.

75.

Guidelines for a Carotid Endarterectomy Trial

D.W. ROWED and J.W. NORRIS (Toronto, Ontario)

The longterm benefit of carotid endarterectomy has not been proven. Design of a prospective study requires certain knowledge of early morbidity and mortality and projection of probable benefit.

Data from the Toronto Carotid Endarterectomy Study indicates a perioperative stroke rate of 3.9% and a death rate of 1.5%, but published combined stroke and death rates range from less than 2% to almost 25%. Projected stroke rate reduction is approximately two-thirds but mortality, which is largely cardiac, is not greatly altered. Time required to show a reduction in stroke and death is at least one year.

The following guidelines are suggested for a prospective trial in symptomatic patients.

1) *Demonstrated* stroke and death rate of approximately 5% in participating centres.
2) Uniform perioperative management.
3) Ethical considerations require data monitoring procedures that would allow early termination of the Study.

Poster Presentations

P-76.

Study of Metabolic and Haemodynamic Aspects of Huntington's Disease by Positron Emission Tomography

A.C. EVANS, C. REDIES, S. GAUTHIER, J.L. TYLER, M. DIKSIC, E. MEYER, Y.L. YAMAMOTO and A. HAKIM (Montreal, Quebec)

PET was used to provide regional measurements in 7 HD subjects, with minimal caudate atrophy, for oxygen metabolism ($rCMRO_2$), oxygen extraction fraction (rOEF), blood volume (rCBV), blood flow (rCBF), pH (rCpH) and glucose metabolism (rCMRGlc). In addition regional rate constants for the transport and phosphorylation of F-18 labelled deoxyglucose (FDG) were measured. Results were compared with similar data from a control group of 6 older normal patients. $rCMRO_2$, rCMRGlc, and rCBF in the caudate nucleus exhibited a coupled depression. Transverse profiles through the head of the caudate body were analyzed with the caudate/cortex index of Kuhl et al.[1] For the control group the index for each parameter was ~20% while in the HD group the indices were 40-50%. Metabolic and haemodynamic measurements in the cortex of the HD patients were not significantly different from those of the control group. The caudate/putamen region showed a 35% reduction in rCMRGlc while $rCMRO_2$ and rCBF were reduced by ~20%. The FDG rate constants are similar for the HD and control groups except for k_2, expressing FDG backflow, in the caudate/putamen. The ratio of k_2 in the cortex to k_2 in the caudate/putamen is a factor of two smaller in HD patients than in controls.

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1) Kuhl DE, Phelps ME, Markham CH, Metter EJ, Riege WH, Winter J (1982) Cerebral metabolism and atrophy in Huntington's disease determined by FDG and computer tomographic scan. Ann Neurol 12: 425-434.

P-77.

Relapsing and Remitting Mononeuritis Multiplex Secondary to Vasculitis in a Patient with Acquired Immunodeficiency Syndrome

L.M. METZ, W.J. BECKER, B.D. McLEOD and B. CURRY (Calgary, Alberta)

Peripheral neuropathies have been reported in association with the acquired immunodeficiency syndrome (AIDS) but the mechanism of the neuropathy has remained unclear.

We present a 51 year old male with a one year history of remitting and relapsing mononeuritis multiplex prior to a diagnosis of AIDS being made. Symptoms included painful paresthesiae, numbness and weakness over a one year period. Physical findings varied over time and included muscle wasting, weakness, decreased sensation and reflex loss. CSF total protein (75 mg/dL) and CSF IgG (10 mg/dL) were both elevated. Neurophysiological studies six months after symptoms began showed widespread denervation. Four months later there was slowing of sensory and motor conduction velocities in three of four nerves tested, and denervation was present on EMG in three of four muscles tested. Sural nerve biopsy showed marked Wallerian degeneration and severe axonal loss. Gastrocnemius muscle biopsy showed patchy neurogenic muscle atrophy consistent with denervation.

Immunofluorescence studies of the sural nerve showed fine granular deposits of IgM, C3 and fibrin in the walls of many endoneurial blood vessels.

This patient with AIDS presented with a neuropathy clinically consistent with a vasculitis, which relapsed and remitted spontaneously and also appeared to respond dramatically to prednisone therapy. Demonstration of immune deposits in this patient is important in that it may lead to a better understanding of AIDS.

P-78.

Cerebellar Blastomycosis: Large Abcess Treated Medically

P. BOURQUE, J.G. D'ALTON and R. SAGINUR (Ottawa, Ontario)

The spectrum of C.N.S. Blastomycosis includes meningitis, intracranial abcess or spinal epidural abcess. Most previously reported cases of cerebellar abscess were documented at necropsy or surgery in the pre-CT scan era.

We report the case of a 50 year old male who presented with a headache, dysarthria and ataxia. Initial evaluation led to a diagnosis of a large cerebellar tumour with secondary obstructive hydrocephalus. Following insertion of a ventriculoatrial shunt, a posterior fossa craniotomy was followed by biopsy of the lesion. Chronic inflammatory changes were noted on histology and Blastomyces Dermatitides was cultured from the patholgical specimen. The patient refused any further treatment for two months. During this time he had increasing cerebellar dysfunction and a CT scan showed several large ring-enhancing lesions which coalesced and involved much of the left cerebellar hemisphere, with compression and displacement of the 4th ventricle. There appeared to be involvement of the petrous bone.

He was treated with Amphotericin B (cumulative dose 2.5g), initially combined with Rifampicin 600 mg daily for six weeks and followed by a course of Ketoconazole 1200 mg daily for 30 days. A follow-up scan after two months of therapy showed a dramatic and complete resolution, persistent at one year.

Once the diagnosis is established, surgical treatment of even large C.N.S. Blastomycotic abcesses can be avoided.

P-79.

Asymmetric Papilledema and Visual Loss in Pseudotumor Cerebri

C.E. Maxner, M.I. Freedman and J.J. Corbett (Iowa City, Iowa)

Pseudotumour cerebri (PTC) is a condition of uncertain etiology characterized by raised intracranial pressure (ICP) in patients with normal CSF profile, no evidence of mass lesions or ventriculomegaly. The patients are usually obese women of child bearing age who present with headaches, blurred vision or diplopia, and papilledema.

We report a 25 year old obese woman who presented with intermittent headaches and blurred vision in her left eye (OS) and on clinical examination had an enlarged visual field blind spot OS with OS optic disc edema. Given the patient's vascular risk factors (obesity, hypertension, 20 pack year smoker, thrombocytosis and migraine), normal CT scan, normal MRI study, and normal lumbar puncture (LP) results (opening pressure = 130 mm CSF, negative profile) a diagnosis of anterior ischemic optic neuropathy was made. At follow-up examination within the month, an inferonasal visual field defect OS was documented and in addition to the marked disc edema OS, slight disc elevation in the right eye (OD) was recognized. A diagnosis of PTC was entertained. Repeat LP pressure was non-diagnostic at 220 mm CSF. Further progression of the OS inferonasal field defect prompted placement of a continuous ICP monitoring bolt and CSF pressures greater than 600 mm CSF confirmed the diagnosis of PTC. An optic nerve sheath fenestration was performed OS because of progressive visual field loss and postoperatively, although the ICP remained elevated, the visual field defect improved and the disc edema almost completely resolved.

This case demonstrates that the visual field defects in PTC may be more extensive than blind spot enlargement and they are potentially reversible; that the papilledema in PTC can be strikingly asymmetric; and that single normal CSF pressure measurements do not rule out PTC.

P-80.

Paroxysmal Kinesigenic Choreoathetosis: A Case Report

M.B.M. SUNDARAM and E.M. ASHENHURST (Saskatoon, Saskatchewan)

Paroxysmal kinesigenic choreoathetosis (PKC) is a rare disorder manifested by brief attacks of uni-or bilateral dystonia, chorea or athetosis. Lack of familiarity with this condition might lead to mistaken diagnosis of psychiatric conditions. We present a case of PKC to highlight clinical features, differential diagnosis and treatment.

This 18 year old male University student presented with 5 year history of brief episodes of involuntary stiffening of the right side of the body; most attacks were precipitated by rising from a chair. Each episode would last several seconds but he would have many attacks daily. There was no associated impairment of consciousness or speech.

Several attacks were witnessed and consisted of low amplitude choreiform movements and subtle dystonic posturing of the right hand and forearm. Some episodes were associated with arching of the right foot and elevation of right eyebrow. Attacks were precipitated by rising from a chair. Passive leg movements were ineffective. EEG during

attacks were normal. Phenytoin completely controlled the attacks but they recurred following discontinuation of the drug.

Differential diagnosis of paroxysmal dystonias will be discussed. Videotape of above described attacks will be shown.

P-81.

Unusual Neuropathological Findings in a Patient Following Surgery for Morbid Obesity: A Case Report and Review of the Literature

R.A. PURDY, V. SANGALANG, E.P. WALTER and S. PHILLIPS (Halifax, Nova Scotia; Saint John, New Brunswick)

We report the case of a 23 year old woman who died of the complications of a pulmonary embolus six months following gastric restrictive surgery for morbid obesity. She presented four months post-operatively with bilateral papillitis, ophthalmoplegia and ascending paralysis resulting in respiratory failure requiring mechanical ventilation.

The neuropathological findings demonstrated marked poliomyelopathy consistent with changes described in Wernicke's disease and more chronic changes of the same type in the diencephalon. There was spongy degeneration of the posterolateral columns of the cord, pyramids and cerebral peduncles as described in B12 deficiency. As well, there were findings reminiscent of Leigh's disease in the dentate, inferior olivary and lower brainstem motor nuclei and substantia nigra. Hypoxic changes were seen in the cerebral and cerebellar cortices.

Review of the recent literature reports several clinical cases of neurological complications of surgery for morbid obesity. The typical pathological findings of Wernicke's disease have been reported as well as one pathological report of a case with polyneuropathy without poliomyelopathy or spongiform degeneration. To our knowledge, the widespread and unusual neuropathological findings in this case and clinical setting have not previously been reported.

P-82.

Graves' Disease and Subarachnoid Hemorrhage: A New Familial Association

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

We describe the familial association of Graves' disease and subarachnoid hemorrhage in 15 members of the same family across 3 generations. The involved individuals are gathered into three groups:

The *first group* consists of 7 females and 2 males with Graves' disease without subarachnoid hemorrhage.

The *second group* consists of 3 individuals with Graves' disease and suspected or confirmed subarachnoid hemorrhage. The first is a female with Graves' disease since the age of 21. At the age of 38 she presented with Grade I subarachnoid hemorrhage from an angiographically confirmed posterior communicating artery aneurysm. The second is a female with Graves' disease since the age of 39. At age 43 she suffered a Grade I subarachnoid hemorrhage confirmed by lumbar puncture. Complete cerebral angiography and CT scan were normal. The third individual is a male with untreated thyromegaly who suddenly collapsed and died at the age of 30 while attending to his usual activites.

The *third group* consists of 3 individuals with suspected or confirmed subarachnoid hemorrhage without evidence of Graves' disease at the time of examination. One male aged 30 who had a brother and sister with Graves' disease and 1 female aged 34 whose mother had Graves' disease, suddenly collapsed and died while attending to their usual activities. The third individual sustained a Grade III subarachnoid hemorrhage from an angiographically confirmed anterior communicating artery aneurysm at the age of 49.

This report suggests a genetic determination for the development of cerebral aneurysms and of Graves' disease in this family. The mode of inheritance of Graves' disease appears to be autosomal dominant with 50% penetrance. The presence of these two disorders in the same individuals and in individuals from the same family suggest that they may be genetically determined and individually transmitted on separate or linked genetic loci.

P-83.

New Daily Persistent Headache: A Benign Disorder

W.J. VANAST (Edmonton, Alberta)

Chronic, benign headache (CBH) is an intractable syndrome combining features of common migraine and tension headache. In contrast to its slow evolution to daily headache (CBDH) we identified a syndrome of new, daily persistent headache (NDPH) in 45 young adult patients (m 19, f 26). 80% of males were age 35-45; females 16-35.

WBC, differential, ESR, monoslide tests, CT scan and neurologic examination were always normal.

Headaches are daily from the onset; steady in 72%; pounding in 38%; unilateral in 38%, temporal (alone or in combination) 23 cases; occipital 21; frontal 12; vertex 8; generalized 5. Associated symptoms include nausea (m 57%, f 53%); vomiting (m 5%, f 19%); light phobia (m 26%, f 42%); noise phobia (m 21%, f 53%); myalgia (1 m); vertigo (2 m, 3 f); drowsiness and lethargy (7 f); near faints (3 f); sore throat (1 f); cold sweats (1 f).

The headache-free state returned spontaneously in 3, 6, 12 and 24 months respectively in 36%, 68%, 80% and 96% of males; 30%, 52%, 58% and 73% in females.

While NDPH pain quality is identical to CBDH, the headache trigger is more suddenly deployed and removed, making these patients an ideal, drug-free group for chronic headache investigation.

P-84.

Persistent Epstein-Barr Virus Infection in Chronic Headache Syndromes: Results of a Pilot Study Using DNA Dot Hybridization

W.J. VANAST, F. DIAZ-MITOMA and D.L.J. TYRRELL (Edmonton, Alberta)

Epstein-Barr Virus (EBV) can induce chronic illness characterized by fatigue, headache, depression and myalgia. Fever is not necessarily associated with this syndrome. Physical examination and standard laboratory tests (WBC, differential, lymphocyte morphology and monoslide test) are usually normal. Symptoms can be chronic or intermittent, recurring several times per year.

These features lead us to postulate that EBV might be responsible for some monosymptomatic idiopathic headache syndromes. Our studies were confined to new daily persistent headaches (NDPH), a syndrome described by us elsewhere. Attempts to establish a correlation between the NDPH syndrome and the excretion of EBV were undertaken. We have previously established that the detection of EBV by the cord blood lymphocyte transformation (culture) correlates well with the detection of EBV genome in cells obtained by throat washing using DNA-dot hybridization. The DNA probe for the DNA-dot hybridization consists of the BamH-1-W subgenomic fragment of the EBV genome (an internal repeat region).

Lymphocytic transformation was positive in 5 of 60 control patients and 6 of 11 patients with NDPH ($p<0.01$). The DNA dot hybridization was positive in 6 of 60 controls, and 13 of 20 patients with NDPH ($p<0.01$).

The preliminary results of this study suggest that EBV oropharyngeal excretion is more common in patients with NDPH than in control patients of similar age and sex.

P-85.

Congenital Lumbar Stenosis — An Unusual Presentation

M.B.M. SUNDARAM, B.B. MALLYA, M. KHAN and S. TCHANG (Saskatoon, Saskatchewan)

L5 and S1 roots are most commonly involved in lumbar canal stenosis (Paine, 75). We now report a patient who presented with isolated bladder and bowel dysfunction. Such isolated S2-S5 involvement, to our knowledge, has not previously been reported.

A 36 year old woman presented with a 3 week progressive history of urinary dribbling, constipation and loss of sensation during micturition, defecation and sexual intercourse. Past history included chronic, intermittent bouts of low backache but without exertional claudication. Examination revealed normal muscle power, tendon reflexes and straight leg raising. Saddle sensations and anal tone were moderately diminished. Evoked potentials (visual, brain stem and somatosensory) and CSF were normal. X-rays showed congenital fusion at L3-4. Metrizamide myelogram showed suggested narrowing of the transverse diameter of contrast column at L4-5. CT scan of lumbar spine with coronal reformation showed moderate narrowing of transverse diameter of spinal canal at L4-5, mainly posteriorly; AP diameter was normal. These findings as well as severe thickening of ligamentum flavum were confirmed at surgery. Following decompression, there was gradual and complete return of sensations and bladder-bowel function.

This case illustrates that i) congenital lumbar stenosis can occasionally present with isolated S2-S5 dysfunction, ii) in some cases, CT reformation at the appropriate level may be necessary to appreciate selective posterior stenosis.

P-86.

Portacaval Shunt Myelopathy with Corticospinal Tract Degeneration

M.R. HANSON, M.L. ESTES, S.M. CHOU and E.WINKLEMAN (Cleveland, Ohio)

Portacaval shunt (PS) myelopathy is a distinct, rare clinicopathologic entity. All patients described have had cirrhosis with surgical or spontaneous PS. Neuropathologic changes include Alzheimer II astrocytosis and corticospinal tract (CST) degeneration principally in the spinal cord. The pathogenesis of the CST change remains unknown. This study adds a case and postulates the cause of CST degeneration.

