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XIV Congrès Canadien Des Sciences Neurologiques

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Société Hoté: La Société canadienne de Neurologie

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I-1

Carotid Endarterectomy: Operative Risks versus Long Term Benefits

J. Ross Fleming, H. Schutz, M. Hogan, P. Hogan, Toronto

A series of 365 consecutive carotid endarectomies, done in the past 20 years by 2 surgeons, has been studied by careful annual follow-up of patients, and by computerized analysis of operative risk and of survival data.

The operative mortality rate has steadily decreased year by year and now approaches zero. There have been no deaths in the past 150 cases.
There is a persisting but small operative morbidity. Lasting neurologic deficit related to the endarterectomy, commencing either immediately or in the first few hours or days postoperatively, occurred in 1.3% of the last 150 cases. Transient neurologic deficit related to the operation occurred in a further 3.3% of these cases, but resolved completely. Postoperative deficits are apparently thrombo-embolic rather than hemodynamic in origin. The long term mortality rate for this series of patients averages 5.2% per year, and most of the deaths are due to myocardial infarction. Strokes related to the side of endarterectomy occurred in 1.5% of patients per year, and strokes related to the opposite hemisphere occurred in an additional 0.9% of patients per year.

Long term survival rates and stroke rates have been examined in various subgroups of patients in an attempt to determine which type of patient should be selected for endarterectomy.

I-2

Amipaque Myelography in Syringomyelia

Allan J. Fox, H. J. M. Barnett, & Gerard Debrun, London

Using a multi-directional fluoroscopy unit, complete myelography can be carried out using Amipaque with films of the whole spinal cord in AP and lateral projections, as well as the cerebellar tonsils. Study can be completed within 10 minutes of the injection of Amipaque either via lumbar or cervical injection. Satisfactory "collapsing cord" studies in both erect and Trendelenberg positions are included. This is a very efficient way of combining myelographic findings in syringomyelia seen previously only in both positive and negative contrast myelograms performed on the same patient. We have performed this type of myelogram satisfactorily in 6 patients, including one with a complex kyphoscoliosis.

I-3

Maternal Epilepsy and Birth Defects:
Correlation with Plasma Anticonvulsant Levels During Pregnancy

Linda Dansky, Eva Andermann, Allan L. Sherwin,
Frederick Andermann and Robert A. Kinch, Montreal

Recent reports associating maternal epilepsy with congenital malformations in the offspring have generated much controversy about the teratogenic effects of anticonvulsant medication. A prospective study was carried out in an attempt to correlate the occurrence of malformation with plasma anticonvulsant levels monitored during pregnancy.

Thirty-six epileptic women have been followed during 41 pregnancies. Where the outcome is known, 7 of 31 pregnancies (22.6%) resulted in malformed offspring: three congenital heart disease, one cleft lip, one club foot, one polycystic kidney, and one child with multiple congenital anomalies.

For diphenylhydantoin, both the mean dosage (5.2 ± 0.3 mg/kg) and mean plasma level (8.8 ± 1.3 μg/ml) were significantly higher in mothers of malformed offspring, compared to mothers who had normal children (4.3 ± 0.3 mg/kg and 5.3 ± 0.9 μg/ml, respectively). The mean plasma levels of phenobarbital and of ethosuximide were also higher in the malformed group, whereas mean levels of primidone were similar for the two groups.

In all patients, mean anticonvulsant plasma levels tended to be near the lower limit of the therapeutic range and to remain relatively constant throughout gestation. Cord blood anticonvulsant levels were almost identical to maternal levels at term.
These results demonstrate a markedly increased frequency of congenital malformations in offspring of epileptic women who took anticonvulsant medication during pregnancy, despite mean plasma levels at the lower limit of the therapeutic range. Furthermore, there is a positive correlation between the risk of malformation and plasma anticonvulsant levels.

I-4

The Gerstmann Syndrome is Alive and Well
and Resides in the Left Parietal Lobe

A. Kertesz, London

The controversy about the validity of Gerstmann syndrome prompted us to examine this entity in our population of 556 patients surveyed for higher cortical function. We found 6 patients who satisfied the criteria of agraphia, acalculia, right-left orientation, and finger agnosia without significant aphasia. None of them were pure examples of the tetrad; 3 had naming difficulty and 3 had constructional apraxia. Three other patients were considered typical clinically, but two had mild Wernicke's and another Transcortical Sensory aphasia in addition. Seven of the nine had a left parietal lesion, confirming the usefulness of the tetrad.

We then established a control group who had significant agraphia and acalculia without aphasia (N-23). Localization of this group (available in 13) still yielded a high number of left parietal lesions (6). There were also 3 frontal, 2 bilaterial, 1 temporal and 1 right parietal abnormality, indicating that the combination of agraphia and acalculia alone, although more common, has less specified localizing value.

I-5

Preoperative Chemotherapy in the Treatment of Malignant Glioma

Derek Fewer and Norman C. Hill, Winnipeg

Despite much clinical research in the postoperative treatment of malignant brain tumours with chemotherapy, very little progress in terms of an increase in long term, functional survival has been achieved. Employing a rationale based on animal data, we have treated 19 patients with preoperative BCNU over the past three years in the context of a Phase I study. Surgery was carried out between eight and twelve days post treatment and no standard use of either radio or chemotherapy was used postoperatively. It is our conclusion that in approximately one half of cases so treated there was 1) an increase in gross necrosis, 2) a more clearly defined margin between tumour and normal brain and, most importantly, 3) a reduction in tumour vascularity. To date, the median survival of the group is eleven months with three long term survivors still alive at 39, 30 and 25 months. There have been no surgical complications related to the chemotherapy. This treatment technique forms part of a protocol being considered by the National Cancer Institute of Canada which has been distributed to all Canadian Neurosurgeons. Participation of all those interested is invited.

I-6

A Clinico-Pathological Study of Malignant Peripheral Nerve Tumors

F. Gentili, N. B. Rewcastle, W. J. K. Simpson, Toronto.

Malignant tumors of peripheral nerves have long interested both clinicians and pathologists because of their rarity and controversial histogenesis. The present study reviews in detail the clinicopathological features of 52 patients with tumors of this type (22 malignant neurilemoma; 25 malignant neurofibroma; 2 malignant Schwannoma; 3 neurogenic sarcoma) encountered during a 34 year period. Twenty patients were females and 32 males with a mean age of 42.2 years. The site of origin was variable including cranial nerves, spinal roots, brachial plexus and extremity nerves. The light microscopic pattern was quite similar in most cases and could not be used reliably to differentiate between these tumors. Likewise, electromicroscopic features including absence or presence of basement membrane, juctional complexes, intracytoplasmic fibrils do not help to distinguish between a Schwann or perineurial cell origin. All patients were initially treated surgically ranging from simple biopsy to radical local excision. Thirty-one patients also received varying amounts of radiation post-operatively. Follow-up has ranged from 2-20 years. The one and five year survival in the malignant neurofibroma group was 72% and 40% respectively. In the malignant neuriloma patients, these figures were 73% and 59% respectively. Twenty-one patients (40%) developed recurrence of their tumors at 4 months and 21 years later. Based on this study, malignant tumors of peripheral nerves are aggressive tumors with tendency to recurrence and until their cytogenesis can be firmly established the distinction between them is unwarranted.

I-7

A Comparison of Extracranial Vascular Procedures and EC-IC Microsurgical Anastomosis for Delayed Post-Occlusion Ischemia of the Internal Carotid Artery

H. Hugenholtz, Toronto, Ont.

40 consecutive surgical cases, with delayed onset of repeated TIA's, progressive stroke & minor completed strokes in the territory of an occluded internal carotid artery, were evaluated for the relative merits of various extracranial vascular procedures & EC-IC microsurgical anastomosis.

Surgical revascularization encompassed internal carotid artery explorations (9), thromboendarterectomies (13), external carotid endarterectomies (8), contralateral carotid endarterectomies (9), subclavian to external carotid bypass graft (1) & EC-IC microsurgical anastomosis (19).

The likelihood of restoring flow was not only related to the time of surgery after suspected time of occlusion, but also to the degree of collateral flow to the carotid siphon. Grading of angiographically demonstrable flow on careful 4-vessel angiography is valuable to determine the optimum vascular procedure in a particular case.

One case was lost to follow-up. The remaining cases were followed for up to 6½ yrs. with an average of 25 mos. Symptoms were arrested in 86% of pts. subjected to extracranial vascular procedures only & in 47% of pts. subjected to EC-IC microsurg. anastomosis. Pts. requiring EC-IC microsurg. anastomosis suffered more complications (8) than pts. who required only extracranial revascularization (3) to arrest symptoms. It is concluded that extracranial vascular procedures to restore flow and/or to augment available collateral supply are frequently adequate to arrest symptoms of delayed post-occlusion ischemia. EC-IC microsurg. anastomosis should only be considered for revascularization of a symptomatic extracranial internal carotid artery occlusion when the occlusion is of long standing duration with little or no collateral flow, and when symptoms continue despite other attempts to improve natural collaterals.

P-I-1

Cis-Platinum Neuropathy. A Clinical and Pathological Study.

J. G. Blain, P. Band, M. Piccoli-Baretta, L. Martin, Montréal

The use of Cis-Platinum in the therapy of solid malignant tumors is proving successful particularly in carcinoma of the genito-urinary tract. Peripheral neuropathy secondary to cis-platinum has been noted twice in the literature. We report on a patient treated with cis-platinum who developed a clinically progressive painful sensory neuropathy involving the four limbs which affected her gait.

Electrophysiological studies demonstrated a mixed sensory motor neuropathy.

Peroneal muscle biopsy shows a mild to moderate tendancy to fibre type grouping. Single fibre and small group muscle atrophy is also present. Sural nerve biopsy demonstrates mild changes at the ultra-structural level. There is an excess accumulation of glycogen in Schwann cell cytoplasm. There is no evidence of demyelination or remyelination. A loss of unmyelinated axons is noted associated with the presence of many collagen pockets in Schwann cells.

The pertinence of the pathological findings of this havy metal neuropathy will be discussed.

P-I-2

Temperature Effects on the Size of Human Sensory Compound Action Potentials

C. F. Bolton, G. M. Sawa and K. Carter, London

The effects of temperature on human sensory compound action potential size has not been well documented. Ten healthy subjects were studied during gradual re-warming of a previously cooled hand and forearm. The mean, finger temperature increased from 22.5 to 33.6°C., a physiological range. Sensory CAPs were recorded with surface electrodes from median digital nerves on antidromic conduction, the radial nerve at the wrist on antidromic conduction and the median nerve at the wrist on orthodromic conduction. The conduction velocity increased, CAP duration decreased, and CAP amplitude was either unaltered or decreased, particularly in digital nerves. The overall result was a progressive decrease in CAP size.

The results stress the importance of considering limb temperature before interpreting CAP size, particularly when recording from digital nerves. The interesting effects on CAP amplitude can be explained by several mechanisms, but our studies suggest that neither changes in latency between recording and reference electrodes, nor in synchrony of nerve conduction, are responsible.

P-I-3

Oculoskeletal Myopathy with Abnormal Mitochondria

V. Bril, N. B. Rewcastle, J. G. Humphrey

Abnormal muscle mitochondria occur as the major pathological feature in a clinically distinct group of patients with progressive external ophthalmoplegia and somatic muscle weakness.

Fourteen adult patients in this group were reviewed. All had bilateral ptosis, and this was usually the presenting complaint. Of these 14 patients, 11 had pronounced external ophthalmoplegia, 11 had mild facial weakness and 12 had somatic muscle involvement. One patient presented atypically with distal muscle weakness. With the exception of sensorineural deafness in one patient, no other neurological abnormalities were noted. Although the family history for similar complaints was negative in 12, the mothers of two patients had bilateral ptosis. Oculopharyngeal dystrophy was the initial presumptive diagnosis in 2 patients. Electromyography done in 11 patients showed myopathic changes in 10, and non-specific findings in one. Muscle biopsy was performed in every patient. Electron microscopy is presently available in 13 of these cases, and 12 have abnormal muscle mitochondria with crystalloid inclusions.

The duration of symptoms ranged from 2 to 50 years with an average of 22 years. This lengthy interval during which only a slowly progressive weakness was apparent indicates the essentially benign nature of oculoskeletal myopathy.

P-I-4

A Mitochrondrial Myopathy in Three Generations

A. K. W. Brownell, L. A. Aucoin and R. M. Preshaw, Calgary

The nosology of muscle diseases characterized pathologically by the presence of abnormal mitochondria is complex and incomplete. We have documented the occurrence of a mitochondrial myopathy in three generations of one family.

The propositus, an eighteen year old female had small muscle bulk, mild generalized weakness that was somewhat accentuated proximally, mild facial weakness and slight restriction of medial, lateral and upward gaze. Her forty-eight year old mother's muscle bulk was small and she demonstrated very mild generalized weakness, but extra-ocular movements were normal. The eighty-two year old grandmother was normal except for a thoracic kyphosis.

Muscle biopsies from each person demonstrated identical abnormalities. In fresh frozen sections stained by the trichrome method subsarcolemmal and intermyofibrillar accumulations of membranous material were observed in a small number of fibers. In serial sections reacted for oxidative enzyme activity increased reaction product was noted in the same fibers. Electron microscopy demonstrated abnormal mitochondrial sizes and shapes and single or multiple paracrystalline inclusions in many mitochondria from the abnormal fibers.

P-I-5

An EMG Rating System for Surgical Decompression in the Cubital Tunnel Syndrome

K. Odusote, A. Eisen, Montreal

Four hundred and ninety-two ulnar nerves were studied in 237 patients with cubital tunnel syndrome and 233 subjects without clinically apparent ulnar neuropathy. Terminal motor and sensory latencies, motor and sensory conduction velocities, sensory action potential amplitudes and dispersions and needle electromyography were analysed by a 0 to 10 rating (EMG score). The patients were divided according to clinical severity and graded 1 through 4. The median EMG scores of the 4 grades were 0.9/10 (N = 70); 1.6/10 (N = 81); 4.7/10 (N = 46); and 7.1/10 (N = 56) respectively. There was a highly significant relationship between EMG score and clinical severity (contingency co-efficient C=0.65, $p < 0.001$). The median EMG score of the controls was 0.6/10 (N = 239) compared to 1.6/10 for all the patients (N = 253). Seventeen (7.1%) of controls had EMG scores greater than 1.6/10. Electrophysiological evidence for cubital tunnel syndrome

(previously defined by Eisen A, Neurology *24*: 256, 1974) occurred in 14.6% of the controls. This incidence was about three times higher in subjects aged over 60 years. Using high gain sensory amplification, the above sulcus sensory action potential dispersion measured 5.3 ± 0.6 msec in 25 controls with EMG scores of 0/10. 84.6% of symptomatic and 70% of asymptomatic (contralateral) nerves of 13 patients with scores of 0/10 had significantly prolonged dispersions. Symptomatic nerves with an EMG score of 4/10 or over should be considered for surgical decompression. Doubtful cases can usually be confirmed by measuring the dispersion of the above sulcus sensory action potential.

P-I-6

Congenital Segmental Spinal Muscular Atrophy

H. Sarnat, Little Rock, Arkanasa; H. Darwish, Calgary, Alberta; C. Archer, St. Louis, Missouri; K. Brownell, Calgary, Alberta

A diagnosis of SMA Group I was made in three children whose subsequent nonprogressive course and differential upper extremity involvement suggested a new entity which we prefer to call congenital segmental spinal muscular atrophy.

At birth, they were noted to have symmetrical diffuse upper extremity weakness and hypotonia. The weakness was more severe distally, and the myotatic stretch responses were absent in the upper extremities. Sensation was preserved. The palmar flexion creases were poorly developed. Subsequently they appeared to improve in tone and, to some extent, in upper extremity distal functions.

Muscle biopsies from the upper extremities showed diffuse neurogenic atrophy, in contrast with the lower extremities, which showed a normal checkerboard pattern. Myelography revealed no abnormalities. The computed tomography of the spine in one patient showed a significantly low density reading for the intraspinal contents in the area of C-7.

The clinical features described and the muscle biopsies suggest a disorder with prenatal onset and a nonprogressive course which is different from juvenile segmental spinal muscular atrophy and the slowly progressive chronic spinal muscular atrophy. The localized atrophy of the spinal cord in one patient leads to speculation that an ischemic insult to the cervical spinal cord in the distribution of the anterior spinal artery occurred early in utero, producing the deficit described.

P-I-7

Progressive Muscular Rigidity with Respiratory Failure in Infancy: A New Myopathy

C. L. Trevenen, J. Hoogstraten, W. DeGroot, S. S. Seshia, Winnipeg

A 7-week-old female infant presented with a 4-day history of respiratory distress requiring assisted ventilation. The chest was normal and there were no abnormal neurological signs but diaphragmatic movements were absent. A tensilon test was negative. Over the next 20 weeks, all of her muscles became increasingly firm, voluntary movements diminished and joint mobility decreased. CPK values ranged from 1765 to 6060 units with elevation of MM and MB fractions. Serial electromyography revealed profuse fibrillation potentials and brief small amplitude motor unit potentials, becoming more marked with time; interference pattern was initially good but became reduced as her clinical state deteriorated. Nerve conduction and repetitive stimulation showed no abnormality. Serial EKG's were persistently abnormal. She died at 6 months of age. Muscle biopsies, performed at 2 and 4 months of age showed widespread fibre degeneration with increasing interstitial fibrosis. By electron microscopy, affected fibres exhibited a variety of changes ranging from focal dispersion of Z bands to complete granular disintegration of Z bands associated with disorientation of myofilaments and loss of mitochondria. The clinical, electromyographic and pathologic features in this patient represent a hitherto undescribed congenital myopathy.

P-I-8

Multicore Muscle Disease, Spine and Joint Stiffness, Spinal Calcification, and Axonal Degenerating Neuropathy

G. V. Watters, G. Karpati, S. Carpenter, P. Humphreys, Montreal

Multicore muscle disease has been reported previously in six children and one adult, all with no evidence of neuropathy.

Onset was before age 2, with slow motor development, proximal limb and trunkal weakness, decreased reflexes, and joint contractures and/or scoliosis.

At age 2½ years our case had a stiff spine. Gradually the stiffness worsened and he developed mild appendicular joint restriction, proximal weakness, loss of reflexes, and peripheral sensory loss. At age 5 electromyographic and nerve conduction studies were normal, but sural nerve biopsy showed an axonal degenerating neuropathy, while gastrocnemius biopsy showed multicore disease.

By age 7½ electrophysiological studies also showed an axonal degenerating neuropathy with absent sensory action potentials. Repeat biopsies were unchanged.

At age 10 synovial biopsy showed non-inflammatory fibrotic reaction. Electrophysiological studies showed deterioration.

At age 11 years spine x-rays for the first time showed extensive calcification with no serological changes.

Thus it seems an axonal degenerative neuropathy may lead to multicore changes in muscle, and suggests other patients with this disorder may also develop or have a neuropathy. The relationship between this neuromuscular disorder and the osseous-connective tissue disease is unknown, but their occurrence together appears to broaden the spectrum of multicore muscle disease.

P-I-9

Retrograde transport of −Nerve Growth Factor in adult mouse sensory neurons — influence of batrachotoxin (BTX), and tetrodotoxin (TTX) on uptake and transport mechanisms

R. J. Riopelle and R. Boegman, Kingston

Both sympathetic and sensory neurons of mature mice have specific uptake mechanisms for βNGF at nerve terminals, and transport the protein in a retrograde fashion to cell bodies in sympathetic and dorsal root ganglia.

In addition to its effect on sodium ion channels in nerve, BTX blocks orthograde transport of labelled protein and neurotransmitter enzyme from the cell body to the periphery (Boegman and Albuquerque, 1979, in preparation).

BTX, when injected into the perineurium, and nerve ligation, prevent the appearance of ^{125} IβNGF in sensory ganglia, and the labelled βNGF is trapped and accumulates distal to the site of toxin injection or ligation. Injections of TTX, which blocks sodium channels but not orthograde transport, or saline injections, have no influence on ^{125}IβNGF retrograde transport.

Kinetic studies reveal that the influence of toxin is localized, and that transport rates distal to the site of perineurial injection are not influenced either by BTX or TTX.

Uptake of Nerve Growth Factor at nerve terminals is not influenced by injections 30 minutes earlier of BTX or TTX into the footpad of the mouse.

The retrogradely transported ^{125}IβNGF is biologically active as assayed in a single cell bioassay for βNGF, and the accumulation of labelled NGF by sensory neurons in the non-injected extremity has been shown to be due in part to a transport mechanism.

P-I-10

Neonatal Myotonic Dystrophy

D. L. MacGregor, A. Hill and E. G. Murphy, Toronto

The neonatal neurology service of the Hospital for Sick Children (Toronto, Canada) has treated three infants with congenital myotonic dystrophy in the past year (1978). These cases will be presented with attention being given to the following features: mode of presentation, clinical course and post-mortem examination (one case).

