Canadian Association of Neuropathologists

Abstracts

of papers presented at
The 29th Annual Meeting
September 7th-9th, 1989
Montreal, Quebec

Summary

The 29th Annual Meeting of the Canadian Association of Neuropathologists was held September 7th to 9th, 1989 at the Hotel Le Grand in Montreal. The scientific session consisted of 19 diagnostic cases, 25 platform presentations and 7 poster presentations.

Two guest lectures were presented:

The Jerzy Olszewski Guest Lecture

Dr. Paul Jolicoeur, Montreal

Title: "Pathogenesis of Retrovirus-Induced Spongiform Myeloencephalopathy: The Retrovirus as a Tool to Probe Normal Cell Functions"

The Royal College of Physicians and Surgeons of Canada Speaker

Dr. Douglas C. Wallace, Atlanta, Georgia

Title: "Mitochondrial Genes and Neuromuscular Disease"

Two awards for presentations by trainees were given:

The Mary Tom Award went to Dr. S. Chukoor of Saskatoon for his paper entitled "Immunohistochemical Study of the Human Foetal Nervous System"

The Morrison H. Finlayson Award went to Dr. Robert R. Hammond of London, Ontario, for his paper entitled "The Neuropathology of Embolized Arteriovenous Malformations"

https://doi.org/10.1017/S0317167100030717 Published online by Cambridge University Press

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Abstracts

1.

The Neuropathology of Embolized AVM's

R.R. HAMMOND and J.C.E. KAUFMANN (London, Ontario)

Many neurosurgical centres utilize the technique of arteriovenous malformation (AVM) embolization as either an adjunct to surgical excision, or as definitive therapy. Several different embolic materials have been employed. At the University Hospital in the past eleven years over 170 patients have received this treatment producing more than 40 surgical specimens and 3 cases coming to autopsy. Two embolic regimens were employed either alone or in combination; isobutyl-2-cyanoacrylate (IBCA) and a mixture of Avitene and polyvinyl alcohol particles (AP). The volume of embolizing agent and the timing of surgery after embolization varied considerably. The embolizing agent(s) could be easily identified in most cases as could vessel thrombosis. Intraluminal and extravascular embolizing agent deposition, recanalization, vessel wall necrosis, acute and chronic inflammatory changes, and gliosis of adjacent brain were also seen.

2.

The Prognosis Following Excision of Brain Tumors

ELLSWORTH C. ALVORD, JR. (Seattle, U.S.A.)

The prognosis following excision of a brain tumor depends upon how much tumor is left behind and its growth rate, in turn defined by its degree of mitotic activity and cell loss. A nomogram has been developed correlating these four factors such that any three should define the fourth or any two should define the limits of the ambiguity of the other two. Obviously, if only one is known, the ambiguity of the other three is very great. What is not so obvious, however, is that generally we know only a fifth factor, the name and grade of the tumor, which is only approximately related (by "degree of malignancy" and "tendency to recur") to one or another of the four major factors: mitotic activity, degree of cell loss, amount of tumor left behind and time to recurrence and/or death.

3.

Specific Patterns of Limbic Deafferentation Linked to Dementia in Lewy Body Disease

Y. ROBITAILLE, P. LEMOINE, R. QUIRION, R. MENA and A. LAROCHE-CHOLETTE (Montreal, Quebec)

We investigated 16 cases of senile dementia (mean age — 78) accessed to the Douglas Hospital Research Center Brain Bank during the past 3 years, which displayed cortical Lewy bodies. They were subdivided in Group 1, which included 10 patients whose dementia followed Parkinson's disease, and Group 2, which consisted of 6 patients who were demented from the onset. In all, Lewy bodies (LBD) were present in highest densities in the lower lamina of the parahippocampal gyrus (PHG), while rostro-lateral temporal, frontal and parietal isocortices harbored minimal LBD's. Both groups had high densities of limbic and isocortical senile plaques, which were the densest in the PHG of Group 2. Group 1 showed intermediate levels of magnocellular basalis cell loss (45.2%, p less than .01), which was severe in Group 2 (80%, p less than .001) compared with age-matched controls. In both groups, temporo-parietal ChAT activity remained within normal limits. Group 1 showed the highest index of Ventral Tegmental Area (VTA) cell loss (82.5%, p less than .01), which was 64% (p less than .01) in Group 2. The magnitude of VTA neuronal loss recorded in 9 non-demented Parkinsonian patients was similar to Group 1. In 4 additional Group 2-like cases from the Saguenay-Lac St-Jean area of Quebec, 2 of which were familial, all were characterized by a neocortical paucity of Alzheimer changes on silver and Congo Red stains. Immunocytochemical reactivity to Alz-50 and core PHF Mab's (Mab 423, Wischik et al, 1988), the latter of high specificity to fetal tau and NFT's, yielded numerous Alz-50 immunoreactive dystrophic neurites and curly fibres markedly predominating in layers II and IV of the PHG. Few PHG NFT's were revealed by Mab 423, none in numerous sections of isocortex. Our results suggest that the combined perforant pathway Alzheimer lesions, PHG LBD's and VTA neuronal loss are major determinants of the dementing process in Lewy Body Disease. Supported by a grant from the Canadian Parkinson Foundation.

4.

Malignant Transformation of a Cauda Equina Ancient Schwannoma

A.S. COMMONS, V.J.A. MONTPETIT, N. GUPTA, M.T. RICHARD and S. DANCEA (Ottawa, Ontario)

A case of malignant transformation and ascending dissemination of a cauda equina ancient Schwannoma is reported. A 66-year-old male with longstanding lumbar back pain presented with a 1 month history of increasing bilateral exertional leg pain and weakness associated with a 20 lb. weight loss. An MRI scan of the thoracolumbar spine revealed an intradural lesion of the cauda equina. The resected tumor consisted of a 1.8 cm encapsulated firm spherical mass possessing a cream coloured homogeneous appearance with a minor central zone of cystic change. At each pole, cylindrical protrusions microscopically identified as nerve fascicles were noted. The extensively hyalinized mass was sparsely populated by stellate cells exhibiting vacuolar degeneration and nuclear pleomorphism and hyperchromasia. No mitotic figures or preserved Antoni A and B areas were discernible. The cells exhibited focal positive staining with S100 protein immohistochemistry while the ultrastructural features were consistent with a Schwann cell origin. Of interest, the capsule was focally infiltrated by loosely arranged atypical cells of undetermined origin. The patient's neurological status deteriorated in an ascending fashion until he developed pneumonia and died 3 months post-operatively. At autopsy, there was extensive infiltration of the leptomeninges, nerve roots and cranial nerves by a malignant neoplasm with multifocal centripetal extension into the spinal cord and brainstem. There was no evidence of generalized neurofibromatosis of distant metastatic disease. Only 3 other cases of malignant transformation of a solitary benign Schwannoma are documented in the literature.

5.

Changes in Cerebral Sulcation in Simple Absence of the Corpus Callosum: Evidence of Rules Controlling Sulcation Patterns

JANS MULLER (Indiana, U.S.A.)