A 65 y/o WF with cirrhosis underwent PS in 1979 following many episodes of hepatic encephalopathy with persistent blood ammonia elevation. 3 years after PS she developed spastic lower extremity weakness with extensor plantar responses. CSF studies and myelography were normal. The spasticity progressed and 1 year later she developed rigidity, akinesia and emotional lability. The disease slowly progressed with death 6 years after PS.

Autopsy showed macronodular post-hepatitic cirrhosis. Neuropathologic examination revealed: Alzheimer II astrocytosis, myelin loss and spongiform change of fiber bundles in the putamen and severe edema and spongiform change of the globus pallidus. Similar but milder changes were seen in the mid-pons. Cortical neurons, particularly Betz cells, were preserved. All spinal segments showed pure, symmetric CST degeneration more pronounced cervically, with prominent axonal swellings in the anterior horns. The CST changes extended into medulla, pons, midbrain and internal capsule (IC).

The extensive CST changes in our patient suggest descending Wallerian degeneration due to IC compression from chronic severe edema in the lentiform nucleus. The relationship of the syndrome to chronic hyperammonemia and pathologic comparison to other reported cases will be discussed.

P-87.

Serum Anti-Brain Antibodies in Neurologic and Psychiatric Disorders and in Normal Controls.

A.V. PLIOPLYS, J. THIBAULT, J.-P. BOUCHARD, C. COCKBURN and R. HAWKES (Quebec City, Quebec)

To investigate the possibility that anti-brain antibodies play a pathogenetic role in a number of neurological and psychiatric disorders a population study was undertaken. Serum samples were obtained from a total of 250 adults, divided into 3 groups: normal and neurologic and psychiatric disorders. The neurologic disorders group included 18 patients with cerebellar ataxias, 22 with various etiologies of mental retardation, 16 with Parkinson's disease, 20 with myasthenia gravis and 5 with other diagnoses. The psychiatric disorders group included 68 with chronic schizophrenia and 4 with other diagnoses. 98 healthy individuals were also studied. The majority of serum samples were obtained when routine blood tests were performed. In the other cases informed consent was obtained. This study was approved by hospital ethics review committees. Serum samples were screened against SDS polyacrylamide gel electrophoretic blots of various normal, autopsy-derived adult human brain regions. The serum was diluted 1:100 for initial incubation and the presence of immunoglobulin labelling was revealed with horseradish peroxidase-conjugated rabbit anti-human IgG. The incidence of immunoreactive banding was 31% in the total studied population. Within the diagnostic groups the incidence of banding was: normals 32%, schizophrenia 28%, mental retardation 27%, cerebellar ataxia 39%, Parkinson's disease 22% and myasthenia gravis 45%. The differences are not statistically significant. There was no significant difference in the numbers and locations of bands between the various diagnostic groups and the normal controls. A previous study reported that the incidence of anti-210K reactivity, corresponding to the high molecular weight subunit of neurofilaments, is 95% in healthy individuals (Science 1985, 228: 1117-9). Our results do not confirm this report in that the overall incidence was only 8%. The similarity in reactivity between the various diagnostic groups and the normal controls suggests that caution must be exerted in interpreting the pathogenetic significance of such findings. This work was supported in part by a MRC fellowship to AVP.

P-88.

Multiple Sclerosis (MS) Patients' Offspring: Sex Ratio, Average Number of Children and Complications Associated with Pregnancy

S. WARREN, M. PATERSON, I. PATTERSON and K.G. WARREN (Edmonton, Alberta)

Some studies have suggested a relationship between the ratio of male to female births and viral infections; eg. an excess of male births has been observed following epidemic measles (Langaney et al, 1979). Alperovich and Feingold (1981) found a significant excess of sons among the children of female versus male MS patients. If the sex ratio of MS patients' children in general revealed an excess of sons when compared to controls, it might implicate a previous viral infection.

At the University of Alberta MS Clinic, 25 male and 78 female patients were matched to friends and non-blood relatives on sex and approximate age. These two groups were then compared on the ratio of

males to females among their offspring. The patients did not report an excess of sons, among either their children born before or after onset age. Nor did the female patients report an excess of sons when compared to male patients. The average number of children reported by patients (2.5) and controls (2.4) was similar, but patients had significantly more of their children prior to onset age ($X^2=6.5$, $P<.02$). Several possible explanations exist; the patients may have started having children younger, or have had their children at closer intervals, than controls. The trend may also indicate that patients were limiting the number of their offspring to avoid social, financial or physical problems. In the case of female patients, there may be some justification for limiting children, in terms of disease course. While no more patients than controls reported miscarriages or other complications of pregnancy following onset age, 10% of the patients reported experiencing at least one MS relapse during a pregnancy and 18% reported experiencing a relapse in the nine months postpartum. Number of children born after onset age did not appear to be associated with disability outcome, however, when duration of disease was taken into account.

P-89.

Powerlessness in Institutionalized Patients with Chronic Neurological Conditions

M. BARABASH and S. WARREN (Edmonton, Alberta)

Neurologists who admit patients to extended care facilities may receive feedback that they have become dependent, uncooperative, non-compliant or possibly hostile. Institutions have been found to impact negatively on patients through loss of privacy, deindividualization, controls on personal autonomy and segregation from the outside world. As a result patients often develop a sense of powerlessness; that is, of having no control over self, others or situations. Powerlessness can lead to feelings of hopelessness, which in turn may affect attitudes towards rehabilitation, be a factor in the development of other illnesses and even lead to death if patients give up the will to live (Miller, 1983).

At Grandview Extended Care Centre (Edmonton), all alert or semi-alert patients admitted are being scored using the Power Behaviour Assessment Scale. This scale measures 4 indicators of powerlessness: verbal expression; emotional response (eg. withdrawal, pessimism); participation in activities of daily living; and interest in learning about health status and care programs.

To date staff have assessed 26 patients with a variety of neurological conditions (such as multiple sclerosis, Parkinson's Disease and epilepsy). This group included 18 females and 8 males, with an average age of 65 and a range from 32 to 95 years. All of the patients exhibited symptoms of powerlessness to some degree. The scale rates severity on the basis of how often a behaviour is manifested (1-never, 2-occasionally, 3-frequently, 4-always). This group's average scores were: verbal expression — 2.5; emotional response — 2.6; participation in activities of daily living — 2.3; and learning about health status and care program — 2.7. The findings indicate that powerlessness was an occasional to frequent problem among them.

If extended care centres could be encouraged to offer programs aimed at helping patients overcome powerlessness, it might benefit both their outlook and health. Physicians could be an important force in encouraging both the establishment of such programs and their patients' participation.

P-90.

Prince Edward Island Spinocerebellar Ataxia — A New Variant

J.M. DOOLEY, J.A.R. TIBBLES and J.P. WELCH (Halifax, Nova Scotia)

We describe 9 patients from PEI with autosomal recessive spinocerebellar ataxia. Their clinical features differ from typical Friedreich's ataxia (F.A.) but are similar to New Brunswick "Acadian ataxia" as described by Barbeau et al (1).

The 9 patients, from 5 families, were 20-38 years of age. The onset of symptoms varied from 5-18 years, with 5 having onset after puberty. The rate of disease progression was slower than in F.A. Of the 5 aged 20-26 years all were still ambulatory and 4 had preserved deep tendon reflexes at the knees. Weakness was less marked than in F.A. and an unequivocally positive Babinski response was found in only 4. EKG examinations and Vitamin E levels were normal in all 9 patients.

The patients were assessed, using the Ataxia Protocol of Pourcher and Barbeau (2) and were compared to groups with F.A. and "Acadian ataxia" (table). Both PEI and "Acadian" ataxia are similarly distinct from Friedreich's Ataxia. A preliminary examination of the available data indicates that these families are genetically related to those previously described as Maritime Acadians by Barbeau (1).

Spinocerebellar ataxia in PEI is more benign than Friedreich's ataxia.

Barbeau et al: Recessive Ataxia in Acadians & "Cajuns" Can J Neurol Sci 1984; 11: 526-533.

Pourcher E, Barbeau A: Field Testing of an Ataxia Scoring & Staging System. Can J Neurol Sci 1980; 7: 339-344.

TABLE: Ataxia Scoring and Staging System

	PEI ATAXIA	ACADIAN ATAXIA	FRIEDREICH
Age of Onset (yr)	11.5 ± 6.5	13.8 ± 0.6	10.2 ± 0.9
Age at Present (yr)	29.6 ± 9.0	28.1 ± 1.7	25.4 ± 1.1
Duration (yr)	15 ± 6	14.4 ± 1.5	15.4 ± 1.4
Severe Ataxia %	55.6	52	91
Muscle Weakness %	2.4	2.8	4.4
Babinski Sign %	44.4	68	100
Scoliosis (max 3)	1	1.6	2.3
Knee Jerk (max 12)	8	12	12

P-91.

Vitamin B_{12} in Alzheimer's Disease

M. FREEDMAN, S. TIGHE, D. AMATO and D. ABBOTT (Toronto, Ontario)

The present investigation was carried out to determine whether Alzheimer's disease was associated with abnormalities in serum B_{12} levels.

Twenty-five patients with Alzheimer's disease were compared to subjects with other causes of dementia ($n=11$) and to neurological controls ($n=20$). The non-Alzheimer dementia (NAD) group included patients with multi-infarct dementia, idiopathic Parkinson's disease and depression associated with cognitive deficits. The neurological controls consisted of patients with peripheral neuropathy, blackouts, headaches, vertigo, and Parkinson's disease without dementia.

Vitamin B_{12} levels were significantly lower in Alzheimer's disease compared to the NAD ($p<0.004$) and the NC ($p<0.005$) groups (see table). There were no group differences in hemoglobin, mean cell volume, or red blood cell folate levels. Our findings are in agreement with others and support the need for additional investigations to study the mechanisms underlying the relationship between vitamin B_{12} and Alzheimer's disease.

TABLE

	Serum B_{12} (pmol/L)	Hb (g/L)	MCV (fL)	RBC Folate (nmol/L)
AD	225	137	92.7	509
SEM	22	2	0.9	41
NAD	418	139	89.4	516
SEM	58	7	1.3	42
NC	426	144	91.7	649
SEM	48	3	0.9	92

P-92.

Implantation of Dorsal Column Stimulator: Psychological Factors

A.G. BLOUIN, E. PETERSON, D. PRESTON and C. ZURO (Ottawa, Ontario)

Patients who complain of chronic pain, but for whom physical cause is difficult to determine, have traditionally been identified by the classical 'conversion V' profile on personality testing. These patients are characterized by an excessive focus on physical complaints and relative psychological naivety. Selecting patients for implant of dorsal column stimulator to reduce pain is made difficult since a legitimate physical history is often accompanied by apparent hypochondriacal symptoms.

Psychological test results (MMPI) were evaluated among 14 patients considered for implantation of a dorsal column stimulator. Surgery was conducted among 6 of these patients and clinical ratings of outcome were obtained. Psychological test results were considered in selecting patients for surgery and those selected evidenced significantly (using stepwise regression) less psychopathology than patients who were not operated on. Implantation of the dorsal column stimulating device resulted in positive clinical outcome for all patients selected, in spite of the fact that these patients generally presented with elevations on the Hypochondriasis and Hysteria scales of the MMPI. It is notable that relatively high levels of depression accompanied this excessive focus on somatic complaints in these patients.

Chronic pain may in fact lead to neurotic features, such as hypochondriacal complaints. Patients presenting with hypochondriacal symptoms have been found to obtain positive clinical benefits from dorsal column implants. These patients are distinguished from those with the classical 'conversion V' profile by having higher levels of depression and a legitimate physical history. The elevated depression probably results from the validity of the physical discomfort experienced by these patients.

P-93.

Repetition and Localization in Transcortical Aphasia

M.E. AWAR and A. KERTESZ (London, Ontario)

Transcortical motor aphasia (TMA) is characterized by poor speech output but good repetition and comprehension and transcortical sensory aphasia (TSA) by preserved repetition and speech output but poor comprehension. We studied language repetition experimentally in a case of each and two controls. The subjects were given a repetitious task consisting of 90 sentences in various categories that included active, passive construction, semantic, syntactic and word order anomalies. Patients were followed in the course of recovery and the lesions causing the distinct syndromes were localized. The experiment revealed that a patient with TMA repeats well with spontaneous correction of long or syntactically anomalous sentences. In contrast, a patient with TSA showed an improvement in the automatic corrective behaviour. The initial inability to carry out any repetition of anomalous sentences indicated that the mechanism of preserved repetition without significant comprehension is still dependent on the structural integrity of sentences in some cases.

P-94.

Cortical Blindness: Evolution and Localization

A. KERTESZ and M.E. AWAR (London, Ontario)

The definition, classification and causes of cortical blindness are reviewed. A case with bilateral infarcts of the occipital lobes, as determined by MRI and CT, is presented and the following stages in the evolution of visual impairment were documented: 1) Cortical blindness; 2) Right homonymous hemianopia with patchy and fluctuating loss of vision in the left hemifield accompanied by confabulatory responses; 3) visual agnosia and impairment of perceptual and visuospatial tasks, and 4) improvement in visual agnosia with persistent prosopagnosia and impaired visual tracing of lines.

The relationship between these stages and visual processing and the localization of the lesion is discussed.

P-95.

A Case of Visual Associative Agnosia and Amnesia

T. BENKE, S. PLÖRER, F. GERSTENBRAND and A. KERTESZ (London, Ontario; Innsbruck, Austria)

This case report describes a patient with a visual object agnosia of the associative type and a persisting impairment of her recent memory. Further symptoms were a right visual field defect, pure alexia, prosopagnosia, color naming impairment, simultanagnosia and loss of mental imagery. Object recognition difficulties were analyzed by testing various categories of stimuli. There was strong evidence for a weakening of processing in the visual modality at the level of intermodality association and, even more severe, of visuosemantic processing. The co-existing visual and verbal memory impairment contributed substantially to the impairment of several cognitive functions. The analysis of our patient's visual agnosia and the review of other comparable case reports strongly suggests a multimodal stage processing of visual stimuli to reach the level of recognition. Our patient's behavioural changes and neuropsychological deficits result from a unilateral brain lesion in the left occipital lobe with extension to the temporobasal region, as shown by CAT scan, disconnecting the visual area from speech and the limbic system. The inferior temporal region therefore has an important role in the evocation of visual memories.

P-96.

Progressive Dementia and Abnormal Movements in Association with Sheehan's Syndrome

M. DUBREUIL (Montreal, Quebec)

Dementia can be a late sequel of post-partum pituitary apoplexy (Sheehan's syndrome). Acute or chronic mental deterioration has been attributed to the associated thyroid or steroid deficiency or to dehydration, electolyte disturbances, hypoglycemia or hypothermia. We report a 67 year old woman who sustained pituitary apoplexy at age 36, following a post-partum vaginal hemmoraghe. Despite irregular menses and failure to lactate, she had another normal pregnancy and delivery at age 41. A brief psychotic episode followed laparotomy for pelvic abcess at age 42. Thyroid hormone supplement was begun at age 55 for hypothyroidism. Progressive mental impairment and asthenia developed in her early 60's. Neurological examination revealed a severe demential state and choreiform movements of the extremities. Serum cortisol was less than 1 mcg/dl and basal and stimulated FSH, LH, TSH and PRL were low. The CT-SCAN showed a small calcification in the head of the right caudate nucleus. Steroid administration and small doses of Clonazepam resulted in marked improvement of her mental status with an almost complete disappearance of the abnormal movements.

P-97.