Frequent findings in neonatal myotonic dystrophy include hypotonia, facial diplegia, talipes, thin ribs and hydramnios with reduced fetal movement during pregnancy. The disorder is transmitted by the mother and about a quarter of the cases are the result of new mutation.

The relevant literature will be reviewed with discussion of the possibility of prenatal diagnosis by amniocentesis for determination of secretor status of the fetus and prediction of inheritance of the allele for myotonic dystrophy based on the Dm-Se linkage.

P-I-11

Hypoxic Myelopathy

H. V. Vinters, J. J. Gilbert, London, Ontario

Although the selective vulnerability to hypoxia of various regions of the brain has long been appreciated, hypoxic myelopathy has only recently been well described (Azzarelli and Roessmann, Neurology,*27* 1049, 1977). From autopsy cases studied in the last four years, we have reviewed the clinical histories and pathologic findings on twelve cases in which variable degrees of hypoxic change were found in the spinal cord. Though the patients had suffered from a wide variety of medical and surgical conditions, the common feature in virtually all cases was a clearly defined anoxic and/or hypotensive episode. Infants and children (5/12 cases) seemed predisposed to show the changes. Pathologic findings in the cord varied from discrete eosinophilia of anterior horn cells to frank infarction of gray matter. The white matter was consistently spared and the thoraco-lumbar region was most often affected. The significance of the changes described has seldom been appreciated pathologically or clinically. The findings may have implications for the clinical course of patients who survive anoxic or hypotensive episodes.

P-I-12

Upper-Dorsal Sympathectomy for Hyperhidrosis

M. Fazl, H. Schutz, Toronto

Excessive sweating of the palms of the hand, more than required for thermoregulatory responses may be occupationally disabling and socially embarrassing. Sympathectomy is the only curative procedure. The authors prefer a one stage bilateral posterior thoracic approach to the sympathetic chain because of the paucity of complications and ready visualization. Our modification of the classical approach to the sympathetic chain will be described and the result of treatment in 5 patients will be discussed.

P-I-13

Passive Transfer of Demyelinating Activity in Experimental Allergic Neuritis

A. F. Hahn, T. E. Feasby, J. J. Gilbert, London, Ontario

To clarify the disputed role of humoural factors in the immunopathogenesis of experimental allergic neuritis (EAN), we have studied the demyelinating activity of EAN serum in vivo using the technique of direct intraneural injection.

Sera from rabbits sensitized with bovine peripheral nerve homogenate plus adjuvant were injected into sciatic nerves of Wistar rats. Focal segmental demyelination developed rapidly at the site of injection. Myelin degradation with preservation of axons evolved within hours, prior to the appearance of inflammatory cells. Sequential studies showed macrophage invasion and phagocytosis of myelin debris. The demyelination was maximal at four days and progressive remyelination was seen beginning by day six. Control injections into the contralateral sciatic nerves were negative. The demyelinating factor(s) was shown to be tissue specific by absorption studies.

These in vivo studies suggest that serum antibodies play a major role in the demyelination of EAN.

Preliminary results from parallel studies of Guillain-Barre Polyneuropathy suggest a similar phenomenon.

P-I-14

Respiratory Evoked Potentials

P. K. H. Wong, A. C. Bryan, A. Froese, Toronto

Cortical evoked potentials (CEP) measured in response to various stimuli (auditory, somatosensory and visual) have provided useful information about the afferent mechanisms involved. In an attempt to quantify sensory input from the respiratory system, we studied the CEP elecited by brief airway occlusion in normal human subjects. Brief occlusions were produced by an electromagnetic valve connected to the subject's mouthpiece. They occurred randomly during each inspiration and lasted 85 ms. Fifty to 100 EEG responses were measured from the Cz - Fp electrode derivation, and were averaged by an on-line computer. EMG of eye and neck muscles were similarly averaged to allow detection of muscle artifact: these could not account for the early CEP components. Significant components of the CEP were noted beginning 15 ms from the time of occlusion. These were absent in control CEP's obtained with the valve by-passed. The early components appear to arise from specific respiratory afferents. Later components (> 80 ms.) are likely to be more non-specific in nature. The origin of the early CEP components is not clear. Contributing sources include muscle receptors from the diaphragm and chest-wall, mechanoreceptors in the airway, or cortical efferent signals.

P-I-15

Scalp-recorded DC Potential Shifts Associated with Hyperventilation in Human Subjects

T. W. Picton, R. T. Pivik and R. Godbout, Ottawa

Scalp recordings of slow potential shifts were obtained from eighteen normal young adult volunteers before, during and after three minutes of hyperventilation. During hyperventilation a negative potential shift of several millivolts consistently developed. Technical controls ensured that this phenomenon was not the result of changes in scalp temperature, skin potential or electrode polarization, and was therefore probably generated in the brain. The negative shift developed slowly, attaining maximum amplitude after the first minute or two of hyperventilation, and it returned to baseline over a similar time course after the end of hyperventilation. The amplitude of this potential was related to the amount of hyperventilation as evaluated by measurements of alveolar CO_2 concentration. The negative shift appeared to relate to the decreased arterial pCO_2 rather than to the activity of hyperventilation, since hyperventilation of a CO_2 mixture so as to maintain a constant alveolar CO_2 concentration was not associated with any change in the DC potential. In reference to an electrode located over the vertebra prominens, the negative shift was maximally recorded at midline frontal and central placements, decreasing symmetrically on either side of midline and falling off quite sharply in the more posterior scalp locations.

II-1

Persistant cranio-pharyngeal canal: report of two cases with unusual clinical and radiological features

Maurice Héon, Domineco Dilenge, C.H.U., Sherbrooke

The persistance of a cranio-pharyngeal canal in the adult was revealed surgically in the first case after the investigation of a post-traumatic rhinorrhea. In the second instance, persistance of the canal was suggested by the demonstration of an intrasphenoidal encephalocele through a bony opening in the floor of the sella turcica.

II-2

Current Management of Acoustic Neuromas

C. H. Tator, J. M. Nedzelski, Toronto

The present report concerns the management of forty patients with acoustic neuromas seen during the past three years. The following factors determined the method of management: tumour size, hearing acuity, presence of hydrocephalus and patient's age. Eight primarily intracanalicular tumours were totally excised using a translabyrinthine approach. Morbidity was minimal and the facial nerve was preserved in all eight cases. Patients with tumours of 2 cm. or less and serviceable hearing (speech reception threshold of less than 50 db and speech discrimination of more than 60%) had tumour excision through the standard suboccipital approach. The facial nerve was spared in all fourteen patients and the cochlear nerve in seven. Pre-operative hearing was maintained in one patient and sound appreciation in another. Eight patients with large tumours in whom hearing was poor were treated by a combined one-stage translabyrinthine-transtentorial middle fossa approach. The facial nerve was spared in all but one. The latter had lost facial nerve function in a previous operation. Five elderly patients (over age 70) with large tumours and hydrocephalus had cerebrospinal fluid shunts only. Two patients with large tumours refused operative treatment, and three elderly patients with small tumours and no hydrocephalus were not operated upon and are being followed.

II-3

Blood Volume Expansion and Induced Hypertension of the Management of Progressive Neurological Deficit Secondary to Ischemia

Q. J. Durward, S. J. Peerless, London

Progressive neurological deficit due to ischemia is most often seen in our institution secondary to:

(i) vasospasm in asociation with sub-arachnoid hemorrhage
(ii) in patients in whom E.C.-I.C. bypass has been performed in conjunction with carotid ligation in treating otherwise inoperable aneurysms, and
(iii) in some patients with thrombo-embolic occlusion of major cerebral arteries either spontaneously or secondary to angiography.

Improvement of blood flow in an ischemic area of brain can theoretically be attained by the following methods:

(i) Increasing the calibre of the blood vessels supplying the ischemic area.
(ii) Decreasing the viscosity of the blood.
(iii) Increasing the cerebral perfusion pressure, either by elevating the blood pressure or lowering the intra-cranial pressure.

In our experience, blood pressure elevation by discontinuation of antihypertensive medications, volume expansion, and pharmacological hypertensive agents has produced immediate and remarkable clinical improvement in certain patients. Fifteen patients with ischemia secondary to one of the above mentioned causes in whom we attempted to stop or improve their progressive neurological deficit are discussed. Ten of the patients improved, and 5 remained unchanged or deteriorated.

The method of B.P., C.V.P. and in certain cases pulmonary capillary wedge pressure monitoring will be described, along with the solutions used for volume expansion and agents for b.p. elevation. Problems we have had with this technique include pulmonary oedema, marked diuresis producing a negative fluid balance and cardiac ischemia.

II-4

Pituitary Apoplexy

S. W. Schatz, A. Talalla, Hamilton

Of 42 consecutive patients with pituitary tumours requiring surgical treatment seven have presented the syndrome of pituitary apoplexy. The clinical features included acute onset of headache and vomiting, disturbance of consciousness, visual failure and/or ophthalmoplegia. Subarachnoid haemorrhage occurred in four patients; two of these had additional neurological deficit. Two patients had been receiving anticoagulant medication and three patients had acute upper respiratory infection. Only one had a pituitary tumour previously diagnosed (and treated by excision and radiation). All patients had gross enlargement or destruction of the sella turcica. Large suprasellar masses were demonstrated in four, smaller in three. By trans-sphenoidal decompression, after intervals from one day to eight weeks, extension of tumour was demonstrated into cavernous sinus in four patients, construction of tumour at the diaphragma sellae in three, and in one of these communication of a large haematoma with the third ventricle. Haemorrhage was prominent in three instances, infarction of adenoma in two; both were present in two. Gratifying restoration of vision and resolution of ophthalmoplegia was documented in five patients. In retrospect earlier diagnosis of pituitary adenoma might have been established for all patients. The high incidence (one in five) of catastrophic apoplexy from large tumours emphasizes the risk of conservative management of patients known to harbour them.

II-5

Unusual Mass Lesions of the Pineal Region in Children

Enrique C. G. Ventureyra, Leslie P. Ivan, and Sin H. Choo, Ottawa

During the past 15 months the authors gained experience in exploring and treating 3 patients with mass lesions of the pineal region. In all 3 instances lesions of benign nature were found. In case No. 1 a large epidermoid cyst araising from the left thalamus was subtotally excised through a transcallosal approach. In case No. 2 a venous malformation of the Galenic system was exposed at surgery through the supracerebellar infratentorial approach. The pre-operative cerebral angiography failed to reveal the vascular nature of this lesion. At surgery "in situ" thrombosis of the venous malformation was achieved. In case No. 3 a choristoma of the pineal gland was exposed and totally excised through a right occipital transtentorial approach. There was no operative mortality or significant morbidity in these series. It was concluded that exploration of all pineal lesions is imperative since the incidence of histologically benign lesions is remarkably high and if these lesions are not treated surgically, they are "blindly radiated". The use of micro technic increased the accuracy and safety of the procedure. The importance of the pre-operative assessment of the patient by means of C A T scan are emphasized as well as for the post-operative follow-up. The three classical approaches to the pineal region were tested and all of them proved to be safe but there was a considerable disporportion in the amount of exposure gained in exploring the pineal region. The authors concluded that the transtentorial approach was by far superior to the other two since it provided the best access to the region allowing excellent control under direct view of the deep venous system as well as access to the posterior and even the anterior third ventricles structures.

III-1

Sensory Deficits Can Impair Recognition of Letters and Faces

D. M. Regan, J. Raymond, A. Ginsburg and T. J. Murray, Halifax

Some M.S. patients have normal Snellen acuity while experiencing reduced visual sensitivity to coarser detail. These patients may experience difficulties in every day vision because sensitivity to coarse detail is necessary for recognition of objects, such as letters and faces.

We tested visual sensitivity to sinewave gratings and obtained plots of contrast sensitivity versus spatial frequency. M.S. patients had abnormal plots. We then used spatially-filtered letters and faces to test the vision of patients whose sensitivity loss was restricted to medium spatial frequencies. The sinewave grating data enabled us to predict the viewing distances at which face and letter recognition would be impaired. Our experimental tests with letters and faces showed that recognition was indeed impaired at the particular viewing distances predicted. (Note: A sinewave grating is a blurred strip pattern. Spatial frequency is the number of bright/dark bar pairs per degree of visual angle.)

III-2

Orientation-specific Contrast Sensitivity Losses in Multiple Sclerosis

J. Whitlock, D. M. Regan, T. J. Murray, and K. I. Beverley, Halifax

Refractive astigmatism that is uncorrected in early life can cause a lasting neural abnormality associated with orientational differences in visual resolution. Such "meridional amblyopia" is more pronounced at higher than at lower spatial frequencies. Abnormal eye movements could also cause orientation-specific contrast defects, but such defects would not be confined to an oblique orientation since oblique saccades are a combination of horizontal and vertical movements that are generated somewhat independently.

We measured grating contrast sensitivities for 4 orientations (vertical, horizontal, 2 obliques), and compared MTF's for the left and right eyes of multiple sclerosis patients and controls. We also compared MTFs for different orientations within a single eye. In a preliminary study we used the method of ascending and descending limits. We have confirmed our conclusions using a 2-alternative forced choice method on 9 patients and 11 controls.

Most patients experienced significantly degraded contrast sensitivity that depended on grating orientation. In some patients these losses were greatest at high spatial frequencies, and in some patients the losses were greatest for a horizontal or vertical orientation. But some patients experienced significant losses of contrast sensitivity that could not be explained as a combination of horizontal and vertical defects, and were restricted to low spatial frequencies. We argue that this defect must be neural, and not due to early astigmatism nor due to abnormal eye movements.

III-3

Conduction Abnormalities in Tourniquet Paralysis

Stephen K. Yates and William F. Brown, London, Ontario

Mechanical injury and ischemia may both contribute to the nerve injuries that can result from use of the pneumatic cuff to control bleeding. The relative importance of the two factors has not been established, however, in man. This problem has been investigated in control human upper limbs by pneumatic cuff inflation to 300 mm Hg for ½-1 hour and measurement of the conduction times in the median or ulnar nerves across the mid-cuff,

proximal and distal cuff border segments. Measurements were compared at intervals prior to, during and after cuff inflation.

Conduction delay and block occurred within 5-10 minutes of cuff inflation at the proximal cuff border followed within minutes by like abnormalities at the distal border cuff edge. Only at 20-30 minutes were reductions in the direct muscle response from stimulation at more distal points along the length of the nerve observed. Conduction block and conduction time increases occurred earlier in sensory than motor fibers. Recovery from conduction block occurred within 1-2 minutes of cuff deflation but conduction delays could persist for ½ or more hours. The observation that nerve function failed first at the levels of the cuff borders suggested that the initial nerve injury was mechanical rather than ischemic.

III-4

Clinical Prognostic Markers in Multiple Sclerosis

D. W. Paty and G. C. Ebers, London, Ontario

In the last 7 years we have seen and catalogued 479 clinically definite Multiple Sclerosis (MS) patients in the MS Clinic at the University of Western Ontario. The mean age of onset was 32 years, and the peak age of onset was 22 years. Fifty-five patients (11%) have run a benign clinical course. Analysis of the initial symptoms showed that 78 (16%) began with retrobulbar neuritis (RBN). This was more likely to occur in females. The interesting finding was that RBN as a 1st symptom in females was associated with a benign clinical course in 18% (10 out of 54) while RBN as a 1st symptom in males was associated with a benign course in only one out of 24 (4%).

Further analysis of this data for prognostic markers is underway. Preliminary data suggests that a benign prognosis was correlated with sex (female), RBN as an initial symptom in females, HLA type, and an initial relapsing and remitting clinical course. Poor prognosis was correlated with initial cerebellar and/or predominant spinal motor involvement.

III-5

Acute Organic Psychosis Caused By Multiple Sclerosis

R. Wilson, J. Bilbao, Toronto, Canada

This paper will describe one case of multiple sclerosis in a young woman who developed an acute organic psychosis and then died from pneumonia shortly thereafter. At autopsy many acute plagues were found throughout both hippocampi and old lesions were present in the spinal cord related to her initial attack.

In the discussion mental symptoms occurring in multiple sclerosis will be reviewed and their anatomic basis will be analysed. Most clinical surveys of multiple sclerosis indicate that emotional disturbances occur throughout all stages of development of the condition, and chronic dementia is primarily found in the more advanced form of the disease. An acute organic psychoses occurring in multiple sclerosis has only been described in a few isolated case reports. Neuropathological analysis of these cases to determine the anatomic basis for the mental changes has rarely been performed.

This case report provides a unique opportunity of studying the clinical-anatomic correlation of an acute organic psychosis occurring early in the course of a case of multiple sclerosis.

IV-1

The Effect of High Dose Barbiturate on the Neuronal Changes of Acute Global Ischemia

M. J. Kendall and F. A. Durity, Vancouver, B.C.

Intensive search for useful therapy of the ischemic brain continues. Although the absolute limits of tolerance of global brain ischemia have not been defined, previous work on the Mongolian gerbil has demonstrated well recognized ischemic cell damage following 15 minutes of bilateral carotid occlusion. The possible protective effect of barbiturates on this process was studied in a group of animals whose ventilation was controlled to avoid purely hypoxic changes. After anesthetic induction, animals underwent 15 minutes of reversible bilateral carotid occlusion. After 4 hours of recirculation they were sacrificed by perfusion-fixation techniques and later multiple histological sections were studied.

No ischemic change was noted in 6 animals after ketamine or pentobarbital induction alone. However, severe cell necrosis occurred in 5 animals (not ventilated) and modest changes in 6 (ventilated) after ketamine anesthesia and 15 minutes bilateral occlusion. Only the occasional ischemic neuron was detectable in 6 animals given 50 mg/kg pentobarbital intra peritoneally just prior to occlusion. However, severe changes were present in 6 given the barbiturate 15 minutes post-occlusion.

These data suggest that, whereas barbiturate may protect against global brain ischemia, by 15 minutes changes may be irreversible.

IV-2

CSF Lactate Levels in Meningitis: A Help or Just Another Test?

R. Lannigan, E. V. Haldane and T. J. Marrie, Halifax

The level of lactate in cerebrospinal fluid has been suggested as a useful diagnostic parameter to differentiate between bacterial and viral meningitis, especially in patients partially treated before admission to hospital. A concentration $>$ 35 mgm/dl, determined by either gas-liquid chromatography or by an enzymatic method, has been considered in several studies to provide definite evidence of meningitis of bacterial origin, whereas a lower level indicates no bacterial involvement. Over the past 18 months, we have analyzed by the enzymatic method the lactate level in 493 spinal fluids submitted from 434 patients with various conditions involving the central nervous system. Fifty-eight fluids had a level of lactate $>$ 35 mg/dl of which 17 were cases of infective meningitis of varying etiology. The 435 specimens with lactate levels within the range considered normal, included 3 cases of infective meningitis, of which 2 were cryptococcal and 1 bacterial. In this study, the lactate level in the cerebrospinal fluid did not provide unequivocal evidence of bacterial infection, and did not provide assistance to any greater degree than the standard parameters of WBC count, protein, and glucose contents in the differential diagnosis of bacterial meningitis from that of any other etiology.

IV-3

Vegetative State After Non-traumatic Coma in Childhood — Evolution and Outcome

S. S. Seshia, J. D. Gillies, Winnipeg

The term "persistent Vegetative State" was used by Jennett and Plum (1972) to describe a clinical syndrome following brain damage in which, after an initial comatose period, patients seem to be in a state of "wakefulness without awareness", and often never regain recognizable mental function. The evolution and outcome of this state have been defined in adults but comparable data are not available for children. We have analysed the data in 14 children who showed this state following an acute illness that resulted in coma. Twelve of the 14 were under 3 years of age. Diffuse anoxia/ischemia (N=10) and meningitis (N=3) accounted for 13 cases. Using a coma scale of 1 to 4, the maximum severity of coma was grade 2 or 3 in 13/14 cases. The duration of coma ranged from 18 hours to 22 days and was under 14 days in 12 patients. Blinking and roving eye movements, occurring within 4 days in 11/14 cases, and decerebrate/decorticate responses, occurring within 4 days in 13/14 cases, were the earliest findings heralding the vegetative state. Clinical sleep/wake cycles were noted within 14 days in 12 cases. Seven children died within 3 months; 6 were severely neurodevelopmentally handicapped and totally dependent (follow-up 3 months to 3 years). One child became ambulant 1 year after the initial insult and now, 4 years later, is moderately retarded. This would suggest that the state need not be persistent, but our experience indicates that the prognosis of children showing the vegetative state is poor.

