Observations on antigens and autoantibodies in multiple sclerosis

This study re-evaluated the role of brain (self) antigens and autoantibodies in MS. The known antigenic changes in MS brain are as follows: Band 1, Band 5, MBP, PLP, breakdown products of GFAP, W., GFAP, z-tubulin, 3 NFPs, two MS specific (high mol. wt) antigens and galactocerebroside. Two new glycoprotein changes (mol. wt 113500 and 138000) were found by sodium borohydride labelling and binding with radioiodinated lectins from surface membrane and myelin fractions in MS white matter autopsy samples. Circulating IgG class autoantibodies for GFAP were found in the CSF of MS cases (n=40, P<0:01) and of brain tumour cases (mlg, P<0:001) for MBP of acute MS (n=14, P<0.02) and SSPE (n=16, P<0:001) and for galactocerebroside of MS (n=42, P<0:001). No correlation was found between different autoantibodies or between serum and CSF. Control patients occasionally showed autoantibodies.

Antigenic specificity of intrathecally synthesized immunoglobulins in multiple sclerosis

In most MS patients the CSF immunoglobulin G (IgG) is strikingly restricted in its heterogeneity, whether selectively increased or not. The oligoclonal pattern of IgG observed in the CSF is unique for each patient and is stable through changes in the clinical course. There is biochemical evidence that the IgG is synthesized intrathecaIly and possibly represents the secretion of plasma cells localized in the vicinity of plaques. In the present combined histological and biochemical study discrete samples from MS brain were analysed and the highest IgG levels were found in MS plaques and adjacent white matter. The IgG extracted from all plaques displayed an oligoclonal pattern on isoelectric focusing. In the three MS brains most fully analysed, there was a poor correlation between IgG levels and histologically identified inflammatory cells in the same piece of dissected tissue. There was close correlation with the degree of astrocytic proliferation and immunoperoxidase staining of samples with human IgG revealed positive staining in astrocytes. The affinity of this cell for macromolecules and particularly IgG must be taken into account in the interpretation of biochemical IgG studies in MS and other diseases.

Corona virus induced demyelination in rats

Central nervous system (CNS) infection of weanling rats with murine coronavirus strain
JHM can result in the following different CNS diseases: Acute encephalomyelitis (AE). This disease develops after an incubation period of 7–12 days. The animals show incoordination, become motionless and die rapidly. Necrotic lesions are predominantly disseminated in the grey matter of the hippocampus, brain-stem and spinal cord. Cell infiltrations are typical for acute inflammations. By immunofluorescence, viral antigen can be found both in neurons and glial cells. Viral particles are detected only in degenerating oligodendroglia cells. Subacute demyelinating encephalomyelitis (SDE). Diseased animals develop clinical symptoms after 13–14 days. The neuropathological lesions consist of demyelinating plaques distributed in the white matter of the optic nerve, midbrain, pons, cerebellum and spinal cord. Within the demyelinated plaques axon and neurons are well preserved. By immunofluorescence, viral antigen is only detectable in glial cells and not in neurons. Cell infiltrations consist of lymphocytes, plasma cells and macrophages. Late demyelinating encephalomyelitis (LDE). After an incubation period of 2–8 months animals develop paralysis. Neuropathological lesions are of typical plaques of primary demyelination as described for SDE. In addition remyelination of the CNS and PNS type are detectable. Infectious virus can be re-isolated from diseased rat by conventional methods. Virus particles are demonstrable in degenerating oligodendroglia cells. The induction of these different types of diseases depends both on the properties of the virus used for infection as shown by temperature sensitive mutants as well as host factors such as age and immunostatus. These different diseases associated with JHM infection offer the possibility to investigate the pathogenic mechanisms of these disorders and provide the basis to analyse the virus-cell interactions which lead to the neuropathological changes. Especially the subacute and late demyelinating encephalomyelitis are of
great interest to analogy to chronic CNS
diseases of man associated with virus infec-
tion.

Webster H. deF. (introduced) (NINCDS, Beth-
esda, MD, USA)

**Immunocytochemical observations in**
multiple sclerosis and other demyeli-
ating diseases

Immunocytochemical studies of several types of CNS myelin lesions suggest that myelin and oligodendroglial targets in demyelinating diseases can be identified by immunostaining lesions with antisera to myelin basic protein (BP) and to an oligodendroglial constituent called myelin-associated glycoprotein (MAG). Hexachlorophene (HCP) intoxication is known to produce intramyelinic edema. In HCP lesions, we observed a normal pattern of periaxonal MAG staining and normal BP staining of compact myelin lamella that surrounded vacuoles. This result is consistent with the fact that the process is reversible and little demyelination is observed. In acute experimental allergic encephalomyelitis (EAE) lesions, areas of altered BP and MAG immunostaining corresponded closely and were similar to histologically detected demyelination. This suggests that in the type of EAE lesion we studied, myelin is the primary target. However, in progressive multifocal leukoencephalopathy (PML), decreased BP staining was confined to areas of demyelination and abnormal MAG staining extended into surrounding white matter that stained normally with BP antiserum and appeared normal histologically. Many oligodendrocytes in these areas contained papova virus. Around multiple sclerosis (MS) plaques, there also were similar areas of decreased MAG staining. Therefore, we suggest that in PML and MS, oligodendrocytes are the primary targets and that demyelination probably is a secondary phenomenon.