Acute Test Doses for Treatment of Dystonia: A Paradoxical Response to Dopaminergic Agents

J.E. PAULSETH (Hamilton, Ontario)

The treatment of dystonia is difficult and very empirical. Several investigators have suggested that the response to test doses of various

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pharmacologic agents be used as the basis for therapeutic decisions. However, as the following case demonstrates, this method has limitations. A 31 year old woman presented with a 7 year history of dystonia that began with blepharospasm and facial grimacing. After 2 years it began to generalize and worsen. At the time of presentation she was incapacitated by it. Family history was negative. From age 15 to 25 she had used alcohol and street drugs including amphetamines, opiates, LSD, solvents and marijuana. She was hospitalized 3 times for manic states or depression. She received haloperidol then fluphenazine for at least 8 months in 1976, 2 years before the onset of dystonia. Examination was unremarkable except for severe generalized dystonia and myoclonic jerks in the arms and trunk. On pharmacologic testing, she had no response to haloperidol 1 mg IM; mild improvement with Sinemet 250/25 p.o.; and improvement but severe sedation after benztropine 2 mg IM. We thus decided to start treatment with dopaminergic agents. She improved mildly at first then gradually worsened. She subsequently developed a manic psychosis on bromocriptine 40 mg, Sinemet 400/100 and clonazepam 2 mg per day. This abated with haloperidol which also improved the dystonia. Dystonia improved further on the dopamine depletor tetrabenazine 175 mg, although trihexyphenidyl 14 mg and clonazepam 1 mg were later required for good control. This case demonstrates that short-term pharmacologic responses are not always predictive of long-term results. Besides the risk of precipitating psychosis, it appears that one may see paradoxical responses to dopaminergic agents. Perhaps low doses decrease dopaminergic activity through a preferential effect on autoreceptors.

P-98.

Metal Concentrations in Drinking Water in Parkinson's Disease and Controls

A.H. RAJPUT, R.J. UITTI, D. O'DONNELL and K. O'DONNELL (Saskatoon, Saskatchewan)

Several workers have suggested a link between drinking water and idiopathic Parkinson's disease (IPD) (Rajput '84, Barbeau '85, Tanner '85) and significant differences in concentrations of some metals between IPD and control brains have been reported (Rajput '84). Nine different metals including Mn, Cu, Mg, and Zn have been implicated in parkinsonism in the literature. Samples of drinking water (well water) in the 18 early onset IPD cases born and raised in Saskatchewan and 36 age and sex matched controls were obtained. We were successful in gaining water from original wells of only 7 patients as other wells were filled in and no longer in use. In those cases where original wells were not usable, samples were obtained from the nearest available source (all within 2.5 miles of the original well). The mean metal concentration of 24 metals: Ag, Al, As, B, Be, Ca, Cd, Co, Cr, Cu, Fe, K, Mg, Mn, Mo, Na, Ni, P, Pb, Se, Ti, V, W, and Zn in these samples was compared in cases and controls.

There were no significant differences in metal concentration for any metals between cases and controls when all samples were considered. When the analysis was limited to the 7 original wells of cases and their respective controls, again no differences were noted. On the basis of these observations, we cannot establish a relationship between metals in drinking water and IPD. It is however conceivable that some other factors might modify absorption or metabolism of some metals and in this way be related to development of IPD.

P-99.

Early Onset Parkinson's Disease and Rural Upbringing

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

The etiology of idiopathic Parkinson's Disease (IPD) is unknown but many researchers believe that the most likely cause is an environmental factor(s). Although clinical features of IPD generally appear around age 60, it has been recognized that the pathological process antedates the symptomatology by many years. Because of the lengthy preclinical stage and increasing mobility of Canadian residents, sound epidemiological studies dealing with a practical number of variables are nearly impossible.

In an attempt to reduce the possible agents under consideration we chose to study environmental factors acting over the first 15 years of life (which has been shown to be crucial for subsequent development of multiple sclerosis) in those patients whose clinical features presented at or before age 40 years. Early Onset Parkinson's Disease (EPD) was recognized in 4% of the IPD cases from the clinical practice of one of us (AHR) and formed the basis of a preliminary report. Since then we have contacted each neurologist and neurosurgeon personally and all physicians in the province by a newsletter. These efforts helped us identify 4 more cases. All cases were seen personally by AHR. This report is based on all 21 EPD cases who were born and resided in Saskatchewan for their first 15 years of life. 19 of these 21 were born and raised exclusively in rural communities (165 persons or less) with birthdates ranging from 1904 to 1947. Based on provincial census data regarding the 1904-1961 time period we conclude that there is a highly significant relationship ($p = 0.0218$) between rural upbringing and EPD.

P-100.

Parkinson's Disease; Treatment with Deprenyl

D.A. CAMERON and D.B. CALNE (Vancouver, British Columbia)

Drugs which inhibit monoamine oxidase A (MAO A) cannot be given to patients receiving levodopa because of hypertensive interactions. Deprenyl, a selective MAO B inhibitor, was developed approximately 20 years ago by Knoll and colleagues (1). Birkmayer et al (2) reported on their experience with 381 patients receiving deprenyl with levodopa and/or dopamine agonists over a 10 year period. From a retrospective analysis they claimed that deprenyl prolonged the course of Parkinson's Disease when compared to patients receiving levodopa and/or dopamine agonists alone. Lees and Stern (3) found that deprenyl decreased fluctuations in response to levodopa.

We present preliminary data with deprenyl as adjunctive treatment in 15 patients with moderate to severe Parkinson's Disease complicated by wearing off reactions. In all cases initiation of deprenyl therapy was achieved without complications. Open observations revealed improvement in clinical status is 3-5 days and this was sustained in all cases over up to 3 months. The doses of dopamine precursor or dopamine agonist were decreased by an average of 25%. Adverse effects were minimal with transient headache in only two cases.

In conclusion, our preliminary experience with deprenyl has yielded encouraging results in the treatment of Parkinson's patients who have wearing off reactions.

(1) Arch Int Pharmocodyn 155 154-164, 1965.
(2) Mod. Prob. Pharmacopsychiatr 19, 170-76, 1983.
(3) Lancet 1 791-795, 1977.

P-101.

Handwriting Analysis of Several Extrapyramidal Disorders

S.G. GAUTHIER, M. BOISSEAU and G. CHAMBERLAND (Montreal, Quebec)

The handwriting of patients with extrapyramidal disorders was studied to identify the presence of any handwriting characteristics that are

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indicative of the disease and to determine what the effects of the drugs used for therapy are on the handwriting. The extrapyramidal disorders studied were:

1. Parkinson with tremor at rest,
2. Parkinson with DOPA-induced dyskinesias
3. Parkinson with akinesia/rigidity
4. Essential tremor
5. Supra-Nuclear Palsy
6. Huntington's disease with chorea.

Our study revealed that each patient possessed a handwriting that was individual to him/her. This individuality was not altered by any of the drugs encountered.

The following observation was made while studying the handwriting samples taken from patients prior to the administration of their medication:

A great variation in the combination of handwriting characteristics listed below was observed amongst each of the patients studied: lack of control, abrupt changes in direction, tremors, slowness, hesitation, rigidity, false starts, no adherence to the base line, micrographia (not frequent) and errors. No pattern was observed for a specific disorder. Hence, we could not relate a handwriting characteristic to a specific extrapyramidal disorder.

The following observations were made while studying the handwriting samples obtained from patients one hour after the administration of their medication:

— Levodopa removed the tremors and reduced the rigidity.

— Levodopa produced an increase in the size of the letters and an elongation of the words in the handwriting.

— One of the anticholinergic drug's side effects was observed in the form of memory errors in the handwriting.

— One patient's handwriting who was taking an antipsychotic agent possessed characteristics that indicated the presence of neurological side effects.

— Propranolol produced variable changes from which no specific trend could be determined.

P-102.

The Natural History of Mutilating Acropathy in a Newfoundland Kinship

W. PRYSE-PHILLIPS (St. John's, Newfoundland)

The clearest definition of the clinical features of autosomal recessive Hereditary Sensory Neuropathy (Type II) to that date was provided by Ogryzlo (CMAJ 1946) who described the features in a Newfoundland kinship. The natural history of the disease has not been reported and the prognosis is not well known. Nor is it known for sure whether this is a degenerative or a static process.

The condition presents as a typical mutiliating acropathy with perceived onset in the first decade. There is predominant thin-fibre function loss in the feet and later in the hands. Motor involvement is minimal or absent.

The index cases of Ogryzlo have been studied and followed over the last 14 years. In this kinship, in which 19 members are now known to be involved, the typical picture has been for progression of sensory deficit, up to the third decade. After this time, the maximum damage appears to have been done and no progression has occurred after the age of 30 in the adult members studied.

The clinical features, the family tree and the pattern of inheritance in this kinship will be discussed.

P-103.

Ophthalmoparesis in Polymyositis: Report of Two Cases with Isolated Bulbar Symptoms in One Patient and Autopsy-proven Extraocular Muscle Polymyositis in the Second Patient.

H.R. JONES, L. FERNANDEZ-HERLIHY, T.H. ARETZ and I.M. LESSELL (Burlington, Massachusetts)

Primary involvement of the extraocular muscles with resultant diplopia is very uncommon in polymyositis. The few cases reported to date with diplopia have initially had significant proximal weakness. In some a diagnosis of concomitant myasthenia gravis has been suggested.

We have followed one patient for 3 years who presented primarily with bulbar symptoms, i.e., diplopia, with a pseudo internuclear ophthalmoplegia, dysphagia, dysphonia and neck flexor weakness but no proximal extremity weakness. This patient had extensive investigations to rule out concomitant myasthenia gravis. These included incomplete response to Tensilon and normal repetitive motor nerve stimulation, single fiber EMG, including the facial muscles and acetylcholine receptor antibodies. CPK was 1496 (110 - normal). Needle EMG showed "acute myopathic" changes mainly in the cervical paraspinal muscles, biopsy of which demonstrated polymyositis. This patient has had an excellent response to steroid therapy.

Another patient with widespread devasting polymyositis had diplopia preterminally. Autopsy demonstrated widespread polymyositis, including the extraocular muscles.

Therefore, polymyositis should be considered in the differential diagnosis of acute diplopia in the adult. One does not always have to implicate an associated myasthenia gravis in this setting.

P-104.

A Case of Motor and Sensory Neuropathy with Striking Involvement of the Upper Extremities.

I. TEIN and E.G. MURPHY (Toronto, Ontario)

Hereditary motor and sensory neuropathies commonly present with distal weakness and atrophy of the lower extremities later followed by milder weakness of the upper extremities. We present a unique case of a 6 year old boy who presented at age 3 with an unsteady gait following which he suffered a rapidly progressive atrophy and weakness both proximally and distally, involving by age 5½ most strikingly the upper extremities, along with optic atrophy, dysarthria, tongue fasciculations, hypotonia and areflexia. CSF protein was normal. Nerve conduction studies showed absent sensory evoked potentials from both sural and median nerves. Motor conduction velocity was normal in the peroneal nerve but very delayed in the median nerve. In both, the motor unit potential amplitudes were decreased. EMG studies were compatible with severe denervational changes more marked in the upper extremities. These findings were consistent with severe axonal degeneration and secondary demyelination. Sural nerve biopsy revealed a loss of large diameter myelinated axons. Myelography revealed a flattened lower cervical cord and upper thoracic cord with a possible delay in the accumulation of dye suggesting a flattened hydromeylia. For this reason the child underwent surgical exploration which excluded the possibility of a local structural etiology for the boy's rapidly progressive course and striking upper extremity predilection.

P-105.

Trigeminal Neuralgia in Association with Charcot-Marie-Tooth Disease

G.P. MURRAY, R.O. HOLNESS, C.W. McCORMICK and L.P. HEFFERNAN (Halifax, Nova Scotia)

Charcot-Marie-Tooth Disease is a primary sensory neuron disorder which usually presents within the first two decades of life. Characteristic clinical findings include wasting and weakness of the muscles sup-

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plied by the common peroneal nerve as well as impairment in distal sensory function. Cranial nerve involvement is not commonly present. Rare exceptions to this include reports of optic atrophy, neurogenic deafness, and electrophysiological evidence of facial nerve involvement.

We report on 4 patients, two of whom were siblings, with clinical and electrophysiological features of Charcot-Marie-Tooth Disease who presented with trigeminal neuralgia. We have surgically treated three of these patients; two by percutaneous gasserian rhizotomy and one by posterior fossa sectioning of the trigeminal nerve.

The association of trigeminal neuralgia with Charcot-Marie-Tooth Disease has only rarely been reported. A common underlying disorder causing involvement of the trigeminal nerve as well as a peripheral neuropathy is proposed.

P-106.

Radial Mononeuropathies Secondary to Misplaced IM Injections: The Clinical and EMG Features in 8 Cases

E. SELESHI and A.J. WILBOURN (Cleveland, Ohio)

The radial nerve can be injured near the spiral groove by misplaced intramuscular injections. Such radial nerve injection injuries (RNII) are rare, constituting ± 6% of the radial mononeuropathies evaluated in our EMG laboratory. We have studied 8 patients with RNII (5 females; 3 males), aged 13 to 70 years.

Although the responsible injections consisted of various medications (antibiotics, analgesics, antiemetics, etc.), the clinical and electromyographic presentations were stereotyped. Clinically, immediate severe burning pain radiated distally, accompanied by paralysis of the wrist and finger dorsiflexors. Atrophy and sensory loss in a radial nerve distribution distal to the elbow subsequently were demonstrable. EMG examinations revealed severe, axon-loss, radial mononeuropathies near the spiral groove: unelicitable motor and sensory nerve conduction responses (recording extensor forearm and base of thumb, respectively) along with abundant fibrillations and absent motor unit potentials in all radial-innervated muscles distal to the triceps/anconeus on needle electrode examination.

While pain was often transient, motor loss remained unchanged for at least 6 months; subsequent recovery was then slow and ultimately incomplete in some.

Conclusion: RNII are rare but serious complications of IM injections which invariably result in prolonged disability.

P-107.

Adult Onset Systemic Carnitine Deficiency: Favorable Response to L-Carnitine Supplementation

M. LEVITAN, J.T. MURPHY, G.W. SHERWOOD, J. DECK and G.M.J. SAWA (Toronto, Ontario)

We report the case of a patient who at age 39 first developed an episode of weakness and transient ketoacidosis with biopsy proven fatty infiltration of the liver. Over the next several years, myopathy ensued, which on biopsy involved extensive deposition of lipid in type I muscle fibers. Further investigations confirmed the diagnosis of systemic carnitine deficiency (SCD) with hepatic, skeletal muscle, and cardiac involvement. The patient has benefited significantly from l-carnitine supplementation. Our case represents an unusually late onset of SCD and highlights the necessity of accurate diagnosis of this rare but treatable disorder. Results of the muscle and liver biopsies are presented along with biochemical results of a 48 hour caloric deprivation test which the patient underwent in hospital. Current concepts regarding the pathophysiology of SCD are reviewed.

P-108.

Livedo Reticularis and Cerebrovascular Lesions: Sneddon's Syndrome

R.N. RANAWAYA and D.R. McLEAN (Edmonton, Alberta)

Sneddon's Syndrome is a rare entity, characterized by the development of generalized livedo reticularis and cerebrovascular lesions. It has a female preponderance and autosomal dominant inheritance is suggested by some reports. Livedo reticularis is the first symptom in the majority of cases and precedes neurologic symptoms by several years. These neurologic symptoms are usually manifested by recurrent transient ischemic attacks and strokes which usually leads to dementia. Cerebral arteriography reveals multiple occlusions in medium sized arteries with extensive collateral vessels. Digital artery biopsies indicate minimal hyperplasia without any inflammatory changes or evidence of arteritis.

We report a 33 year old housewife who developed diffuse progressive livedo reticularis at age 14 and subsequently suffered many transient ischemic attacks culminating ultimately in a right hemisphere infarction. She is mildly demented with a left hemiparesis. CT Scan, cerebral angiograms and photographs of her skin lesions will be presented.

This entity is not mentioned in standard neurologic texts. We present this case of a rare and fascinating neurological syndrome with the hope that interest will be stimulated and effective treatment developed.

P-109.