IV-4

The Cerebral and Cardiac Response to Nitroprusside Controlled Hypotension in Neurosurgical Patients

W. W. Stoyka, W. A. Tucker, Toronto

Ten patients requiring neurosurgery for aneurysms arterio-venous malformations, posterior fossa explorations or brain tumours were selected for this study. Informed consent was obtained for placement of an internal carotid artery catheter and 133 xenon injection for cerebral blood flow (CBF) measurement. Anaesthesia was induced with sodium thiopentone, tracheal intubation and muscle relaxation was facilitated with pancuronium bromide and anaesthesia was maintained with N_2O, O_2 and enflurane and artificial ventilation with moderate hypocarbia. An intra-carotid cannula was inserted for arterial pressure monitoring, blood gas determinations, and an injection site for 133 xenon. A Swan Ganz thermodilu-

tion cardiac output catheter was advanced from a peripheral vein into the pulmonary artery for determination of central venous pressure, cardiac output (CO); pulmonary artery pressure or wedge pressure. With the patient supine, dual CO and CBF baseline values were obtained. Subsequent CO and CBF's were measured following changes in posture, rapid mannitol infusion and sodium nitroprusside controlled hypotension at various levels. A comparison of baseline values and results obtained with posture, mannitol or nitroprusside hypotension will be discussed. The most significant features were the maintenance of normal CBF at low arterial pressures with nitroprusside and the discovery of the minimum safe level for controlled hypotension for each individual patient.

IV-5

Valproic Acid and Plasma Levels of Phenobarbital

J. Bruni, B. J. Wilder, R. J. Perchalski, Gainesville, FL

The concurrent administration of valproic acid with phenobarbital (PB) may lead to important interactions. A significant rise in phenobarbital level may occur. The kinetic mechanisms underlying this interaction have been poorly understood. A number of factors could be responsible: increased PB absorption, decrease in the volume of distribution, inhibition of hepatic metabolism, or decreased renal execretion of phenobarbital. Our earlier observations failed to demonstrate a pH dependent renal mechanism for the rise in PB levels. PB and hydroxyphenobarbital (OHPB) excretion were measured in the urine of four patients during treatment with valproic acid. The amount of OHPB excreted in the urine generally decreased despite increases in PB plasma concentrations. More important, the urinary OHPB/PB ratio was constantly reduced ($p < .025$) in all four patients. The average ratio before treatment with valproic acid was $0.48 \pm .0.26$ (SD) and 0.31 ± 0.19 (SD) during concurrent administration. These data are indicative of inhibition of the hepatic microsomal enzymes that metabolize phenobarbital. This inhibition is responsible for the rise in PB plasma levels observed in the majority of patients during concurrent administration of PB and valproic acid. From our data and on the basis of knowledge of PB pharmacokinetics an increase in the absorption or a decrease in the volume of distribution of PB are not involved.

V-1

Volume-Pressure Studies in Adult Hydrocephalus

A. L. Amacher, London

Several methods have been proposed for predicting the outcome of surgical treatment of adult communicating hydrocephalus. These have included 24 hour pressure recordings, infusion tolerances, characteristics of air encephalography and isotope cisternography, etiology of the condition, and cerebral blood flows.

In this preliminary study, 20 patients with communicating hydrocephalus and 4 with aqueduct stenosis have been studied awake or under anaesthesia, using ventricular infusion by continuous or bolus injection at various rates. A search for outcome predictability factors has been made among the parameters of infusion tolerance, cerebral compliance and "ventricular strain", and characteristics of the volume-pressure curves.

Two patients (2/5) with ventricular infusion tolerances of more than 2.0 cc. per minute have shown improvement, and 12 of 17 with infusion tolerances less than 2.0 cc. per minute have been benefited by shunting.

In the majority of cases, the volume-pressure curve shows a reduction in pressure response to unit volume injection as higher intracranial pressures are reached. Whether such a curve pattern reflects a sudden change in cerebral compliance or in fluid absorption or flow is unknown.

To date, no reliable predictive factors have been uncovered relating to outcome of shunting procedures in adult communicating hydrocephalus.

V-2

Trigeminal Neuralgia: Percutaneous Rhizotomy versus Microvascular Decompression

G. G. Ferguson, D. C. Brett, S. J. Peerless, and J. P. Girvin, London, Ontario

We have reviewed our experience with percutaneous trigeminal rhizotomy and microvascular decompression (Jannetta procedure) in the treatment of trigeminal neuralgia.

Percutaneous rhizotomy was performed in 40 patients. The average age was 65 (45-86) and the average follow-up is 20 months. Twenty-seven patients (67%) have been totally free of pain since their initial procedure. Four cases were immediate failures. In nine cases there was delayed recurrence of pain. There was no mortality and no significant morbidity. Sensory loss has been well tolerated except in one case.

Sixteen patients have had posterior fossa craniotomy and microvascular decompression of the trigeminal nerve. The average age was 55 (39-70) and the average follow-up is 13 months. Some degree of vascular cross-compression of the trigeminal nerve was found in every case except one in which a small unsuspected cholesteatoma was found. While 13 patients (80%) have had no pain since surgery, three patients have had some degree of recurrence. There was no operative mortality but a number of minor, largely transient, complications were noted.

The suggestion that microvascular decompression will result in life-long cure for tic patients seems uncertain as the short-term results in our series are not appreciably better than those with percutaneous trigeminal rhizotomy.

V-3

An Improved Treatment of Sagittal Synostotis

W. Howes, Halifax

The results of linear craniectomy in the treatment of scaphocephaly, the skull deformity of sagittal synostosis, have been less than ideal. Prompt recurrence of suture refusion has led to techniques based on inhibition of bone growth i.e. the use of silastic sheeting.

Based on Moss's concept that the basic cause of synostosis is not in the suture itself which is physiologically passive, but is rather secondary to abnormal dural tensions, a modification of linear craniectomy is described. This technique utilizes closing wedges of the parietal bones with immediate improvement of skull appearances.

10 cases followed up to 2 years are described.

V-4

Embolization of Cerebral Arteriovenous Malformations (Brain Angiomas) with Bucrylat

G. Debrun, A. Fox, F. Vinuela, S. Peerless, and C. Drake, London, Ontario

Brain angiomas are often inoperable because they are located in the basal ganglia or in the rolandic area of the dominant hemisphere, or when they are too extensive. Different types of embolizing material have been used and will be discussed. The most recent is an acrylic substance which hardens instantaneously upon contact with blood (Bucrylat). Incomplete and complete disappearance of the AVM will be shown and the limits of the technique will be emphasized. Medicolegal problems will be discussed.

V-5

Derivation Lombo-Peritoneale dans la Syringomyelie

J. Francoeur, Québec

Le traitement chirurgical de la syringomyélie demeure controversé. Les techniques chirurgicales employées, (libération d'adhérences aux trous de Magendie et de Luschka avec ou sans oblitération du canal épendymaire à l'obex, drainage du syrinx dans l'espace sous-arachnoidien, simple dérivation ventriculocardiaque, ventriculostomie lombaire), ont donné des résultats discutables. Nous avons eu l'occasion de traiter il y a deux ans, une jeune fille de 26 ans chez qui on venait de porter un diagnostic de syringomyélie. La maladie avait débuté à l'ège de 11 ans et avait évolué cliniquement comme une maladie démyélinisante. La cavité syringomyélique s'étendait sur toute la hauteur de la moelle. Nous avons procédé à une laminectomie lombaire et au drainage du syrinx dans l'espace sous-arachnoidien puis dans un même temps opératoire à une dérivation lombo-péritonéale. Immédiatement après la chirurgie, sa condition neurologique s'est améliorée considérablement. La patiente a cependant dû être soumise dernièrement à un drainage du syrinx dans l'espace sous-arachnoidien cervical à cause d'une récidive de symptômes. La chirurgie a de nouveau amélioré considérablement la patiente. Nous croyons qu'il y aurait avantage à considérer le traitement de la syringomyélie à l'aide d'une dérivation lombo-péritonéale après avoir drainé le syrinx dans l'espace sous-arachnoidien. Ce genre de traitement pourrait satisfaire les tenants des différentes théories et s'avérer un traitement satisfaisant de la pathologie en cause.

V-6

Thalamic Stimulation for Denervation Pain

I. M. Turnbull, Vancouver

Injury to sensory pathways may cause chronic pain. Unlike the pain of noxious stimulation, denervation pain can not be suppressed, except temporarily and unreliably, by interrupting sensory pathways central to the lesion. An electrode in the principal sensory relay nucleus of the thalamus can activate tertiary neurones to produce a tingling sensation which feels as if it originated in the denervated part of the body. The hypothesis that stimulation of thalamic neurones deprived of their normal peripheral connections would arrest denervation pain was tested clinically by Adams and Hosobuchi in anesthesia dolorosa from trigeminal nerve section and by Mazars and colleagues in a variety of denervation pains. These encouraging initial reports stimulated the work to be reported.

Since 1975, thalamic electrodes have been implanted in 16 patients and established for long term use in 12. Ten of the 12 are continuing to obtain pain relief by regular stimulation. The procedures, quality of pain control and problems that have arisen will be discussed.

VI-1

A Simplified Analysis of Somatosensory Responses in Multiple Sclerosis

A. Eisen and K. Odusote, Montreal

The short latency responses recordable from the cervical spine and scalp evoked through median nerve stimulation have several components. The N_{14} and N_{20} peaks are the most easily identifiable and their latencies measured 13.7 ± 0.8 msec and 19.1 ± 0.9 msec respectively (N = 50). The difference between these latencies (N_{20} - N_{14}) reflects a central conduction time from the cervical cord to the cortex. It measured 5.45 ± 0.7 msec. The frequency with which abnormalities of the N_{14} or N_{20} peaks occurred in 105 patients with or suspected of having multiple sclerosis (MS) was analysed. Responses were considered abnormal if (1) they were absent, (2) their latencies were prolonged, (3) there was prolongation of (N_{20} - N_{14}), or (4) the side to side difference of any of these values was greater than the normal means +3 SD. Abnormalities were documented in 82.8% of 29 patients with definite MS; 87.5% of 24 patients with early probable or latent MS; 68.2% of 22 patients with progressive probable or possible spinal MS; and 40% of 30 suspects. A significant side to side difference of (N_{20} - N_{14}) was the sole aberration in 8 of the 12 suspects who had electrophysiological abnormalities. We conclude that in MS, the diagnostic value of simply measuring the N_{14} and N_{20} peaks compares favourably to more complex analysis of other components recordable from the neck and scalp.

VI-2

Contrast Sensitivity in Multiple Sclerosis: abnormal buildup and recovery from adaptation

J. Raymond, T. J. Murray and D. M. Regan, Halifax

We recently reported that a considerable proportion (20/48) of multiple sclerosis patients experienced a loss of contrast sensitivity, even though Snellen acuity was unimpaired. Our conventional methods, however, confounded depressed contrast sensitivity with (a) abnormally rapid and/or severe adaptation to contrast, and (b) abnormally slow recovery from adaptation. Here we report measurements of the rate of rise of contrast threshold during adaptation, and the rate of threshold recovery after cessation of adaptation for multiple sclerosis patients and for control subjects. Our adapting stimulus was a 7 c/deg sinewave grating of 70% contrast whose luminance was similar to that in our earlier report.

The affected eye(s) of multiple sclerosis patients recovered slowly compared with patients' unaffected eyes or control subjects' eyes. The buildup of adaptation was also abnormal in multiple sclerosis patients. Contrast threshold was still rising after 60 secs adaptation in the affected eye(s) of multiple sclerosis patients, whereas threshold had levelled out within 40-60 secs for control subjects and in patients' good eyes. This may relate to Enoch *et al.*'s finding of abnormally great adaptation in MS (though their gratings were 10-100 times brighter than ours).

Of two amblyopic eyes tested, neither showed abnormal recovery from adaptation. This is tentative evidence that our findings may not be entirely unspecific for multiple sclerosis.

VI-3

Long Latency EMG Responses to Load Perturbations in Hemiplegic Patients

R. G. Lee, G. L. Rohs, and D. G. White, Calgary

In normal subjects, mechanical perturbations at the wrist joint give rise to a characteristic EMG response from the forearm muscles consisting of an early component (M1) beginning after 30-35 msec. and one or more late components (M2, M3) occuring after a latency of 55-60 msec. The long latency responses may be related to the clinical phenomenon of muscle tone and in an earlier study it was shown that there was a marked accentuation of these components in patients with Parkinsonian rigidity.

In the present study, 21 hemiplegic patients were examined at varying intervals following strokes resulting from ischemic or hemorrhagic lesions of one cerebral hemisphere. The M1 component was accentuated in all subjects. Alterations in the long latency responses fell into three categories. In a small group of patients, there was no EMG activity following the initial M1 response. The remaining patients showed either an accentuation of the late response similar to what is seen in Parkinsonism or an unusual pattern in which an initial complex burst of EMG activity was followed by a second almost identical component occuring after a latency of 90-110 msec.

Changes in the long latency responses were determined by several factors including the anatomical site of the lesion, the extent of sensory impairment, and the length of time since the original stroke. However, it was not possible to establish any consistent correlation between the type of late EMG response and the degree of spasticity assessed clinically, and it is concluded that long latency reflexes determined by this method do not play a major role in the pathogenesis of increased muscle tone in hemiplegics.

VI-4

Spinal and Cortical Potentials Evoked by Tibial Nerve Stimulation in Controls and Multiple Sclerosis

S. Chayasirisobhon, A. Eisen, L. Ridsdale, Montreal

In multiple sclerosis (MS) the diagnostic yield of somatosensory responses (SERs) evoked through median nerve stimulation is lowest in progressive spinal MS and MS suspects. SERs evoked by stimulating lower extremity nerves although rarely reported should be diagnostically more useful since they reflect conduction through the whole neuraxis. In 25 normal subjects sequential stimulation of both tibial nerves at the ankles was used to evoke SERs which were simultaneously recorded from the lower thoracic spine (T_{12}) and scalp (C_Z). The main negative peak of the response from T_{12} (designated N_{21}) had a latency of 21.5 ± 1.5 msec. The initial components of the scalp SER are designated as P^{30}, N_{30}, P_{40}, N_{50} and P_{60}. Their respective latencies were 30.6 ± 2.3 msec, 32.0 ± 1.9 msec, 38.4 ±2.5 msec, 49.0 ± 1.8 msec and 60.8 ± 2.1 msec. Of the three earliest components, P_{40} was the most easily recognized and was invariably present. The difference in the latencies of (P_{40} - N_{21}) reflects a conduction time from T_{12} to C_Z and was 16.7 ± 1.7 msec with a side to side difference of 0.8 ± 0.4 msec. All of a small group of 10 patients with progressive spinal MS had prolongation of P_{40} and/or (P_{40} - N_{21}). It is anticipated that SERs evoked by tibial nerve stimulation will also be valuable in the diagnosis of MS suspects.

VI-5

Motoneuronal Excitability During Wakefulness and Non-REM Sleep: *H-Reflex Recovery Function in Man*

R. T. Pivik and L. Mercier, Ottawa

The present study reports on sleep-wakefulness comparisons of H-reflex modulation determined by the recovery function technique in which pairs of reflexes are elicited by equal intensity stimuli delivered at graded inter-stimulus intervals. A recovery function curve is then generated based on amplitude comparisons of the second reflex to the first as a function of inter-stimulus intervals (500-5000 msec). An evaluation of motoneuronal excitability during sleep using this method has not been previously reported in human adults.

Direct and reflex responses were elicited by stimulation of the posterior tibial nerve and muscle action potentials recorded from the triceps surae during wakefulness and all-night sleep recordings in 13 subjects. EEG, EOG and EMG recordings were taken during sleep and sleep stages defined according to standard criteria (Rechtschaffen and Kales, 1968). A marked

decrease in the peak of facilitation present in the waking data at 200 msec was observed during non-REM sleep stages 2, 3 and 4.

Possible bases for the sleep-related absence of facilitation will be discussed.

VI-6

Antibody to Proteolipid and Myelin Basic Protein in Multiple Sclerosis (MS) Sera

William Sheremata, Miami, Florida, Denise D. Woods, Toronto, Mario A. Moscarello, Toronto

Proteolipid (PL) is a major structural myelin protein. Its lack of solubility has limited investigations as to its possible role as an antigen in experimental and clinical demyelinating disease. Antibody to PL occurs in EAE and has been shown to cross react with myelin basic protein (BP). As in EAE studies, we used double immunodiffusion plates with acrylamide gel slices containing PL or BP to assay 90 human control and 101 MS sera for specific antibody.

Only 1 of 32 normals but 14 of 58 with other neurological disease (OND), and 55 of 101 MS patients showed positive responses to BP. In contrast, 1 normal, 13 OND and 6 MS patients showed positive responses to PL. While 75% of convalescent MS sera had BP antibody, only 11% had PL antibody; although both antibodies occurred equally in OND.

These assay results may only reflect physiochemical differences between BP and PL, and the limitations of the assay system. However, they suggest that in MS during convalescense there is an active humoral immune or B cell response to BP, but not PL.

VII-1

2-Deoxy-Glucose Metabolism in Generalized Seizures Arising from a Kindled Focus

A. H. Handforth, D. C. N. Howse, Kingston, Ontario

The pattern of metabolic activity arising from generalization of a seizure focus has been studied in the adult rat brain employing the technique of autoradiography using (^{14}C)-2-deoxy-D-glucose (2DG). A seizure focus in the right amygdala was created by recurrent intermittent, brief stimulations (the kindling effect) until generalized (class V) seizures developed. An intra-arterial pulse of 25 uCi of 2DG was administered to alert awake animals followed by stimulation-induced seizures, and the animal was sacrificed 45 minutes later. Autoradiographic analysis was carried out using a computerized densitometric system. Generalized motor seizures were associated with a marked bilateral increase in activity in the substantia nigra and a less intense but symmetrical increase in hippocampal metabolic activity. Minimal changes were observed in the stimulated amygdala and neocortex. These findings emphasize the importance of specific subcortical mechanisms in seizure generalization.

In addition, a study of the phenomenon of post-seizure inhibition was carried out. After a series of 14 seizures were administered at hourly intervals to kindled animals a marked elevation in seizure threshold occurred, attaining a maximum at 48 hours. An autoradiographic study using 2DG was carried out and the results will be discussed.

VII-2

Sodium Valproate in the Treatment of Intractable Seizure Disorders of Childhood

D. Keene, K. Metrakos, G. V. Watters, and A. Sherwin, Montreal

65 children with intractable seizure disorders, who had had adequate trials of multiple anticonvulsants without achieving control, were selected from the Montreal Children's Hospital seizure units and placed on Sodium Valproate. The purpose is to report on the pharmacokinetic and clinical findings in these patients.

Rapid oral absorption of Sodium Valproate leads to peak serum levels in 1-3 hours (later peaks occurring if administered after meals.) A mean serum half-life of 12.3 hours was obtained. Correlation between oral dosage and plasma levels was poor. The occasional side effects which occurred were mostly gastrointestinal. Interactions with Phenobarbital, Dilantin, and Clonazepam presented some difficulties. If possible Clonazepam should be discontinued before starting Valproate.

Classification as to type of epilepsy in these patients proved very difficult when using the presently available classifications. Many of our patients had changing or mixed seizure and EEG patterns. Though the clinical results are not outstanding, a few obtained complete control; but the majority of the generalized seizure patients showed a decrease in seizure frequency with a secondary benefit of improved awareness and decrease in behavior disturbance. The addition of Valproate makes a trial of this drug warranted in all cases of intractable seizure disorders of childhood.

VII-3

The Effects of the Anticonvulsant Valproic Acid on Cerebral Indole Amine Metabolism

V. MacMillan, Toronto

Valproic acid (VA) produces increased cerebral concentrations of 5-hydroxyindoleacetic acid (5-HIAA) which has suggested that altered serotonin (5-HT) synthesis may explain its anticonvulsant properties and reported effectiveness in the treatment of postanoxic action myoclonus. The effects of 1h exposure to VA (500 mg/kg) on indole amine metabolism were studied in rats by measurement of cerebral hemisphere contents of tryptophan, 5-hydroxytryptophan (5-HTP), 5-HT and 5-HIAA. Tryptophan and 5-HIAA were increased at 1h exposure to VA, whereas 5-HTP and 5-HT remained unaltered from control. The accumulation of 5-HTP after decarboxylase inhibition with 3-hydroxybenzyl hydrazine was not altered by VA and thus indicated that the tryptophan hydroxylation rate was not altered by VA or by the elevated brain tryptophan levels. The accumulation of 5-HT after monoamine oxidase inhibition with pargyline was also not affected by VA and thus suggested that the synthesis of 5-HT was not altered. The combination of VA and probenecid resulted in a 5-HIAA level which was equal to that of VA alone. The results indicate that VA increases brain 5-HIAA by inhibition of the transport mechanisms which remove 5-HIAA from brain.

