PROCEEDINGS OF THE FIFTY-FIRST MEETING OF
THE BRITISH NEUROPATHOLOGICAL SOCIETY AT
THE UNIVERSITY OF LIVERPOOL, 15–17 JULY 1976

PRESIDENT: P. O. YATES

FRIDAY 16 JULY

Miles J. (introduced) & Buxton P.H. (Centre for Pain Relief, Regional Department of Medical and Surgical Neurology, Liverpool)
The manner in which pituitary alcohol injections relieve pain

We applied the technique of transphenoidal alcohol injection to a wide range of cancer patients with encouraging results. We used a radio-opaque contrast medium and found in a proportion that the contrast medium tracked up the pituitary stalk, and across the floor of the IIIrd ventricle into the ventricular system. We, therefore, suspected that the pain relief might be due to chemical hypothalamotomy. Post-mortem study with india ink mixed with a radio-opaque contrast medium confirmed that fluids injected into the pituitary gland, propagate through the stalk and into the region of the hypothalamus.

Lipton S. (introduced) (Neurological Unit, Walton Hospital, Liverpool)
Percutaneous cervical cordotomy

Bowsher D. (introduced) Department of Anatomy, The University of Liverpool, Liverpool L69 3BR
Neurophysiological mechanism of acupuncture in pain relief

The essentials of acupuncture stimulation are that it is carried out at a frequency of 2–3 Hz at an intensity sufficient to excite Aδ primary afferents. The characteristics of the giganto-cellular reticular formation in the lower brain stem include the requirement of Aδ activation in order to produce excitation, and a failure to respond to peripheral stimulation at frequencies above 2–3 Hz. Cells in this region have reticulo-spinal axons which are capable of inhibiting transmission in spinal interneurons forming a link in the pathway giving rise to ascending anterolateral fibres.

McConnell P. (introduced) & Berry M. (Department of Anatomy, University of Birmingham)
Effects of undernutrition on the developing rat cerebellum

The effects of undernutrition on the developing cerebellum were studied in 30 day old rats undernourished from birth by restricting access to the lactating mother. These animals showed a significant reduction in cerebellar weight, and a 34% reduction in total area of the vermis and increased density of both granule and Purkinje cells. Network analysis of Golgi-Cox preparations showed a significant increase in the density of the dendritic fields of Purkinje cells but a 52% decrease in overall network size, due to a reduction in the total number of dendritic segments and to a reduction in the length of terminal segments.

Knowles J.F. (introduced) (The Medical School, Birmingham B15 2TJ)
Short-term effects of ethyl nitrosourea on the subependymal layer of neonatal rats investigated by autoradiography and microdensitometry
Ethyl nitrosourea (ENU) and $^3$H-thymidine when injected together into 1 day old rats, enabled changes in the cell-cycle of subependymal cells to be studied. They were killed at various intervals during the following 28 h. During this period, two main peaks were seen in the percentages both of labelled mitoses and of degenerate cells. In test animals the peaks of percentage-labelled mitoses occurred at approximately the same time as those in controls, although the first peak was decreased and the second increased, indicating that ENU affected the progress of cells through their cycle of division. The variation in the percentage of degenerate cells showed that the cytotoxic effect of ENU induced at least two waves of cell death. The majority of degenerate cells were unlabelled, although smaller peaks in the percentage of labelled degenerate cells occurred at the same time. Feulgen microdensitometry showed that degenerate cells contained only a diploid amount of DNA and, therefore, were probably in a post-mitotic phase.

King, R.H.M., Thomas P.K. & Kocen R.S. (Royal Free Hospital and Institute of Neurology, London)

Ultrastructural changes in peripheral nerve in late onset metachromatic leukodystrophy

Observations have been made on nerve biopsies from two cases of late onset metachromatic leukodystrophy and compared with the findings in the late infantile and juvenile forms. Contrary to some recent reports (e.g. E. Joosten et al. (1975) Acta Neuropathologica 33, 165) the nature of the intracellular inclusions was not found to differ between the late onset and the earlier onset forms. Hypertrophic changes of onion bulb type were more prominent in the late onset cases and macrophages were less numerous, these features presumably being attributable to the chronicity of the process.