If the cerebral cortex be severely damaged (early porencephaly) or malformed (pachygyria-microgyria complex), it cannot provide many crossing fibres to the corpus callosum; which, having lost its raison d'être, will be largely absent: secondary to symptomatic callosal aplasia. There are however cases in which the cerebral cortex is perfectly normal but there is some midline factor preventing the development of the corpus callosum. It has been known since Davidoff & Dyke (1934) that the medial hemisphere wall then will assume a radial gyrational pattern. Not reported is that this verticalization of the sulcation pattern also can be observed on the lateral surface, specifically the frontal lobe, making the diagnosis of a callosal deficiency apparent from the lateral aspect alone. If the cortical plate is considered as a continuously and uniformly extending plate, expanding at a greater rate than the underlying

white matter, it follows that the plate will be forced to fold. Folds will occur depending on pre-existing radius of curvature of the structure; they can be predicted following simple geometric rules. If the medial and lateral surfaces of the cerebral hemisphere are considered together, the corpus callosum acts as a brake or dam to the extension of the cortical plate; the corpus callosum will impose a predictable sulcation pattern on the hemispheral cortex, with the first sulcus (often double), the cingulate, paralleling the dam. By the same token, the absence, either partial or whole, of the corpus callosum will allow an entirely different pattern of sulcation to develop, both on the outer and on the medial surface. It should be emphasized that these sulcation patterns can only be expected in a normal cerebral cortex and that therefore the presence of these patterns — say in radiologic studies — can be taken to mean that the cortex is histologically normal. The predictability of these patterns lends force to a general theory of sulcation to explain other hemispheral abnormalities, stenogyria in hydrocephalus for example, or the pattern in holoprosencephaly.

6.

Pituitary Asymmetry and Hyperprolactinemia Due to Massive Diffuse Prolactin Cell Hyperplasia

V. JAY, K. KOVACS, E. HORVATH and H.S. SMYTH (Toronto, Ontario)

Diffuse prolactin cell hyperplasia is well recognized in the setting of pregnancy and lactation and to a lesser extent in states associated with disturbances of dopaminergic regulation due to tumorous or nontumorous lesions of the hypothalamus or infundibulum. Rarely, prolactin cell hyperplasia has been observed in association with prolactin and ACTH secreting adenomas and in patients with primary hypothyroidism. We report an unusual case with hyperprolactinemia due to prolactin cell hyperplasia unassociated with pregnancy, overt hypothyroidism or drug therapy. This 38-year-old woman with two children aged 11 and 17 years was investigated for headaches and irregular menses. The headaches, presumably unrelated had been noted for about 2.5 years following a motor vehicle accident. The patient had irregular menstruation in the preceding 11 years. Her last menstrual period had been about 6 months prior to admission. There was no associated galactorrhea. The patient did not use oral contraceptives. The serum prolactin level was 256 mcg/L with an exaggerated response to TRH testing with a baseline of 199 mcg/L increasing to 1101 mcg/L. The patient was clinically and biochemically euthyroid. CT and MR scans showed evidence of increased tissue on the left side involving the adenohypophysis. Exploration by a transsphenoidal approach revealed no discrete adenoma. Examination of the specimen showed nontumorous adenohypophysis composed predominantly of chromophobic cells interspersed with acidophilic and scattered basophilic PAS-positive cells. The reticulin network was preserved but markedly distorted. The large majority of the cells were immunoreactive for prolactin with a predominant Golgi-pattern of immunoreactivity. Growth hormone cells appeared to be markedly reduced in number. Electron microscopy showed active prolactin cells with extensively developed rough endoplasmic reticulum and Golgi complexes and secretory granule exocytosis. Extracellular endocrine amyloid was found in association with the stimulated prolactin cells. This case represents a primary prolactin cell hyperplasia of the pituitary with no established cause. Further work is needed to clarify the mechanism of prolactin cell proliferation in this form of pituitary disease.

7.

Cysts of the Neuraxis of Endodermal Origin

I. MACKENZIE and J.J. GILBERT (London, Ontario)

Colloid cysts of the third ventricle have an obscure origin with a wide variety of sources proposed in the literature. Ultrastructural studies have suggested similarities with respiratory and intestinal epithelium. To further investigate this possible endodermal derivation, we examined the histologic and immunohistochemical features of five colloid cysts and compared them with two enterogenous cysts of the spinal cord, lesions of accepted foregut derivation. All seven lesions contained columnar and cuboidal, with ciliated areas. This epithelium was positive with a variety of mucus stains (PAS, Alcian Blue, Muci Carmine). Immunohistochemistry showed the colloid cysts to be positive for cytokeratin, EMA and CEA (5/5), occasionally positive for S-100 protein (3/5) and negative for GFAP and vimentin (0/5). These findings were similar to the enterogenous cysts — cytokeratin, EMA, CEA positive (2/2), S-100 positive (1/2) and GFAP and vimentin negative (0/2), and suggests a similar origin from primitive foregut endoderm. An epithelial lined cyst from the fourth ventricle with the same histologic and immunohistologic appearance is presented, as it may represent a developmental lesion of similar etiology in an unusual location. We conclude that colloid cysts of the third ventricle and enterogenous cysts of the spinal cord are two members of a group of cystic lesions derived from foregut endoderm. These lesions may arise in a variety of locations along the midline of the neuraxis.

8.

Cytokinetics of Human CNS Neoplasm Using the Monoclonal Antibody Ki-67

ANA MARIA C. TSANACLIS, FRANÇOISE ROBERT and STEVEN BREM (Montreal, Quebec)

Ki-67 is a mononuclear antibody to a nuclear antigen expressed by proliferating cells in all phases of the cell cycle except G_0. For tumors, the labeling index (LI), the fraction of labeled cells over the total number of cells counted, represents a measure of the proliferative rate and malignant potential of the replicating cells. The LI of 17 intracerebral tumora was measured using a computerized image analyzer (Leitz, "Bioquant"). There was a striking difference between benign tumors (a low-grade astrocytoma, an acoustic schwannoma, and an angiolipoma) that had an LI typically less than 1%, versus malignant tumors that had much higher values: an anaplastic oligo-astrocytoma, 7.1%; anaplastic astrocytomas (n = 2), $\bar{x}$ = 10.0%; and glioblastomas (n = 5) $\bar{x}$ = 8.6%. The highest LIs were observed in metastic carcinomas (n = 4), with a mean of 35.8%. These results correspond to prior studies and suggest a close relationship between the LI and the clinical evolution of a brain tumor. This technique is a sensitive, accurate, and reproducible method to assess the growth rate of a tumor. Because of the biologic and prognostic implications of the LI, cytokinetic studies with the Ki-67 is a promising marker to complement the standard histopathology in the management of patients with brain tumors.

9.

Cerebral Amyloid Angiopathy with Granulomatous Angiitis Ameliorated by Steroid Treatment

T.I. MANDYBUR and G. BALKO (Cincinnati, U.S.A.)