VII-4

Epileptic Twilight State

M. Newman and A. J. Gomori, Winnipeg

3 cases of continuous partial seizures or epileptic twilight state are described with EEG's taken during and between attacks. One patient had a history and EEG evidence of only generalized seizure activity as in the cases described by Lennox as Petit Mal Status. The other two had clinical and electrographic evidence of unilateral temporal lobe disturbance. The immediate and continuing treatment of this type of epilepsy is discussed and the differentiation between Petit Mal Status and complex partial status advocated by J. Engel, Belawsky and others is disputed.

VII-5

Forebrain Commissurotomy for Intractable Seizures

Juhn A. Wada, Peter D. Moyes, Vancouver, B.C.

Our experimental studies involving non-epileptic rhesus monkeys as well as epileptic Senegalese baboons, suggest that forebrain commissure plays a vital role in secondary generalization of clinical seizure originating from one hemisphere but also in the development of primary generalized convulsive seizures. In addition, our results suggest that the anterior 2/3 bisection is sufficient to achieve this goal for control of convulsive seizure of temporal lobe origin.

Based upon these experimental observations, two patients have undergone forebrain commissurotomy. Both patients had bilateral multi-focal abnormalities. Their seizure included automatism with or without convulsive seizures, severe behaviour disturbance and atonic seizure with loss of consciousness. These seizures were medically refractory in spite of intensive monitoring and treatment with multiple medications. Since they underwent commissural bisection 20 and 8 months ago (at the time of this writing), they have remained free of habitual seizure on continued medications.

Some controversy exists in the results of animal experimentation, suggesting that commissural bisection may increase susceptibility. Our own study suggests that the findings obtained in —non-epileptic- animals are quite different from those obtained from 'epileptic' animals. Our limited clinical experience also suggests that forebrain commissure of man with severe seizures is not only a major transhemispheric transmission route of

epileptic discharge, but also appears to play a major role in facilitating intra- as well as interhemipsheric ictal process.

We believe that forebrain commissurotomy is a beneficial alternative for those medically intractable patients who do not qualify for open classical excisional surgery.

VII-6

High Dose Short-acting Barbiturates in Refractory Status Epilepticus

G. B. Young, Saskatoon, W. T. Blume, London, Ontario; K. G. Warren, Edmonton, and C. F. Bolton, London, Ont.

Parental high dose barbiturates have recently received considerable attention in the treatment of raised intracranial pressure. We feel another indication is the treatment of refractory status epilepticus.

5 patients aged 19-62 years were treated for grand mal status epilepticus unresponsive to intravenous phenytoin, phenobarbital or diazepam as well as rectal paraldehyde. 2 patients had chronic static cerebral lesions and a previous history of grand mal seizures. 2 others had acute encephalitis and 1 had post-infectious encephalomyelitis due to measles.

3 patients were treated intravenously with Thiopental + 2 with Pentobarbital in doses sufficient to require assisted ventilation + to produce a burst-suppression pattern on the EEG, for 4-12 days. None received skeletal muscle relaxants. In each case the seizures were stopped successfully. The 2 patients with chronic cerebral lesions recovered to their former state. 1 patient with encephalitis recovered completely. The other patient with encephalitis and the patient with post-infectious encephalomyelitis have moderate mental impairment but are continuing to improve.

In conclusion: 1) high dose barbiturates are effective in stopping refractory grand mal status epilepticus, 2) the treatment may have to be maintained for several days, 3) skeletal muscle relaxants are unnecessary in this treatment.

P-II-1

"Bobble-Head Doll" Syndrome

Peter B. R. Allen, Edmonton

An unusual, involuntary movement of the head and neck occasionally occurs in association with lesions of the third ventricle. The evolution, recognition, management and results of treatment are described in association with a review of similar cases described in the literature.

P-II-2

Meningiomas Associated with Cerebral Cysts

W. S. Tucker, H. Nauta, W. J. Horsey, J. M. Bilbao and C. G. Gonsalves, Toronto

Three cases of cystic meningioma encountered over a one year period are presented and their pathological features together with the pitfalls of diagnosis and treatment are discussed. It appears from a review of the literature and an analysis of these three cases that large xanthochromic cerebral cysts may be associated with meningiomas in any of three configurations: 1) centrally within the tumour 2) peripherally within the tumour 3) in the adjacent brain. Regardless of which configuration applies, the C.T. appearance of such cystic meningiomas may mimic that of a glial tumour with cystic or necrotic change and lead to an incorrect presumptive diagnosis of malignant glioma. This false impression may be perpetuated by the gross appearance at operation, which likewise can mimic malignant glioma. Although several radiologic features should alert one to the possible presence of a cystic meningioma, we know of no definitive radiologic means to differentiate this lesion from the more common malignant glioma. This finding should underscore the need to biopsy cerebral neoplasms regardless of how much their appearance on C.T. Scan may suggest malignant glioma.

P-II-3

Treatment of Pathological Fracture Dislocation of the Spine due to Metastatic Cancer

R. G. Perrin and K. E. Livingston, Toronto

Pathological fracture dislocation of the spine, a potentially disastrous complication of systemic cancer, is rarely reported.

We have treated 20 patients with symptomatic pathological fracture dislocation of the spine, including eighteen women and 2 men ranging in age from 30 to 74 with a mean of 46 years.

Culpable primaries included breast (12 women), thyroid (2), uterus (2), lung (1), lymph (1), skin (1) and one unknown.

The cervical spine was most commonly involved (10), followed by thoracic (6) and lumbar (4) levels.

Local neck or back pain was the presenting symptom in 19 patients. At the time of surgery, 10 patients were ambulatory, 7 were bedridden, and 3 showed no clinically detectable voluntary movement.

Treatment involved skeletal traction, posterior decompression of the cord and stabilization of the spine (with rib strut or Harrington instrumentation). All patients were considered for postop radiotherapy and chemotherapy.

Fourteen patients reported pain relief after treatment. Fourteen were ambulatory, 4 were improved, and 2 were unchanged following surgery. One patient died during the early postoperative period of disseminated disease and 7 patients survived an average of 5 months. Twelve patients are living an average of 15 months after surgery.

A satisfactory result (walking and continent 6 months after treatment) has been achieved in 9 cases.

Spinal metastases may present as pathological fracture dislocation of the spine. Critical neurologic sequellae can be avoided or reversed by urgent decompression of the cord and stabilization of the spine.

P-II-4

Intracranial Pressure Monitoring with the Epidural Fiber-Optic Transducer in Children

L. P. Ivan, E. C. G. Ventureyra, S. H. Choo, Ottawa

Observations on 28 patients with continuous I.C.P. monitoring are reported. The authors used the fiber-optic transducer with digital readout and paper recording facilities in the Intensive Care Unit of the Children's Hospital of Eastern Ontario. Eighteen patients were suffering from severe head injuries, ten from other conditions requiring I.C.P. monitoring. Intracranial pressure monitoring with this technique using an epidural sensor, proved reliable and very valuable in the management of patients in coma. No infection occurred in this series, nor were there any other complications arising from the technique. Apart from 3 episodes of breakage of the transducer cable, the authors did not encounter technical difficulties with the system.

The findings are analyzed and good correlation between pressure readings below 20 mm. Hg and above 50 mm. Hg was found in predicting the outcome of severe head injuries. Pressure readings between 20 and 50 mm. Hg. cannot be used for predicting outcome according to our observations. Seven patients were managed with therapeutic deep barbiturate coma, which was found extremely useful to reduce increased intracranial pressure and to improve the outcome of severe head injuries.

P-II-5

A Review of Clinical Experience with Diaphragm Pacing

R. G. Vanderlinden, S. W. Epstein, Toronto

The indications for diaphragm pacing include paralysis of respiration due to transection of the upper cervical cord and ventilatory insufficiency due to impaired respiratory centre control.

The selection of patients requires evaluation of function of the respiratory centre, as well as the phrenic nerves, lungs and diaphragms, and ideally, the latter three components are normal. The evaluation includes response to hypercarbia and hypoxia, arterial blood gases during sleep, phrenic nerve viability, flow-volume curves and fluoroscopic assessment of diaphragm function.

The pacing apparatus consists of an electrode implanted around the phrenic nerve in the neck and connected to a radio receiver. A battery powered radio frequency transmitter emits adjustable trains of pulses that induce current in the receiver.

The first case of total ventilatory support by diaphragm pacing in Canada was successfully instituted in 1973 at the Toronto Western Hospital in a patient with high cervical cord transection. Since then we have had experience with diaphragm pacing in three more quadriplegic patients, one baby with neonatal apnoea, and two patients receiving nocturnal pacing

for primary alveolar hypoventilation. Considerable clinical and physiological information has been recorded.

The results in these seven patients indicate that diaphragm pacing is a practical clinical method of managing chronic ventilatory failure in carefully selected cases.

P-II-6

Anterior Cervical Discoidectomy without Fusion. An Effective and Safe Procedure

Gerard Leblanc, Québec

The author presents 13 cases of anterior cervical discectomy without fusion performed with magnification and using a unilateral approach. It will be shown that total discectomy without fusion may provoke subluxation, but that a unilateral approach will not do so. A follow-up period of 18 months with progress X-rays shows good stabilisation of the cervical spine with rapid bony fusion of the vertebral bodies from three to six months in a high percentage of cases. The operation procedure is simple, safe, less time consuming and with a short post-operative course. The author feels that this technique should be the procedure of choice for the acute herniation of a cervical disc and for unilateral radiculopathy consequent to foraminal narrowing by osteophytes.

P-II-7

An Unusual Case of a Partly Calcified Arachnoid Cyst at D7 and Meningioma at D8-D9 causing Paraparesis

E. Berger, J. Ashby, C. Auger, G. Duckett, Y. Mayrand, A. Neaga and M. Villota, Montréal

A 69 year old female was admitted with a history of progressive paraperesis. Myelography showed an almost complete block at D8-D9. Laminectomy and intra-dural exploration led to the removal of a meningioma causing flattening of the cord at the D8-D9 level as well as of an archnoidal globular cyst partly calcified and attached to the inside of the dura in its posterior aspect at D7. The calcified plaque measured 1.2 + 1 + 0.2 cms. The calcified plaque extended in a semicircular fashion over the posterior half of the dura sub-durally. Rapid post-operative recovery, patient now walking and even dancing.

Although intra-cranial meningiomas associated with disseminated arachnoidal calcifications have been reported in the medical literature, a Medline search using the computor service of the McGill Medical Library failed to reveal similar entities in the spinal canal in a review of recent medical literature.

P-II-8

Extradural Tumours in the Region of the Foramen Magnum in Children

Q. J. Durward, A. L. Amacher and J. Shillito, London and Boston

Extra-medullary tumours in the region of the foramen magnum in children are rare. Only five such cases have been described to date and of these, only one was extradural.

We have encountered three cases of extradural tumours in this region; a 6 year old girl with an extradural sarcoma lying anteriorly between the foramen magnum and the odontoid process, a 7 year old boy with an osteoma arising laterally from the occipital condyle, and a 5 year old boy with Ewing's sarcoma of the odontoid.

The points of interest regarding these three cases are: i) bizarre and varied clinical presentations; ii) a surprising lack of physical findings, and iii) the problems of surgical approach to tumours in this region in children.

We shall discuss the difficulties in diagnosis, the problems of surgical approach, and the risks inherent in surgical and radiation therapy, when such lesions are encountered.

P-II-9

Transdural Anastomoses Stimulated by Craniotomy

Allan J. Fox, Gary Gerguson, & Gerard Debrun, London

Transdural anastomoses separate from the microsurgical EC/IC bypass has been seen to develop in follow-up angiograms of 8 patients who underwent EC/IC surgery for cerebral ischemia. Seven of these had the angiographic appearance of "poor" EC/IC function, and one had development of meningeal anastomosis in addition to a well-functioning bypass. None of these dural anastomoses were present on pre-operative angiograms, and all developed near the edges of the craniotomy defects. These observations suggest that craniotomy alone will stimulate some transdural anastomoses to cerebral cortex which is relatively deficient in supply in some cases. Post-operative angiography of EC/IC cases therefore, needs to clearly distinguish superficial temporal from meningeal arteries.

P-II-10

A New Technique for Rapid Vascular Anastomosis

W. M. Lougheed and F. Gentili, Toronto

Despite advances in microsurgical techniques, problems in cerebrovascular reconstructive surgery remain, including that of providing an adequate blood volume to the brain and maintaining blood flow while the microscopic anastomosis is being created. We have utilized a technique based on the development of a specially devised anastomotic clip which allows for rapid vascular anastomosis without the need for placement of any sutures. An autogenous vein graft is used. Each end is prepared and mounted on the second ring of the clip. When allowed to close the design of the clip brings the junctional areas of the graft and vessel together firmly and allows for the lumen of the vein graft and recipient vessel to be automatically aligned. Time taken for carrying out the anastomosis has averaged ten to fifteen minutes. We have used this technique in 20 vascular anastomoses in the dog using both carotid and femoral vessels. The patency rate in animals followed for 6 to 12 weeks with serial angiography has been 100%. Post mortem histological and scanning electronmicroscopic studies have revealed excellent junctional anastomosis with no evidence of thrombosis. This experimental work demonstrates the technical feasibility of this procedure which in man could be applied to the treatment of inaccessible intracranial regional stenotic lesions of the internal carotid, middle cerebral and vertebral arteries and in dealing with large complex aneurysms.

P-II-11

Cervical Stenosis

Drs. O. F. Veidlinger, J. C. Colwill, H. S. Smyth and R. G. Elgie, Toronto

A distribution curve of cervical canal saggital diameters in 40 patients presenting with cervical myelopathy showed a shift to the left when compared with 200 controls. Detailed analysis of 100 additional cervical canals at each level is made, taking into account the distortion found in the standard six foot lateral projection. 75% of the symptomatic cases could be classified as having cervical stenosis with a canal diameter under 15 mm. Additional encroachment on the canal by hard bars in older patients, soft discs in younger patients, infolding of the ligamentum flavum and cord edema, produce a variety of clinical pictures which often lead to misdiagnosis, especially in the longstanding cases. A rationale for surgical treatment must consider the fact that most cases had multiple levels of compression. Results are analyzed by individual symptoms and were favorable even in longstanding cases of compression and did not depend on the specific procedure used. Some complications can be prevented by preservation of the hypophyseal joints for stability and avoidance of foraminal instrumentation, to minimize interference with the spinal blood supply.

P-II-12

Pathogenesis of Coning in Acute Fatal Stroke

O. B. White, J. W. Norris, V. C. Hachinski and A. Lewis, Toronto

Eight hundred and sixty-one patients were admitted to the Stroke Unit at Sunnybrook Hospital over three and a half years, and 163 died within the first month of whom 56 cases came to autopsy. There was a marked difference between the mode and timing of death in the cerebral hemorrhage cases compared to those with cerebral infarction.

Twenty-three of 27 hemorrhagic stroke patients died from cerebral coning, 13 of these dying within the first 24 hours, the remainder dying during the next 10 days. The remaining four cases of this group died from pneumonia or pulmonary embolism. Ten of 29 ischemic stroke cases died from cerebral coning between days 2-10, but none died within the first 48 hours. Five patients died from acute myocardial infarction within the first five weeks. The remaining 14 patients in this group died in the acute phase from either pneumonia, pulmonary embolism or congestive heart failure.

Death in the first 24 hours in patients with acute cerebrovascular lesions appears to be due to the overwhelming mass effect of accumulation of blood within the brain. Thereafter, the hazard of coning from acute cerebral edema in either the hemorrhagic or ischemic stroke patients is no longer present after 10 days.

P-II-13

Glioblastoma Following Radiation Therapy

Renn O. Holness, Virgilo E. Sangalang, Halifax

Therapeutic irradiation has been incriminated occasionally in the development of malignant intracranial neoplasms. These have been usually mesodermal and very rarely glial in origin.

In the present case the patient, a young man with acromegaly had received 4000 rads. to the pituitary region 6 years previously. He presented in Oct. 78 with seizures, then again in Jan. 79 with raised intracranial pressure and rapid onset of a transtentorial pressure cone. Investigation and subsequent surgery confirmed a left temporal lobe glioblastoma. The patient expired despite surgery.

Autopsy findings are presented in detail. The pituitary tumor was still viable correlating with elevated serum growth hormone levels prior to death. The glioblastoma was situated within the previous field of irradiation. Furthermore, histological evidence of radiation induced changes existed alongside frankly neoplastic cells suggesting a pathogenetic connection between the two. A relevent literature review is given.

P-II-14

Diving may be a Breakneck Affair

Charles H. Tator and Virginia E. Edmonds, Toronto

Diving accounted for 10.6% of a series of 358 patients with acute spinal cord injuries admitted to Sunnybrook Hospital and Toronto General Hospital from 1948 to 1973, and was by far the commonest cause of spinal cord injury sustained during sports or recreational activities. The median age of the 38 patients injured while diving was 21. Thirty-two were males and six were females. The commonest vertebral level of injury was C5-6 in 14 patients followed by C4-5 in eight patients. Anterior fracture-dislocations, posterior fracture-dislocations, and compression fractures were the most frequent types of vertebral injuries. Twenty-five patients had total motor and sensory loss below the level of the lesion, eight had total motor loss and some sensory preservation, and five had some motor and sensory preservation below the level of the lesion. Recovery of cord function was poor in those with major initial deficits.

Greater public awareness of the hazards of shallow water diving should lower the incidence of these injuries. Indeed, diving as a cause of cord injury in this series was higher than in most series from other countries.

VIII-1

Axillary (Circumflex) Nerve Palsy following Blunt Trauma to the Shoulder Region

Vera Bril and Henry Berry, Toronto

Although the commonest type of axillary nerve palsy occurs following shoulder dislocation or humeral fracture, another form is seen after blunt trauma to the shoulder region without associated fracture or dislocation. The former usually goes on to a full recovery whereas a failure to recover is common in the latter group. In our review of 13 patients with palsy after blunt shoulder trauma, 7 patients showed minimal or no recovery of deltoid muscle function and 6 patients went on to complete or near complete recovery. Serial electromyographic examinations usually revealed the lesion to be in continuity although clinical recovery was not satisfactory in a number of these patients. The mechanism of the palsy appears to involve a stretch injury and this was confirmed at operation in 2 patients. Glenohumeral fixation can be a troublesome complication and did limit the recovery of function in 4 patients. Further details of the type of trauma, clinical and electromyographic examination, assessment and management are presented and discussed.

VIII-2

Glucose Transport and Oxidation in Myotonia Dystrophica

E. Mably, K. P. Strickland, G. J. M. Tevaarwerk and A. J. Hudson, London

Previous studies have shown that insulin binding to monocytes in myotonia dystrophica (MD) is reduced. Accordingly, insulin binding was further studied by investigating the effect of insulin on the transport of 1-^{14}C-2-deoxy-glucose (2dog) and the oxidation of 1-^{14}C-glucose in chopped adipose tissue from 15 MD patients with two age- and size-matched control subjects for each. The transport of 0.55 mM 2dog was measured over 3 min at 37° with or without 32 ng/ml of insulin and stopped with 400 mM glucose before isolation and washing of the tissue on a millipore filter. Oxidation was determined at 37° for 90 min by absorption of $^{14}CO_2$ from a system containing 0.55 mM glucose with or without 50 ng/ml of insulin. Results per 10^5 cells were calculated using diameters measured on collagenase-isolated cells and lipid content of chopped tissue samples for each patient. Mean basal values (± S.D.) for transport in MD and control subjects were 231 ± 121 pmoles and 318 ± 154 pmoles, respectively. Stimulation of transport by insulin was significant at 321 ± 158 pmoles ($p=0.01$) for MD and 541 ± 273 pmoles ($p<0.001$) for control subjects. Basal oxidation (mean ± S.D.) in MD was 1.46 ± 0.78 nmoles and for the controls was 1.68 ± 0.59 nmoles. Stimulation of oxidation by insulin was significant with an increase to 1.74 ± 0.89 nmoles ($p\ll0.001$) in MD and 2.04 ± 0.80 nmoles ($p<0.001$) in the controls. Control-matched paired comparisons showed that in MD patients the transport of 2dog is similar to control levels basally ($p=0.1$) but is significantly less with insulin ($p=0.02$). By identical comparisons no difference in oxidation was found ($p=0.4$). Thus, insulin-stimulated glucose transport, but not oxidation, is impaired in MD. This finding provides further indication of a cell surface membrane abnormality in this disease. MRC #MA-5702

VIII-3

Déjerine-sottas Disease in Children

A. Hill and D. A. McGreal, Toronto

Déjerine-Sottas Disease also known as hypertrophic interstitial neuritis is a rare progressive peripheral neuropathy accompanied by enlargement of the spinal and peripheral nerves.

Seven cases of Déjerine-Sottas Disease will be presented and the following aspects will be reviewed: — mode of inheritance (autosomal recessive or dominant), age and mode of presentation, the value of spinal x-rays, myelography, CSF protein and sural nerve biopsy in diagnosis, variation in course and severity, spinal cord signs and symptoms secondary to massive spinal nerve swelling compressing the spinal cord.