Protective Effect of Therapeutic Ultrasound on Hypoxic Brain

E.W. PETERSON, G.V. FORESTER, O.Z. ROY and J.R. SCOTT (Ottawa, Ontario)

Earlier studies from our laboratory have indicated that therapeutic ultrasound improves the contractility of hypoxic myocardium. This study investigated whether direct application of therapeutic level ultrasound (1 W/cm^2 SATA at 1 MHz) would protect the hypoxic brain. Nine cats were used in these experiments. Visual Evoked Potentials (VEPs) were recorded by averaging. We compared the VEPs under normoxia (pO_2 180-220 mmHg) and during transient global hypoxia (pO_2 21-30 mmHg). As expected hypoxia was deleterious to the VEPs affecting both the fast and slow components. Treatment of the brain with ultrasound before, during, and after hypoxic episodes tended to prevent these changes. These results suggest a direct effect of ultrasound on cerebral cell function, possibly by facilitating the utilization of the limited oxygen supply. Since ultrasound produced some heating of the brain, control experiments were performed with whole body heating. They revealed that simple temperature elevation did not produce the protective effect seen with ultrasound. These results suggest that ultrasound may have a therapeutic effect on brain tissue subjected to hypoxia.

P-110.

Aphasia and Right Cerebral Hemisphere Infarction in Right Handed Patients

A. SHUAIB, T.P. SELAND and L.A. METZ (Calgary, Alberta)

Aphasia usually results from a lesion of the third frontal gyrus (Broca's area) or the superior temporal gyrus (Wernicke's area) in the left hemisphere. In right handed people the incidence of aphasia resulting from a right hemispheric lesion is unknown, but is considered rare. Documented cases have mostly resulted from infarction in the middle or

anterior cerebral artery regions. The aphasia is usually non-fluent, with moderately impaired comprehension and a good recovery.

In the last two years (1984-1985) we have observed three right handed patients with right hemispheric infarction associated with left hemiplegia and aphasia. All three patients suffered from severe cardiac disease. In two patients cardiac embolus was the presumed etiology. Both had congestive heart failure and atrial fibrillation and required anticoagulation (AC). After complete recovery one patient had recurrence of the same symptoms with a second embolus to the right hemisphere while still on AC. The second AC patient suffered a hemorrhage into the infarction requiring surgical evacuation. The third patient had two episodes of transient ischemic attacks (TIA's) with aphasia and left sided weakness which was followed by a subsequent right hemispheric infarction with similar symptoms. In all three patients there was cranial CT evidence of right hemispheric infarctions with no abnormalities evident in the left hemisphere. Recovery was rapid but partial in two patients and minimal in the third.

Aphasia from right hemispheric lesions in right handed individuals although considered rare may be under-reported. TIA's with subsequent infarction or recurrent embolic strokes involving the right hemisphere presenting as aphasia and left hemiparesis would strongly support an important role of the "non-dominant" hemisphere in aphasias.

P-111.

PET Evaluation of Blood Flow and Metabolic Changes Induced by PGI_2 Therapy in Patients with Ischemic Stroke

R. POKRUPA, A. HAKIM, J. VILLANUEVA, E. MEYER, M. DIKSIC and A. EVANS (Montreal, Quebec)

Prostacyclin (PGI_2) has been proposed as therapy for ischemic stroke. Its actions may be to facilitate reperfusion or to offer "cellular protection". 11 patients with acute ischemic strokes were studied by PET within 48 hours of symptom onset. They were then enrolled in a randomized double blind study of PGI_2. After completion of the infusion, 5-7 days later, they were restudied with PET. We report the results of Cerebral Blood Flow (CBF) and Oxygen Matabolism ($CMRO_2$) measurements and assess the impact of PGI_2 on these parameters. At the time of the initial scan infarcted tissue was identified on the $CMRO_2$ scan as cortical regions (I) with $CMRO_2 < 67$ μmoles/100g./min. CT and neurological deficits correlated with an index of infarct size and agreed with the location of infarcts noted on PET. CBF in I on the initial scan was either hypo or hyperfused relative to the "normal" contralateral hemisphere mean values. Two placebo and one PGI_2 case with areas of reduced CBF initially had normal $CMRO_2$, corresponding to current concepts of an ischemic penumbra. ¾ PGI_2 patients and ⅓ placebo subjects displayed initial hyperperfusion. In the hypoperfused infarcts, both groups had partial recovery of the CBF when the initial infarct and adjacent hypoperfused areas were small. In the placebo cases adjacent penumbral areas later satisfied criteria for infarction. Overall size of I increased more in the placebo group than in the PGI_2 group but these changes did not reach statistical significance. From this study it was difficult to identify a beneficial metabolic or perfusion response to PGI_2. This conclusion is limited by the unexpectedly variable pattern of early stroke. In future studies PET assessment of infarcts in the early stage will allow stratification of cases for better evaluation of response to treatment.This research was supported in part by the Medical Research Council of Canada, the Upjohn Company of Canada and Wellcome Research Laboratories.

P-112.

Diagnostic Discriminative Value of BAER Latency and Amplitude in Multiple Sclerosis

M. JAVIDAN, D.R. McLEAN, A. FARID and K.G. WARREN (Edmonton, Alberta)

Discriminant analysis provides functions with maximum potential to distinguish between two or more different groups.

The discriminative value of BAER latencies, amplitudes and various combinations were studied in 99 definite MS patients and 34 normal controls. The latency of Wave I-V were measured and III-I, V-III and V-I (central conduction time = CCT) were calculated. The amplitude of Waves I-V were measured. The summated amplitude of Waves III, IV, and V(CA) and the Wave V/I and III/I amplitude ratios (ARs) were computed.

Stepwise discriminant analysis proved that the combination of Wave V amplitude (VA) and latency (VL), Wave IV amplitude (IVA) provides the best discriminating function. The function developed was .64VA − .50VL + .42IVA. Among various manipulated combinations, CA was more valuable than CCT or other conduction measurements while ARs failed to provide further differentiation. The function developed was .74CA − .52CCT.

Discrimination using weighted individual latencies and amplitudes exceeded the results utilizing individual latencies, individual amplitudes, or any combination of CA, CCT, ARs in separating MS patients from controls.

P-113.

Central Habituation of the Somatosensory Evoked Potential and Newly Defined Middle Latency Components Elicited at Slow Stimulation Rates

A.A. EISEN, A.E. GOODRIDGE, M. HOIRCH and C. HERSHLER (Vancouver, British Columbia)

Several studies have reported amplitude decrements of visual and auditory evoked potentials at stimulus rates conventionally employed to elicit somatosensory evoked potentials (SEPs). Angel et al (EEG and Clin Neurophysiol; 60:335, 1985) described an amplitude reduction of > 50% of the mechanically elicited SEP with repetition rates of 0.3 Hz.

We have explored the decremental influence of different stimulus rates on the SEP. Median and posterior tibial SEPs were elicited by electrical stimuli of intensity 3-4 times sensory threshold. The decrement in SEP amplitude was exponential with amplitudes reaching 90% of maximum only at interstimulus intervals above 10 secs. At stimulation rates below 0.1 Hz the SEP amplitude was 2-3 times greater than obtained using conventional frequencies of 1-5 Hz. The N20/P40 components were augmented by additional middle latency negativities N60/N75, N160/N170 and N290/N320. They were clearly identifiable after averaging only 20 responses and were obliterated at stimuli delivered faster than 0.5 Hz.

The findings are taken to indicate a normal central habituation of the SEP. We speculate this will be lost in some CNS diseases whilst in others it will be exaggerated. It is postulated that the newly described middle latency components are mediated via very slowly conducting peripheral and central myelinated fibers. Their latencies might be a useful measure of disease affecting these slowly conducting pathways.

P-114.

Magnetic Resonance Imaging: Pathological Correlations in Temporal Lobe Epilepsy

R. KUZNIECKY, V. de la SAYETTE, R. ETHIER, D. MELANÇON, Y. ROBITAILLE, S. BERKOVIC, F. ANDERMANN, A. OLIVIER and W. FIENDEL (Montreal, Quebec)

Radiological investigations in patients with temporal lobe epilepsy are usually unsatisfactory in the absence of well defined structural lesions. To define the value of Magnetic Resonance Imaging (MRI) in temporal lobe epilepsy we studied 41 patients prior to surgical treatment and correlated it with the pathological findings.

All patients had pre-operative investigations including CT Scan and MRI (Philips Gyroscan 0.5 Tesla). Blind interpretation of the MRI's, CT Scans and controls were done by two radiologists. Of the 41 patients, 39 showed abnormalities (atrophy, abnormal signal intensity or well defined lesions) on the MRI in comparison with 23 on the CT Scan. Of the 39 patients with abnormal MRI, 11 had tumours or vascular lesions that were well defined on the MRI. CT Scan was abnormal in 7 of these. Increased signal intensity on T2 weighted spin echo sequences was seen over mesial temporal structures in 10/13 patients with sclerosis of one or all of the mesial temporal structures, and in 4/9 patients with minimal to moderate gliosis. Six patients with no significant pathological findings showed minimal atrophy of the affected temporal lobe.

These results indicate that well defined lesions in MRI correlate with tumours or vascular lesions. It also showed a good correlation between increased signal T2 weighted spin echo images and sclerosis. Thus, MRI is a valuable technique in localization of lesions in patients with intractable temporal lobe epilepsy.

P-115.

Focal Cortical Dysplasia and Gliomas: An Unusual Association

R. KUZNIECKY and Y. ROBITAILLE (Montreal, Quebec)

Taylor et al described focal cortical dysplasia in some patients with intractable epilepsy. This entity has distinctive pathological characteristics and can be differentiated from the neurocutaneous syndromes.

We report 2 patients with intractable epilepsy who underwent surgical treatment for their seizures. The first patient was a 9 year old boy who developed focal seizures at the age of 4. His seizures became uncontrollable by the age of 7. MRI revealed a right parasagital lesion. He underwent surgical resection. Histological examination demonstrated abnormally layered cortex with large dysplastic neurons and numerous foci of densely aggregated fibrillary astrocytes which extended deeply into the adjacent white matter. The second patient was a 4 year old girl who developed seizures at the age of 9 months. Her physical exam was normal. Her seizures remained resistant to treatment. Radiological investigations (MRI, CT Scan) suggested a diffused abnormality over fronto-temporal regions. Histological examination revealed large number of dysplastic neurons in the cortex and increased fibrillary astrocytic proliferation in the surrounding areas.

The association of astrocytomas and focal cortical dysplasia has not been described previously to our knowledge. The occurrence of these two entities may provide some evidence for a relationship between dysgenetic abnormalities and neoplasms.

P-116.

Focal Pattern Sensitivity Without Light Sensitivity

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

A 31 year old right handed housewife has had complex partial, secondary generalized, and simple partial seizures since age 3 years. CT scan and neurological examination including visual fields are normal. Her simple partial seizures consist of an opaque multicolored spinning wheel in the centre of her vision which gradually expands symmetrically encompassing her entire visual field. Rare episodes of generalized dimming of vision occur. No environmental factors, including visual, precipitates her seizures.

Interictal EEGs showed frequent spikes in the right posterior temporal-occipital region, sporadic generalized bisynchronous spike and waves maximum over the right hemisphere and a low voltage persistent delta over the right occipital, posterior temporal parietal region.

Pattern reversal evoked potentials were performed for full field and both hemifields using a sequential stimulation technique. Full field and left hemifield stimulation evoked spikes over the left hemisphere while right hemifield stimulation gave little or no evoked potential. In contrast, photic stimulation failed to evoke spikes.

This is the only instance of regional pattern sensitivity of which we are aware, and certainly the only one without flash sensitivity.

P-117.

The Postictal EEG

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

We studied the postictal EEG manifestations of 51 focally originating seizures.

The EEG reverted immediately to its preictal characteristics in 16 patients (31%). Regional delta appeared in 8 (16%); background activities were attenuated in an additional 5 (10%). 21 patients (41%) manifested both delta and attenuation, and one had rhythmic theta only.

Postictal changes lasted longer among the 18 patients whose seizures developed into bilaterally synchronous epileptiform discharges, but the type of change was unaffected. Ictal bilaterally synchronous discharges were more likely to occur in patients with multiple independent spike foci interictally.

In our material, location of regional postictal alterations always corresponded to locus of origin (although we recognize exceptions to this in clinical practise).

The duration of postictal changes varied considerably (7-2450 seconds) with complex changes lasting longer than those with a single morphological feature.

P-118.

Benzodiazepine-receptor Activity in Human Epileptogenic Cortical Tissue

P.A. HWANG, W.M. BURNHAM, S.J. KISH, H.J. HOFFMAN, L.E. BECKER and E.G. MURPHY (Toronto, Ontario)

Samples of focal and extra-focal neocortical tissue excised from patients undergoing surgical resection for intractable epilepsy were analysed using a filter assay for benzodiazepine-receptor binding.

"Focal" and "extra-focal" areas were defined by electrocorticography, the "focus" being the area showing maximal interictal epileptiform activity and the "extra-focal" area being that area which showed least. Samples were frozen in liquid nitrogen within five minutes of excision and stored at −70°C until analysis.

Saturation isotherms of 3H-flunitrazepam binding were generated according to the method of Placeta and Karobath (1979). Unlabelled clonazepam was used to define non-specific binding. Samples were analysed "blind" and the focal and extra-focal samples from any given patient were assayed in parallel. The maximal receptor density (Bmax) and binding affinity (l/Kd) were estimated from Scatchard plots.

Preliminary data were obtained from 8 patients, 4 males and 4 females, aged 12-18 years, all with long-standing complex partial seizures, on anti-convulsants. The Kd's for the focal and extrafocal samples were almost identical, being 1.26 ± 0.06 and 1.24 ± 0.06 nM respectively.

The Bmax values were 782 ± 75 fmoles/mg protein for the focal samples and 869 ± 48 for the extrafocal samples. This difference was not significant with the present sample size but does suggest the possibility of decreased benzodiazepine receptors in the human epileptogenic focus. Additional samples are being collected as well as early studies on GABA-mediated alterations in the cortical tissue being initiated.

P-119.

Bromide in the Treatment of Seizures in Porphyria

J. BRUNI and D.A. DOTTEN (Toronto, Ontario)

A 37-year-old female patient presented to The Wellesley Hospital with generalized tonic-clonic seizures. She had a previous nine year history of porphyric attacks secondary to variagate porphyria characterized by crampy abdominal pain, nausea, vomiting and the production of dark urine. Urinary collections demonstrated elevated levels of coproporphyrin and uroporphyrin. Both valproic acid and clonazepam resulted in the aggravation of her porphyric crises. Other conventional antiepileptic drugs were not used because of their known potential to aggravate porphyria. The patient was subsequently treated with bromide with successful control of her seizures without aggravation of her porphyria, and with normalization of the EEG. The role of bromide in the treatment of porphyric seizures will be discussed.

P-120.

Use of Lorazepam in the Treatment of Status Epilepticus

J. BRUNI (Toronto, Ontario)

Recently lorazepam has been approved for the treatment of status epilepticus. In this report the results of treatment in twenty-three episodes of status epilepticus in twenty-two patients are presented. Four patients presented with myoclonic status, three patients presented with partial motor status and fifteen patients experienced tonic-clonic status epilepticus. An initial intravenous dose of 2 to 4 mg at a rate of 1 mg/minute was administered and repeated a second time if necessary. Seizure control was achieved in 19 episodes of status. The majority of patients were subsequently treated with a second anticonvulsant usually phenytoin for maintenance therapy. Two patients developed mild respiratory depression. Lorazepam is an effective benzodiazepine for the treatment of status epilepticus. It has a rapid onset of action, has a low incidence of cardiopulmonary depression and may be effective in status refractory to diazepam.

P-121.

Tripole Spike Discharges

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

Focal spike discharges having a very complex and interesting potential field were observed in 11 children between the ages of 4-14 years (mean 9 years).

On routine EEG recordings (using cheek or hand reference) these discharges were found to have centrotemporal positivity with simultaneous frontal and posterior negativity. This "tripole" field was seen in conjunction with normal background activity. Often there were also one or two independant dipole spike discharges involving either the temporal, frontal, or occipital regions. All discharges had a wide field usually involving both hemispheres and having the appearance of a "generalized" sharp and slow wave.

Clinically there was a history of infrequent nocturnal partial or 2° generalized seizures in nine children, slow speech development in one, and precocious puberty in one. The development history and neurological exam were normal in all but 2 cases where slow speech development and spina bifida were noted.

It is hypothesized that the tripole field is created by a single complex generator near the lower rolandic region. This generator may be orientated vertically with superficial positivity and deep negativity. The deep negativity, conducting through brain tissue, is surfacing in the frontal and occipital regions and appears to surround the positivity.