Chopra J.S. (introduced) & Banerjee A.K. (introduced) (Departments of Neurology and Pathology, Postgraduate Institute of Medical Education & Research, Chandigarh, India)

Paralytic rabies

Hydrophobic rabies is frequently seen in India, but an ascending paralytic form without hydrophobic symptoms is rare. Hurst & Pawan (1932) (Journal of Pathology and Bacteriology 35, 301) and Banerjee & Chopra (1974) (Neurology India 22, 83) have described the paralytic rabies in detail. This study is based on single nerve preparations of sural, lateral popliteal, ulnar and spinal nerves taken at necropsy from five male patients (aged 14–56 years), all presenting with symptoms and signs of ascending paralysis. Negri bodies were demonstrated in the CNS of all cases. Marked changes of segmental demyelination and minor changes of wallerian degeneration were observed in the teased single nerve preparations. There was invariably a moderate loss of myelinated nerve fibres.

Rewcastle N.B. (introduced) (University of Toronto, Ontario, Canada)

The 15 nm filament neurofibrillary tangle

Neurofibrillary tangles composed of the 10 nm filament and the 22 nm ‘twisted tubule’ or bifilar helix have become associated with certain experimental models and specific human diseases. Recently, neurofibrillary tangles composed of filaments of 13–15 nm have been described in two cases of progressive supranuclear palsy (Powell et al. (1974) Journal of Neuropathology and Experimental Neurology 33, 98). The occurrence of tangles of 15 nm filaments in two seemingly unrelated cases is described, one with a progressive Parkinson-dementia syndrome, the other with an obscure progressive brain stem disorder with diffuse brain stem tangles.

Cumming W.J.K. (introduced) & Hudgson P. (Muscular Dystrophy Group Research Laboratories, Newcastle upon Tyne NE4 6BE)

Focal nodular myositis

‘Focal nodular myositis’ has been used pathologically to describe the sparse, inflammatory cell infiltrate sometimes seen in the muscles of patients suffering from rheumatoid arthritis and other autoimmune conditions. Here we described three male patients with painful, nodular myositis, in two of whom the nodular process
evolved into a generalized myopathy with dysphagia and in one case a skin rash. In each, muscle biopsy showed intense interstitial inflammatory infiltration of muscle with focal muscle-fibre necrosis and regeneration resembling infarcts. We believe that this to be an unusual variant of polymyositis rather than a pathological entity in its own right.

Nanda R.N., Boyle F., Gillespie J.S., Johnson R.H. & Keogh H.J. (all introduced) (University Department of Neurology, Institute of Neurological Sciences, Glasgow G51 and Department of Pharmacology, University of Glasgow, Glasgow G12)

Adrenergic innervation of peripheral blood vessels in patients with neurogenic orthostatic hypotension

Evidence was found in four patients with neurogenic orthostatic hypotension (OH) of interruption of reflex pathways controlling blood pressure. There was a marked pressor response in all patients to infused noradrenaline (NA) and phenylephrine. A pressor response to infused tyramine was present in three patients, but not in the fourth. In skin and muscle biopsies adrenergic innervation of blood vessels was present in all four patients. Absent catecholamine-specific fluorescence in biopsy tissue has been previously reported from patients with OH who had no demonstrable pressor response to infused tyramine (Kontos et al. (1975) Annals of Internal Medicine 82, 336). One patient did not respond to tyramine infusion, suggesting that his orthostatic hypotension was due to a failure of NA release from blood vessels adrenergically innervated. Thus, orthostatic hypotension may be due to failure of release of NA despite adrenergic innervation of peripheral blood vessels.