VIII-4

A "Partial Syndrome" of Myotonic Dystrophy

W. Pryse-Phillips, G. J. Johnson & B. Larsen, St. John's

Among 144 subjects of a single large kindred examined by a Neurologist, an Ophthalmologist and by EMG, a definite diagnosis of Myotonic Dystrophy (DM) was possible in 33. The most significant diagnostic features were orbicularis weakness, reduced intraocular tensions and decreased frequency and amplitude of blinking. A characteristic facial expression, apathy and a typical EMG findings were the other most frequently detected abnormalities. The agreement between the ophthalmologic and neurologic diagnosis was completed both for affected and unaffected cases. However, 16 of the subjects had equivocal features, again with full agreement between ophthalmology and neurology. Such included posterior capsula colored specks, ptosis, wasting of masseters, sharp mouth, slow relaxation of hand grip or eye closure, and abnormal, not myotonic, EMG findings.

The characteristics of this group and their likely classification and significance will be discussed. In view of the expected numbers of affected subjects, such patients are thought unlikely to have a true syndrome of DM although their appearance may represent the phenotypic results of transmission of small amounts of the determining genetic material. Other hypothesis will be discussed in the light of the finding within this study of a new genetic marker.

VIII-5

Infantile Neuroaxonal Dystrophy; Clinical and Neuropathological Diagnosis

V. Sangalang, Peter Camfield & J. A. R. Tibbles, Halifax, N.S.

In 1952 Seitelberger described infantile neuroaxonal dystrophy (INAD) and it has since been the subject of many reports. The earlier cases were diagnosed at necropsy. The disorder may sometimes be recognized clinically but confirmation of the diagnosis during life by light and electron microscopy of cerebral biopsies has been limited, particularly in the early stages of the disease (Herman et al, Toga et al). Recent reports of axonal lesions in peripheral nerves, intramuscular nerves, and unmyelinated nerve fibers of conjunctival biopsies if confirmed, may obviate the need for brain biopsies.

We describe the clinical features and light and electron microscopic findings of cerebral, sural nerve and muscle biopsies from two cases of INAD diagnosed during life at a relatively early stage. The pathogenesis of the axonal lesions is discussed in the light of current knowledge of axonal biology. The study provides an opportunity to re-evaluate the consistency and specificity of some of the axonal lesions recently described in peripheral nerves.

VIII-6

Malignant Hyperthermia: A Cause of Unexplained Elevation of Serum Creatinine Phosphokinase (CPK)

A. S. Gordon, B. A. Britt, Toronto

The individual who has an elevated serum CPK in the absence of any easily definable neuromuscular disease, cardiac disease, hypothyroidism. psychosis, or trauma poses a difficult and challenging problem. We have recently seen 9 patients referred primarily because of an unexplained elevation in CPK (MM band). The clinical features included muscle cramps, pains and tenderness, ptosis and a high degree of anxiety. One man had bilaterally ruptured biceps muscles and only two had mild proximal myopathy. In none was an anesthetic reaction a prominent complaint. At the time of muscle biopsy, a strip of muscle was subjected to the caffein-halothane contracture test of Kalow and Britt. This test is highly diagnostic for MH and it was abnormal in 7 out of 9. Based on detailed anesthetic history, cardiac evaluation, and clinical, CPK and biopsy screening of family members, 3 out of 7 have definite MH. One of the patients belongs to a previously unrecognized large Italian kinship, members of which have had documented anesthetic reactions, unexplained sudden death, and muscle complaints. A fourth suspect belongs to a kinship with an unexplained myopathy but no hyperthermic reactions. The remaining three positive patients are considered isolated MH suspects.

The CPK is high in some but not all patients with MH. This disease should be considered in anyone with a persistently elevated CPK.

VIII-7

Startle Disorders of Man: A Unifying Concept

Daniel L. Keene, Eva Andermann, Frederick Andermann and Louis Felipe Quesney, Montreal

Startle is a protective reflex common to man and animals. Our studies of two families with hyperexplexia, as described by Suhren, Bruyn and Tuynman, lead us to propose a unifying concept of the startle disorders of man, all of which appear to share certain common pathophysiological features.

Abnormal startle is encountered alone in essential startle or startle disease (Gastaut); in association with echopraxia and echolalia in the Jumpers of Maine (Beard, 1878); and in a percentage of patients with Tourette's Syndrome, where echopraxia and echolalia may also occur.

We found hyperexplexia to be a dominantly inherited disorder with variable expressivity which may present in two forms within a family: hyperexplexia minor, where only intermittent excessive startle occurs; and hyperexplexia major, where the abnormal startle is associated with hypertonia in infancy, falling spells, episodes of nocturnal myoclonus of the legs, hyperreflexia and insecure gait. All symptoms of this often undiagnosed disease respond best to clonazepam. The incidence of epileptogenic electrographic discharges is high; yet, the clinical symptomatology does not appear to be epileptic per se.

By contrast, in startle epilepsy, the stimulus activates epileptic discharges and symptoms appropriate to the underlying focal or generalized epileptic disorder.

IX-1

Spontaneous Dissection of the Internal Carotid Artery

B. G. Benoit and N. L. Nabavi, Ottawa

Three examples of this uncommon condition were recently treated at the Ottawa Civic Hospital, and details are presented to further define the management of this potentially lethal condition.

Two males, age 37 and 42 years, presented with hemicranial pain, and ipsilateral Horner's syndrome. Angiography revealed the "string sign" with distal "pouch", and both patients were subsequently treated by anticoagulation. The condition stabilized, the only residual being a mild Horner's syndrome. Interval angiography on both patients, demonstrated an improvement in lumem size but persistance of the distal "pouch".

A 36 year old male, presented with peri-orbital pain, visual blurring, and Horner's syndrome, which went unrecognized for ten days. Subsequently, he suffered a massive right cerebral infarction, and died within 48 hours. Angiography revealed a long segment of arterial narrowing, but the patient's advanced clinical condition precluded definitive treatment. At autopsy, the cervical carotid artery, was found to be almost occluded, due to an intimal flap raised by hemorrhage in the media.

Most cases of spontaneous carotid dissection, begin with headache, facial pain, oculo-sympathetic palsy, with or without transient neurological deficits. Angiography reveals distinctive changes, which vary from a long segment of stenosis, to a tapering type of occlusion, frequently with distal localized aneurysmal dilatation of the artery.

The precise etiology is unknown, but it would seem that the dissection begins in an area of medial necrosis, for which numerous causitive factors have been described.

Proper management, consists of early diagnosis and angiography. Anticoagulant therapy, or surgical intervention, should then be undertaken promptly, in order to prevent the dissection with its potentially devastating consequences.

IX-2

Routine rCBF Monitoring During Carotid Endarterectomy

M. I. Vilaghy, D. W. Rowed, J. W. Norris and V. C. Hachinski, Toronto

Using a new type of probe holder especially designed for regional cerebral blood floow (rCBF) measurements in the operating room, we have evaluated rCBF and carotid stump pressures during carotid endarterectomy in 23 patients. Marked discrepancy between stump pressures and rCBF recordings after carotid occlusion were seen in 45% of cases. An explanation for the unreliability of stump pressure as a guide to cerebral perfusion will be proposed.

There was no relationship between the degree of arterial stenosis seen on angiogram compared to the observed rCBF values, and little or no change in rCBF values post-operatively even when high grade stenoses were present. Our experience indicates that previous empirical levels of "ischemic" rCBF should be revised in the light of our experience with individual cases.

Routine intraoperative rCBF determination reduces operation time by decreasing the frequency of arterial shunting. The exposure required is less extensive and the high carotid bifurcation is more reasonably accessible. Routine shunting does not eliminate the risk of intra-operative embolization and appears to be required only in a minority of cases. We, therefore, believe that routine intraoperative rCBF determination is an important adjunct to carotid endarterectomy

IX-3

Cerebellar Infarction — Review of Recent Experiences

W. B. Woodhurst

Cerebral infarction is an underemphasized condition which untreated carries a high mortality rate. This report reviews seven cases of cerebellar

infarction seen by the V.G.H. neurosurgery service during the past two years. The patients ranged in age from 44 to 69 (average 56). There were four men and three women. The common initial symptoms were vertigo, headache, nausea, vomiting, and ataxia. Physical findings, often minimal at onset included; obtundation, gaze paresis, nystagmus and limb or gait ataxia. Most patients (5/7) demonstrated progressive deterioration from posterior fossa mass effect and/or hydrocephalus. Four patients underwent posterior fossa craniotomy and resection of the infarcted cerebellar tissue. Of these four patients three were unconscious at the time of operation; two recovered, one died, and one was drowsy and recovered. One other patient had a ventriculoperitoneal shunt for hydrocephalus and made a progressive recovery. Two patients recovered without surgical therapy. The CT scan often demonstrates the infarct if a good quality examination is obtained.

The treatment of patients with progressive signs of deterioration is surgical decompression of the posterior fossa by resection of the infarcted tissue. Shunting for hydrocephalus may alleviate some of the secondary effects of the mass lesion. Early recognition of the clinical and radiographic features and prompt treatment are essential for recovery.

IX-4

Barbiturate Therapy — A Report of Fifteen Cases

H. Hugenholtz, Toronto

An anecdotal account is given of fifteen patients subjected during the past year to barbiturate therapy for global hypoxia, cerebral oedema of various etiologies and vasospasm.

Barbiturate therapy was combined with mild hypothermia (31°dC. to 32.5°C) in eleven cases. The dose of barbiturates was titrated to maintain low serum levels (less than 1.5 mg. per dl.) and thereby avoided the need for controlled assisted ventilation in 14 cases. The I.C.P. was monitored in all patients.

Problems encountered in the management of these patients are presented as well as the current use of such a barbiturate protocol in the early surgical repair of ruptured intracranial aneurysms.

The presentation includes an outline of the prerequisites required before undertaking this method of treatment, the problems encountered in the management of these patients.

Based on this limited clinical experience, there appears to be a potential role for barbiturate therapy in the early operative intervention of ruptured intracranial aneurysms.

IX-5

Antiplatelet and Anticoagulant Failure in Carotid Artery Occlusion

R. T. Ross, Winnipeg

Thirty patients with unilateral occlusion of one internal carotid artery were studied. Twenty of the patients presented at the time of diagnosis with a history of transient ischemic attacks. In fifteen of the twenty the T.I.A.s arose in the middle cerebral artery ipsilateral to the occluded internal carotid artery. All patients had some collateral blood flow to the ipsilateral middle cerebral and more than half of the thirty patients had two collateral sources. Twelve of the thirty patients had adequate controlled therapy with a variety of antiplatelet or anticoagulant medication. The outcome was poor in all.

IX-6

Carotid Endarterectomy and Prevention of Stroke

J. Barwinsky and M. Newman, Winnipeg

131 consecutive patients underwent 152 operations of carotid endarterectomy for T.I.A. at St. Boniface Hospital and were followed for up to nine years. The results are assessed to indicate whether a controlled study of surgical versus medical treatment would be ethical or adivsable. In the first four weeks after surgery, no patient died but six suffered strokes, a major complication rate of 4%. 112 patients were followed for a year after surgery. Of 77 normotensives, one suffered a stroke in the territory of the operated vessel and three strokes involved other arteries. Of 35 hypertensives, two strokes involved the operated vessel, two other arteries and one had hypertensive encephalopathy. In 56 patients followed five years, or to the time of stroke, there were five strokes in the operated vessel and 12 in others. When comparing the efficacy of medical and surgical therapy for T.I.A.'s, the important criterion is prevention of stroke in the relevant carotid territory. These figures are at least as good as any published on treatment with aspirin or anticoagulants. The proper controlled trial should compare a combination of medical and surgical therapy, with surgery alone and the groups must be matched for age and hypertension. The end point should be stroke.

IX-7

CBF Measurement as a Guide to the Safety of Internal Carotid Occlusion in the Treatment of Carotid Aneurysms

G. G. Ferguson, J. K. Farrar, C. G. Drake, G. A. Varkey, London, Ontario

Carotid ligation remains a technique to consider in the treatment of certain unusual carotid aneurysms. Recent reports from the Institute of Neurological Sciences in Glasgow have suggested that CBF measurement in conjunction with trial occlusion is a reliable guide to the safety of carotid occlusion.

Our experience with the "Glasgow technique" in five carotid-cavernous and two carotid-ophthalmic aneurysms treated by internal carotid artery occlusion has been reviewed. In every case the reduction in CBF values during temporary cross-clamping was less than 25% of control values and safety of permanent occlusion was predicted. Six patients tolerated the permanent occlusion uneventfully. However, one patient had a major delayed stroke. In this case there had been no reduction in CBF during trial clamping. Angiography revealed a saddle embolus at the intracranial carotid bifurcation and it is almost certain that the stroke occurred as a result of an embolus from the aneurysm rather than from hemodynamic ischemia.

Details of the evolution of this technique together with the recent application of the detachable balloon catheter. and potential pitfalls in the method will be outlined.

In general our experience supports the concept that hemodynamic safety of carotid ligation may be predicted by CBF measurements, but caution is still indicated as the risk of embolization following occlusion cannot be predicted.

X-1

Microvascular Morphometry in Hippocampal Cortex of Aged and Demented People

M. J. Ball and M. A. Bell, London, Ontario

Quantitative studies have shown significant differences in severity of the histopathological lesions of mesial temporal cortex not only between patients with Alzheimer's dementia and mentally normal aged persons, but also in both populations between various microscopic "zones" within the hippocampus itself. In order to explain this striking regional predilection of some "zones" and relative sparing of their immediate neighbours, a morphometric survey of the arteriolar-capillary system was undertaken as part of a larger investigation of the complete posterior cerebral artery tree.

Serial celloidin sections of the entire hippocampal formation from brains from aged and demented patients were stained with the alkaline phosphatase method. The density of, and internal diameters of the arterioles and capillaries were measured in up to 15,000 samples per brain from photographic enlargements with a digitizer and a particle size analyser. Data indicate that in some of these "zones" there are highly significant differences between the anatomy of the intraparenchymal microvasculature of aged people and of patients with Alzheimer's disease. The implications of this for understanding the pathogenesis of dementia will be presented.

X-2

The Effects of Ventricular Shunting on the Intellectual Functions of Patients with Normal Pressure Hydrocephalus

B. A. Ridgley, B. Dibkin, C. H. Tator, D. W. Rowed, Toronto

Despite the findings that dementia is an important symptom of the clinical triad in normal pressure hydrocephalus, very few studies have investigated changes in dementia after ventricular shunting with standardized and objective measures of brain functions. Based on subjective rating scales or on clinical impression, investigators have reported varing effects of shunting with different patient populations. Quantifiable measures of the changes in intellectual functions associated with surgical intervention could be useful in establishing a better criteria for patient selection.

In the present investigation twenty-four (N=24) patients with normal pressure hydrocephalus were assessed with various neuro-psychological tests before and after ventricular shunting. Fourteen (n=14) had a known etiology and nine (n=9) patients had an idiopathic history. All patients received the Wechsler Adult Intelligence Scale, the Wechsler Memory Scale and the Halstead-Wepman Aphasia Screening Test. Pre and post-operative between and within group comparisons are presented for the neuropsychological subtests in conjunction with various neurosurgical and neuroradiographic findings.

The idiopathic and known etiology groups did not differ significantly on pre-operative measures of their neuropsychological status. A statistically significant improvement was recorded post-operatively for the known etiology group. Instances of significant individual improvement was observed in the idiopathic and known etiology groups.

The difficulties inherent in conducting retrospective studies on the effects of ventricular shunting are outlined and the parameters necessary for controlled prospective investigations are discussed.

X-3

The Effect of Age on Intravenous Cerebral Blood Flow and Rise Time Measurements in Normal Subjects

Michael Schwartz, Gerald Mintz, Michael Joy, Macey Skopitz, Toronto, Ontario

Regional cerebral blood flow studies by the intravenous injection of Xenon-133 were performed on 18 resting subjects with neither symptoms nor signs of neurological illness. Their ages ranged from 39 to 78 years with a mean of 62. The flow index determined by 2 compartment analysis of the washout curve, and the rise time, that is the time interval between 10 and 90 percent of peak brain radioactivity were calculated. There was a strong correlation for both parameters with age: rCBF declined with age, whereas rise time increased. At age 62, the mean flow index value for our method was 47 ml/minute/100 gms. and the mean rise time was 0.62 minutes. The slope of the curve relating the mean cerebral blood flow and age was -0.5, that is at age 42, the expected normal value was 57, whereas at age 82 "normal" was only 37. Similarly, the normal rise time at age 42 was 0.49 minutes and at 82 was 0.75 min. The standard deviation from region to region within individuals for blood flow values was 6.46. For a biological measurement to be considered unequivocally abnormal, it is generally required to be at least 2 standard deviations from the mean. At age 62 in our subjects, therefore, low values are less than 33 and high ones greater than 59. The lesser value is well within the normal limits for a subject aged 82 and the greater value would be normal at age 42. Similarly, with a standard deviation of 0.098 for the rise time values about a mean of 0.62 minutes at age 62, the limits of normal for that age are well within the normal limits for subjects at the extremes of age in our sample. In conclusion, age is a very strong co-variant in cerebral flood flow measurements and must be considered in the assessment of any individual.

X-4

Alzheimer Paired Helical Filaments in Vitro

D. R. Crapper and U. De Boni, Toronto

A crude saline extract of Alzheimer affected brain induced paired helical filaments (PHFs) in neurons in fetal brain explants after 14 to 36 days. Since employing strict aseptic techniques the PHFs have only occurred after the addition of the extract from Alzheimer affected brain and have not been observed to have occurred spontaneously in untreated neurons or after treatment with chemicals or hormones. Material from four senile and pre-senile Alzheimer affected brain have induced PHFs. Employing centrifugation as a method for examining the size of the particle associated with PHF induction indicates a particle larger than 10s but smaller than 80s. Preliminary ultraviolet radiation studies indicate resistance to 10^5 erg/mm^2. While it is presently unknown whether the PHF inducing agent contains nucleic acid, the data suggest that induction is unlikely to be associated with a conventional virus.

X-5

A Familial Movement Disorder

Jeannine Talbot, R. D. Macdonald, Toronto

We will present a family in which five of twelve siblings suffer from abnormal movements with varying degree of severity. The movements are 1) fine choreic movements of the tongue, fingers, hands and toes, 2) proximal shock-like myoclonic jerks affecting mainly the neck, shoulders and abdomen, 3) a postural tremor, 4) dystonic posture of the neck and the arms. (A movie will be shown demonstrating these features.)

All cases had a rapid onset of abnormal movements in early childhood with no subsequent progression after the age of eight. The movements were increased by fatigue, stress and voluntary efforts to control them; they disappeared completely during sleep and following a moderate intake of alcohol. There was no associated epilepsy, progressive neurological deficit or dementia. A pharmacological trial was performed in one patient.

In the literature two conditions "Benign Familial Chorea of early onset" and "Hereditary Essential Myoclonus" differ by the description and definition of the movement disorder. They are otherwise similar in terms of heredity, age of onset and clinical features. The abnormal movements seen in our patients overlap both of the above conditions which we will propose represent a single entity.

X-6

Familial Cerebellar Degeneration, Polyneuropathy and Splenomegaly due to an Adult Form of Lipid Storage Disease

R. Wilson, J. Bilbao, S. Lowden, A. Hudson, Toronto

This paper will describe a familial condition in which there is a progressive cerebellar degeneration, a mild demyelinating polyneuropathy and a marked splenomegaly developing in a brother and sister in their fourth decade. Nerve conduction tests indicate a moderate generalized slowing of peripheral nerve conduction. No sphingomyelinase activity is present in the peripheral leukocytes. Electron microscopic examination of a sural nerve biopsy demonstrates a demyelinating neuropathy and accumulation of lipid in Schwann cells and pericytes which is immunofluorescent.

In the discussion an attempt will be made to classify this condition. It will be emphasized that even though there is an absence of sphingomyelinase activity in these two patients, no presently accepted form of Niemann-Pick disease is similar to their clinical picture. Because of the immunofluorescence of the lipid deposition the question of a relationship between this condition and the adult form of neuronal ceroid lipofuscinosis will be raised, and their differences discussed. It will be suggested that this condition may represent a new adult form of Niemann-Pick disease or a link between Niemann-Pick disease and the neuronal ceroid lipofuscinoses.