Identification of this tripole field of a focal discharge is important to avoid misinterpretation of this field as a generalized discharge.

P-122.

Epileptiform Spikes Evoked by Tactile Stimulation

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

Epileptiform discharges evoked by sensory stimulation are thought to be rare (incidence 0.7%). Previous report suggested that this phenomenon has a high association with later development of childhood epilepsy. We encountered this finding in 37 children aged 0.2 to 17.5 years (mean 5.9 years), during routine EEG examination, and wish to report our dissenting experience.

This presenting history included seizure disorder, developmental delay, mental retardation, learning disability, febrile convulsion, behavioural disturbance, encephalitis, meningitis, headache, failure to thrive or attention deficit. Twenty five of the 37 children had a history of seizures. Seizure types included partial (7), absence (7) and tonic-clinic (3). There was no patient with reflex epilepsy or neuronal storage disease. CT head scans were normal in 8 of 10 children tested.

The spontaneous EEG spikes were all in the central Rolandic area, and could be consistently evoked by mechanical stimulation of the contralateral hand. The optimal stimulus was a rapid extension flick of the fingers. Computer averaging of these discharges showed a characteristic morphology and topography.

Evoked spikes did not have prognostic significance in our patients. Our data do not support any association between evoked spikes and particular pathology or syndrome including epilepsy, contrary to previous report.

P-123.

Withdrawn

P-124.

Value of Interictal Scalp EEG in Determining Site of Seizure Origin

J. BORGHESI and W.T. BLUME (London, Ontario)

Identification of the epileptogenic focus most responsible for a patient's habitual and medically refractory seizures is the principal concern in evaluating the patient's suitability for surgical intervention.

The study addresses the value of interictal scalp EEG and supplementary laboratory data in providing lateralizing evidence equivalent to that currently supplied by ictal scalp and/or invasive EEG.

Interictal delta and spike activity was analysed in 2 past surgical groups: i) temporal lobectomies (n = 40), ii) frontal lobectomies (n = 20), to ascertain what lateralising features were reliably consistent and

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whether findings differed for the two groups. Whilst delta and spike activity was almost completely ipsilateral to the site of epileptogenesis in Temporal Lobe cases, findings from the Frontal Lobe cases are expected to be more diverse.

Neuroradiology and neuropsychology were also examined to ascertain whether findings were in concordance with the interictal EEG data.

P-125.

Benign Epilepsy with Occipital Spike-Waves: A Family Study

R. KUZNIECKY, B. ROSENBLATT and K. METRAKOS (Montreal, Quebec)

The concept of "Functional Focus" is best exemplified by benign epilepsy with rolandic spikes. Recently, Gastaut has described "Benign epilepsy with occipital spike-waves" (BEOSW) adding a new entity to the group of functional benign epilepsies. The EEG and clinical features have been documented but there is no evidence for a definite genetic component. We studied four siblings, three of which had the typical seizures and four of which had the typical EEG pattern (occipital spike and waves enhanced by eye closure when the patient was young evolving into occipital paroxysmal sharp and slow irregularities as the patient got older).

A family study including 25 relatives in three generations was done. All members were interviewed and 19 had EEG's. Our results showed a typical pattern, characterized by intermittent sharp-slow waves over occipital regions in 5 members (26%). Among the 8 members in the third generation, 3 (37%) had the occipital pattern, where as in the second generation, 2 out of 8 (25%) had the pattern.

These findings suggest that BEOSW may be inherited with an autosomal dominant pattern with variable expression of the seizure disorder and an EEG pattern that is age dependant.

P-126.

Seizures in the Elderly

M.B.M. SUNDARAM (Saskatoon, Saskatchewan)

67 elderly patients over the age of 60 (37 males, 40 females; mean age — 70 years) were newly diagnosed to have seizures during an 18 month period in our hospital. They were prospectively followed for a mean period of 13 months from seizure onset. 57 had at least 1 EEG and 58 had CT scan of brain.

Etiology was unknown in 23 cases (34%). Seizures were partial in 9 (based on history only in 6; from EEG findings in another 3) and generalized in 14; seizures were exclusively nocturnal in 8 of 14 cases with generalized attacks. Number of attacks were 4 or less during the follow-up period in 17 of 23 cases (15 with and 8 without therapy).

Seizures in 16 of 17 tumour patients (metastatic — 7, meningioma — 5, glioma — 4, tuberculoma — 1) were partial. In 12 of them, seizure was the presenting neurological symptom; 5 of these 12 had normal initial neurological examination (4 meningiomas, 1 glioms); however, only 1 of them had normal initial EEG but his seizures were partial by history.

Other etiologies were: stroke — 14 (at onset — 7; as late complication — 6; both — 1), metabolic — toxic encephalopathy — 5, subdural hematoma — 3, Alzheimer's disease — 2, drug-withdrawal — 2 and cerebral contusion — 1.

Conclusions: when seizures begin after 60 years of age i) cause is unknown in approximately ⅓ of cases; seizures in this group are often nocturnal but attacks tend to be infrequent. ii) routine CT scan may not be necessary in those with generalized seizures (based on history and lack of focal findings in EEG) and normal initial neurological examination.

P-127.

"Not All That Meets The Eye . . ."; A Comparison of the Manifestations of Psychogenic Seizures As Described By Sir William Gowers And Video-EEG Telemetry.

S. OPPENHEIMER and R.M. SADLER (London, Ontario; St. John's Newfoundland)

Sir William Gowers' (1845-1915) major contributions to neurology have at least partly been made through his powers of observation and his meticulous recording of clinical symptoms and signs. The accurate diagnosis of psychogenic (PG) seizures is facilitated by such attention to detail and Gowers was one of the first clinicians to differentiate the features of "hysteroid fits" from those of true epilepsy.

Recent technological advances allow the modern clinician to record patients' behavior on videotape while simultaneously monitoring the electroencephalogram (EEG). These recording systems have facilitated the diagnosis of PG seizures and allow detailed analysis of ictal events.

A literature survey was performed and publications describing the behavioral events of PG seizures as proven by simultaneous video-EEG recording were selected for comparison with Gowers' observations.

We conclude that Gowers' observations of "hysteroid" (PG) seizures are in fair agreement with those made with the aid of video-EEG techniques in the following categories: (a) age; (b) predominance of females (but with a sizeable male contribution; (c) nonspecific warnings; (d) iatrogenic precipitation of attacks; (e) motor features of clonic, tonic and co-ordinated movements; (f) common occurrence of eye closure; (g) absence of tongue biting; and (h) extremely rare urinary incontinence. The major areas of disagreement concern (a) frequency of opisthotonic posture; (b) frequency and type of vocalization; (c) duration; and (d) mode of termination. Further, some ictal phenomenon thought to be typical of "hysteroid fits" by Gowers (kicking, thrashing, pelvic thrusting) have been recently demonstrated to occur in partial complex seizures of frontal lobe origin (Williamson PD et al. Ann Neurol 18: 497-504, 1985).

P-128.

Somatosensory Evoked Potentials in Comatose Children

L.J. DE MEIRLEIR and M.J. TAYLOR (Toronto, Ontario)

Somatosensory evoked potentials (SEPs) were performed in 57 comatose children upon admission in the Intensive Care Unit, and were studied in respect to initial neurological status and final outcome. SEPs were recorded over the cervical spine and contralateral sensory cortex in response to median nerve stimulation. The mean age of the patients was 7.5 years (range 1 month to 19 years). They were divided into 5 groups: Trauma (21), Hypoxic-ischemic encephalopathy (9), CNS infection (6), Toxic-metabolic encephalopathy (5), Reye's syndrome (5), and others with coma of various etiologies (11).

SEP results were graded I to IV: normal, increased interpeak latencies or asymmetrical cortical, unilateral or bilateral absent cortical, absent cervical and cortical responses. On admission 40 patients scored on the Glasgow Coma Scale ≤7, 22 survived, but 15 with severe neurological sequellae, and 18 died. Of the 40 patients only one had normal SEPs, while 29 had unilateral or bilateral absent cortical responses. None of the 21 patients who died had normal SEPs. Only 2 of these had mild abnormalities with asymmetrical cortical responses and increased interpeak latencies, while 19 had SEPs grade III and IV. The 10 patients with normal outcome had normal (7) or only mildly abnormal (3) SEPs.

In 34 of these patients auditory brainstem responses (ABRs) were also studied. Of the 12/34 patients who died, 5 had normal ABRs; other abnormalities such as increased interpeak latencies and/or absent waves were equally represented in this group. However, 11/12 of these patients

had severely abnormal SEPs with unilateral or bilateral absent cortical responses.

Repeat testing was done in 33 patients. The SEPs were found to be stable over the intensive care course of the children, except in those with Reye's syndrome.

This data clearly supports the usefulness of SEPs (in contrast to the ABRs) in predicting neurological outcome of comatose children.

P-129.

Selective Brainstem Injury in an Asphyxiated Newborn: Correlation of Clinical, Radiological and Neuropathological Features

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

Several distinct patterns of cerebral injury have been documented in asphyxiated newborn infants. Neuropathological studies in experimental animals and in human infants have demonstrated disproportionate injury to brainstem and thalamus following an episode of acute, total asphyxia. We report the clinical, radiological and neuropathological features of the poorly documented entity of brainstem injury in an asphyxiated term infant.

The patient was a 4300 gram term infant who sustained an episode of acute, total asphyxia at birth. Apgar scores remained at one at 1, 5, and 10 minutes. The child remained comatose and had persistent brainstem dysfunction. The gaze was dysconjugate and the corneal, oculocephalic, oculovestibular and gag reflexes were absent. There was facial diplegia with gaping of the mouth and retrognathia. Marked fasciculations of the tongue were observed and recorded on video tape. There was hypotonia of the limbs and clonus at the ankles. The CT scan of the head demonstrated decreased attenuation in the region of the basal ganglia consistent with hypoxic-ischemic injury. Repeat scan at one month showed focal atrophy of the basal ganglia with isolated dilation of the third ventricle. Neuropathological examination at four months showed infarction and gliosis of thalamus, basal ganglia and brainstem with relative preservation of the cortex.

These observations clearly demonstrate prominent brainstem signs in an asphyxiated infant in whom there was neuropathological evidence of selective thalamic and brainstem infarction. Although this pattern of injury in the newborn is a recognized neuropathological entity, the clinical and radiological correlates are appreciated rarely.

P-130.

Children with Migraine Have Similar Anxiety, Personality Profiles, and Life Events Compared to Their Headache-Free Friends

P.J. COOPER, H.N. BAWDEN, P.R. CAMFIELD and C.S. CAMFIELD (Halifax, Nova Scotia)

Anxiety and stressful life events are thought to be major precipitants of childhood migraine. This unproven assumption was examined by comparing a group of consecutive children referred for evaluation of headache with their same sex and age matched headache-free best friends. Prior to assessment, 39 children (average age 11 years; 20 girls and 19 boys) and their parents completed several standard anxiety scales, the Personality Inventory for Children (PIC), and life events scales. The same scales were administered to the control children and their parents. All subjects (and no controls) met Prensky's criteria for migraine. All were neurologically normal, with no serious chronic disease.

Family unit was traditional in 74% of migraineurs and 85% of controls. 27 patients had a first degree relative with migraine. Headache duration averaged 35 mos. (3-132 mos.). No statistical differences were found between patients and controls, or between the two groups of parents on any of the anxiety or life events scales. Children's anxiety scores were not related to parents' anxiety scores. Personality profiles (PIC) of patients were very similar to controls, differing only with respect to higher ratings for patients on somatic complaints and depression scores ($p<0.001$).

Although these findings may contradict prevailing dogma, we conclude that children with migraine are not more anxious or stressed than their friends. Either childhood migraine is most often triggered by non-stress related factors or, more likely, normal amounts of stress and anxiety lead to the expression of their migraine tendency.

P-131.

Multicore Myopathy and Hypohydrotic Ectodermal Dysplasia: A New Autosomal Recessive Syndrome in an Acadian Kindred

P.R. CAMFIELD, C. GALLIANI, J.B. ROSS, J. KLOTZ and J.P. WELCH (Halifax, Nova Scotia)

Two double first cousins from highly consanguineous Acadian families are described with a unique combination of myopathy and hypohydrosis. Case 1 is a moderately retarded 9 year old boy with moderate proximal weakness (unable to rise from the floor without help). He has never produced sweat or tears and becomes flushed and uncomfortable in moderate heat. Case 2, his 5 year old cousin has mild speech difficulties with mild proximal weakness (unable to jump from the floor). She shows similar heat intolerance and lack of sweat. Weakness has not progressed over 3 years followup. Both have similar facies with long narrow nose, depressed nasal bridge and prominent forehead. Both have lightly scaling skin, fine hair but normal nails and only carious teeth. All parents and sibs have normal strength and sweating.

Investigations were the same in both. Starch iodine testing documented severe hypohydrosis. Normal tests included CPK, chromosomes and skin biopsies (normal sweat glands by light, electron and scanning microscopy). EMG was consistant with a myopathy. Quadriceps biopsy showed multicore myopathy characterized by Z-band streaming.

Ectodermal dysplasia has been associated arthrogryposis, periodic hypokalemic paralysis and congenital insensitivity to pain, but not previously reported with multicore disease. The specificity of multicore myopathy is unknown; some have suggested a neuropathic origin. We postulate that these patients have a previously undescribed autosomal recessive disorder which affects both muscle strength and the ability to sweat.

P-132.

Obstructive Hydrocephalus in Nephropathic Cystinosis

G.M. RONEN, M. FARIDI, W.D. HENEGHAN, P.S. PARFREY and W.D. SPRAGUE (St. John's, Newfoundland)

CNS complications have rarely been recorded in cystinosis patients. Ross and associates (Neurology 32: 1320, 1982) described communicating hydrocephalus and proposed that the deposition of cystine crystals in the meninges interfered with CSF absorption. We describe a 9 year old boy with infantile nephropathic cystinosis, maintained on hemodialysis, who developed obstructive hydrocephalus at the level of the aqueduct. Symptoms consisted of occipital headache, vomiting and periodic coughing developing overnight into coma and a focal right sided motor status epilepticus. CT scan showed dilation of the lateral and third ventricle, a normal sized fourth ventricle, subtle periventricular edema and absence of subarachnoid space. At the time the VP shunt was inserted the CSF pressure was extremely high. The patient slowly regained consciousness but remained with a right sided hemiplegia and dysphasia. Repeat

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CT scan showed decreased ventricular size, prominent sulci on the right and hypodensity involving the whole left hemisphere.

Previous neuropathologic studies have demonstrated early in the course of the disease an abundance of cystine crystals in the choroid plexus. Depositions in the meninges and the brain parenchyma were found at a later date. The hydrocephalus in our case, therefore, could be explained by deposition of cystine crystals with possible inflamatory changes in the aqueduct of Sylvius.

Physicians taking care of cystinosis patients should be aware that both obstructive and communicating hydrocephalus may occur more often as these patients live longer with modern renal care.

P-133.

Familial Autosomal Recessive Hydrocephalus with Sensorineural Deafness

G.M. RONEN, F.C. FRASER, W.D. HENEGHAN, C. HOBEIKA, J.C. JACOB and F.B. MAROUN (St. John's, Newfoundland; Montreal, Quebec)

Inherited hydrocephalus is almost always inherited as an x-linked recessive trait. Autosomal recessive inheritance is extremely rare; its existence has been disputed. We describe a unique familial syndrome with autosomal recessive inheritance, consisting of hydrocephalus, sensorineural deafness and mild to moderate neurodevelopmental retardation. The probands are a sister and brother and a male cousin. The pedigree indicates parental consanguinity in both sibships. Head circumference (HC) exceeded the +2.5 SD in all three. The two males required early VP shunting while the girl's HC stabilized and grew along the +2.5 SD. CAT scan in all three shows significant asymmetric dilation of the laternal ventricles, mildly dilated third and a normal sized fourth ventricle, suggesting aqueductal stenosis. All three have marked sensorineural deafness and subnormal neurodevelopment.

This second report (the first: J. Genet. Hum. 29: 155) of autosomal recessively inherited hydrocephalus due to aqueductal stenosis, associated with sensorineural deafness, indicates not only the existence of this mode of inheritance in hydrocephalus but also suggests an association with sensorineural deafness.