Boullin D.J. (introduced), Adams C.B.T. (introduced) & Mohan J. (introduced) (Radcliffe Infirmary, Oxford)

Reversal of cerebral arterial spasm with dopamine

Cerebral arterial spasm (CAS) which following subarachnoid haemorrhage (SAH) after rupture of cerebral aneurysms is believed to be caused by vasoactive substances in blood or CSF. In a search for vasoactive substances causing spasm, and drugs which may reverse or prevent spasm, it was found that isolated human basilar artery contracts to six prostaglandins and to 5-hydroxytryptamine, noradrenaline, histamine and adrenaline, the latter effects being blocked by specific antagonists (Boullin D.J., Mohan J. & Grahame-Smith D.G. (1976) Journal of Neurology, Neurosurgery and Psychiatry. 39, 756.) Moreover, CSF from patients with CAS (spasm CSF) produces contractions not blocked by antagonists. Propranolol (Boullin D.J. & Mohan J. (1976) British Journal of Clinical Pharmacology. In press) and dopamine relax basilar arteries. Dopamine also prevents and antagonizes spasm CSF induced contractions. In baboons, intracisternal blood produces arterial spasm and this is reversed by 10 μg/kg intracisternal dopamine. In five SAH patients, following operation for clipping of cerebral aneurysms, intracranial dopamine has been perfused into the region of the aneurysm through inflow and outflow catheters implanted during surgery. Postoperative angiography using the superficial temporal artery shows that dopamine perfusions decreased postoperative spasm in three out of five patients.

Franks A.J. & Khalili A.H. (introduced) (General Infirmary, Leeds, LS1 3EX)

Prognostic factors in ruptured berry aneurysms—the significance of hypertension. A retrospective study

The incidence of hypertension in fatal and non-fatal episodes of subarachnoid haemorrhage (SAH) from ruptured 'berry' aneurysms has been analysed. In males a significant difference in incidence is found between fatal and non-fatal episodes (28% and 7% respectively), whilst a smaller but definite difference is present in females (fatal, 29.5%, non-fatal, 19%). The incidence of hypertension among both males and females surviving an episode of SAH was comparable with that expected in the general population. Some possible intracranial mechanisms of this higher mortality among hypertensive patients have been examined, but no single factor emerges to explain the observed differ-
Hypertensive patients who die have a higher incidence of multiple aneurysms than other groups, a lower incidence of middle cerebral artery aneurysm rupture than normotensive fatalities, and are more likely to rupture their aneurysm at or below 10 mm diam. Hypertension seems to be a definite, but not essential, factor in development and rupture of aneurysms, and, especially in males, a poor prognostic factor.

Hewlett R.H. & Brownell B. (Frenchay Hospital, Bristol BS16 1LE)
Necrotizing vasculopathy in microgliomatosis (microglioma-reticulum cell sarcoma)

Post-mortem material from 10 cases of microgliomatosis was examined. The distribution of lesions and their macroscopical appearances were remarkably similar in each case, as were their clinical features. Histological examination was especially directed to the incidence of argyrophilic cells and compound granular corpuscles, and to the vasculature of areas of neoplastic infiltration and of the surrounding brain. In addition to the typical proliferation of perivascular reticulin which has been observed in all previous accounts of this tumour, one case in our series showed an occlusive and necrotizing vasculopathy which could not be simply related to tumour necrosis; this pathological feature, associated with an elevated serum IgG in life, is a new observation in microgliomatosis.

Brown A.W., Levy D.E. (introduced), Calverley J. (introduced), Kublik M. (introduced), Harrow J. (introduced) & Brierley J.B. (MRC Laboratories, Carshalton, Surrey)
Selective chromatolysis in the gerbil brain; a consequence of epilepsy induced by ischaemia

After bilateral carotid occlusion (14–30 min), 21 gerbils were perfusion-fixed with FAM for LM and 8 with glutaraldehyde for EM. Survivals were 3½–24 h. After 1 h unilateral occlusion, 14 gerbils were pre-treated with Dilantin. All were perfusion-fixed with FAM at 48 h. Typical ischaemic cell change (ICC) was seen in striatum hippocampus and cerebral cortex in about 40% with unilateral occlusion and in all with bilateral.