We report a case of a 62-year-old black woman with a history of hypertension and type II diabetes mellitus who 7 months prior to death developed confusion, inappropriate behavior and difficulties with her vision. There was no dementia. CT scan revealed focal mass within the right posterior parietal lobe with minimal enhancement. MRI showed an ill-defined area of abnormal signal in the right posterior parietal white matter. A biopsy of the right parietal mass displayed granulomatous angiitis and severe cerebrovascular amyloidosis but not tumor. Chronic inflammation with an occasional multinucleated giant cell was seen about the amyloid infiltrated vesssels. The cortex demonstrated gliosis but no plaques or tangles. Subsequently, the patient was treated with steroids and cytoxan which resulted in improvement in her neurologic status. Six months later, the patient developed persistent fever and diarrhea which was treated with antibiotics. Repeat CT scan of the head revealed enlargement of the right parietal lesion. The cytoxan dose was

increased with some improvement in the patient's mental status. However, the patient subsequently developed congestive heart failure, hemorrhagic cystitis and finally hypoxemia, progressively worsening to respiratory failure. She expired 8 months after initial onset of symptoms. Autopsy revealed opportunistic bronchopneumonia as cause of death. The biopsied area of the brain showed laminar cortical atrophy with gliosis (infarct?) and amyloid and angiopathy but of a much lesser degree than in the biopsy. Scant perivascular inflammatory infiltrates were seen only focally and no giant cells were observed. Neurofibrillary tangles were absent. The amyloid, both in the biopsy and autopsy material, was of the A4 type. This case suggests that steroid and cytoxan treatment could have ameliorated the angiitis and the amyloid angiopathy as well. Of additional interest was lack of plaques within the cortex despite the A4 type of the amyloid angiopathy.

10.

Microinjection of Antibodies into Cultured Motor Neurons: Labeling of Perikarya and Dendrites by SMI31 Against Phosphorylated Epitopes on Neurofilament Proteins

H.D. DURHAM (Montreal, Quebec)

SMI31 and SMI32 are monoclonal antibodies that distinguish between phosphorylated and non-phosphorylated epitopes, respectively, on the medium and high molecular weight neurofilament proteins (Sternberger and Sternberger, Proc Natl Acad Sci USA 1983; 80: 6126). SMI32 labels perikarya, dendrites and axons in fixed spinal cord sections or cultures, whereas SMI31 labels mainly axons. In order to study the mechanisms involved in neurofilament organization in motor neurons and the significance of neurofilament phosphorylation, SMI31 and SMI32 were microinjected into living motor neurons in culture. Dissociated cultures of spinal cord were prepared from 13 day embryonic mice and maintained for at least 4 weeks in culture. Solution containing 2 to 8 mg/ml of antibody was microinjected through a glass micropipette into large motor neuron-like cells using an Eppendorf pressure-injection unit. In some experiments, Lucifer yellow 0.25% was included in the injection buffer as a marker. At various times after microinjection, cultures were fixed in methanol, then acetone both at –20°C. Injected antibody was visualized by incubation with goat anti-mouse IgG conjugated to Texas Red. To visualize epitopes on neurofilaments not occupied by injected antibody, cultures were then incubated with SMI31 or SMI32 followed by goat anti-mouse IgG conjugated to AMCA. *In vivo* labeling with microinjected SMI32 was similar to that of SMI32 in fixed cells. However, when microinjected, SMI31 labeled large filament bundles in perikarya and dendrites as intensely as did SMI32. This was not due to change in the phosphorylation state of neurofilament proteins since neuronal perikarya microinjected with SMI31 were still labeled by SMI32 postfixation and microinjection of Lucifer yellow alone did not alter the labeling of perkaryal filaments by SMI31 post-fixation. Nor was labeling of cell bodies observed when high concentrations of SMI31 were applied to fixed cells. A number of reports indicate that antibodies against phosphorylated neurofilament epitopes label cell bodies and various perikaryal inclusions in pathological states. The results of this study indicate explanations other than increased phosphorylation could account for these changes in antibody binding and suggest caution in their interpretation.

11.

Chromogranin A-Like Immunoreactivity (CgA-li) in the Maturing Human Visual Cortex

L-C. ANG and D.G. MUNOZ (Saskatoon, Saskatchewan)

Chromogranin-A is a calcium-binding protein and a precursor of modulatory peptides. In addition to its widespread presence in secretory granules of neurocrine cells, CgA-li is observed in a large variety of neuronal populations in mammalian species as well as in the human brain (Munoz, et al, Abs Soc Neurosci 1988). In the neocortex, the distribution of CgA-li exhibits regional variability corresponding to the different cytoarchitectonic areas. We have studied the effect of maturation on the expression of CgA-li in the human calcarine cortex from 8 patients, ages ranging from 4 months to 88 years. Frozen 50μ sections of the calcarine cortex were immunostained with the monoclonal antibody LK2H10 using the avidin-biotin technique. The CgA-li was restricted to neurons. Staining was particulate in the somata; dendrites and occasional proximal segments of the axons were also stained. On the basis of the shape of their somata and dendritic pattern, the majority of the labeled cells were felt to be pyramidal in nature. In the calcarine cortex of a 4-month-old, CgA-li was restricted to only a few large pyramidal cells at layer V. Immunoreactivity was also seen in the neuropil as dense collections of puncta in layer IV. By 15 months CgA-li was expressed in increasing numbers of neurons in layer V and some neurons in layers IV and VI. At 12 years many more neurons were stained in layer IV. At 25 years there was an increasing number of neurons in layers III and IV with some perikaryal staining also appearing in layer II. The laminar pattern of the visual cortex was quite distinct even though the subdivisions of layer IV were not clearly demarcated. Only at the age of 35 years did CgA-li exhibit clear demarcations in the different subdivisions of layer IV. The laminar pattern of staining was well maintained to the age of 88 years, though there was less intense staining of the neuropil in layer IV. The major change in CgA-li after the age of 15 months indicates continuing maturation of the primary visual cortex after this period; a change not appreciated with classic staining techniques such as the Nissl stain.

12.

Preferential Incorporation of Chromogranin A-Like Immunoreactive (CgA-li) Peptides in Senile Plaques of Alzheimer's Disease

M.C. CARO and D.G. MUNOZ (Saskatoon, Saskatchewan)

One of the current hypotheses for the mechanism of formation of senile plaques states that the deposition of amyloid precursor protein is followed by nonselective incorporation of neurites containing diverse neurotransmitters in numbers proportional to their relative abundance in the surrounding neuropil. To test this hypothesis we have compared the density of neurons immunolabelled for several peptides in the amygdala and entorhinal cortex of nine normal controls and six patients with Alzheimer disease with the density of neuritic plaques labelled for the same peptides in Alzheimer's disease. Results for the basal nucleus of the amygdala as shown in the table.

	CgA-Li	Som 28(1-14)	CCK	Calbindin
Neurons/mm², Controls	3.2	5.1	8.2	24.9
Neurons/mm², Alzheimer	0.7	4.1	7.8	19.3
Plaques/mm², Alzheimer	11.2	1.4	1.3	0.04

CgA-li neurons were less common than those labelled with antibodies against any other peptide examined, but the reverse was true for plaques incorporating neurites labelled with each of these peptides. Results in other nuclei of the amygdala and in the entorhinal cortex are consistent with this conclusion. These results indicate that the incorporation of neurites into senile plaques is a selective process, some neuronal types being more prone to participate in the formation of these structures.

13.