P-134.

Skin Biopsies in Rett's Syndrome

S. NAG and P.M. MACLEOD (Kingston, Ontario)

Rett's syndrome is a disorder affecting females who are apparently normal until 6 to 12 months of age, and then develop progressive loss of motor and cognitive skills, inappropriate social interaction, deceleration of head growth and an inability to communicate. The condition is considered to be a sporadic x-linked dominant mutation lethal in males.

Skin biopsy has proved useful for the diagnosis of many neurological diseases. In this study skin biopsies of eight cases of Rett's syndrome were studied by electron microscopy to determine whether any consistent abnormality occurred which would aid in the diagnosis of this condition. Seven of the eight cases examined and all the controls showed no ultrastructural abnormality of the skin.

Large vacuoles, some empty and some containing fibrillogranular material were seen in the secretory cells of sweat glands in one case of Rett's syndrome. Vacuoles were also noted in fibroblasts and endothelium and in cultured fibroblasts derived from the skin. Although these findings strongly resemble the observations in known storage diseases special stains of paraffin and frozen tissue failed to reveal the nature of the material in the vacuoles and an abnormal metabolite was not detected on urine screening.

Our studies thus far suggest that skin biopsies are not helpful in the diagnosis of Rett's syndrome. Perhaps Rett's syndrome includes a heterogenous group of conditions and the single positive biopsy represents an undiagnosed storage disease.

P-135.

A Longitudinal Study of Short Latency Somatosensory Evoked Responses in Healthy Newborns and Infants

E. LAUREAU, A. MAJNEMER, B. ROSENBLATT and P. RILEY (Montreal, Quebec)

Maturational changes in short latency somatosensory evokes responses (SER) were studied in 18 healthy full term newborns in the first week of life and consequently repeated at two to three months of age. Both median nerves were electrically stimulated individually and evoked responses were recorded at three levels: Erb's point (EP), second cervical vertebrae (CII), and contralateral parietal scalp (C'c). Results of 32 were recorded in all cases. At the parietal level, potentials were present in 85% of cases, absent in 9% and questionable in 6%. Parietal potentials were occasionally noted on one side only. Repeat examinations at 2-3 months of age demonstrated significant maturational changes in the SER. These changes included decreased interpeak latencies (CII to C'c), increased amplitude and markedly diminished dispersion of parietal potentials. In contrast, minimal changes in wave-form configuration and latency were noted at the EP and CII level. These findings most likely reflect myelination and increased synaptic efficiency predominantly in the central sensory pathway. The purpose of this investigation was two-fold: the first objective was to delineate a reliable technique for SERs in newborns that could be applied to the clinical setting. Secondly, normative data was established in newborns and infants as this will help us in accurately differentiating a normal from an abnormal group of neonates.

P-136.

Morphological Characteristics of the Auditory Brainstem Evoked Response (ABR) in Healthy and High Risk Neonates

A. MAJNEMER, B. ROSENBLATT and P. RILEY (Montreal, Quebec)

The auditory brainstem evoked response (ABR) assesses the functional integrity of the auditory pathway and as such, is a useful diagnostic tool in the neonatal intensive care unit. Interwave latencies and amplitude ratios are commonly used as measures of neural transmission, whereas waveform morphology has only been briefly described in the literature. In a prospective study, ABRs were performed on 20 healthy full term newborns and 70 high risk neonates. A scoring system was devised so that morphological characteristics could be quantified objectively. Results show a significant difference in morphology between the two groups. 23.7% of the high risk group had abnormal scores, and the abnormalities typically involved wave III. Follow-up testing at 2 and 6 months conceptional age revealed a persistence of these abnormalities. Furthermore, chi square analysis demonstrated a significant relationship between the neonatal morphology score and adaptive and reasoning skills (as measured by the Griffiths developmental scale) at 1 year conceptional age. Neurodevelopmental testing is presently being carried out to evaluate the relationship between neonatal waveform morphology and developmental scores at 3 years of age.

P-137.

Oligoclonal Banding and Immunoglobulin G Index in Cerebrospinal Fluid of Children

E.H. ROLAND, K. FARRELL, G. LOCKITCH and N. URQUHART (Vancouver, British Columbia)

Neurological disorders in children may be associated with an immunological response, resulting in qualitative and quantitative changes in proteins of the cerebrospinal fluid (CSF). Oligoclonal banding (OCB) and Immunoglobulin G (IgG) Index reflect abnormal intrathecal formation of IgG. This study attempts to define more precisely the diagnostic and therapeutic implications of OCB and IgG Index measurements.

Paired samples of CSF and serum were obtained from 100 children with neurological problems. The samples were examined in blinded fashion with quantitive radial immunodiffusion and high-resolution agarose electrophoresis. The IgG Index [(CSF/serum IgG)/(CSF/serum albumin)] was calculated.

Oligoclonal banding occurred in 10 children with congenital/chronic viral infections (8) and methotrexate leukoencephalopathy (2). The IgG Index was elevated in 30 patients with subacute viral infections (13), focal seizures (7), cerebral tumours (2), miscellaneous (8). A CSF/serum albumin ratio suggestive of abnormal blood/CSF barrier or decreased CSF flow occurred in 8 patients with relapsing polyneuropathy (3), choroid plexus tumours (2), and degenerative disorders (3). Fifty-eight patients had no OCB and normal IgG Index. These included nonspecific mental retardation (8), generalized epilepsy (10), autism (8), and nonspecific headache/behaviour problems (8).

Fifty percent of children with abnormal intrathecal IgG production had progressive neurological symptoms. All patients with disturbed blood/CSF barrier showed a progressive clinical course. Oligoclonal banding or IgG Index did not predict accurately which patients were responsive to steroid therapy. This study demonstrates that OCB and elevated IgG Index may provide adjunctive evidence for chronic inflammatory disease involving the nervous system in children.

P-138.

Immunocytochemical Localization of Brain Edema in a Rat Glioma Model

C.L. FARRELL and R.F. DEL MAESTRO (London, Ontario)

Brain tumours are associated with vasogenic edema which is a critical determinant of morbidity in these patients. Effective patient management is facilitated by an understanding of the mechanisms of production and spread of edema. The C_6 spheroid implantation glioma model is suitable for the investigation of edema because it is a simple and reproducible rat model with pathological similarities to human glial neoplasms. Since edema is characterized by the extravasation of serum protein, the sites of production and subsequent distribution of edema were investigated in this experimental tumor model by the use of markers for serum albumin. Fluorescein-conjugated antibodies against serum albumin were used to immunocytochemically localize the source and regional distribution of serum protein on slices of rat brains containing tumours. In the viable regions of tumour tissue, primarily in the periphery in large tumours, there was abundant fluorescence. There was some fluorescence in the peritumor areas and little or none in the central necrotic portions of the tumour. Around individual vessels in the viable tumour tissue, a decreasing gradient of intensity of fluorescence from vessel to surrounding tumour tissue was observed. In the peritumor tissue, some vessels also demonstrated this pattern. Vessels in the contralateral hemisphere were negative. These results suggested that edema arises predominantly from vessels within the viable tumour mass and that there is a small population of vessels in the peritumor regions which appear to contribute. These conclusions are consistent with data obtained by spectrophotometric measurements of Evans Blue, another marker of serum albumin, in tumour, peritumor and normal tissue extracts, and also with quantitative morphometry studies of the blood-brain barrier characteristics in these tissues.

P-139.

The Possible Cerebral Carcinogenic Effect of Prophylactic Cranial Radiotherapy in Acute Lymphocytic Leukemia

G. L'ESPÉRANCE and P. OUELLET (Quebec City, Quebec)

The treatment of children's acute lymphocytic leukemia (A.L.L.) is generally effective, but can lead to serious complications such as the appearance of secondary neoplasms. We have recently had under our care a nine year old boy who was in remission of A.L.L. with good control of his disease over a period of five years. Unfortunately, symptoms of rapidly progressive intracranial hypertension led to a diagnosis of a frontal glioblastoma multiforme which progressed very rapidly to his death. As this type of tumour is in itself rare among children, we reviewed the pertinent literature and found two similar cases. In view of these findings, it is worth questioning the role of the possible cerebral carcinogenic effects of the prophylactic therapy utilised in A.L.L.

P-140.

Steroid Induced CT Scan Changes in Patients with Recurrent Malignant Gliomas

D.R. MacDONALD, J.G. CAIRNCROSS, J.H.W. PEXMAN and R.K. COATES (London, Ontario)

Adrenocorticosteroid hormones (steroids) are known to decrease the enhancement, mass effect and edema associated with brain tumours. Since clinicians are relying increasingly on the computed tomographic (CT) scan to judge the response of malignant brain tumours to investigational treatments, it is crucial that the magnitude and time course of steroid induced CT scan changes be analyzed. It may be necessary to develop a strategy to distinguish CT scan improvement due to steroids from that due to other treatment modalities. This is especially relevant to the interpretation of phase II chemotherapy studies. At the time of recurrence many patients with malignant brain tumours are given steroids to control symptoms, followed immediately by investigational chemotherapy. The baseline CT scan documenting recurrence is performed prior to steroids. Treatment begins (ie., steroids and antineoplastics) and the CT scan is repeated several months later. CT stability or improvement is attributed to chemotherapy without considering the role of steroids. To address this important clinical concern we have analyzed pre- and post-steroid CT scans in a small group of patients with recurrent malignant gliomas. Our methods and preliminary results are discussed.

P-141.

Interventional Neuroradiography for Symptomatic Spinal Metastases

R.G. PERRIN, J.S. McMAHON, H. GROSMAN and R.J. McBROOM (Toronto, Ontario)

Interventional neuroradiography has evolved as an important therapeutic adjunct in efforts to control pain and reduce hemorrhage in various disorders.

Among the outstanding features of symptomatic spinal metastases are the prominent presenting pain syndrome, and the notoriety for

intra-operative hemorrhage (in our experience, the average blood loss during neurosurgical decompression in two hundred patients with symptomatic spinal metastases was 3.5 litres). These aspects should be amenable to arterial embolization.

We have used pre-operative interventional neuroradiography in the management of four patients with hypernephroma and symptomatic spinal metastases.

In our experience this technique proved useful: (1) to enable pre-operative visualization of the vascular feeding pattern and, (2) in enabling arterial occlusion of various tumour feeders thereby reducing intra-operative hemorrhage. There was no significant benefit for pain control.

P-142.

Photodynamic Therapy of Malignant Brain Tumours: Intraoperative Measurement of Light Penetration Through Brain

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

The degree of tumour cell killing which occurs during the course of photodynamic therapy [PDT] is dependent on the concentration of the photosensitizer in the tumour cells, the light energy absorbed by the cells, and, the inherent cell sensitivity to the photodynamic effect. The degree of tumour cell light energy absorption is in part dependent on the transmission of light through the tissue.

We have measured relative light flux intraoperatively in 6 patients with malignant gliomas who underwent PDT in order to determine the light penetration depth [the distance in mm that results in a reduction to 37% in light intensity] in brain tissue in vivo. An argon dye pump laser was the light source and an inflatable laser coupled balloon was the light delivery system.

For each case the laser was tuned to a wavelength of 630 nm; the wavelength was confirmed with a spectroscope [26-6270 Hartridge revision spectroscope]. The total light energy delivered ranged from 810 to 3888 Joules and the light dose ranged from 15 to 68 J/cm^2.

An optical fiber probe consisting of a single 400 um, cleaved end fiber fixed in a 17-gauge biopsy needle was coupled to the 88XL photometer with a model 150 sensor head. Readings of the detected light flux were taken as the fiber was passed radially into the brain towards the centre of the irradiation volume. In each of the 15 data sets, the regression of the ln relative flux [ln(RF)] on R was well fitted to a straight line. The penetration depth was calculated as the reciprocal slope. The light penetration depth ranged from 1.2 to 4.9; the mean and s.d. was 2.53 $\pm$1.04.

In cases 1-4 the tumours were large and in all but one patient the tumours were recurrent; a subtotal tumour resection was carried out in each case. In these cases the 8 data sets likely represented measurements of malignant astrocytic tumour tissue in vivo. In cases 5 and 6 the tumours were smaller, were not recurrent and had radical surgical resections. In these patients the 7 data sets likely represented measurements of edematous brain in vivo. The mean PD values in the "tumour" group and the "brain" group was 3.16 $\pm$ 1.02 and 1.80 $\pm$ 0.41, respectively [p 0.005]. We attribute this significant difference to the differences in the absorption and scattering properties of brain and tumour.

P-143.

The Effect of Porphyrin Photosensitizers on the Toxicity of BCNU in C57BL/6J Mice

P.J. MULLER and K. CHADA (Toronto, Ontario)

The most widely used agents for PDT are the porphyrin photosensitizers. It has been shown that HPD can cause murine marrow hypercellularity and splenic hypertrophy. We have examined the effect on survival and marrow cellularity of high dose BCNU after HPD or DHE pretreatment in C57B1/6J mice.

The lethal toxicity of the LD50 + 10% dose of BCNU [60 mg/kg] was significantly reduced by pretreatment with hematoporphrin derivative [HPD] when the HPD was administered at least 3 days prior to the BCNU. HPD administered 1 or 2 days prior to BCNU or after BCNU had no effect. The % death rate was reduced from 80% to 0% when HPD was administered 7 and 5 days prior to BCNU. No alteration of the lethal toxicity rate of BCNU at doses of 80, 60, and 40 mg/kg were identified with dihematoporphyrin ether [DHE] pretreatment although some increase in median survival was noted in 2 groups. A significant reduction of marrow cell depletion was found at low dose schedules. High doses of DHE resulted in marrow depletion. Both HPD and DHE altered the toxicity of BCNU.

Should porphyrin photosensitizers, which alone have little toxicity, prove to protect against nitrosourea toxicity then an important dose limiting factor [myelotoxicity] could be altered if no reduction in the tumoricidal activity occurs.

P-144.

Angioendotheliosis (NA): An Elusive Diagnosis

A. SHUAIB and W.J. MURPHY (Calgary, Alberta)

Only 24 cases of NA (a malignancy with proliferation of neoplastic cells in blood vessels at multiple sites) with CNS involvement have been reported. The diagnosis was made ante mortem in only five patients, always after a meningeal-brain biopsy. We report a case with an unusual, rapidly progressive course with no focal neurological signs until late in her illness.

A 77 year old female was admitted with a three week history of severe constant headache and transient episodes of left-sided numbness and inability to speak. Neurological examination, cranial CT and routine lab work were normal. Cerebrospinal fluid (CSF) exam showed an increased protein (1.98g/L) and (19 WCB/mm^3). Intermittent episodes of aphasia, confusion and agitation without localizing neurological findings between episodes occurred over the next four weeks. Repeat CT and CSF exam were unchanged. An angiogram showed only a six millimeter aneurysm of the posterior communicating artery. One week later, a partial third nerve palsy, internuclear ophthalmoplegia and skew deviation occurred, but a repeat cerebral angiogram and CT showed no new abnormality. A further CT scan nine weeks after admission showed three hypo-dense lesions, and a biopsy was done. The meningeal biopsy was inconclusive, but the brain biopsy was compatible with NA. Her hospital course included recurrent respiratory failure, pulmonary emboli, abdominal pain, silent myocardial infarction and progressive renal failure. Treatment included high dose steroids and a partial course of radiation therapy. Prior to death, mid position fixed pupils and ophthalmoplegia suggested a midbrain lesion. Autopsy examination showed NA at multiple sites, and a hemorrhage in the upper brainstem. No primary tumour could be found.

In the appropriate clinical setting, awareness of the possibility of NA and early biopsy of CT demonstrated brain lesions may lead to early diagnosis.

P-145.

Brain Tumours Presenting as TIA's and Strokes

D. KONDZIOLKA, M. BERNSTEIN, L. RESCH and C.H. TATOR (Toronto, Ontario)

A retrospective review was conducted on 685 randomly selected charts of patients with brain tumours (excluding pituitary) treated

surgically between 1970 and 1985. Attention was focussed on patients presenting with clinical symptoms and signs of occlusive cerebrovascular disease referable to the cerebral hemisphere with the tumour. Patients either had transient ischemic attacks (TIA's) characterized by hemisensory symptoms, hemiparesis, or dysphasia lasting less than 24 hours, or completed stroke with variable recovery. Patients presenting with a seizure or sudden obtundation suggesting a hemorrhage, were excluded.