An entirely different alteration, 'selective chromatolysis' (SC), was restricted to hippocampus (h.l.) and deep neocortex. Unlike ICC it was not recognizable before 3½ h. and appeared to have a slow time course. At 24 h. there was striking preservation of organelles but disruption of rough ER. Brief bilateral occlusion produced minimal ICC but considerable SC. The latter was related to the extent of major epilepsy. Unilateral occlusion after Dilantin produced minor focal seizures. SC was minimal. Apparently SC is a consequence not of ischaemia but of epilepsy.

Ailt G. & de la Motte D.J. (introduced) (The Middlesex Hospital Medical School, London, W1P 6DB)
A study of vascular permeability changes in wallerian degeneration using horseradish peroxidase

Ultrastructural observations were made of rat peroneal nerve after crush, employing horseradish peroxidase (HRP) as a tracer protein to indicate changes in vascular permeability. Up to 2 days after crush there was extensive exudation of HRP from damaged capillaries at the site of injury but leakage was absent from vessels proximally and distally. At the site of crush, vessels were composed of fragmented and separated endothelial cells. Proximally and distally vessel walls showed normal fine structure; vesicles containing HRP were absent and tight-junctions between endothelial cells remained intact. Twenty-one days after crush, transudation of HRP from endoneurial capillaries was found both at the site of crush and along the distal segment. Ultrastructural changes in vessel walls were limited to a marked increase in vesicles filled with HRP.

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SUNDAY 17 JULY

Hutchinson W.M. (introduced), Kirk J. (introduced) & Allen I.V. (Institute of Pathology, Belfast BT12 6B2)
EM observations on demyelination in multiple sclerosis

Electron microscopy has been done on plaques
and white matter from two patients with long-standing MS on whom necropsy was carried out shortly after death. In the plaque margin oligodendroglia showed vacuolation and increase in volume of cytoplasm with loss of normal organelle structure in the cell body, in the cytoplasm of the paranodel sacs, and in the inner and outer tongues. This swelling was associated with splits in myelin lamellae along major dense lines. Irregular balls of disrupted myelin were seen lying adjacent to myelin sheaths and naked axons. Microglia and their cell processes were frequent in the plaque margin with phagocytosis of myelin debris, but there was no evidence of active stripping of myelin lamellae from the sheaths. Inside the plaque margin microglia showed an increased cytoplasmic volume with transformation of myelin debris into less osmiophilic lamellar structures, typical lyre-bodies and circular clear and electron-dense inclusions. Similar phagocytic cells with inclusions were seen in the perivascular spaces inside plaques. No virus-like material was observed in any of the cells examined. From these observations it is suggested that demyelination in multiple sclerosis may be secondary to oligodendroglial degeneration.

Hubbard B.M. (introduced) & Hopewell J.W. (Churchill Hospital, Oxford)

Changes in the cellular density of the spinal cord of the rat after exposure to X-rays

Myelopathy associated with extensive white matter necrosis develops in the rat spinal cord approximately 4 months after exposure of a 16 mm length of the cervical region to 4000 rad of X-rays. The glial cell populations of normal and irradiated spinal cords have been measured before and during the appearance of myelopathy. Three to four months after irradiation astrocyte and oligodendroglial populations were significantly reduced compared with controls. At the onset of paralysis there was a greater deficiency of oligodendrocytes than astrocytes. The control spinal cords showed an increase in the density of oligodendrocytes with age. The astrocyte population of normal rats remained fairly constant over the period of study. Mitotic figures were occasionally observed amongst the glia of both control and irradiated spinal cords, and ARG studies using ⁹H-thymidine indicated that glial cells synthesize DNA.

It was concluded that the development of white matter necrosis in the irradiated spinal cord is primarily due to the loss of oligodendrocytes. In addition the glial cell population of the spinal cord appears to have a slow turnover rate accounting for the long latent period before the onset of necrosis.

van der Kogel A.J. (introduced) (Radiobiological Institute TNO Rijswijk, The Netherlands)

Late radiation damage in the rat spinal cord: dose dependence of different types of lesions

Male 3 months old WAG/Rij rats were locally irradiated with single and fractionated doses of 300 kV X-rays on region L2-L4 or C5-T2 of the spinal column. The tolerance dose for the induction of paralysis is for both regions about 1500 rad single dose. However, histologically the lesions are considerably different.