X-7

Neurotoxicity of Aluminum

S. J. Karlik and D. R. Crapper, Toronto

In Alzheimer pre-senile dementia, there is a statistically significant increase in cerebral cortical intra-nuclear aluminum content compared to age matched controls. Aluminum also accumulates within nuclei from the senile brain. Sub-nuclear fractionation indicates aluminum is isolated with DNA. The aluminum ion exists in solution in a complex equilibrium with many mono- and polynuclear hydroxides. The interaction of many metal ions with DNA can be altered through a change in metal concentration. Unique to aluminum is the observation that a different hydration state also alters the interaction of aluminum with the biopolymer DNA. At least two complexes exist: Complex I which raises the DNA Tm and Complex II which lowers the Tm. Complex II produces reversible DNA crosslinks similar to those produced by Cu^{+2}. The data is consistent with the presence of Al^{+3} and $Al(OH)^{+2}$ producing Complex II and Complex I respectively. Therefore, it is important to consider the species which exists in the varied disease states where aluminum is found. An underlying pathological process might alter the ionic balance, shifting the equilibrium from a benign form to a neurotoxic ionic configuration.

P-III-1

Isolated Vein of Galen Thrombosis: Clinical and Pathological Features

W. J. Becker, O. H. Huhn, R. West, T. P. Seland, H. A. Swanson, Calgary

This study reports a patient with cerebral thrombophlebitis limited to the vein of Galen and its tributaries.

A 21 year old female initially presented with unilateral throbbing headaches after starting oral contraceptive medication (Norinyl 1/50). Several months later she presented to the Emergency Department with a depressed level of consciousness and bilateral extensor plantar responses, but without lateralizing signs.

Lumbar puncture showed an opening pressure of 250mm of H_2O, no WBC, and 56 RBC/mm^3. CSF protein was 328 mg/dl.

She rapidly deteriorated and within 20 hours of admission was bilaterally decerebrate. Despite mechanical ventilation, she died 4 days after admission.

An EEG showed alpha activity, despite a stuporous state. Angiography showed good filling of the dural sinuses and superficial cerebral veins, but with complete lack of filling of the Galenic venous system.

At autopsy, she showed infarction of the corpus callosum, basal ganglia, and midbrain tegmentum. The cerebral cortex was intact. The vein of Galen was completely thrombosed, while all dural sinuses were open.

Isolated thrombosis of the Galenic venous system can cause coma without lateralizing neurologic signs and with alpha activity in the EEG. The diagnosis can be confirmed by early angiography.

Clinicopathologic corelations and the possible relationship of this syndrome to oral contraceptives are discussed.

P-III-2

Spontaneous Intracerebellar Hematoma — a 60% Mortality

Q. Durward, H. W. K. Barr, London

Despite clinical awareness and the accuracy of C.T., intracerebellar hematoma remains a lethal condition. McKissock's comprehensive report, consisting of 34 cases with a 74% mortality, has not been substantially improved despite a two decade interval.

We reviewed 20 cases seen over 10 years; the survival rate is dismal. It is proposed that surgical decompression may not be the only method of treatment.

Twelve out of 20 patients died (60%). Thirteen patients were subjected to craniotomy, 8 died (62%). Seven were treated conservatively, with 4 deaths (57%). This is a highly selected series and one cannot compare the two treatment approaches, but the outcome is related to the rapidity of the ictus and clinical status at the time of diagnosis. The 5 survivors in the surgical group were all able to follow commands pre-operatively. Four patients in the conservative group were moribund at the time of presentation or diagnosis, and surgery was declined. Three survivors were considered for surgery, but were improving, had purposeful responses to pain and only mild 4th ventricle compression.

In selective cases without deterioration or 4th ventricular obstruction, conservative treatment may be entertained. A comatose patient, without brain stem reflexes, will not survive, despite surgical decompression. Surgical evacuation is life-saving in selected cases, but despite the C.T. examination, early clinical recognition remains of paramount importance.

P-III-3

Cardiac Lesions Following Acute Stroke

John W. Norris, Vladimir C. Hachinski, and A. Kolin, Toronto

We have previously reported on the increased incidence of cardiac arrhythmias ($p < 0.001$), elevated serum cardiac enzymes ($p < 0.05$), and raised serum catecholamines ($p < 0.005$) in acute stroke patients when compared to controls. During these studies, we have sometimes observed areas of myocardial necrosis at autopsy in patients dying from cerebral infarction or hemorrhage.

In a prospective study of 36 patients dying with a variety of acute cerebral lesions including meningitis and brain tumor, the myocardium was examined by routine H & E sections. In three patients, there were acute myocardial infarctions. In the remaining 33 patients, the nine that showed multiple areas of myocytolysis all died from acute cerebrovascular lesions. Three had hemispheric infarctions, two brain stem infarctions, three hemispheric hemorrhages, and one ruptured aneurysm.

These cardiac lesions may play a role in the subsequent prognosis of acute stroke patients.

P-III-4

Value and Limitations of Doppler Scanning in Cerebrovascular Disease

M. I. Vilaghy, V. C. Hachinski and J. W. Norris, Toronto

A study was undertaken to establish the limits of clinical usefulness of Doppler scanning in 200 consecutive patients with cerebrovascular disease examined by this ultrasound technique. Sixty of these cases had cerebral angiography.

Doppler scanning was 93% as accurate as angiography in assessing arterial lesions with greater than 50% stenosis, and there were 9% false positive tests and 5% false negative results. Conversely, angiography significantly underestimated the degree of stenosis at carotid endarterectomy in 5% of cases. In five patients in whom angiography was contraindicated, extensive extracranial arterial disease was demonstrated by Doppler scanning and was felt to be a critical factor in syncopal episodes. The technique was found especially valuable in screening patients for asymptomatic bruits, in elderly or debilitated patients where angiography was contraindicated and in follow-up.

Limitations of Doppler scanning are the failure to visualize intracranial vasculature and the inability to detect reliably arterial narrowing below 50%. Allowing for these restrictions, our observations indicate that this non-invasive procedure adds useful information to the clinical assessment of patients with cerebrovascular disease.

P-III-5

Carotid Injury due to Intraoral Trauma

W. B. Woodhurst, G. B. Thompson, W. D. Robertson, M. Borozny, Vancouver

Internal carotid artery injury after penetrating and non-penetrating intraoral trauma is a rare childhood injury. Many cases with major infarction and increased ICP have died. We report the case of a twenty-five month old child who sustained a right internal carotid injury from a fall on the sharp end of a "rat-tailed" comb. Initial injury appeared trivial but at twenty-four hours post injury she was noted to have major right hemisphere deficits. Angiograms demonstrated right ICA occlusion 1 cm. above its origin. The intracranial carotid was filled by collaterals but the proximal middle cerebral artery was occluded.

Seventy-two hours post injury she deteriorated with signs of progressive transtentioial herniation. A subdural screw was placed for ICP monitoring and ventilation with sedation and intermittent mannitol was used to control her elevated ICP. By eighty hours later the ICP was refractory to this therapy and a thiopentone infusion was begun. This dramatically reduced the ICP for the next four days after which therapy was gradually withdrawn.

The child remained with a severe left hemiplegia at the time of discharge from hospital 36 days after injury.

This case demonstrates the importance of careful observation of children after intraoral trauma and the benefits of intensive programs for control of increased ICP from major infarction.

P-III-6

Antifibrinolytic Therapy in the Management of Subarachnoid Hemorrhage

R. O. Holness, W. S. Huestis, A. Badejo, Halifax

100 consecutive patients with subarachnoid hemorrhage were reviewed. Most harbored ruptured aneurysms which were eventually treated surgically. Our medical regimen includes 36 grams of Amicar daily, bed rest, sedation, and in certain cases steroids and anti-hypertensive agents. Ruptures of an aneurysm in the pre-operative period has become uncommon in our experience and occurred in less than 5% of the present series. This has allowed us to extend our pre-operative period to two or three weeks in many instances with resultant decrease in post- operative morbidity.

Possible side effects of Amicar therapy were studied. The most common were minor in nature; mucosal dryness was frequent whereas nausea and abdominal pain occurred in a few cases. Three patients developed acute gangrenous cholecystitis requiring emergency surgery. One patient had ischaemia of her bowel. Another had angiographic appearances of cerebral

arteritis but without associated clinical findings. The angiogram returned to normal after Amicar was discontinued. No patients developed myopathies, venous thromboses, or bleeding disorders. The incidence of cerebral infarction and hydrocephalus did not appear to be increased in incidence.

Antifibrinolytic therapy has few adverse effects and our experience supports the view that it represents a real advance in the management of subarachnoid hemorrhage.

P-III-7

The Happy Puppet Syndrome

J. M. Dooley, D. L. MacGregor and J. M. Berg, Toronto

The happy puppet syndrome was first described in 1965 by Harry Angelman. There have subsequently been 17 cases reported in the literature. Our poster presentation describes 5 new cases and 1 case which was previously reported by one of us.

All of our cases fit classically into the clinical picture of this syndrome with an unusual ataxic gait, severe mental retardation and seizures of varying type associated with abnormal EEG's. All have microbrachycephaly with prognathism and tongue protrusion and all exhibit inappropriate laughter with absence of speech development. Our investigations included electroencephalographic, chromosomal, dermatoglyphic, biochemical and radiographic studies.

Previous reports have described cerebral atrophy on pneumoencephalography. C.T. scanning of the head has not been previously reported and although we performed scans on all of our patients no uniform abnormality was found.

Our poster presentation includes photographs of all the patients, a summary of the classical features with a review of the literature and representative EEG's and C.T. scans.

We propose that this syndrome is probably more common than was previously thought and that the appearance, despite varying ethnic background, is very similar.

P-III-8

Role of the Putative Amino Acid Transmitters GABA, Glutamic Acid and Aspartic Acid in Thiamine-Deficient Encephalopathy

E. Hamel, R. F. Butterworth and A. Barbeau, Montreal

Experimentally-induced thiamine deficiency in rats bears certain clinical and pathological similarities to thiamine deficiency in man, as exemplified by the Wernicke-Korsakoff syndrome, an affliction of the central nervous system. Neurological symptoms in man include ataxia, nystagmus, memory dysfunction and polyneuritis; in rats, thiamine deficiency results in ataxia, opisthotonus and loss of righting reflex.

During progressive depletion of the vitamin, it is predominantly brain thiamine diphosphate (TDP) that is decreased while free thiamine and thiamine monophosphate remain fairly constant. TDP acts as cofactor for the pyruvate and α-Ketoglutarate dehydrogenase complexes with the result that the activities of these enzyme complexes (and subsequently the oxidation of pyruvate and α-Ketoglutarate) are diminished in the brains of symptomatic thiamine-deficient rats. While impaired pyruvate oxidation appears to have no effect on cerebral ATP or acetylcholine levels, studies in our laboratory have shown that the concentrations of the amino acids GABA, glutamic acid and aspartic acid are significantly diminished in many regions of the brain and spinal cord of symptomatic thiamine-deficient rats when compared to pair-fed controls.

As there is now good evidence that these amino acids serve as neurotransmitters in many parts of the CNS, changes in their concentrations could lead to severe neuronal dysfunction and the observed neurological manifestations of thiamine-deficient encephalopathy.

P-III-9

The Distribution of Vagal Sensory Fibres to the Area Subpostrema of the Cat

R. A. Leslie, D. G. Gwyn and D. A. Hopkins, Halifax

The area subpostrema (ASP), a subdivision of the nucleus of the tractus solitarius (NTS), is not clearly distinguishable with routine light microscopic staining methods. The area was recognised as a separate entity within the NTS only as a result of a characteristic staining pattern following cholinesterase histochemical experiments on the feline brainstem. An earlier study in our laboratory using a silver impregnation technique indicated that the vagus nerve projects heavily to the ASP as well as to other parts of the NTS. More sensitive methods have been used to elucidate further details of this vagal afferent projection. These consisted of autoradiography following injection of 25μCi of (^{3}H)-leucine into the nodose ganglion, histochemical demonstration of horseradish peroxidase (HRP) following injection of 30% HRP into the nodose ganglion or stomach wall, and electron microscopy of degenerated vagal terminals one to three days following removal of the nodose ganglion. Autoradiography revealed a profuse vagal projection to the ipsilateral ASP, and a light projection to the contralateral area. HRP labelled fibres and terminals were seen in the ipsilateral ASP following injection into the nodose ganglion. However, following injection of the protein into the stomach wall, labelling was seen bilaterally in the ASP. Subsequent to an injection of 200mg of HRP into the anterior stomach wall, labelling was seen not only in the ASP, but also in more ventro-lateral parts of the NTS and bilaterally in the commissural nucleus. At the ultrastructural level, degenerating vagal terminals which were seen in the ASP following ganglionectomy made synaptic contact with small dendritic elements and contained round clear vesticles and occasional dense-cored vesicles.

P-III-10

Retinal Functions in Light Deprived Animals Studied with Electrical Stimulation of Retina (T.R.S.)

S. Molotchnikoff and I. Lessard, Montréal

In humans, sensations of light (phosphenes) can be evoked by applying alternating current to the eye. In animals, recordings from ganglion retinal cells have shown that electrical stimulation of the retina (T.R.S.) activates in a specific manner either the ON or OFF retinal channels which are responsible for brightening and dimming sensations. From these relationships it has been proposed that electrical stimulation "mimics" diffuse light action. The purpose of this experimental investigation is to compare responses evoked by light and electrical stimulations of the retina in normal and dark raised rabbits. Responses were recorded in adult urethane anaesthetized animals with a tungsten micro-electrode aimed stereotaxically at the optic nerve. In normal animals 85% (n=46) of ganglion cells responded to T.R.S. with a typical pattern of alternating periods of excitation and inhibition. Only cells with a slow conduction. ($V \leqslant 6$m/sec) are unresponsive to such stimuli (15%). In contrast to normals, rabbits raised in darkness showed that only 13% responded to T.R.S. with a pattern comparable to that of the control group. Since Sodium Aspartate abolishes the T.R.S. evoked responses, it follows then that, the T.R.S. acts at the level of the retinal outer plexiform layer. Thus, the poor responsiveness obtained in dark reared animals, indicates that the total absence of light sensations weakens or alters synaptic transmission at retinal level.

P-III-11

Steroid Modification of Responses to Mitogens and Specific Neural Antigens in Multiple Sclerosis (M.S.)

Steven Kobetz, William Sheremata, and Diana Lopez, Miami, Florida

Lymphocyte PHA responses are reported to be decreased in M.S. Different steroid regimens have led to variable PHA assay results being reported. A steroid reversible reduction of PHA response by MS serum has previously been reported. However, in other studies steroids have augmented responses to central nervous system myelin basic protein (BP). Steroid and serum effect on Conclavin-A (Con-A) responses have not been reported.

Responses to PHA 10μ/ml, Con-a 4μ/ml and CNS BP and 100μ/ml peripheral nervous system and P_2 10μ/ml protein and the effect of homologous and heterologous serum was studied in 69 subjects. Serial study of ACTH in 6 patients in acute attacks and during stable disease was performed. Mean counts per minute (cpm) in PHA stimulated cells from normals, other neurological disease (OND), and MS were 75,300, 56,410, and 79,950 respectively. Cpm in Con-A stimulated cells were 74,730, 41,030 and 62,120 BP stimulated cells 6,180, 1,120 and 3,300 and in P_2 stimulated cells 5,190, 1,110 and 1,970. Only serial studied acutely ill patients showed a dramatic increase in response to BP (which was decreased by MS serum), accompanied by a variable response to PHA, and a slight but consistent decrease in Con-A response.

These results suggest that steroids may reduce already altered suppressor cell function allowing proliferation of stimulated clones of lymphocytes. This treatment however does suppress lymphokine production. These results may thus explain "steroid rebound", which was observed in the joint study of ACTH in multiple sclerosis.

P-III-12

Electrophoretic Analysis of Human Erythrocyte Membrane Proteins

C. C. Liew, I. H. Fraser and A. S. Gordon, Toronto

Human erythrocyte ghosts were prepared by the method of Dodge *et al.* Assays of protein kinase activity of cell ghosts were carried out in 50 mM Na-acetate —pH 6.0), 10 mM Mg-acetate, 0.3 mM EGTA and γ-^{32} P-ATP (10 μm) as described by Roses and Appel.

Membrane proteins were either solubilized in SDS or extracted by phenol-buffer. Both methods extracted similar proteins which could be separated into 8 major and at least 10 minor fractions by one-dimensional SDS-polyacrylamide gel electrophoresis (PAGE). The membrane proteins were further resolved by two-dimensional-PAGE using isoelectrofocusing in the first dimension and SDS-PAGE in the second. The phenol extraction method gave the best electrophoretic profiles in the two-dimensional PAGE.

No differences were found in the specific activity of protein phosphorylation in erythrocyte membranes between Duchenne muscular dystrophy (30.8 ± 2.8 (8) pmol/mg/min), and their age-matched controls (29.2 ± 3.8 (6) pmol/mg/min). In addition, autoradiograms of [^{32} PÇ-labelled phosphoproteins from both Duchenne muscular dystrophy patients and their age-matched controls separated by either SDS-one-dimensional PAGE or by the two-dimensional gel system were similar.

P-III-13

Allergy and the Brain

D. Keene, C. Melmed and F. Andermann, Montreal

Anoxia due to asthmatic attacks leading to anoxic convulsions and also to epilepsy had been well described in children, but not adults, by Nellhaus.

A 28 year old woman with childhood onset asthma presented at age 16 with attacks which had a stereotyped pattern. She would awaken from sleep with a sense of dyspnea; while reaching for her Ventolin inhaler would lose consciousness and have a tonic attack lasting less than 1 minute. A reduction in her theophylline resulted in status asthmaticus and innumberable tonic attacks leading to severe anoxic encephalopathy. Subsequently, with adequate control of her asthma, she has been free of further tonic seizures. The attacks were considered to represent anoxic convulsions. In contrast, a 21 year old woman with unconsciousness induced by severe asthmatic attacks presented no tonic or tonic-clonic manifestations.

Cerebral anoxia is not the only cause of encephalopathy accompanying acute allergic events. A 4½ year old girl presented with attacks of rhinitis, conjunctivitis, and urticaria which proceeded to a stereotyped acute neurological syndrome and coma. She was hospitalized on 20 occasions and became steroid dependent. Her attacks of acute encephalopathy also responded to steroids. The mechanisms of cerebral involvement in these attacks remains unclear. They diminished progresively, but she went on to develop generalized photosensitive epilepsy.

Asthma inducing hypoxia with coma or anoxic seizures can occur in adults and should be treated appropriately and energetically. Other mechanisms of acute encephalopathy triggered by allergic attacks remain speculative.

P-III-14

Protein Binding and Salivary Concentrations of Valproic Acid in Epileptic Patients

J. Bruni, J. M. Gallo, C. Lee, B. J. Wilder, Gainesville, FL

Knowledge of antiepileptic drug (AED) plasma concentratins is important in titrating doses of drugs to achieve optimal seizure control without producing unacceptable toxicity. Salivary concentrations of AED's are also useful in patient monitoring because of their convenience and the likelihood that they represent unbound or pharmacologically active drug. Single of multiple saliva, total and free plasma determination of valproic acid were made in 16 epileptic patients. The mean plasma protein binding of valproic acid was $89.4 \pm 4.7\%$. The concurrent administration of other AED's did not affect the protein binding of valproic acid. The mean saliva to total and free plasma level ratios were 0.03 ± 0.03 (1 S.D.) and 0.33 ± 0.34 respectively. The correlation coefficient was low in both cases. A therapeutic saliva level was not apparent due to the poor correlation between salivary levels and pharmacologic response. The pk_a of valproic acid in relation to salivary and plasma pH provides the best explanation of why salivary levels are inadequate predictors of plasma concentrations. In vitro studies to determine the effect of phenytoin on the protein binding of valproic acid were carried out with a dialyzing system. These confirmed the lack of effect of phenytoin on valproic acid binding.

XI-1

The Effect of Spinal Distraction on Regional Spinal Cord Blood Flow in Cats

E. J. Dolan and C. H. Tator, Toronto

Distraction is considered to be a factor in many spinal cord injuries. Using a specially designed distraction apparatus and the ^{14}C-antipyrine autoradiographic technique, the effect of distraction on spinal cord blood flow (S.C.B.F.) in cats was studied. Distraction was performed at L2-L3 at a rate of 0.25 cm/10 min, and the spinal evoked potentials (S.E.P.'s) were monitored by stimulating the sciatic nerve and recording at T-13. S.C.B.F. was assessed in 5 control animals; four animals when the S.E.P. was abolished; five animals after the S.E.P. had been abolished and an additional 0.5 cm distraction applied. Arterial pO_2, pCO_2, pH and body temperature were within normal limits at the time of the S.C.B.F. measurement.

Control animals had grey and white matter flows of 49.14 ± 0.24 (S.E.M.) and 10.08 ± 0.05 (S.E.M.) ml/100 gm/min respectively. Distraction to the point of S.E.P. loss caused a 50% loss of S.C.B.F. at and caudal to the distraction site. An additional 0.5 cm distraction produced total abolition of S.C.B.F. in all areas examined.

For the first time it has been shown that spinal distraction causes cord ischemia similar to that seen with other types of spinal cord injury. In addition, distraction severe enough to cause loss of the S.E.P. has already produced severe cord ischemia.