Homocystinuria with Spongy Degeneration of the White Matter

K. MEAGHER-VILLEMURE, K. SILVER and A. O'GORMAN (Montreal, Quebec)

The authors are reporting a case of a 5½-month-old baby who presented since birth with some dysmorphic features, cataracts, microcephaly and significant neurological impairment. The baby's parents are consanguinous. Homocystinuria was later diagnosed in this child and the patient was refractory to vitamin B_6 treatment. The child presented

https://doi.org/10.1017/S0317167100030717 Published online by Cambridge University Press

with repeated episodes of respiratory infections and developed myoclonic seizures, events from which he finally died. A CT scan done had shown diffuse involvement of the white matter. At autopsy, the central nervous system was severely involved with spongy degeneration of the white matter, microcystic cavities, poor myelin formation and a severe reactive gliosis. Minimal axonal changes were seen. Similar cases have been rarely reported and the same histological changes have been reproduced experimentally in animals by ingestion of cycloleucine, a drug causing homocystinuria.

14.

Renal Blastema and Various Types of Lower Dysraphism: A Report of Four Cases

MOHAMED HÉDI SAGUEM, JEAN MICHAUD and JACQUES DUBÉ (Montreal, Quebec)

Dysraphic lesions are the most frequent malformations in man. Most are found at the caudal end of the neural tube where a wide spectrum of morphological anomalies are found. We report four cases, aged five days to four years (one already published: Masson P. Ann Anat Pathol 1959; 3: 379-389) with congenital lumbo-sacral dysraphism. They were associated with subcutaneous, intra-spinal or intra-dural "lipomas", one with a meningocele and one with a myelomeningocele. In all, localized fibrous areas harboring islands of renal blastema with tubular and glomerular structures were found. In one instance, neuroglial tissue was admixed in the fibrous tissue. Mitoses were found in the immature portion in two cases. Immunohistochemical reactions are compatible with nephrogenic tissue, particularly at the level of differentiated tubular structures which were positive for vimentin and cytokeratin. Both kidneys were, by clinical investigations, normal in all patients. This very rarely reported finding is of unknown pathogenesis. It could be related to a concomittant developmental defect involving the axial mesodermal and the intermediate mesodermal structures. These findings can also be related to extrarenal nephroblastomas and to neural differentiation in nephroblastomas.

15.

Neuropathological Differences Between Ischemia and Hypoglycemia

ROLAND N. AUER (Calgary, Alberta)

Ischemic and hypoglycemic brain damage have usually been considered to have the same pathogenesis, under the rubric of energy failure. Recent experimental evidence indicates that a unifying theme in the pathophysiology of brain damage due to these two conditions is the release of endogenous excitatory amino acids, causing selective neuronal necrosis. In some experimental and clinical situations, endogenous brain lactic acidosis gives rise to pan-necrosis, where glia are killed as well. Lactic acidosis is impossible during hypoglycemia, which is characterized by a tissue alkalosis. This may explain the absence of infarction usually seen in hypoglycemia as opposed to ischemia in both experimental and clinical situations. Although both ischemia and hypoglycemia are global insults to the brain, the cerebellum is characteristically spared in hypoglycemia, whereas global ischemia causes necrosis of Purkinje cells. The cerebellar sparing in hypoglycemia is likely due to a more efficient glucose transporter in that brain structure. Another morphologic difference between ischemia and hypoglycemia is a characteristic involvement of the dentate gyrus in hypoglycemia. Review of clinical material reveals some cases where a characteristic involvement of the dentate gyrus, usually extremely resistant to ischemic brain damage, is seen. Knowledge of neurochemical similarities and differences between ischemia and hypoglycemia is important in understanding the pathogenesis of brain damage in these two conditions. In addition, knowledge of the structural differences which sometimes may allow the clinical neuropathologist to clearly differentiate hypoglycemic from ischemic brain damage, may be useful in certain clinical or medico-legal situations where it is necessary to differentiate hypoglycemic from ischemic brain damage in the human.

16.

Neuroaxonal Dystrophy and Trans-Synaptic Caudate Nucleus *Degeneration in Parkinson's Disease*

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

The ultrastructure of biopsied caudate nucleus (CN) specimens of two patients with advanced Parkinson's disease (PD) were compared with CN biopsy obtained during passage to deeply-seated frontal tumor. The CN of both PD patients displayed frequent dystrophic neurites filled with numerous dense bodies, myelin figures, profiles of smooth endoplasmic reticulum and mitochondria. Dystrophic changes could be traced to the axonal terminals still in the synaptic connections with other neurites or neuronal somata. A few distended neurites displayed two separate pools of dissociated microtubules and neurofilaments. Occasional myelinated and unmyelinated fibres showed varicosities with focal accumulation of the content similar to that present in dystrophic neurites, chiefly mitochondria. Some synapses were attached to very dense post-synaptic neurons or neuritic processes, characteristically seen in trans-synaptic degeneration. Many neurons were normal but a few also showed degeneration. The number of astrocytes and macrophages were clearly increased often in the proximity to dystrophic axons. Morphometric studies indicated approximately a 20% reduction in the number of mitochondria in the neuropil of the CN of both patients. Other morphometric assessments were carried out only in one patient. They revealed that the number of terminal neurites per area in the control and PD were similar. These findings suggest remodeling of the synaptic connections and possibly process of reinervation of some CN neurons in PD. The total area of the terminal neurites was significantly increased. This enlargement of the terminal neuritic processes may represent the initial event in dystrophic changes. The HLPC assessment of the level of neurotransmitters in one patient revealed approximately 90% reduction in the amount of dopamine and drastically lowered levels of dopamine metabolites. Light microscopic and immunohistochemical examination for GFAP, neurofilaments, tyrosine hydroxylase, Ricinus communis lectin, Ia antigen and ubiquitin performed in one patient, showed no evident pathological changes. The presence of widespread dystrophic changes in CN suggests abnormal axonal transport in Parkinson's disease. Enlargement of the neuritic terminals may represent an early stage of this process. The occurrence of trans-synaptic degeneration indicates that some patients may not benefit from transplanation because of the progression of neuronal degeneration to the second set neurons within the caudate nucleus in advanced stages of Parkinson's disease.

17.

Intracranial Hemorrhage as a Complication of Traumatic Carotid-Cavernous Sinus Fistula

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

Spontaneous intracranial hemorrhage is an uncommon complication of carotid-cavernous sinus fistulas, and because of the few published descriptions of the pathogenesis of this complication, the following case is reported. A 24-year-old man, one month after a motorcycle accident during which he sustained a basal skull fracture, developed a carotid-cavernous sinus fistula manifested by headache, proptosis of the left eye, and diplopia. These symptoms worsened over the ensuing five months and culminated in his sudden collapse which was preceded by occipital headache, loss of hearing in the left ear, and vertigo. When admitted to hospital he was found to be deeply comatose. A CT scan of the head disclosed acute hemorrage within the basal subarachnoid space and ventricular chambers. The patient's neurological status deteriorated and he died the day following his ictus. Autopsy confirmed the presence of a large fistula between the posterior intracavernous portion of the left internal carotid artery and the adjacent cavernous sinus in conjunction with massive ectatic enlargement of the sinus and its drainage route via the ipsilateral superior petrosal sinus. There was an associated compression

neuropathy of the left cranial nerves III, V (ophthalmic branch), and VI. In the left lateral brain stem plexus of veins that drained into the superior petrosal sinus there were similar features of engorgement and arterialization including varicocele formation. One of these venous varicies at the level of the pontomedullary junction had ruptured with fresh hemorrage into the lateral recess, subarachnoid space, and through the torn ipsilateral inferior and middle cerebellar peduncles into the fourth ventricle to track along the cerebral aquaduct into the third and lateral ventricles. In absence of a demonstrable arteriovenous malformation in the left cerebellopontine angle it is proposed that the arterialized changes and rupture of the lateral brain stem venous plexus was caused by retrograde flow of blood at arterial pressure from the superior petrosal sinus due to the arterial-venous shunt created by the carotid-cavernous sinus fistula. In the clinical literature the occasional reports of intracranial homorrhage as a complication of carotid-cavernous sinus fistulas have speculated upon the pathogenic role of venous hypertension. This current case report provides rare pathological confirmation.