Region L2-L4: After doses from 2000-5000 rad, the general pattern of the lesion consists of severe demyelination and necrosis of the nerve roots, and the cord appears normal. With increasing dose, the spinal cord is also affected, and after 8000–10 000 rad it shows severe destruction due to haemorrhagic and ischemic infarction.

Region C5-T2: After doses of 1850–1950 rad, about 25% of the rats develop paralysis during their lifespan, due to extensive haemorrhages in grey and white matter. After doses of 2000–5000 rad, necrotic areas are found almost exclusively in the white matter, without damage to the nerve roots. The observations can be related with the different syndromes of radiation myelopathy in man.

Hopewell J.W., Edwards D. (introduced) & Wiernik G. (introduced). (Churchill Hospital, Oxford and Mersey Regional Centre for Radiotherapy and Oncology, Clatterbridge Hospital, Merseyside)

The sex dependence of intracranial gliomata in the Merseyside region 1961–70
The age and sex distribution of 1223 cases of intracranial gliomata diagnosed in the geographical area covered by the Mersey Regional Cancer Registry over the period 1961-70 have been analysed. In the majority of these cases (820) diagnosis was confirmed by histology. In both children and adults intracranial gliomas were more common in males, incidence rates indicating a sex ratio of 3 to 2.

In adults, tumour incidence was first found to increase with age in both sexes, reaching a peak in the age group 60–64 years. Glioma incidence declines rapidly in older age groups. The difference in tumour incidence between males and females was only observed from in the age group 45–49 years. Previously reported animal studies (Hopewell J.W. & Hubbard B.M. (1975) Neuropathology and Applied Neurobiology 1, 103) have demonstrated glioma induction to be sex-hormone dependent. The observed pattern of glioma incidence in man is compared with known changes in hormone levels with age.

Williams B. (introduced) & Timperley W. (Midland Centre for Neurosurgery and Neurology, Warley B67 7JX and Royal Infirmary, Sheffield S6 3DA)

Three cases of communicating syringomyelia secondary to midbrain gliomas

Three cases were discussed in which hydrocephalus presented at ages 21, 13, and 7 years from aqueduct obstruction due to tumour. After shunting operations each case developed progressive visual and midbrain symptoms. Symptoms of syringobulbia and impotence supervened later in the first patient, ataxia and blindness progressing to a triplexia in the second, and ataxia and syringomyelic cord symptoms in the third. Post-mortem examination showed midbrain gliomas in all, with invasion of the cerebellum in the first and third cases. In the first case cavities were demonstrated from the midbrain through the pons and medulla to the syringomyelia by injection studies, macroscopic and microscopic examination. A more usual site of communication at the obex was present in the two younger patients. The significance of the combination for the understanding of mechanisms producing the cavitation was discussed.

Diemer N.H. (introduced) (Institute of Neuropathology, University of Copenhagen, Denmark)

Gliarial nuclear changes in rats with hepatic, portosystemic, and hyperammonaemic encephalopathy

Differential counts of astrocyte- and oligodendrocyte-nuclei in corpus striatum have been performed in rats with portocaval anastomosis (PCA), CCl4-induced liver cirrhosis and urease-induced hyperammonaemia.

The counts showed an increase in the number of nuclei classified as astrocyte nuclei. Thus the astrocyte nuclei constituted 29% of the total number of glial cells in the PCA-animals, 27% in the CCl4-group, and 24% after urease (control animals 15%). The total number of astrocytes plus oligodendrocytes was not increased in any of the experimental groups, which is in accordance with the fact that cell divisions were not seen. Animals with the most severe liver disease showed a slightly reduced number of glial cells.

It is postulated that nuclei, normally regarded as oligodendrocyte nuclei may assume the characteristics of astrocyte nuclei and develop Alzheimer type II changes after immersion fixation.