XI-2

The Value of Early Relief of Persisting Spinal Cord Compression after Acute Cord Compression Injury

E. J. Dolan and C. H. Tator, Toronto

Persisting spinal cord compression after acute injuries has empirically been considered deleterious to functional recovery. Using a rat spinal cord injury model this laboratory has defined the relationship between the force compressing the spinal cord, and the length of time the compression was maintained. The injury device was a modified aneurysm clip and the force of compression could be accurately measured. Forces of 20, 70 or 180 gm compressing the spinal cord for 3, 30, 60 or 300 seconds were studied using 7 animals for each force-time combination. Clinical recovery was followed weekly for 8 weeks by assessing the ability of the animals to maintain themselves on an inclined plane.

The results clearly showed that both the force and duration of compression are important interrelated factors in determining recovery from acute compression injury of the spinal cord. For all forces examined, early relief of spinal cord compression resulted in significant improvement in functional recovery.

XI-3

Sciatic Nerve Grafting of Spinal Cord Defect

B. Bratten, New Orleans, A. Hudson, Toronto

Eight female Wistar Rats were anaesthetised and 1.5 cm. dorsal spinal cord was resected. Nerve roots adjacent to proximal and distal cord stumps were avulsed. Sciatic nerve autographs were inserted between the cord stumps.

Paraplegic rats were maintained by bladder expression 5 times/24 hours. None developed automatic bladder emptying.

Animals were re-anaesthetised at intervals through 14 weeks and proximal cord, graft and distal cord removed en bloc. Tissues were fixed by immersion in Gluteralderhyde.

RESULTS: All grafts were found in continuity with proximal and distal cord stumps. Light and E.M. study of graft showed typical appearance of

reinnervated peripheral nerve graft. Most fibres were contained within fascicles and few were in the extrafascicular tissues.

Proximal cord biopsies (Biodian and L.F.B.) showed numerous axons and ongoing degeneration at anastomosis. Aggregates of ependymal cells were present. Occasional myelinated fibres of peripheral type were noted next to astrocytes and central myelinated and unmyelinated fibres. Distal cord stump showed some degeneration and many fiable fibres.

It is tempting to interpret the numerous graft fibres as being of central origin, but there is a very marked discrepancy between dense fibre concentration in graft and sparse fibre concentration in distal cord. Histology of periphery of the graft at the proximal anastomosis resembles traumatic neuroma, and in many instances regenerating fibres appear to be following peripheral vascular spaces in manner analogous to Schwannosis seen in regenerating peripheral roots. Our conclusion is that great care is advised in accepting results of this and analogous experiments as evidence of graft transmission from central to peripheral structures. We believe that majority of fibres in the graft are derived from peripheral structures.

XI-4

Regeneration Following Sciatic Nerve Grafting to the Rat Spinal Cord

P. M. Richardson, U. M. McGuinness and A. J. Aguayo, Montreal

In 24 young adult female rats, a segment of the thoracic spinal cord was resected and replaced by an autologous sciatic nerve graft. From 10 days to 4 months later, the animals were sacrificed and the graft and its junctions with the spinal cord were studied with the light and electron microscope. All grafts of more than 3 weeks duration were richly innervated with myelinated and unmyelinated axons. This was true, even in 8 animals in which the dorsal spinal roots entering the pia at the graft site were avulsed together with their ganglia. Many fibres appeared to pass from the graft to the subpial zone of the spinal cord. However, at the border of the CNS tissue, myelinated and unmyelinated axons were observed within dome-shaped structures, each filled with astrocytic processes and surrounded by a basal lamina. Occasional nodes of Ranvier were seen in which one heminode had peripheral myelin and the other had central myelin. The origin and termination of axons in the graft and axons which cross the CNS-PNS interface have not yet been determined.

XI-5

Severe Cauda Equina Compression From Acute Herniated Lumbar Disc

A. Joern, M. Laplante, P. Richardson, R. Ford, J. Stratford, Montreal

Six patients with severe cauda equina compression secondary to herniated intervertebral discs are reported. Four men and two women with a mean age of 44 were treated. All but one had prior symptoms of low back pain and/or sciatica lasting as long as eight years. The onset of the presenting symptoms was sudden and painful. This clinical feature helped differentiate the lesion from other processes such as metastatic tumor. Three to fourteen days passed before the patients were referred to the neurosurgical service. Upon admission each patient demonstrated bilateral weakness, sensory loss and absence of deep tendon reflexes associated with distended, atonic bladder and diminished anal tone. Lumbar myelography disclosed complete blocks in each case. The levels involved varied: L2-3 (two); L3-4 (one); L4-5 (one) and L4-S1 (two). Prompt surgical decompression revealed extruded disc fragments in all cases. Recovery was characterized by return of motor and bladder function with mild residual sensory and reflex dificits. The preoperative duration of neurological deficit was not closely correlated with the time required for postoperative return of function. In this series of cases the return of bladder function was better than previously reported.

XII-1

Ontogeny and Regional Distribution of Neurite Outgrowth Factors in Embryonic Chick

R. J. Riopelle and D. Cameron, Kingston

A single cell bioassay for Nerve Growth Factor (βNGF), has been used to measure neurite outgrowth activity in developing chick embryos.

In ontogeny, neurite outgrowth activity can be detected in whole embryo extract as early as 2½-3 days of embryonic life and increases thereafter. The neurite outgrowth activity is present at least 3 days before mediodorsal neurons of dorsal root ganglia respond *in vitro* to βNGF and bear high affinity surface receptors for the protein.

The regional distribution of neurite outgrowth activity has been measured at 8 days of embryonic life. High levels of activity are detected in extracts of skeletal muscle, gut and heart, but little or no activity can be measured in brain, spinal cord or sensory ganglia.

Only some of the neurite outgrowth activity at any embryonic age or from any region has immunological cross-reactivity with mouse βNGF. At concentrations of rabbit anti-mouse βNGF antibody that are four orders of magnitude (10^4) higher than concentrations producing 50% inhibition of βNGF-induced neurite outgrowth, dose response plots have plateaued at 40-50% inhibition of extract-induced neurite outgrowth.

XII-2

Defective Bile Acid Metabolism in Cerebrotendinous Xanthomatosis (Cholestanolosis)

V. MacMillan, Toronto

Cerebrotendinous xanthomatosis (CTX) is a rare inherited lipid storage disease that is characterized by central nervous system and tendon xanthoma which contain large amounts of 5-α-cholestan-3-β-ol (cholestanol). A 33-year-old male with juvenile cataracts, mild mental retardation, ataxia, spasticity and achilles tendon xanthoma is presented. The biochemical findings of a normal blood cholesterol (175%), elevated blood cholestanol (1.8 mg%) and a biopsied tendon xanthoma containing 10% of the total lipids as cholestanol were characteristic for CTX. The patient's bile acid secretory pattern showed abnormalities with a diminished total bile acid production, reduced percentages of chenodeoxycholic acid (11%) and deoxycholic acid (4%) and the presence of large amounts (12%) of unidentified compounds which are tentatively identified as aberrant bile alcohols. The biochemical findings are in agreement with the recent proposal of Salen that the basic abnormality in CTX is a defective 24S-hydroxylation in the cholic acid biosynthetic pathway. The rationale for the use of oral chenodeoxycholic acid in the treatment of CTX is discussed.

XII-3

Ultrastructure of the Dorsal Motor Nucleus of the Vagus Nerve in the Cat

J. H. McLean and D. A. Hopkins, Halifax

The dorsal motor nucleus of the vagus nerve (DMV) receives projections from several central sources including the amygdala and hypothalamus as well as the lower brain stem. Despite the importance of these structures in the regulation of visceral functions, the synaptic organization in the DMV has not been described previously. Therefore, in the present study the normal ultrastructure of the DMV in the cat was examined. Two types of neurons were distinguished. The majority were oval medium-sized neurons (20-30 μm in length) with non-invaginated nuclei. Smaller neurons (9-16 μm in diameter) with invaginated nuclei were scattered throughout the neuropil. Small numbers of axo-somatic synapses of types similar to more numerous axo-dendritic synapses were observed. In the neuropil, the majority of dendritic profiles ranged between 1 and 3 μm. Axo-dendritic synapses contained round or pleomorphic vesicles. Dense-cored vesicles were often found in association with pleomorphic vesicles in symmetrical synapses but were more frequently found with round vesicles at asymmetrical synapses. These results provide a basis for an ultrastructural analysis of afferent connections to the DMV. Supported by the Medical Research Council of Canada.

XII-4

Microiontophoresis of Excitatory Amino Acids and Antagonists on Identified Medial Hypothalamic Neurons

L. P. Renaud, A. Padjen, E. Arnauld and B. S. Layton, Montreal

Electrophysiological studies in pentobarbital anaesthetized Sprague-Dawley rats have demonstrated that the excitability of medial hypothalmic neurons is altered by electrical stimulation in the amygdala, lateral septum, midbrain and dorsal hippocampus. Preliminary neuro-pharmacological studies performed with microiontophoretic techniques examined the sensitivity of these identified medial hypothalamic neurons to acidic amino acids. The majority of neurons demonstrated an increase in excitability during applications of L-glutamate, L-aspartate, DL homocysteate, kainate and ibotenate. Responses evoked by glutamate, aspartate and homo-

cysteate were usually of similar magnitude, and brisk in onset and termination. Kainate evoked responses were characteristically delayed in onset and recovery, often tending to excessive depolarization at the peak of the responses with subsequent 'cell loss'. Ibotenate responses were usually biphasic, an initial excitation preceding a prolonged period of decreased excitability. Application of the diethylesters of glutamate and kainate decreased both glutamate and aspartate evoked excitations and had no effect on synaptic evoked excitation; their use in the evaluation of the excitatory neurotransmitters in the medial hypothalamus appears dubious.

XII-5

The Usefulness of Isoelectric Focusing in Polyacrylamide Gel (IEF-PAGE) in Demonstrating Oligoclonal Banding in MS CSF

G. C. Ebers and D. W. Patty, London, Ontario

The most characteristic laboratory finding in MS is the presence of distinct IgG bands as demonstrated by numerous electrophoretic techniques. Although agarose gel electrophoresis demonstrates an abnormality in approximately 85-90% of clinically definite MS patients, the remainder do not show the banding pattern. Furthermore, a much larger number of patients with possible MS do not show any eletrophoretic abnormality.

The present study concerns isoelectric focusing of MS CSF in polyacrylamide gel (IEF-PAGE). Preliminary experience with this method had indicated its greater sensitivity for IgG separation. The method resolves pooled gamma globulin and normal IgG into faint bands. Accordingly pooled and individual IgG fractions are run in parallel with MS CSF samples. 25 patients with clinically definite MS have been studied. 24 have shown banding by this method. The number of bands detectable has ranged from 2-24. 2 and 4 of these were not detected by agarose gel or cellulose acetate electrophoresis respectively. Faint bands in MS serum correspond to CSF bands in over 1/3 of patients. Routine pH 3-10 gels used in this study were prepared prior to use but are available commercially. The region of interest which lies mainly in the pH ra-ge of 7-9 can be expanded greatly using gels which establish a gradient of pH 7-9. This provides little or no diagnostic usefulness over the pH 3-10 gels.

IEF-PAGE provides a modest improvement over other methods in demonstrating the oligoclonal banding pattern so characteristic of MS CSF.

XIII-1

Usefulness of Bromocriptine in Advanced Fluctuating Parkinson's Disease

J. David Grimes, Ottawa

Ten patients with longstanding (average 10 years) and moderately advanced (Yahr 111-IV) disease were chosen from a Parkinson's Disease Clinic population. The patients were selected because of the presence of daily fluctuations in level of function of varying types and severity including, severe ON-OFF phenomena, end of dose deterioration, and freezing episodes. Bromocriptine was started in low dosage (2.5 mg BID or less) and slowly (4-12 weeks) increased to a dose of maximum improvement (15-50 mg, average 28 mg per day). Sinemet reduction varied from 0 (3 patients) to 625 mg (2 patients) (average 192 mg).

Eight of the ten patients were moderately to very significantly improved. Fluctuations in level of function, especially minor ones, were very much improved in most patients. Four patients with marked disabling bradykinesias in addition to fluctuations were very much improved. One of the two patients with severe ON-OFF phenomena (disabled one-half of the day) had remarkable improvement with no further prolonged spells of disability. Five patients had definite reduction of dyskinesias. Four of four patients with disturbed nocturnal sleep, were improved.

Bromocriptine addition, combined with variable Sinemet reduction, appears to be a very worthwhile drug adjustment in the therapy of advanced fluctuating Parkinson's Disease.

XIII-2

Powassan Encephalitis Resembling Herpesvirus Encephalitis and Treated with Adenine Arabinoside (ARA-A)

P. R. Camfield, F. Mehrmanesh, and J. Embil, Halifax

An 8-year-old boy, vacationing for 2 days in Nova Scotia, had a "flu-like" prodrome, then suddenly gustatory hallucinations and repeated left-sided seizures. On admission to the I. W. Killam Hospital for Children in Halifax, he was febrile and confused with a mild left hemiparesis. Initial spinal fluid showed 91 mononuclear cells and a protein of 60. Carotid arteriograms and nucleotide brain scan were normal. An EEG within 12 hours showed focal delta waves over the right temporal lobe and, 24 hours later, a repeat EEG showed bitemporal delta. A brain biopsy was not performed. A presumptive diagnosis of herpesvirus encephalitis led to treatment with ARA-A 15 mg/kg/d for 9 days. He had further gustatory hullucinations, but gradually improved during the treatment period. Four months later, he was normal. The diagnosis of Powassan virus encephalitis was established by a diagnostic rise in CF and HI titers. No rise in antibody titer to other neurotropic viruses, including herpesvirus, was demonstrated. Prior to his visit to Nova Scotia, this boy lived in the same area of New York State where the majority of previously reported Powassan cases have occurred. ARA-A did not adversely affect his outcome. Its efficacy in herpesvirus encephalitis is only apparent with prompt treatment in the conscious patient. Since herpesvirus encephalitis cannot always be diagnosed correctly, either clinically or with biopsy, further documentation of no adverse effects of ARA-A in other encephalitities such as Powassan is important.

XIII-3

Primary Lymphomas of the Central Nervous System

R. M. Gladstone, W. S. Tucker and J. M. Bilbao, Toronto

An unusual evanescent multifocal encephalopathy, found at autopsy to be due to multicentric lymphoma of the brain, prompted a review of this uncommon and frequently undiagnosed tumour.

15 cases of primary C.N.S. lymphoma were included; 14 lesions involved brain and a single unusual example involved the cervical spinal cord primarily. There were 9 male and 6 female patients, ranging in age from 27 to 68 years (average 53 years).

8 patients presented with focal neurological disturbances, 2 with raised intracranial pressure, 2 with dementia and 3 with focal seizures. No patients had evidence of paraneoplastic or immunological disorder. Assessment suggested multiple lesions in 3 cases. The commonest site (6 cases) was callosal, with involvement of both cerebral hemispheres. 3 cases were diagnosed as having demyelinating disease; in one the diagnosis was revised and a tissue diagnosis obtained.

A surgical diagnosis was attempted in 13 cases, and was positive in 12 cases. A course of radiotherapy was given in only 1/3 of the cases and these patients had the longest and best quality of survival.

The varied clinical presentations of this unusual (but radiosensitive) tumour may lead to misdiagnosis unless it is considered and a tissue diagnosis obtained.

XIII-4

Fibroid Radiculopathy: An Unusual Neurological Complication of a Common Benign Uterine Neoplasm

L. P. Heffernan, R. C. Fraser and R. A. Purdy, Halifax, Nova Scotia

A 28 year old (22 week) primigravida presented with distal left lower extremity swelling and numbness. Examination disclosed evidence of left venous obstruction and radicular (L5) dysfunction. This was confirmed by electromyography which further delineated a retroperitoneal site of involvement. Ultrasound revealed a single fetus plus a large mass in the area of the posterior uterine wall representing either a subserosal myoma or retroperitoneal tumor. Exploratory laparotomy revealed a gravid uterus with multiple fibroids, a huge one being located on its posterior aspect adjacent to the pelvic brim. A spontaneous miscarriage ensued the day after surgery following which there was no further progression of the neurological dysfunction. Subsequent veinography demonstrated bilateral iliofemoral thrombosis this being as well extensive throughout the entire left lower extremity.

Literature search failed to document a similar clinical presentation. Deep vein thrombosis and radicular pain without weakness have frequently been reported in association with huge fibroids. A recent review of the neurological complications of pregnancy fail to mention radicular compression via a leiomyoma. It is postulated that the presence of a gravid 22 week uterus plus a large posterior fibroid were significant in combination to result in radicular compression leading to neurological dysfunction.

XIII-5

Mercury Intoxication of the Nervous System in Canada (Chronic Minamata Disease)

O. Kofman, Toronto D. Simard, Quebec City D. Marsh, Rochester

The acute of subacute form of methylmercury intoxication of the nervous system described by Hunder & Russell in 1940 has subsequently been documented in Japan, Iraq, United States, Etc.

Of particular current interest are some recent reports from Japan and Canada which have suggested the occurrence of a chronic and possibly delayed onset form of 'Minamata Disease' which developed gradually some years after the initial exposure to methylmercury.

In order to assess the significance of this increasing problem a comprehensive study of 306 Cree Indians, most of whom had known mercury exposure was recently completed. An additional small control group was studied although a full epidemiological survey was not available. A combined group of 18 neurologists and ophthalmologists from 6 university centres conducted extensive clinical examinations during 1977-78. Multiple other factors including mercury analysis of blood and hair, age nutrition, fish, drug and alcohol ingestion, etc. was all carefully assessed. Special problems were further assessed by means of EMG, EEG C.T. Scan, nerve conduction tests, CSF examination, myelography, etc. In many cases elevated levels of organic mercury were detected in blood and hair. Other findings included tremor, ataxia, peripheral neuritis, visual disorders, etc. However, no individual revealed a constellation of symptoms and signs that conformed to the suggested concept of chronic Minamata Disease.

This conclusion is compatible with our previous experience elsewhere in Canada as well as with reports from Sweden. It does, however, differ significantly from other recently published studies in Quebec and Japan. Some reasons for this apparent discrepancy will be considered. The conclusions drawn from this survey should have significance relative to similar contemplated studies in other global areas.

XIV-1

Ultrastructural Appearance of Peripheral Nerve Fibers Demyelinated with Lysophosphatidyl Choline (LPC)

G. M. Bray, I. D. Duncan and A. J. Aguayo, Montreal

Intraneural injections of LPC cause a rapid, localized breakdown of myelin which leads to segmental demyelination and reversible conduction abnormalities. The present study was designed to determine if the axon and Schwann cell specializations, which are necessary for impulse conduction in myelinated fibers are derranged in LPC-induced demyelination. Sciatic nerves in Sprague-Dawley rats weighing 150 g were injected with 1% LPC. Two, 4 and 6 days later, groups of animals were perfused with fixative solution. Demyelinated segments of the injected sciatic nerves were cut transversely into 2 mm blocks. Alternate blocks were processed for thin-section and freeze-fracture electron microscopy.

Two and 4 days after injection, the demyelinated areas contained large amounts of myelin debris. By 6 days, much of this debris had been removed. In longitudinal sections, demyelination of individual fibers terminated at former nodal regions producing a "heminode"—a relatively normal paranode contiguous with an axonal segment ensheathed by a thin Schwann cell process. Internodal segments of the demyelinated fibers were ensheathed by Schwann cell processes containing no myelin; unensheathed axonal segments were not observed. In freeze-fracture replicas, the demyelinated internodal segments resembled normal internodes and no special contacts were observed between axons and their overlying Schwann cells. Because LPC demyelination differs from that induced by diphtheria toxin, where many fibers show paranodal demyelination only, the study of LPC-demyelinated fibers may provide new insights into different patterns of demyelination and their effects on function.

XIV-2

Infantile Mixed Polyneuropathy

H. Darwish, K. A. Brownell, S. T. Myles, Calgary

Defective myelination throughout the peripheral nervous system has been reported independently in three case reports of severe early infantile polyneuropathy. This is a case report of a fourth child with similar pathological findings, whose course has been quite benign.

The patient was first assessed at the age of 4 years because of his peculiar gait. He did not walk until age 18 months and was a floppy infant. Motor nerve conduction velocities were slowed and muscle biopsy showed atrophy. His course was subsequently stable and characterized by newly acquired motor skills.

At 10 years of age, moderate weakness, more prominent in the distal muscle groups, hypotonia, arreflexia, and pallanesthesia and hypothesia in a glove-stocking distribution, were noted. Motor and sensory nerve conduction velocities were markedly slowed. CSF examination was normal.