18.

The Central Nervous System in AIDS: A Review of 86 Cases

JEAN MICHAUD (Montreal, Quebec)

The neuropathological examination of the human central nervous system (CNS) in the acquired immune deficiency syndrome (AIDS) discloses a wide variety of lesions. Variations according to age groups, countries and patient subgroups as related to the etiology of the syndrome are now recognized. We report our findings in 86 patients with AIDS. Twelve were in the pediatric age group: seven females and five males aged between three and 66 months. Seventy-four were in the adult group: 68 males and five females aged between 19 and 58 years. Over 90% of both pediatric and adult groups had significant morphological findings that could be classified in three main groups: HIV-related lesions, opportunistic infections and primary CNS tumors. In approximately 14%, more than one pathological process was found. Human immunodeficiency virus (HIV) encephalitis was found in 58% of pediatric cases and 27% of adult cases. If one adds the patients with the diffuse non specific leucoencephalopathy (fibrillary gliosis, microglial cells, myelin palor and microglial nodules), 67% had HIV-related lesions. Opportunistic infections were found in 25% of pediatric cases (2 CMV and 1 Candida encephalitis) and in 54% of adult cases, Toxoplasma gondii, cytomegalovirus, papovavirus and cryptococcus neoformans being the most frequent organisms. Primary lymphomas were discovered in four adult cases. The spinal cord was available in all pediatric cases. A mild vacuolar myelopathy was found in one case but six showed a cortical spinal tract degeneration. In adults, the spinal cord was rarely submitted in our material. Non AIDS-related lesions were also relatively frequent and were mainly cerebrovascular complications. This series enhances the very important role of HIV in the neurological complications of AIDS patients, confirms the paucity of opportunistic infections in the pediatric age group and their importance in the adult one and the frequency of multiple patholgical processes in the same patients. Differences with other large series will be explored, mainly in relation to risk factors.

18.

Hereditary Sensory Neuropathy, Dysautonomia and CNS Degeneration in Two Siblings

DIMITRIS P. AGAMANOLIS and PAMELA G. GALLOWAY (Akron, U.S.A.)

Two siblings, boy and girl, were initially investigated because of severe hypotonia and failure to thrive. The boy had areflexia, insensitivity to pain, mutilation of his tongue, absent corneal reflexes and absence of sweating. Tearing was present. He had unexplained temperature fluctuations, gastroesophageal reflux and repeated aspirations. He developed infantile spasms and died at fourteen months of age. Work-up for metabolic disorders was negative. Autopsy revealed loss of unmyelinated and small myelinated axons in peripheral nerves, degeneration and loss of sensory and autonomic ganglionic neurons, loss of intermediolateral cell column neurons and degeneration of dorsal columns. In addition, there was cerebral atrophy due to neuron loss and gliosis of cortex and white matter, and a vacuolar myelinopathy of brainstem tracts. The hippocampus was normal. The girl was unable to suck or swallow and had no tendon reflexes. She developed seizures when she was two weeks old and died at six months of age. She had no laboratory evidence of a metabolic disorder. She had CNS changes identical to those of her brother. These patients, who were of German-Swiss, English-Scottish and Hungarian ancestry, had a hereditary neuropathy which is pathologically identical to Familial Dysautonomia (Riley-Day Syndrome, HSN type III). In addition, they had changes compatible with a CNS degenerative disorder. A similar combination of central and peripheral nervous system changes has not been previously reported.

20.

Development of Multiple Oligodendrogliomata in a Patient with Myelinoclastic Transitional Sclerosis

K. CHANDLER and D.G. MUNOZ (Saskatoon, Saskatchewan)

There are approximately 20 reports of glial tumors developing in patients with multiple sclerosis (MS). The majority of these tumors were astrocytomas but in a few cases (less than 5) oligodendramatous components were identified. We are presenting a female patient who received a diagnosis of MS at age 23 and had a progressively downhill course, with multiple exacerbations and remissions. From age 30 she complained of headaches. One year prior to death she had focal seizures. Computed tomography showed a left frontal mass. She expired at age 41. At autopsy, the cerebral hemispheres showed diffuse, confluent, microcystic cavitary white matter lesions, which spared the subcortical U-fibres. The brainstem and spinal cord showed classical MS plaques. There were multiple, separate, infiltrating tumor nodules in the cerebral hemispheres and the mesencephalon. Conventional and immunohistochemical staining showed each tumor was an oligodendroglioma. Each tumor originated within demyelinated areas. We hypothesize that the oligodendrogliomata originated in a background of hyperplastic oligodendroglia secondary to demyelination and subsequent remyelination. It has been shown in experimental animals that mature oligodendroglia can be stimulated to divide as a part of the glial reparative response to demyelination. This situation may be analogous to the well known neoplastic transformation of a variety of cell types chronically stimulated to divide in the course of response to injury.

21.

Intracranial Fibromas in Children: Report of Three Cases and a Review of the Literature

STEVEN C. BAUSERMAN and CHARLES S. CHANG (Temple, U.S.A.)

Fibrous intracranial tumors in children present a difficult differential diagnostic problem for the diagnostic pathologist/neuropathologist. One of the main considerations is meningioma which may be sclerotic in this age group. We present clinical, radiographic and pathologic material from three cases with immunohistochemistry and electron microscopy as adjunctive studies in each instance. There is long-term follow-up in the first case whose history includes two instances of recurrence or persistence of a cerebral lesions first encountered in an eleven-year-old female. She is now alive and well after 13 years. The second case, that of a four-year-old boy died of surgical complications following a second resection of his cerebello-pontine angle mass. The most recent case is without evidence of residual tumor after three months, having presented with clinical and radiographic features suggestive of choroid plexus papilloma in the right lateral ventricle. In spite of the disparate locations of the lesions (cerebral subcortical, extra-axial in cerebello-pontine angle, and intra-ventricular), we conclude that these share

histologic identity and should probably remain distinct from meningioma in their classification among intracranial tumors of children. These rare tumors appear to be benign with a tendency to recur if incompletely excised. Their histogenesis and their precise classification as neoplasm or hamartoma remain somewhat speculative at this point in part due to their rarity.

22.