Seventeen of the 685 patients (570 supratentorial tumours, 115 infratentorial tumours) presented with occlusive cerebrovascular disease as the initial working diagnosis. The mean age of the patients was 61 years (cf. 53 years for the 685). There were 10 males and 7 females. Eleven patients had TIA's, of which 8 were single and 3 multiple. The TIA's were sensory in 5 cases, motor in 2, dysphasia in 3, and mixed in one. There was no case of amaurosis fugax. Five patients had completed strokes — 3 motor, one dysphasia and one mixed. One patient had a single sensory TIA followed two days later by unresolving dysphasia. Tumour pathology was glioblastoma in 9 cases, meningioma in 6, oligodendroglioma in one, and metastatic squamous cell carcinoma in one. The mean interval from the initial cerebrovascular presentation to craniotomy for tumour was 8.0 months (8.0 months for meningiomas, 3.3 months for glioblastomas, 4 years for the oligodendroglioma, one month for the squamous carcinoma). Sixteen of the 17 patients had angiograms of which 7 revealed plaques of the extracranial internal carotid artery.

In summary, 3% of patients with supratentorial tumours in the present series presented with a clinical history highly suggestive of occlusive cerebrovascular disease. This may represent the coincidence of two separate disease processes, or the ability of a neoplasm to transiently or permanently alter the regional metabolism and/or blood flow of the brain.

P-146.

The Use of the Intraoperative Monitoring of Somatosensory Evoked Potentials to Determine the Need for Temporary Bypass Shunting in Patients Undergoing Carotid Endarterectomy

F. GENTILI, W.M. LOUGHEED, K. YAMASHIRO, H. GHATE and C. CORRADO (Toronto, Ontario)

The purpose of the present study was to determine the value of intraoperative monitoring of somatosensory evoked potentials (SSEP) in detecting impending cerebral ischemia during vascular clamping and thus the need for temporary bypass shunting in patients undergoing carotid endarterectomy.

Intraoperative monitoring of SSEP has been carried out utilizing a standard protocol and analysis of data in 90 patients. Based on normative intraoperative data, tolerance limits and a grading system (I-IV) for SSEP changes was established. In patients with minimal SSEP changes (I and II), 3 had postoperative deficits, 2 of which were delayed (6 days, 1 week). Of patients with Grade III and IV changes, 8 had postoperative deficits. In patients with Grade I and II changes at the time of clamping, there was no significant difference in outcome regardless of whether a shunt was used. Of patients with Grade III and IV changes at the time of clamping, 4 of 5 without shunting had postoperative deficits. Of 20 patients with Grade III and IV SSEP changes at clamping that were subsequently shunted, 14 reverted to Grade I and II with no postoperative deficit. Of 6 with persistent Grade III and IV changes, 4 showed postoperative deficits.

The results suggest that Grade III and IV changes which could not be reversed with shunt placement or blood pressure manipulation are a significant prognostic indicator for postoperative deficit. Comparing SSEP recordings with EEG studies in 10 patients revealed that SSEP is the more sensitive indicator for cerebral ischemia. At present, SSEP changes are being used as the sole criteria for temporary shunting during carotid endarterectomy. In our last 40 patients using these criteria, we have had no postoperative deficits and only 15% have required shunt placement.

P-147.

Endarterectomy Without Shunts and Electrophysiologic Monitoring

K. REDDY and M. WEST (Winnipeg, Manitoba)

The use of intraoperative shunts, patch grafts, and electrophysiologic monitoring methods in carotid endarterectomy is still very controversial. A prospective series of 100 carotid endarterectomies in 89 patients, performed over a three year period by a single surgeon, is presented here. All but 5 procedures were performed for transient ischaemic attacks, reversible ischaemic neurologic deficits, or minor strokes. All patients were preoperatively grouped according to the Mayo Clinic System, and 65% of the patient population was found to be in the III and IV groups. All the procedures were performed under general anaesthesia, without using intraoperative shunts, electrophysiologic monitoring methods and patch grafts. Mild hypervolemic hemodilution was utilized to improve perioperative cerebral oxygen delivery. Results are analysed in terms of major and minor morbidity, major morbidity being that interfering with active daily living. There were no mortalities in this series. One patient had permanent stroke due to technical problems. Details of the minor morbidity are discussed. Our results confirm that for a successful outcome in carotid endarterectomy, intraoperative shunts, patch grafts and electrophysiologic monitoring are not essential. The hemodilution may have had a positive influence on the results of this series.

P-148.

Cerebral Blood Flow and Metabolism Following Extracranial to Intracranial Bypass

R. LEBLANC, J.L. TYLER, G. MOHR, E. MEYER, M. DIKSIC, L. YAMAMOTO, A. HAKIM, L. TAYLOR and S. GAUTHIER (Montreal, Quebec)

Pre- and postoperative positron emission tomography (PET) was performed in 6 patients undergoing extracranial to intracranial (EC-IC) bypass for the treatment of symptomatic extracranial carotid occlusion. The 6 males were aged 52 to 68 years and had transient ischemic attacks (5 cases), amaurosis fugax (2 cases), and completed stroke with good recovery (1 case). PET was performed within 4 weeks prior to surgery and between 3 to 6 months postoperatively using 15-O-labelled O-2, CO-2, and CO and 18-Fluorine-Fluorodeoxyglucose. Cerebral blood flow (CBF), cerebral blood volume (CBV), cerebral metabolic rates for oxygen and glucose (CMRO-2 and CMRGlu) and the oxygen extraction fraction (OEF) were measured.

Preoperatively, compared to elderly control subjects, patients had increased CBV, a decreased CBF/CBV ratio, and decreased CMRO-2 bilaterally. These findings indicate hemodynamic compromise and depressed oxygen metabolism. The CMRO-2/CMRGlu ratio was below 5.5 in 5 cases, possibly indicating anaerobic metabolism. CBF was decreased only in 1 patient with bilateral carotid occlusion, OEF, CMRGlu, and CMRGlu/CBF values were variable.

All bypasses were patent and all patients were asymptomatic following surgery. Postoperatively PET showed decreased CBV and an increased CBF/CBV ratio bilaterally indicating improved hemodynamic status. This was not associated with increased CMRO-2 except in patients in whom the postoperative OEF also increased. The CMRGlu and

CMRGlu/CBV ratio were increased in 5 patients. Changes in CBF, CMR-02, OEF and CMRO-2/CMRGlu ratio were variable. One patient with progressively decreasing CBF and CMRO-2 and progressive dementia documented by serial neuropsychological testing had improved CBF, CBV and CMRO-2 postoperatively, concomitant with improved neuropsychological functioning.

Symptomatic carotid occlusion is associated with bilateral hemodynamic compromise, reflected by an increased CBF/CBV ratio, and depressed oxygen utilization. Revascularization improves the hemodynamic status but changes in oxygen metabolism are variable.

P-149.

Current Management of Cerebral Arteriovenous Malformations

R. LEBLANC and J. THÉRON (Montreal, Quebec)

We report our recent experience with the treatment of cerebral arteriovenous malformations (AVM) with reference to: 1) Cortical mapping under local anesthesia for the treatment of AVMs related to eloquent brain regions (7 cases); 2) Intra-operative fluorecein angiography with videotaped replay to identify major feeders and normal cortical arteries assuring that blood supply to eloquent cortex is preserved (6 cases); 3) Pre-operative and intra-operative embolization to reduce the size of the nidus and the risk of intra-operative bleeding (2 cases); 4) Embolization of inoperable AVMs to reduce intracranial shunting and arrest symptomatic cerebral ischemia (4 cases).

One or more of these techniques were used in 6 males and 6 females aged 18 to 62 years (mean: 37.7) who presented with intracranial hemorrhage (6 cases), seizures (5 cases), and headaches (1 case). Four patients had a focal neurological deficit, one had a progressive organic brain syndrome and one had depressed level of consciousness following cerebral hemorrhage. Seven patients had a normal neurological examination. Ten AVMs were larger than 5 cm. Seven involved the dominant hemisphere and 2 were in the corpus callosum. Eight patients had surgery and the AVM was completely excised in 5 cases. Surgery was complicated by normal perfusion pressure breakthrough bleeding in 1 case and there was worsening of a previously severe hemiparesis in another. Four AVMs were embolized only. This partially reduced the size of the lesion in all cases and improved hemiparesis in 1. There were 2 cases of transient neurological deficit and 2 cases of mild permanent focal neurological deficit in the embolization group.

We conclude that the current armamentarium of endovascular and surgical techniques can satisfactorily be used in the treatment of some complicated AVMs.

P-150.

Post-Traumatic False Aneurysm of the Superior Cerebellar Artery

J.-L. CARON and R.P. POKRUPA (Montreal, Quebec)

Traumatic cerebral aneurysms occur mainly after severe blunt and penetrating head injuries. For them to occur on the posterior circulation is unusual and even more so secondary to a minor blunt head injury. A case is described of a false cerebral aneurysm located on a branch of the rostral trunk of the superior cerebellar artery in the ambient cistern. Four days following a blow to the occiput, without loss of consciousness, the patient presented with a subarachnoid hemorrhage (SAH) and acute hydrocephalus. Initial angiography appeared normal, however an examination 16 days later revealed the aneurysm which appeared mycotic. At operation, the aneurysm was between the inferior colliculus and the fourth cranial nerve, beneath but closely apposed to the tentorial edge. Its wall was composed of layers of clot. The feeding artery was clipped. Because of the history, location and absence of an infectious etiology, we attribute this aneurysm to trauma. The cerebral incisura is thus identified as a potential site of anatomic vulnerability for cerebral vascular injury following minor blunt head trauma. A discussion of the pathophysiology and a review of the literature are presented.

P-151.

Lymphocytic Adenohypophysitis Presenting as Pituitary Tumour

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Lymphocytic adenohypophysitis is an uncommon disorder in the spectrum of pituitary disease. It occurs exclusively in women, often during pregnancy or the postpartum period and can mimic the clinical picture of a pituitary adenoma.

Fewer than 20 cases have been reported in the literature. We report 2 cases of lymphocytic adenohypophysitis and review the pathology, etiology, and immunology of this disorder.

The diagnosis should be considered in a patient who presents clinically with a nonfunctioning pituitary tumour and evidence of hypopituitarism.

P-152.

A New Technique for Posterior Cervical Fusion

E.G. DUNCAN, H. SCHUTZ and T. MINAS (Toronto, Ontario)

A new technique for posterior cervical fusion is described. Following exposure of the laminae of the vertebrae to be fused Kirshner wires are passed through the bases of the spinous processes above and below the level of the proposed fusion. The wires are trimmed so that 1-2 cm lengths protrude bilaterally. Fixation is then achieved by a figure-of-eight technique employing heavy (16) gauge wire. The procedure is completed by laying cortical slab bone grafts harvested from the iliac crest onto the suitably prepared laminae.

This method has several advantages over those presently in use. Firstly, sub-laminar dissection and passage of wires with the potential for spinal cord damage is avoided. Secondly, immediate internal fixation of the unstable segments is obtained without the disadvantages of techniques using acrylic. Thirdly, because of the arrangement of the Kirshner and figure-of-eight wires rotational and lateral as well as antero-posterior stability is achieved. Finally, because a heavy gauge wire is employed the internal fixation is strong enough to allow immediate post-operative mobilization without external fixateurs. Only light cervical ruffs are used, chiefly for patient comfort.

The technique is described in detail with intra-operative pictures to illustrate the technique. A series of twelve patients operated on over a five year period are presented and the indications, complications and results of this method discussed.

P-153.

Laser Surgery of Extramedullary and Intramedullary Spinal Cord Lesions

N.A. RUSSELL, B.G. BENOIT and V.F. DA SILVA (Ottawa, Ontario)

We have used a CO2 laser unit combined with the operating microscope in the treatment of twenty-three extramedullary and intramedullary

spinal cord lesions. The extramedullary group totalled fifteen, comprising seven meningiomas, three schwannomas, one exophytic ependymoma and two metastases. The eight intramedullary lesions included one ependymoma, one metastasis, two lipomas and four syringes.

In extramedullary tumours the technique involves coagulating the surface with a low power defocused beam. This causes capsular shrinkage which tends to retract the tumour away from the spinal cord. The capsule is then incised using a focused beam of slightly higher power. Removal proceeds using a combination of laser vaporization and ordinary instruments. Tumour remnants are efficiently destroyed by the laser. In no case was there post-operative neurologic deterioration. One meningioma recurred after four years and was again removed. In the intramedullary tumours the cord was incised with a focused beam, the tumour delivered and the remnants vaporized. One diastematomyelic spur was easily vaporized, there being no need to retract the surrounding cord. Four syringes were fenestrated. The laser was not helpful in treating two lipomas.

We conclude that the CO2 laser is useful as an adjunct in the surgery of various intradural spinal cord lesions. It facilitates the removal of those tumours in less accessible locations. Manipulation of the spinal cord is minimized. However, on the basis of this experience, we cannot describe it as being essential, since all of these cases could have been adequately managed by conventional techniques.

P-154.

Surgery of Lumbar Discs and Lumbar Stenoses: A Complex Venture

A. GODON (Montreal, Quebec)

Much remains unknown about the physiology and the pathophysiological mechanisms of the lumbosacral spine in disease.

Surgery remains but one of the alternatives in treating mechanical lumbosacral problems. Other forms of treatment are now often more effective.

Choosing patients for surgery remains of utmost importance, and specific criteriae and approaches have been developed by the author over the years.

Three specific indications do remain for surgery:

1. *The sequestrated acute one level* lumbar disc herniation with its clinical, physiological and neuroradiological correlations.
2. *Central* spinal stenosis (congenital, acquired, mixed) with intermittent secondary claudication of the cauda equina.
3. *Lateral* spinal stenosis (mainly acquired) with secondary unilateral claudication.

Clinical and precise neuroradiological examinations are important adjuncts. Adding the surgical microscope to the surgical procedure has greatly lessened operative trauma and improved results.

The use of the scalpel in solving low-back related neurological conditions is becoming indeed more and more rare.

The author will also mention the advantages of multi-disciplinary approaches and will dwell upon a nine year experience in the use of neurostimulators for pain, with the help of Pain Clinics.

P-155.

Demographic and Medical Characteristics of Adult Head Injuries in a Canadian Setting

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This study consisted of a review of the charts of head-injured patients who had been admitted to Sunnybrook Medical Centre in either 1978 (N = 219) or 1982 (N = 268). The purpose was to describe the demographic characteristics of this patient population as well as to describe various aspects of their medical and surgical treatment in hospital. We report information on frequency of occurrence by age and sex, type of injury, length of stay, frequency and type of extracranial complications, mortality, and (for 1982) Glasgow Coma Scale distribution. In addition, some of the psychosocial correlates (such as use of alcohol and the possible role of suicidal intent at time of accident) of these groups are described. These data are compared to those of three previous Canadian studies of head injury in Canadian adults.

P-156.

Motor and Somatosensory Evoked Potentials Recorded from the Rat

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

Motor and somatosensory evoked potentials (MEP and SSEP) were recorded from 20 normal rats. MEPs were elicited by applying constant current anodal stimuli to the sensorimotor cortex (SMC). The responses to the stimuli were recorded from *Pt/Ir microelectrodes stereotactically inserted into the spinal cord at T10 (MEP-C) and from a bipolar electrode placed on the contralateral sciatic nerve (MEP-N). A total of 512 MEP responses were averaged on a Cadwell 8400 signal averager. SSEPs were elicited by stimulating the sciatic nerve and recorded from the T10 cord and the contralateral SMC. A total of 1024 SSEP responses were averaged.