A fascicular biopsy of the sural nerve was performed. The pathologic features noted by light microscopy included a moderate decrease in the axons and early onion bulbs. Teased fibre studies showed excessive variability in myelin thickness and globule and sausage formation. A few fibres were undergoing wallerian degeneration. Electronmicroscopy confirmed the findings. A biopsy of the gastrocnemius muscle demonstrated group atrophy, histochemical fibre type grouping and large numbers of target fibres.

Although the principal lesion occurs in myelin, primary axonal degeneration is also present. These active degenerative changes in the peripheral nervous system are surprising in view of his continuing clinical improvement.

XIV-3

Globoid Leukodystrophy. Motor End-Plate Ultrastructure Simulating Neuroaxonal Dystrophy

J. Hoogstraten and S. S. Seshia, Winnipeg

Muscle biopsy, with ultrastructural study of motor end-plates and intromuscular nerves, has been advocated as a means of establishing the diagnosis of neuroaxonal dystrophy, without having to resort to the more formidable procedure of cerebral biopsy.

Muscle biopsy of a three year old girl was interpreted as indicative of neuroaxonal dystrophy.

The child exhibited clinical evidence of a progressive neurological disorder, beginning at nine months of age with hypotonia, progressive failure of vision and hearing, terminating in a vegetative state.

Autopsy at six years of age revealed the morphological features off globoid leukodystrophy, rather than neuroaxonal dystrophy.

This experience indicates that the specificity of motor end-plate alterations indicative of neuroaxonal dystrophy, must be regarded with reservation.

XIV-4

Nephrotic Syndrome, Epileptic Seizures, and Friedreich's Ataxia in a Family

G. V. Watters, B. S. Kaplan, S. H. Zlotkin, K. N. Drummond, Montreal

In a family of four children, the mother and several of her relatives have generalized epilspsy. Her first born child had neither Friedreich's ataxia, nephrotic syndrome, nor seizures; the second child had Friedreich's ataxia; while the third and fourth children had Friedreich's ataxia, nephrotic syndrome and epileptic seizures.

The third child died and at autopsy had findings compatible with Friedreiich's ataxia and in addition loss of cerebellar Purkinje cells and atrophy of the dentate nucleus.

No evidence of an immunological abnormality was found which would account for the nephrotic syndrome, or the spino-cerebellar degeneration, or relate these two disorders to one another. Prolonged corticosteroid therapy for the nephrotic syndrome did not appear to affect the course of the neurologic disorder.

The possibility that the epileptic seizures in the two siblings were due to the expression of an electroencephalographic spike-wave trait inherited from the mother is proposed. This may be an explanation for the occurrence of seizures in other patients with spino-cerebellar degenerations previously considered to have dysnergia cerebellaris myoclonica.

XIV-5

The Preclinical State of Duchenne Dystrophy

G. Karpati and S. Carpenter, Montreal B. Lemieux, Sherbrooke

Two cousins were found to have 10-12 fold increase of serum creatine kinase (CK) activity in the neonatal period as a result of a routine screening

program. Their mothers' serum CK activity was also increased 4x above normal confirming their carrier state. The motor development of the children at least until the time of their muscle biopsy at 10 and 18 months of age respectively was normal, but their serum CK activity further increased to 250-400x above normal. Examination then was unremarkable except mild enlargement of the calves. Biopsy of biceps brachii of both patients revealed numerous groups of muscle fibers undergoing segmental necrosis or regeneration. Hypercontracted fibers were common; connective tissue excess was present. By electron microscopy, gaps of the plasma membrane were seen in non-necrotic muscle fibers which had dilated membrane bound spaces. Focal breakdown of plasma membrane leads to necrosis unless it is repaired. In support of this suggestion, we found muscle fibers in which single or multiple layers of basal lamina were separated from a dimpled surface of the cell. Empty basement membrane sheaths indicating failure of regeneration were present.

The study of these patients indicate that destruction of muscle cells is extremely active in very early life in Duchenne dystrophy, but until muscle fiber loss reaches a critical degree, overt clinical weakness is not evident. Our personal experience (and that of others) with fetal muscles from suspected cases does not yet permit to establish if and when specific pathologic changes are first detectable in Duchenne dystrophy during embryonic development.

XIV-6

The Peripheral Neuropathy of Diabetes Mellitus: A Corroborative Argument for an Ischemic Etiology

Virgilio E. Sangalang and L. P. Heffernan, Halifax

Two distinct forms of peripheral neuropathy occur in association with diabetes mellitus: a) distal, predominantly sensory, symmetric polyneuropathy and b) mononeuropathy or mononeuropathy multiplex. When the latter presents as an acute or subacute, often painful, asymmetric or symmetric, pelvic girdle weakness without sensory impairment it has often been referred to as diabetic amyotrophy.

The pathology of the usually clinically reversible mononeuropathy or mononeuropathy multiplex, though infrequently documented has been attributed to ischemic infarction whereas the usually clinically progressive distal symmetrical form has been attributed to "metabolic" dysfunction. The case to be reported is that of a 60 year old female insulin-dependent diabetic who developed an acute, severe, asymmetric pelvic girdle mononeuropathy multiplex combined with a distal symmetrical polyneuropathy in whom focal destructive lesions (infarcts) were demonstrated in a sural nerve taken at biopsy. Further examination (light and electron microscopy) revealed the microangiopathy so characteristic of diabetes mellitus. The paper discusses the significance of this microangiopathy and its possible role in the genesis of the ischemic lesions detected in this neuropathy. Furthermore, to be proposed is the contention that such a vasculopathy may itself be explicable on the basis of a metabolic abnormality specific to diabetes.

XIV-7

Myxedematous Polyneuropathy

R. Wilson, J. Bilbao, A. Hudson, Toronto

The occurrence of a polyneuropathy in association with myxedema is rare. Pathological examination of the peripheral nerves in this condition has been limited to a few isolated reports, the largest series being two cases.

This paper will describe two cases of myxedema with a polyneuropathy studied with serial nerve conduction tests after thyroid replacement and a sural nerve biopsy done before starting treatment.

The pathological findings of the electron microscopic examination of each case is different than the reports published up to the present time. In one case there is primarily axonal degeneration and onion bulb formation is present in the second case.

Based upon reports that thyroid hormone may influence axoplasmic flow, the possibility that the hypothyroid state produces a polyneuropathy by direct interference with neuronal metabolism and axoplasic flow rather than disturbing Schwann cell metabolism will be discussed.

XV-1

Blink and Jaw Jerk Reflexes in Multiple Sclerosis

Stephen K. Yates, William F. Brown, Donald Paty, London, Ontario

Electrophysiological investigations are helpful in multiple sclerosis to detect CNS lesions not evident to clinical examination. Evoked potential methods, however, are complicated by the requirement for electronic averaging. Methods to look for abnormalities in the chin tap evoked masseter reflex and blink reflex discharges in response to Vth nerve stimulation or light flash are technically less difficult and test the integrity of the respective brainstem connections. The light flash blink discharge tests, moreover, the integrity of the optic nerves, tracts and diencephalon. The combination of the above tests requires usually less than ½ hour and is not uncomfortable.

Abnormalities in one or more of the above tests have been observed in 80% of patients with chronic progressive myelopathy. The tests have also been abnormal in 90% or more of clinically definite MS patients. In patients with possible MS, abnormalities have been detected in 40-50% of patients. These tests have proven helpful in the detection of lesions of the brainstem and visual pathway lesions not obvious to clinical examination. The tests, therefore, help to confirm the clinical diagnosis of multiple sclerosis by providing evidence for extra lesions in the central nervous system.

XV-2

Congenital Oculomotor Apraxia of Cogan in Twelve Children

G. V. Watters, T. H. Kirkham, R. C. Polomeno, Montreal

Twelve children, five boys and seven girls, including one sibling pair, had the onset in the first year of life of congenital oculomotor apraxia of Cogan (COMAC) a defect in saccadic gaze, which is compensated for by a quick lateral head movement (head thrust), head drop, or blink.

Differential diagnosis included hemianopsia, strabismus, and in two children blindness. Ocular structures were normal, but two had rotatory nystagmus. Defects in saccadic gaze were bilateral in 10, and unilateral in 2. Horizontal optico-kinetic nystagmus (OKN) was abnormal (absent) in all; while vertical OKNs were usually normal.

Pregnancies and delivery were normal in most. There was delayed motor development in most; with gradual improvement in some to the low normal range. The prominence of head thrust decreased with age.

Three of the 12 have close to normal development; three have diverse unusual abnormalities of the nervous system; and six have shown a pattern of mild facial diparesis, hypotonia, general clumsiness, and delayed motor milestones, which has been the clinical picture of many of the children with COMAC. CT scans and pneumoencephalograms have not shown abnormalities in our patients, nor in most of the other reported patients. Recently, agenesis of the corpus callosum has been documented in some patients with this disorder.

The mechanism for the abnormality of oculomotor function is still to be established, but would appear to be of diverse etiologies.

XV-3

Primary Aberrant Regeneration

D. Boghen, P. Laflamme, T. Kirkham, and M. Aubé, Montreal

The clinical and neuroradiologic features of four cases with the syndrome of aberrant regeneration of the third nerve are presented. By contrast with what is commonly seen, the syndrome was not preceded by a third nerve palsy.

A petrous apex-cavernous sinus meningioma was the underlying lesion in all the cases. Surgical and pathological confirmation of the diagnosis was obtained in three. Regardless of whether the other ocular motor nerves are spared (as in our cases) or involved (as in other cases reported in the literature) primary aberrant regeneration of the oculomotor nerve appears to be highly characteristic of a cavernous sinus meningioma.

XV-4

Respiratory Coordination Changes with Cerebellar Stimulation

P. K. H. Wong, A. Froese, H. J. Hoffman, Toronto

Cerebellar Stimulation (CS) is being used with increasing frequency in the treatment of cerebral palsy (CP). In our group of 5 CP children, 4 had frequent severe respiratory infections prior to CS. Following chronic CS, they all showed a marked decrease in the incidence of such infections. Using

coil magnetometers, we measured rib-cage (RC) and abdominal (ABD) AP diameter excursions during quiet respiration and active maneuvers — max. inspiratory volume and max. respiratory rate. The tests were performed on 3 occasions (at least 1 week apart): with CS off for 24 hrs. ("off"), then with CS left at its usual intensity ("on"), and again "off". Attention was paid to the respiratory rhythm and phase relationship between RC and ABD movements. In all 5 patients studied, the "off" trials were associated with RC movements being more out of phase with ABD movements (paradoxical respiration), while "on" trials had less paradoxical respiration. Such paradoxical respiratory movements represent incoordination of the diaphragm and intercostal muscles, and lead to impaired cough and decreased clearance of respiratory secretions. These preliminary results suggest that CS improves coordination between respiratory muscle groups.

XV-5

Development of Head Position Control in Cerebral Palsy Patients by Angular Displacement Feedback

Peter Humphreys and Robert Forget, Montreal

Head position control was measured in ten cerebral palsy patients (aged 3-23) unable to maintain an upright head position while seated. 5 had severe athetosis due to birth asphyxia, 5 spastic quadriplegia of various etiologies. Head deviation from the vertical position was assessed by a helmet device containing mercury switches recording angular displacement of the head in both sagittal and coronal planes. Continuous recording of the number and duration of head deviations outside preset limits was carried out. After their normal head control achievement had been documented, the patients underwent a training period during which they received instantaneous auditory and visual feedback whenever head deviations exceeded preset limits. All patients, regardless of intelligence level, demonstrated a striking progressive improvement in head control during the feedback training period. Following cessation of feedback, two of the best motivated adult athetoids had complete retention of their improved head control (up to 6 months later). The remainder (8) had a partial regression but demonstrated a significantly improved head control in comparison with the baseline. These data suggest that severely involved cerebral palsy patients can learn to improve head control with the aid of angular displacement feedback.

XV-6

The Borderland of Migraine

A. Hill, K. Farrell and Da. A. McGreal, Toronto

Migraine is common and complicated migraine is not uncommon in children. Transient hemisensory defects, hemiparesis and visual field defects are the most common neurological manifestations and will not be included in this presentation.

Several more bizarre forms of complicated migraine have been seen by the authors during the past two years at the Hospital for Sick Children, Toronto. The importance of considering migraine, albeit as a diagnosis of exclusion, in many patients with unusual neurological signs and symptoms is reinforced by the following group of patients: — ophthalmoplegic migraine (2), post-traumatic migraine (6), confusional states (7), basilar migraine (3), cortical blindness (1), focal seizure (1), epilepsia partialis continua (1), permanent neurological deficit (2), transient monocular blindness (2). Some patients had more than one of the above types. Two cases of migraine accompanying thrombocytopenia are included.

Angiographic, C.A.T. scan and neuropsychological data will be presented.

XV-7

Literal, Verbal and Sentence Alexia

A. Kertesz and W. Harlock, London, Ontario

The varieties of alexia are taxonomically defined in an asphasic population. The reading performance of 245 aphasics, who had complete language assessment and the reading subtests of the Western Aphasia Battery and who had been classified according to the test scores was studied. Twenty-three percent were considered not alexic by virtue of achieving a standardized cut-off score. The rest were divided into the various groups of alexia taxonomically, according to their sentence-reading-comprehension, word-reading and letter-reading scores. A synoptic table was constructed to define the alexic syndromes unequivocally, and the rationale for these will be presented. The incidence of each variety was determined in each asphasic group. The results indicate that Literal alexia occurs most frequently with Broca's aphasia. Verbal alexia is the least common variety, but is seen relatively frequently with Transcortical Sensory, Wernicke's and Broca's aphasia. Globals commonly have Global alexia. Wernicke's tend to display either Global or Sentence alexia. The majority of Conduction and Anomic aphasics suffer from Sentence alexia, followed by a Diffuse alexia involving all elements of reading. In conclusion, the taxonomic analysis of aphasic alexia indicates that, while most aphasics, with the exception of Anomics, are alexic, the type of alexia varies with the type of aphasia.

XVI-1

Neurological Disorders and Immigration. A Progress Report.

Frederick Andermann, Henry B. Dinsdale, Laughlin B. Taylor, and Robert W. Wood, Montreal, Kinston, Ottawa

The new Immigration Act permits admission to Canada for people who do not present a danger to the public and do not have excessive requirements for medical or social services. Thus, nobody will be barred from admission to Canada simply because of a diagnosis of any specific neurological or other disorder.

Each individual will be assessed by Canadian Medical Officers, and the findings scored on a grid taking into account the criteria just mentioned. A handbook has been prepared by the Department of National Health and Welfare, Medical Services Branch, to assist the Medical Officer in his decision. It includes sections on epilepsy, multiple sclerosis, mental retardation and other neurological disorders prepared by us. A review board including members of this society is available for further consultation in the case of difficult problems.

Project 45 involving re-evaluation of about a thousand individuals presently in Canada under Minister's Permit, because of previous inadmissibility on medical grounds, provided experience and practical testing of the new system. For instance, controlled epilepsy is no longer a reason for nonadmission and provisions are available for re-evaluation in cases where control is poor but improvement may be anticipated.

The new law and mechanisms for medical assessment involving ongoing consultation with neurologists and other medical specialists bring criteria for immigration to Canada into line with our current approaches to neurological disease and provide a forum for ongoing examination of the government's and the public's views of these disorders.

XVI-2

Manpower Planning in Neurology: Observations from Ontario

H. B. Dinsdale, Kingston

The issue of physician manpower will remain with the profession for the foreseeable future. Factors of uncertain potential only a few years ago, such as restriction of physician immigration and limitation of government funding of residency positions, are now major elements influencing manpower projections. A national committee on physician manpower reported in 1971 that production was adequate to meet national needs in adult but not in child neurology.

To review Ontario's needs, a subcommittee on Postgraduate Manpower of the Council of Ontario Faculties of Medicine was appointed to: (1) indicate the relevance of training programs to manpower needs of the province, and (2) suggest means of coordinating programs to avoid unnecessary duplication. Twenty study groups looked at present and future provincial and out-of-province needs. The first report in 1975 forecast that production in Ontario of neurologists would be roughly in balance with projected needs. However, survey of the five Ontario university centres in 1979 reveals up to 15 adult and 7 child neurology appointments available during the next two years, if appropriate individuals can be found. Community hospitals recognize a need for a further 9 neurologists. Questionnaires demonstrate that 25% of Ontario program graduates locate elsewhere in Canada and 15% outside of Canada.

Considering attrition, population growth, choice of location of practice, and special university needs, there is currently a shortfall of neurologists in Ontario.

XVI-3

Familial Fatal Parkinsonism With Alveolar Hypoventilation and Mental Depression

R. A. Purdy, Halifax, A. Hahn and H. J. M. Barnett, London, Ontario

The clinical, pathological and neurochemical characteristics of a newly recognized inherited neurological disorder are reported.

Lethargy and mental depression are early symptoms, followed by mild parkinsonism and progressive weight loss. Failure of automatic respiratory control develops and may result in sudden death.

Advanced degeneration of the substantia nigra, cell loss and gliosis of the basal ganglia and focal gliosis in the medulla are seen on pathological study.

Degeneration of the nigral-striatal dopaminergic system is evidenced by low levels of tyrosine hydroxylase (TH), dopamine, homovanillic acid and L-Dopa decarboxylase in postmortem brain samples. Taurine concentrations in fasting plasma and CSF and brain contents of taurine are within normal limits.

XVI-4

Familial Agenesis of the Corpus Callosum with Sensorimotor Neuronopathy: Genetic and Epidemiological Studies of over 170 Patients

Eva Andermann, Frederick Andermann, Denis Bergeron, Pierre Langevin, Richard Nagy and Jean Bergeron, Montreal, Chicoutimi and Québec

This syndrome consists of complete agenesis of the corpus callosum, mental retardation, sensory and motor neuropathy, and associated dysmorphic features. Diagnosis can be suspected in infancy because of hypotonia, most marked in the lower extremities, areflexia and retardation, and can be confirmed by computerized axial tomography, conduction studies and peripheral nerve biopsy. Initial progress in motor ability to the level of standing or walking with crutches at four to six years of age, is followed by motor deterioration, with most patients confined to a wheelchair by the early teens. Extreme scoliosis develops, and most patients have died by the third or fourth decade.

The syndrome is inherited as an autosomal recessive trait, and is seen only in French-Canadian families originating from the Baie St-Paul-La Malbaie region of Quebec. Most new cases are now diagnosed in the Chicoutimi-Lac St-Jean area, where the population has migrated. The gene frequency of the syndrome in this population of 300,000 is extremely high, and founder effect has been demonstrated by genealogical studies.

Two patients have shown florid hallucinatory psychosis and possible dementia. At least five patients show the typical neuromuscular syndrome and retardation, but do have a corpus callosum. Thus the callosal agenesis in this syndrome may be an intrauterine manifestation of a widespread and progressive disease process. However autopsy confirmation is still not available.

Recognition of the syndrome has led to earlier diagnosis, genetic counselling, and prevention of recurrence within sibships. Although carrier detection is still unavailable, prenatal diagnosis by ultrasound may be feasible.

XVI-5

Some Differential Effects of Infrasound on Humans

D. S. Nussbaum, S. Reinis, Waterloo, Ontario

In an attempt to assess individual reactivity to low frequency sound, 63 subjects were exposed to 8Hz pure tone at 130dB SPL for 30 minutes, 211 controls were exposed to amplifier burn in the same soundproof booth. Five of the subjects had episodes of headache, dizziness, nausea and fatigue 3 to 5 hours after the exposure; eight other subjects had at least two of the symptoms. These sensitive persons had longer time estimates and differed in their EEG, heart rate and vascular response during the exposure to the intrasound. The sensitive and non sensitive persons did not differ in the short-term memory personality tests and past medical history.

XVI-6

Noise Induced Vestibular Damage

W. Pryse-Phillips, St. John's

Noise induced hearing loss is well recognized. Its mechanisms are not clearly defined but a number have been proposed and will be discussed.

A case of noise induced vestibular damage will be presented and discussed in the light of scanty similar case reports to be found in the literature.

The Co-incidence of both cochlear and vestibular damage as a result of noise trauma might suggest similar mechanisms for their causation and the relative likelihood of hair cell damage and mechanical trauma in the two syndromes will be examined.

XVI-7

The Effect of Simulated Sonic Booms on the Auditory Thresholds of Rhesus Monkeys

S. Reinis, J. W. Featherstone, C. Tsaros, Waterloo, Ontario

Repeated simulated sonic booms of medium intensity, about 100 Pa, have been found by this laboratory to cause bleeding into the basal turn of the cochlea of C57 BL/6J mice and chinchillas. Single superbooms of 200 to 500 Pa have the same effect. High frequency sounds are perceived in the basal turn of the cochlea. Rhesus monkeys that were exposed to repeated simulated sonic booms showed a threshold shift after 24 hours to tones with the frequency in their middle threshold range of 8KHz, 30 KHz and 35 KHz. Threshold changes were still present after four months at 24KHz and 30KHz. This indicated that repeated exposure to sonic booms will cause a permanent threshold shift in the high frequency range.