An Embolic Mechanism for Cerebral Watershed Infarction: Neuropathological and Experimental Studies

M.S. POLLANEN and J.H.N. DECK (Toronto, Ontario)

Selective embolization of thrombotic material to the borderzone regions between major cerebral arterial territories was found to be the cause of watershed infarction in three cases. None of the cases had clinically documented hypotension, but all had an embolic source. Neuropathologic findings were maximal in the anterior-middle cerebral arterial watershed region where infarcts of varying ages corresponded to thromboemboli occluding subarachnoid arteries with a mean diameter of approximately 200 μm. These findings support the hypothesis that small emboli are not randomly distributed in the cerebral arterial supply but are preferentially distributed to terminal arterial branches located in the watersheds. Previous *in vitro* studies indicate that small particles suspended in laminar flow remain in a central column of rapidly moving fluid, and tend not to diverge into branches which emerge from the major trunk. We propose that the cerebral arterial branching pattern is a special case of this phenomenon where the asymmetric branching pattern of arteries prior to the watershed zones determines the route of distal propagation of emboli. In an attempt to reproduce the selective distribution of emboli, we perfused the internal carotid arteries of suitable cadavers with 90-210 μm microspheres suspended in whole blood. Preliminary results show that artificial emboli in the 150-210 μm size range are preferentially distributed to the subarachnoid arteries of the watershed zone, while particles <150 μm are randomly spread throughout arterial territories. Further experimental work and relevant literature will be discussed.

23.

Neuronal Messenger RNAs are Maintained in Surviving Neurons of Amyotrophic Lateral Sclerosis

A.W. CLARK, P.M. TRAN, I.M. PARHAD and C.A. KREKOSKI (Calgary, Alberta)

Amyotrophic lateral sclerosis (ALS) is characterized by progressive degeneration of motor neurons, with minor involvement of certain other neuronal populations. The sequence of cellular events leading to death of motor neurons in ALS is unknown. One plausible hypothesis is that DNA repair is defective, resulting in impaired transcription and, ultimately, defective protein production (Bradley and Krasin. Arch Neurol 1982; 39: 677-680). To characterize neuronal gene expression in ALS, we quantitated 4 neuronal mRNAs and a glial mRNA in spinal cords of 7 subjects with ALS and 11 controls. *In situ* quantitation was performed on surviving motor neurons of ALS and control cases for the human neurofilament light subunit (NF-L) mRNA. For all Northern analyses, equal amounts of total RNA from each ALS case and each control were evaluated. Despite extensive loss of lower motor neurons, the ALS spinal cords showed no loss of mRNA for NF-L when assessed with *in situ* hybridization, Northern analysis, and RNase protection assay; and no loss of mRNA for neuron specific enolase, B-50/GAP-43, or the Alzheimer amyloid precursor protein on Northern analysis. ALS cords also showed no decrement in neuronal/glial mRNA ratios when compared to control cords. Our findings do not support the hypothesis of a generalized impairment of neuronal gene transcription in the pathogenesis of ALS. The possibility that certain neuronal mRNAs may be overexpressed in this disease warrants further investigation.

(Supported by the Amyotrophic Lateral Sclerosis Society of Canada. Neurofilament, enolase, amyloid precursor, GAP-43, and GFAP DNAs used in this study were gifts of JP Julien, S Forss-Petter, D Liston, R Neve and N Cowan, respectively.)

24.

Immunohistochemical Study of the Human Fetal Nervous System

S. SHUKOOR and L-C. ANG (Saskatoon, Saskatchewan)

We performed immunohistochemistry on 23 normal human fetuses with gestational ages (GA) ranging from 5 weeks to 28 weeks. The gestational ages were determined by measurement of the Crown/Rump length by ultrasound or direct measurement during pathological examination. The specific antisera used were directed to neuron specific enolase (NSE), glial fibrillary acid protein (GFAP), neurofilament protein (SMI31), S100 protein, prealbumin, alpha-fetoprotein, Leu-7, and cytokeratin. Cytochemical staining of biotinylated lectins were performed with concanavalin A (Con A) and Ricinus communis agglutinin I (RCA). GFAP positive processes started to appear in the spinal cord at 8 weeks GA and in the cerebrum at 10 weeks. NSE was demonstrated in the neuropil of the spinal cord, dorsal root ganglia and inner lining of the central canal approximately at 6½ weeks and in the anterior horn cells at 10 weeks. S100 was mainly expressed in the Schwann cells and the dorsal root ganglia as early as 6½ weeks but was only seen in the spinal cord at 9 weeks. It was also noted in the subependymal region of the cerebrum and the choroid plexus at 22 weeks. Prealbumin and RCA were expressed in the lining of the ventricle at the site of the primordial choroid plexus epithelium at 5 weeks. SMI31 was expressed in the spinal and peripheral nerves at 6½ weeks and in the posterior column of the spinal cord at 9 weeks. The cytokeratin was negative in the CNS except in the choroid plexus at 11-12 weeks. Both Leu-7 and Con A were expressed extensively in the CNS at 5 weeks GA and staining diminished by 28 weeks. Immunohistochemistry provides a useful approach in the investigation of the cytogenesis of the CNS, but most of the previous studies except those on intermediate filaments have been performed on animals rather than on humans. Nevertheless, our present study confirms some of the results of earlier studies in humans such as the earlier appearance of GFAP immunoreactivity in the spinal cord in comparison to the cerebrum. We also demonstrated that the primordial choroid plexus epithelium could be identified by the use of prealbumin and RCA as early as 5 weeks gestation, long before it could be distinguished by morphology, or by S100 and cytokeratin immunoreactivity.

25.

The Human Pituitary in Pregnancy

B.W. SCHEITHAUER, T. SANO, K. KOVACS, W.F. YOUNG and N. RYAN (Mayo Clinic, U.S.A.; Toronto, Ontario)

The pituitary undergoes reversible enlargement during pregnancy due to the proliferation of chromophobic "pregnancy cells". No comprehensive immunocytochemical studies of the pituitary in pregnancy have been reported. We undertook a study of 69 autopsy pituitaries of women age 17 to 44 (mean 31 years) who died in various phases of pregnancy, post abortion or in the post partum period. Accumulation of pregnancy cells was noted; they were immunoreactive for prolactin (PRL) but not for other adenohypophyseal hormones. Mitotic figures were encountered in such cells, indicating they arise by multiplication of PRL cells. Using "mirror section" techniques, no mammosomatotrophs, i.e., cells immunoreactive for both GH and PRL, were identified. Hyperplasia of PRL cells was evident at one month of pregnancy and gradually disappeared within several months following delivery; the process of involution was retarded in the one lactating patient investigated. In some cases, hyperplastic foci of PRL cells resembled microadenomas; indeed, at times, it was difficult to distinguish hyperplasia from adenoma formation. Another striking change in the pituitaries of pregnant women was reduction of immunostaining of FSH/LH cells; the reduction was apparent at 2.5 months and extensive at 6

months. This process was reversible in that positivity assumed normal intensity within as little as 1 month following delivery or abortion. Immunoreactivity for GH, ACTH, TSH, and alpha subunit did not appear to be affected. Eight adenomas (12%) were encountered in patients 1 month pregnant to 24 months postpartum. All were noninvasive microadenomas measuring 1 to 4 mm; seven contained PRL only, whereas one plurihormonal tumor contained PRL TSH, and alpha subunit. Prolactinomas were no more numerous and/or larger than similar tumors in nonpregnant women and adult males; thus pregnancy neither initiates adenoma formation nor accelerates their growth. Furthermore, the pituitaries of two multiparas (gravida 14 and 17) were devoid of adenomas, suggesting that protracted stimulation of lactotrophs does not result in an increased frequency of prolactinomas. In pituitaries harboring prolactinomas, massive pregnancy cell hyperplasia was evident outside the tumor indicating that PRL production by adenoma cells does not suppress the proliferation of prolactin containing pregnancy cells.