Buxton D. (introduced) (Moredun Institute, Edinburgh EH17 7JH)

Studies into the site of action of Clostridium welchii (perfringens) type D epsilon toxin in the brains of mice

*Cl. welchii (perfringens)* type D produces non-lethal epsilon prototoxin which is converted to a lethal toxin by the action of trypsin. Epsilon toxin causes a breakdown of the 'blood–brain barrier' in mice allowing the extravasation of the vascular tracer, horseradish peroxidase (Morgan et al. (1975) Journal of Comparative Pathology 85, 461). It has been shown that this leakage can be prevented by the prior administration of formalinized epsilon prototoxin and that the inhibition produced is competitive. Immunoperoxidase studies demonstrate that formalinized epsilon prototoxin binds to the luminal surface of blood vessels in the brain. It is suggested that the toxin exerts its effect directly through specific receptor sites on the vascular endothelium.
Coronavirus encephalitis in mice: preliminary observations

The coronavirus group includes mouse hepatitis virus, infectious bronchitis virus of chickens, and transmissible gastroenteritis virus of pigs. Coronaviruses have been isolated from patients with colds, and have also been implicated in endemic (Balkan) nephropathy. Coronavirus OC43 derived from a patient with a cold, initially grown in human embryonic tracheal culture, was injected intracerebrally into mice and serially subpassaged in brain suspension. It produced a fatal encephalitis when injected into the brain of newborn mice, the period between inoculation and death being 48 to 60 h. Mice older than five days appear not to be susceptible. Animals were killed by perfusion-fixation at 24 and 48 h after inoculation. A prominent periventricular inflammatory response was present, with apparent fusion of groups of intraventricular cells. There was marked disruption and oedema of the corpus callosum. Glial, fibroblastic and vessel wall proliferation was prominent. Neuronal damage was marked at 48 h, especially in the hippocampus, with eosinophilic intracytoplasmic inclusions. Virus particles resembling coronavirus and measuring 80-90 nm were seen extracellularly and within dilated cisternae of endoplasmic reticulum.

BOOK REVIEWS

Bradley W.G.

Disorders of peripheral nerves

316 pages, Blackwell Scientific Publications, Oxford, London, 1974. £9.75

In so many ways this is a useful and practical book, certainly the copy in our EMG department is frequently consulted on points of neuroanatomy and electrophysiology. These areas, as well as neurochemistry, are attacked con bravura and the author should be congratulated on this score. However, it is the practising clinician to whom this book is mainly addressed. Regretfully it must be said that at the clinical level Professor Bradley has not been entirely successful, and although his book claims to offer more than undergraduate neurology texts it is often rather disappointing in its approach to diseases of the peripheral nervous system. It could be that for all his obvious enthusiasm and intelligence, the author does not have quite the breadth of experience for him to be able to present a completely rounded view of his subject.

Serological tests for syphilis in all patients with peripheral neuropathy (cf. p. 85)? Laryngectomy in motor neuron disease patients with bulbar palsy (p. 240)? Dubious advice. Peripheral nerve lesions in malaria and schistosomiasis (p. 200)? Indeed! Some of the accounts of the clinical pictures of peripheral nerve diseases, common as well as rare, are too perfunctory to be really useful at a postgraduate level. Elsewhere, carcinomatous neuropathies are dealt with in slight and uncritical fashion. The pattern of neuropathy seen in untreated patients with uraemia is not clearly distinguished from that in patients on haemodialysis. The relation of liver failure to the development of peripheral neuropathy is more controversial than might be gathered from pages 168 and 172. Autonomic involvement is insignificant, rather than late, in the Rukavina type of primary amyloidosis (p. 227), and is more apparent in the van Allen type.

In other places an irritating superficiality of approach can be detected. The first sentence of p. 162 and the last paragraph of p. 294 do not need to be spelt out. To write, apropos motor neuron disease (p. 239), that there are a number of pointers which may be of aetiological significance, is overoptimistic—if not downright self-delusory. A penchant for the resonant epithet is not always gainful, despite the