The grand mean MEP-C consisted of an initial D wave (mean latency 1.25 ± .08 ms and conduction velocity 66.7 m/s), and 4 subsequent I waves, I1-I4. The threshold for eliciting the MEP-C was a 4 mA pulse, 50 us in duration. The response amplitude increased and the latency decreased with increasing stimulus intensity. The MEP-N required stimuli of higher current and wider pulse width for a response to be elicited. The initial positive wave of the MEP-N (mean latency 3.09 ± .19 m/s) travelled with a conduction velocity of 55.0 m/s) and was followed by several slower components which were attenuated by repetition rates exceeding 8.2 Hz. The SSEP consisted of 7 peaks: P1, 3.47 ± .24 ms; P2, 7.33 ± .81 ms; N2, 13.69 ± 2.11 ms; P3, 30.75 ± 5.79 ms; N3, 42.30 ± 2.65 ms; and P4, 58.34 ± 2.95 ms. Sectioning of the dorsal columns of the cord markedly attenuated the SSEP while sparing the MEP. Complete cord transection abolished both the MEP and SSEP.

This is the first systematic study of both the MEP and SSEP in the rat, and indicates that combined recording of these two modalities should prove useful in assessing the functional integrity of the motor and sensory tracts following experimental spinal cord injury.

*Platinum-Iridium

P-157.

Carbonic Anhydrase Activity in the Normal and Injured Peripheral Nervous System of the Rat

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The carbonic anhydrase (CA) reactivity of primary neurons and axons was studied in the rat peripheral nervous system, before and at various times after surgical procedures including transection of the spinal cord, unilateral removal of dorsal root ganglia (DRG), and section of ventral, dorsal roots or spinal nerves. The CA-reactivity in

medium and large size DRG neurons was not affected by dorsal rhizotomy but rapidly diminished after a spinal nerve section. Dorsal root reactive fibers were myelinated and included all calibers except the smallest range. No enzymatic activity was found in spinal cord motoneurons, despite the presence of CA-stained axons in ventral roots. These most likely represented gamma motor axons, according to their size and their disappearance after a segmental cord lesion or in the distal segment of a ventral root after section. CA-stained sympathetic cells were not seen in the superior sympathetic ganglia, but were found scattered in the thoracic, lumbar and caeliac ganglia.

P-158.

Effect of Cortical Lesions on Striatal D_2 Dopamine Binding Sites: Autoradiographic Studies

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(Halifax, Nova Scotia)

In addition to differing pharmacologically, D_1 and D_2 dopamine receptors differ in anatomical location; it appears that D_1 dopamine receptors are located post-synaptically. D_2 dopamine receptors are also found post-synaptically but a substantial number of D_2 receptors are also reported to be found presynaptically on glutamatergic terminals. Evidence for this is both direct and indirect. Unilateral decortication produces an approximately 35% decrease in the density of D_2 dopamine binding sites as measured using *in vitro* binding of ^{3}H-spiroperidol displaced with (+)-butaclamol. In support of the direct evidence for pre-synaptic D_2 receptors on glutamatergic fibres originating in the cortex, activation of dopamine receptors inhibits calcium-dependent glutamate release from rat striatal slices *in vitro*. Furthermore, these D_2 receptors become supersensitive after destruction of the nigro-striatal pathway. Drugs effective in both Parkinsonism and schizophrenia appear to act on D_2 and not D_1 receptors. Knowledge of the precise distribution of D_2 receptors is therefore of importance. Autoradiographic localization of D_2 receptors was studied in serial sections from 3 hemidercorticated rats. [^{3}H]-Spiroperidol was used to label D_2 sites and specific labelling was defined using 10 μM domperidone. Semi-quantitative microdensitometry was carried out using a computer-aided densitometer. The average loss in D_2 sites on the decorticated side was about 30% in reasonably good agreement with the value (38%) obtained in homogenate binding studies from our laboratory. However, microdensitometry on autoradiograms permitted us to confirm the heterogenous distribution of D_2 receptors within the striatum and to show, for the first time, that a large part of the loss of D_2 receptors after decortication is from dorsolateral regions of the striatum. These regions are, not surprisingly, heavily innervated by fibres of the corticostriatal pathway. These studies confirm for the first time autoradiographically the loss of D_2 receptors. This work was supported by the MRC, the Parkinson Foundation and Dalhousie Medical Research Foundation.

P-159.

A Comparison of the Effects of Carbon Monoxide Intoxication and Low Oxygen Gas Mixtures on Cerebral Biogenic Amine Metabolism

V. MacMILLAN (Toronto, Ontario)

The effects of 1% CO on cerebral biogenic amine metabolism was studied by measurement of cerebral hemisphere contents of 5-hydroxytryptamine (5-HT), 5-hydroxyindoleacetic acid (5-HIAA), dihydroxyphenylalanine (DOPA) and dopamine (DA). The results indicated that 1% CO is associated with an increased cerebral hemisphere content of DA. In CO animals treated with the carboxylase inhibitor, 3-hydroxybenzyl hydrazine, the rate of tyrosine hydroxylation was not significantly altered. This combination indicates that CO either reduces DA release or inhibits the deamination of DA.

In decarboxylase inhibited CO animals the rate of tryptophan hydroxylation was reduced. When the duration of exposure to a given range of arterial oxygen content was matched to that of a group exposed to 5% O_2, the rates of tryptophan hydroxylation were equivalent. Since tryptophan hydroxylation is a linear function of tissue oxygen tension, these results indicate that at a given arterial total oxygen content the tissue oxygen tension and supply are equivalent in low oxygen or CO hypoxia.

P-160.

Neurofilament Antigen Expression in the Rat Cerebral Cortex: Differential Sensitivity to Hypothyroidism

A.V. PLIOPLYS, C. GRAVEL and R. HAWKES (Quebec City, Quebec)

Neurofilaments are an integral component of the cytoskeleton and play a central role in establishing and maintaining neuronal form. In particular, high neurofilament concentrations are characteristic of many classes of axons in the central nervous system. Isolated neurofilaments from rat brain consist of three distinct polypeptides with apparent molecular weights 210K, 160K and 68K. A murine monoclonal antibody, mabN210, has been produced which specifically recognizes an epitope associated with the high molecular weight subunit and this antibody has been used to explore the regulation of neurofilament expression during brain development. It has been shown that in the rat cerebellar cortex, the expression of mabN210-immunoreactivity in basket cell axons is severely suppressed in hypothyroidism while neurofilament antigen expression in other cerebellar axons seems not to require thyroid hormones (Can. J. Biochem. Cell Biol. 63 (1985): 564-576). In view of the well-known cortical deficits in hypothyroidism, these studies have now been extended to include the developing rat cerebral cortex and selected cortical afferent and efferent axons. In hypothyroid rats there is a marked suppression of mabN210-immunoreactivity in the cerebral cortex and corpus callosum and, to a lesser extent, there is a reduction in staining in the internal capsule. By contrast, hypothyroidism did not reduce mabN210-immunoreactivity in the lateral olfactory tract or the stria medullaris. In rats, serum thyroid hormone starts to rise to adult levels on postnatal day 4. It appears that axons that have attained their mature distribution prior to the onset of thyroid hormone expression are not affected by hypothyroidism whereas mabN210-immunoreactivity is suppressed in those axonal tracts that reach a mature distribution after P4. This work was supported by grants to R.H. from the Medical Research Council of Canada and Fonds de Recherche en Paralysie cérébrale, by a M.R.C. fellowship to A.V.P. and by F.C.A.C. studentship to C.G.

P-161.

Applications of Quantum Mechanics to the Theoretical Prediction of a Putative Endogenous Antiepileptic Peptide

D.F. WEAVER (Halifax, Nova Scotia)

The pathogenesis of idiopathic epilepsy remains obscure. Many workers have implicated the role of "endogenous anticonvulsants", and there have been numerous attempts to isolate such compounds. Indoles, purines, prostaglandins and β-carbolines have been put forth as possible candidates. Spero has suggested an oligopeptide (MW ~ 500) capable of binding to the phenytoin receptor site (Spero, Lancet, 2, 1319, 1982). An alternative approach to isolating an endogenous anticonvulsant experimentally is to predict its structure theoretically.

To achieve this goal, the electronic and geometric properties of a

series of heterocyclic (hydantoins, succinimides, oxazolidinediones) and acyclic (amides, carbamates, biurets) anticonvulsants were determined theoretically using a CNDO/2 quantum mechanical method (Pople, J. Chem. Phys., *43*, 5129, 1965). Physiochemical parameters, such as the octanol-water partition coefficient also were determined theoretically (Klopman, J. Comp. Chem., *6*, 28, 1985). A computational pattern recognition approach was devised to search these descriptors, and thus to define a region of structural commonality. Having ascertained the morphology of the antiepileptic bioactive surface, peptides with similar conformational properties were then designed. A family of cyclic dipeptides (diketopiperazines) was synthesized to model the putative endogenous antiepileptic peptide. The properties of these diketopiperazines were compared to a recently designed family of antiepileptic linear dipeptides (Weaver and Wolfe, *in preparation*) as well as to known neuropeptides. Finally, a similar semi-empirical quantum mechanical approach was used to investigate the properties of a receptor molecule capable of binding this putative endogenous antiepileptic peptide.

P-162.

Ependyma of the Central Canal of the Rat Spinal Cord: Normal and Pathological

K. REDDY, J.E. BRUNI and W.A. ANDERSON (Winnipeg, Manitoba)

The ependymal lining along the length of the central canal was examined in untreated S/D rats and its response to injury of the thoracolumbar (TL) cord determined. The central canal was lined for the most part by a single layer of uniformly arranged cuboidal-columnar ependymal cells with large basally located nuclei and apically displaced organelles. Prominent membrane fusions and condensations of filaments were consistent features of the apical region of the cells. Their basal poles terminated bluntly on the subjacent neuropil and occasionally (1-5 cells/section) were drawn out into radially directed processes. Experimental animals received either a small unilateral scalpel incision in the lateral funiculus of the TL cord or a puncture wound in the dorsolateral medulla that did not impinge on the ependyma and were sacrificed from 2-21 dpo. Randomly selected lesioned and control rats received colchicine (0.2 mg/100 g) s.c. 6 h prior to sacrifice at 1-4 dpo. In rats with TL lesions, the lumen of the central canal was collapsed and lined by irregularly contoured ependyma which was multilayered in appearance. Ependymal cells were often radially elongated and possessed filament-filled basal processes. Compared to sham controls, the number of cells lining the lumen was significantly reduced at 2 and increased at 3 dpo. Daily mitotic rates among ependymal cells of lesioned rats reached a maximum of 3.34% at 2 d compared to 0.21% and 0.28% in intact and sham controls respectively. Mitotic activity declined progressively thereafter and approached control values by 4 d. A similar but less marked pattern of proliferative activity was seen 5 mm distal to the lesion site in the cord but essentially no proliferative activity was observed in fourth ventricular ependyma of rats with comparable lesions in the medulla. Proliferation of ependyma in the rat spinal cord, unlike the fourth ventricle, is a significant reactive event triggered by localized injury and elucidation of the factors involved merits further study.
(Supported by a grant from the MRC of Canada.)

P-163.

The Release of Arachidonate from Phospholipids of Red Cells in vitro and in Brain in vivo

R.R. BAKER and H.-y. CHANG (Toronto, Ontario)

The pathology associated with brain hemorrhage may be related to the breakdown of red blood cells in nervous tissue. The release of arachidonic acid from red cell lipids may lead to the generation of icosanoids or other potentially damaging derivatives of arachidonate in brain. To study the catabolism of red blood cell lipids, red cells were isolated from rat blood and were labelled in vitro in incubations with ^{3}H arachidonate. After 60 minutes at 37°C 9-26% of the arachidonate was incorporated into the complex lipids of the red cells. The free arachidonate was removed by washing the red cells with saline containing bovine serum albumin. Of the radioactive complex lipids, phospholipids accounted for > 95% of the label and of these, phosphatidylcholine possessed the most radioactivity (70-76%). When the labelled red cells were incubated in Krebs ringer-glucose or serum at 37°C there was a release of radioactive free fatty acid with time until this accounted for 25-42% of the total red cell radioactivity, after 16h. The increased levels of radioactivity in the free fatty acid could be accounted for largely by decreases in red cell phosphatidylcholine labelling. The radioactive red cells were also injected into rat brain and after sacrifice, a decline in phosphatidylcholine radioactivity was seen in brain. Radioactive fatty acid did not accumulate in brain but was recycled into other phospholipids. The results indicate a release of arachidonate from red cell lipids in vitro and in vivo.
(Supported by the Heart and Stroke Foundation of Ontario.)

P-164.

Incorporation of Arachidonic and Docosahexaenoic Acids into Bis (Monacylglycero) Phosphate and Other Lipids of Fibroblasts from Control and Neimann-Pick Subjects

J.R. WHERRETT and S. HUTERER (Toronto, Ontario)

Accumulation of the lysosomal phospholipid bis (monocylglycero) phosphate (BMP) occurs in inherited and acquired phospholipidosis. To further characterize disturbances in metabolism of BMP, the incorporation of fatty acids into complex lipids of mutant and control fibroblasts was studied. Following incubation of cells in serum-free medium with either 5uM ^{14}C arachidonic or ^{14}C docosahexaenoic acids phospholipids and neutral lipids were readily labelled. After 60 minutes, the distribution of arachidonic acid label was: phosphatidylcholine (PC) 51%, phosphatidylethanolamine (PE) 12%, phosphatidylinositol (PI) 9.5% and BMP 2.3% and the distribution of docosahexaenoic acid label was 36, 19.5, 2.6 and 10.3% respectively. PI had the highest specific activity when arachidonic acid was added, whereas BMP (1.3% of total phospholipid P) had the highest when docosahexaenoic was added. After incubation prolonged to 21 hours, the proportion of arachidonic acid label had fallen in PC and BMP to 42 and 0.7% and had increased in PE and PI to 30 and 12.5%. In comparison, the proportion of docosahexaenoic acid label had fallen in PC and PI to 20 and 2.2% and increased in PE and BMP to 45.1 and 12.7%. In cultures from 3 Niemann-Pick phenotypes incubated for 60 minutes, uptake and distribution of fatty acid label was similar to control cultures. After 21 hours of incubation, distribution of label was also similar to controls except that in cultures from types A and B but not C, the proportion of label in BMP was elevated, in the case of arachidonic acid to the value observed at 60 minutes and in the case of docosahexaenoic acid to a value greater than that at 60 minutes. These findings demonstrate highly selective incorporation of exogenous docosahexaenoic acid into BMP of fibroblasts and suggest decreased deacylation-reacylation reactions involving polyunsaturated fatty acids of BMP in those mutants that have a deficiency of lysosomal lipid phosphodiesterase.

P-165.

Counts of Corticospinal and Rubrospinal Neurons Reflect Severity of Spinal Cord Injury

M.G. FEHLINGS, R. MIDHA, C.H. TATOR, J.A. SAINT-CYR and A. GUHA (Toronto, Ontario)

This paper describes an objective, quantifiable technique for assaying the severity of spinal cord injury. Twenty-one rats underwent a C7-T1

laminectomy: 12 received a C8 spinal cord clip compression injury with forces of either 2.3, 16.9 or 53.0 gm; 4 had cord transection at C8; and 5 had no cord lesion. Post-operative clinical neurological assessment was performed by the inclined plane method. At 4 weeks the spinal cord injured rats underwent a T10 transection and insertion of a Gelfoam pledget impregnated with horseradish peroxidase (HRP). HRP was similarly administered to 9 normal rats. Longitudinal sections of the spinal cord encompassing the injury site were stained with luxol fast blue and coronal sections from the cerebrum and midbrain were processed for HRP reactivity with tetramethylbenzidine. Labelled corticospinal and rubrospinal neurons were counted in every 6th section to derive a cortical score (CS) and a red nucleus score (RNS) for each animal.

The CS decreased with increasing injury severity in a dose dependent fashion ($P < .0001$). However, only the animals injured with the 53.0 gm glip had a significantly lower RNS than the other groups ($p < .0006$). The degree of preservation of the dorsal columns at the injury site correlated with the CS, whereas the RNS was related to the degree of preservation of the lateral columns. Counts of rubrospinal neurons, but not corticospinal neurons, correlated closely ($r = 0.96$) with the inclined plane results, suggesting the importance of non-pyramidal tracts in modulating gross motor function. Thus, counts of corticospinal and rubrospinal neurons are useful for quantifying the severity of spinal cord injury. The method should be helpful in assessing the value of various therapeutic modalities for this condition.

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