This study was supported in part by grant MP 6349 awarded by the Medical Research Council of Canada and by the generous contributions of Mr. and Mrs. Ellis I. Levitt.

Posters

P1.

Intraspinal Bronchogenic Cyst: Ultrastructural Study of the Lining Epithelium

K.L. HO and R. TIEL (Detroit, U.S.A.)

Intraspinal enterogenous (neuroenteric) cysts are rare and their histogenesis and embryogenesis remains unclear. Intraspinal cyst formed of tissue proper to the tracheobronchial tract has been referred to as bronchogenic cyst. While the histological characteristics of their lining epithelium have been well described at the light microscopic level, there are rare ultrastructural studies of the epithelial cells. This report described the ultrastructural characters of the lining epithelium of a symptomatic intraspinal bronchogenic cyst of the CT-T2 level of a 21-year-old woman. Six distinct cell types were recognized: ciliated cells, non-ciliated cells, and goblet cells that reached the lumen, and basal cells, Kulchitsky cells and undifferentiated cells that were basally located and did not reach the lumen. The microvilli of non-ciliated cells were coated with granulofibrillary material. Discharge of granular contents from goblet cells was noted. Abnormal cilia, particularly compound cilia, were frequent. Complex interdigitations of cytoplasmic membrane with prominent desmosomes were present in the pseudostratified region. Kulchitsky cells contained characteristic membrane-bound dense-core neurosecretory granules. Intraepithelial unmyelinated axons were observed but none were closely associated with Kulchitsky cells. The cell types of the lining epithelium of the present cyst and their topographic distribution within the epithelium are very similar to those of the normal tracheobronchial epithelium.

P2.

Intraspinal Bronchogenic Cyst: Ultrastructural Study of Abnormal Cilia

K.L. HO and R. TIEL (Detroit, U.S.A.)

Ultrastructural study of the intraspinal and intracranial cysts is rare. Abnormal cilia of the lining epithelium have been mentioned. However, only the cilia with abnormal numbers of microtubules and compound cilia were described. In this report we described the detailed morphological alterations of cilia of the lining epithelium of an intraspinal bronchogenic cyst from a 21-year-old woman. Cilia abnormalities could be categorized as follows: (A) cilia with abnormal axonemal microtubules, including addition and deletion of doublets, dislocation of doublets or singlets and partial or complete disarray of microtubules with incomplete or no recognizable ring pattern; (B) swollen cilia with normal or abnormal axonema; (C) compound cilia with multiple axonemal microtubules ensheathed by a common ciliary membrane; (D) naked cilia with no lining ciliary membrane and (E) intracytoplasmic cilia and aggregates of microtubules with no ring pattern. Of these, compound cilia and swollen cilia were most common. Deficiency of dynein arms, a characteristic feature of immotile cilia syndrome, was not found. Ciliary abnormalities found in the present cyst are very similar to those described in the human bronchial epithelium with various diseases. The present findings suggest that the epithelium of intraspinal broncogenic cyst shares similar ciliogenesis and susceptibility to abnormal ciliary formation as that of the bronchial epithelium. In the absence of exogenous irritations, the epithelial damage and the subsequent abnormal ciliary formation in the present cyst was probably related to the pressure effect from intraluminal accumulation of the secretions.

P3.

Late Spinal Cord Metastases From Pineal Neoplasms

R.R. HAMMOND and J.J. GILBERT (London, Ontario)

Pineal region tumors make up <1% of primary intracranial neoplasms in North America. These tumors are more common in Oriental populations (3-5%) and in children and adolescents. There is a male preponderance (5 to 12.5:1). The majority of these tumors are germinomas; the remainder pineocytomas, pineoblastomas, teratomas and other rare forms. We present two cases of late spinal cord metastases of pineal tumors. A 64-year-old male presented with headaches and ataxia. A head CT scan showed a pineal mass and hydrocephalus. In the second case, a 35-year-old male presented with headaches and blurred vision. A head CT scan showed a pineal mass and hydrocephalus. Both patients received radiotherapy (patient 1 had a ventriculoperitoneal shunt). Despite presumed cures, with complete resolution clinically and radiographically both patients returned after several disease-free years (4 years 9 months and 5 years 9 months, respectively) with spinal cord metastases. Subsequent autopsy in the first case disclosed a pineocytoma with diffuse dissemination in the ventricles and subarachnoid space. In the second case, biopsy of a cervical intramedullary mass disclosed a germinoma. The patient is receiving further radiotherapy.

P4.

Ultrastructural Morphology of Microfibrillar Paracrystalline Inclusions (MPI) within Dorsal Root Ganglia (DRG) of Ferrets, Dogs and Humans

S. DANCEA, N. MIKHAEL, D. STEWART and V. MONTPETIT (Ottawa, Ontario)

MPI consist of large aggregates of regularly arranged filaments measuring 50-85 nm in diameter located in the perikarya and proximal processes of neurons in humans and various animal species. Since their description in locus ceruleus by Marinesco in 1902, they have been reported to occur in substantia nigra, thalamic and caudate nuclei of normal human brains as well as in the cervical sympathetic ganglia of cats and mice. Pena (1980) was unable to detect them in the thalamus of normal children's brains, although they were easily found in the same structure of normal adult brains. We found similar MPI in the perikarya and proximal processes of DRG of ferrets, dogs and humans. In the ferrets, MPI were a prominent finding in cisplatinum treated animals and controls and were located in the periphery of perikarya and in proximal unmyelinated axons (PUMA). MPI were occasionally seen in dogs treated with high doses of pyridoxine and in humans on cisplatinum chemotherapy. Ultrastructurally, MPI were made up of bundles of

straight filaments 50-60 nm in diameter arranged in highly parallel fashion with intervals of 5 to 6 nm in between and with regular transverse striations 5 to 7 nm apart. On cross section, the filaments form arrays of squares with a 5 nm side. In perikarya, MPI were surrounded by ribosomes and lipofuscin granules. In cisplatinum treated humans they seemed to be responsible for the focal distention of PUMA. MPI are reminiscent of the lattice web of Hirano bodies (HB) and the skein of thin filaments seen in the neocortex of bridled mouse. However, HB consists of sheets of parallel filaments 10 nm in diameter, intersecting each other at variable acute angles and giving rise to characteristic appearance of rows of regularly spaced punctate densities. The MPI share the same immunohistochemical features as HB being immunoreactive with actin but not with tubulin and neurofilament antibodies. These findings support a common nature for these inclusions, i.e., that of actin polymers. Actin is a common component of the cytoskeleton of neural cells with a proven role in the maintenance of tridimensional cell architecture. The difference in the aggregation status of actin polymers seen in these two types of inclusions is probably secondary to abnormalities of actin itself or actin-associated proteins in a modified neuronal homeostasis.

P5.

Structural Changes in Cerebral Vessels Following Amyloid Deposition

T.I. MANDYBUR (Cincinnati, U.S.A.)

To determine the structural damage in the cerebral vessels showing deposition of the A4 type of amyloid, ten cases with cerebral amyloid angiopathy of this type were stained with reticulin stain, van Gieson-elastica stain, Congo red, thioflavine S, actin, factor VIII and A4 antibody and examined. The pathological changes within the vessel walls differed depending upon the caliber and type of the vessel involved and upon the severity of the amyloid angiopathy. In all vessels, including those with severest involvement, the endothelial lining appeared complete, without sloughed off areas. The elastica in the larger leptomeningeal arteries were preserved, these vessels showing accumulations of amyloid only in the adventitia and on and between the outer smooth muscle cells of the media. The smaller arteries here showed a more diffuse amyloid deposition in the media, the smooth muscle cells being reduced proportionately to the degree of amyloid accumulation, which was followed by dilatation of the vessel and disappearance of elastica. In extreme instances, the smooth muscle cells disappeared completely, together with amyloid, new media being organized subendothelially (double bareling). The cellular elements of intracortical arterioles seemed to withstand amyloid accumulation better, usually without dilatation of the lumen (rather with narrowing), the smooth muscle cells undergoing reduction, too, but to a lesser extent.

P6.

Central Nervous System Involvement in Cystinosis

D.G. VOGEL, M.E. CORNFORD, M. MALEK-ZADEH and H.V. VINTERS (Los Angeles, U.S.A.)

Cystinosis results in a wide range of organ system injury in affected individuals. Clinically, patients may manifest hypothyroidism, retinopathy, and usually die from renal involvement. With the use of dialysis and renal transplantation, patients with cystinosis now frequently live into adulthood. Autopsy examination of a 28-year-old man with cystinosis, who had been successfully treated several years previously with renal transplantation, revealed deposition of cystine crystals in multiple organs. The transplanted kidneys, however, were spared. The brain showed extensive cystine deposition, as assessed in frozen sections of brain tissue examined by polarization microscopy. Particularly severe involvement was noted in the basal ganglia, which had undergone cystic necrosis. Elsewhere, the brain showed foci of glial scarring of the neocortex, multifocal patchy demyelination and extensive dystrophic calcification of the white matter, which was even apparent on cut sections of the cerebral hemispheres. Spongiform change and vacuolization was seen focally within the neocortex, white matter and brainstem. Ultrastructurally, characteristic cystine crystals were found, particularly around cerebral microvessels within pericyte-like cells. The patient also had unilateral hippocampal sclerosis, presumably secondary to a long-standing seizure disorder which was attributed to the cystinosis. *Conclusion:* Extensive cerebral deposition of cystine can occur in nephropathic cystinosis, a disorder in which it is commonly believed there is minimal brain involvement. As patients survive for an extended period of time following renal transplantation, neurologic complications of this disorder may become the major, even the fatal ones. Systemic therapy should be aimed at multiple organs (including the central nervous system), not simply the kidneys.

P7.

Rapid Immunoperoxidase Staining of Nerve Biopsies

G.S. DAVIDSON (London, Ontario)

During surgical reanastomosis of damaged or severed nerves, or following muscle and nerve transplants, surgeons may want to know if the ends of the nerves that are about to be joined contain healthy axons, or are fibrotic, or shows signs of traumatic neuroma formation. If a choice of fascicles is possible, the ones with a healthy population of axons must be identified. Conventional frozen section and H&E staining produce poorly oriented specimens which reveal little histological detail and do not allow these questions to be answered. By aligning the nerve specimen inside the groove of a 'V'-shaped piece of metal foil, rapidly freezing the specimen in liquid nitrogen, and re-embedding it in a vertical position, freezing artefact was avoided and perfect cross-sections were obtained. Using both H&E staining and the immunoperoxidase technique with high concentrations of monoclonal antibody against neurofilament with a haematoxylin counterstain, axons were selectively stained. Their numbers and diameters could be easily assessed, and myelin was readily visible. Individual fascicles could be easily identified and chosen for anastomosis. The amount of faintly staining material between nerve fibres allowed assessment of fibrosis, and axonal disorganization and preponderant obliquity made the diagnosis of actual or incipient traumatic neuroma formation possible. The entire procedure was accomplished in twenty minutes, allowing intraoperative use of the technique.

DIAGNOSTIC CASE PRESENTATIONS

1. **Fusarium meningoencephalitis.**
   P.G. GALLOWAY, D.P. AGAMANOLIS (Akron, U.S.A.)
2. **Cerebral oxalosis due to ethylene glycol toxicity.**
   A.H. KOEPPEN (Albany, U.S.A.)
3. **Alzheimer's disease with cerebellar degeneration, query grumose degeneration of dentate nucleus.**
   H. HATTORI, T. UEMA, S. TANAKA, H. KONDO, T. NISHIMURA, E. KADOTA, S. HASHIMOTO (Osaka, Japan)
4. **Adult onset Hallervorden-Spatz syndrome or Seitelberger's disease with late onset: variants of the same entity? A clinicopathological study.**
   S. GAYTAN-GARCIA, J.C.E. KAUFMANN, G.B. YOUNG (London, Ontario)
5. **Tropical Spastic Paraparesis.**
   Y. ROBITAILLE, G. FRANCIS (Montreal, Quebec)
6. **Alveolar soft part sarcoma.**
   F. KIM, L. RESCH (Toronto, Ontario)
7. **Epithelial metaplasia in glioblastoma multiforme vs choroid plexus carcinoma and glioblastoma multiforme.**
   J.M. BONNIN (Indianapolis, U.S.A.)
8. **Brain tissue emboli to lungs and systemic arterial circulation, predominantly brain.**
   N.B. REWCASTLE (Calgary, Alberta)

9. **Cerebral venous thrombosis in inherited antithrombin III deficiency.**
   J.B. LAMARCHE (Sherbrooke, Quebec)
10. **Proliferative vasculopathy and hydranencephaly-hydrocephaly with multiple limb pterygia.**
    M.G. NORMAN (Vancouver, British Columbia)
11. **Familial peripheral neuropathy associated with agenesis of the corpus callosum.**
    S. CARPENTER, G. KARPATI, F. ANDERMANN, J. MATHIEU (Montreal; Chicoutimi, Quebec)
12. **Adult Leigh's disease with biochemically documented severe cytochrome C oxidase deficiency.**
    B. LACH, D. ATACK (Ottawa, Ontario)
13. **Carcinoid tumor, query primary.**
    J.H.N. DECK (Toronto, Ontario)
14. **Recurrent cerebellar hemorrhages secondary to amyloid angiopathy.**
    F. ROBERT (Montreal, Quebec)
15. **Primary leptomeningeal astrocytoma.**
    D.A. RAMSAY, S. NAG (Kingston, Ontario)
16. **Cerebral microangiopathy in hemolytic-uremic syndrome.**
    M. HRYNCHAK, L.C. ANG, D.G. MUNOZ (Saskatoon, Saskatchewan)
17. **Cylindrical spirals in skeletal muscle biopsy in a patient with 4 P-syndrome.**
    W.C. HALLIDAY (Winnipeg, Manitoba)
18. **Cladosporium trichoides cerebral abscess.**
    B.W. SCHEITHAUER (Rochester, U.S.A.)
19. **Astrocytoma.**
    F. KIM, L. RESCH (Toronto, Ontario)