Suckling A.J., Wilson N.R. & Rumsby M.G.
(all introduced) (University of York, York YO1 5DD)

**Mechanisms of demyelination in chronic**
relapsing experimental allergic encepha-
lomyelitis

Chronic relapsing experimental allergic encephalomyelitis (CREAE) occurs in guinea-pigs with relapsing and remitting clinical signs and evidence of perivenous inflammation, reactive gliosis and demyelination with axonal sparing. CREAE may be a model for multiple sclerosis, but there are differences in how the plaque arises. In the thoracic cord and optic nerve from strain thirteen guinea-pigs with CREAE at various stages of the disease, demyelinating lesions occur with participation of macrophages and astrocytes. Piecemeal myelin degeneration also occurs without the participation of any cell type. In these areas myelinolysis occurs in intercellular spaces. Remyelinating axons with centrally remyelinated sheaths also show evidence of myelin degradation. Thus, several types of myelin-damaging events occur in different areas of plaques in time.

Lassmann H., Kitz K. & Wiśniewski H.M. (all
introduced) (Brain Research Institute, Vienna, Austria)

**Possible mechanisms of demyelination in**
chronic relapsing experimental allergic encepha-
lomyelitis and multiple sclerosis. **Ultrastructural observations and passive transfer studies**

While studying the pathology of several variants of chronic relapsing and chronic progressive EAE in guinea-pigs it became apparent that the structural features of the lesions depend upon the interval between sensitization and plaque formation. These include the extent of demyelination, remyelination, gliosis, inflammation and vascular pathology. Similar differences occur when the pathological changes of acute and chronic MS are compared. A possible explanation for the differences could be different concentrations of demyelinating and myelinating inhibiting antibodies in sera and CSF of the animals. We investigated the demyelinating activity of sera from animals with chronic relapsing EAE in vivo by injecting it into the CSF of normal recipient animals. The majority of sera from the early and late chronic stages of
the chronic EAE were able to induce demyelination in the CNS and PNS of normal recipients. As in the primary disease, demyelination occurred via myelin stripping or vesicular disruption of myelin. Sera from animals with acute EAE were only rarely effective. Sera from control animals did not induce demyelination. These findings indicate an important role of humoral factors in the pathogenesis of demyelinating lesions.

Szuchet S. (introduced) (Pritzker School of Medicine, University of Chicago, USA)

**Studies on cultured oligodendrocytes**

We have examined the changes in morphology which follow the seeding of oligodendrocytes isolated by our procedure using phase-contrast, scanning and transmission electron microscopy. Fourteen hours after being placed on plastic culture dishes 'floating' cell clusters predominate; these attach after several days. The ultrastructure of the floating cells resembles that of light oligodendrocytes described by Mori & Leblond (1970); i.e., unlike cells fixed immediately after isolation, they reveal an electron lucent cytoplasm, no clumped nuclear chromatin and abundant intracellular organelles. Clustered cells have apposed plasma membranes reminiscent of gap junctions. Attached cells extend long membranous processes which contain large numbers of microtubules and cytoplasmic organelles. Cultured oligodendrocytes incorporate labelled precursors into components of myelin. They also accumulate components of their own plasma membrane. The specific activities of lactic and malic dehydrogenases, enzymes involved in carbohydrate metabolism increase with time in culture. High levels 2', 3'-cyclic nucleotide phosphodiesterase and glycerol phosphate dehydrogenase, two putative markers of oligodendrocytes are detected early, but the specific activities of these enzymes decline with time in culture. Thus, cultured oligodendrocytes mimic oligodendrocytes *in vivo* and provide a good model for study of the role of these cells in multiple sclerosis.

Hirano A. (introduced) (Montifiore Hospital and Medical Center, New York, USA)

**Pathology of the periaxonal space**

Fine structural studies of myelinated fibres under a variety of pathological conditions have revealed that the periaxonal space is remarkably resistant to dimensional change. Under conditions where one might expect the periaxonal space to be compressed, such as enlargement of the axon or of the inner Schwann cell collar, it generally retains its original width. In other conditions such as axonal shrinkage, the periaxonal space is usually maintained; sometimes at the expense of the widening of the space between the inner Schwann cell collar and the innermost lamella of compact myelin. In those unusual cases where the periaxonal space is indeed widened the inner Schwann cell collar is usually missing from those regions. The loss of the collar may be brought about by an increase in the caliber of the space within the sheath or, perhaps, by the degradation of Schwann cell cytoplasm.

Lam D.K.C. (introduced) & Pratt O.E. (Institute of Psychiatry, London)

**Reduced effectiveness of the blood–CNS barrier in experimental allergic encephalomyelitis**

The effectiveness of the blood CNS barrier in excluding substances of differing molecular size from the brain and spinal cord was studied during the development of EAE in Lewis rats inoculated with guinea-pig spinal cord in complete Freund's adjuvant. To do this, a steady level of each test substance, radioactively labelled, was maintained over a short time in the blood stream (Daniel et al. (1975) Med. Biol. Engng. 13, 214). The effectiveness of the barrier begins to fall, especially in the spinal cord, several days before clinical signs become evident and the fall continues during the acute attack. The reduction in effectiveness (i.e. leakage) is greatest for the entry of small molecules like mannitol but appreciable even for large molecules like serum albumin. These findings are of interest in relation to the long-standing observation that multiple sclerosis plaques are commonly related to blood vessels.
Banerjee A.K. & Chopra J.S. (introduced) (Postgraduate Institute of Medical Education and Research, Changigarh-160012, India)

**Does multiple sclerosis exist in India?**

A survey of the literature reveals that multiple sclerosis (MS), diagnosed on clinical criteria, occurs throughout India. The disease is, however, much rarer than in the West, and in India affects males more often. Visual impairment and spinal cord involvement are most common. Neuropathological features have been reported in only four cases. In three, the total duration of neurological illness was 1–6 months, and showed predominantly acute lesions. The duration in the other was 3 years and 4 months with two remissions. Pathologically, relatively more destructive and confluent lesions were observed. Autopsy proven classical causes of MS have not been reported. In the elucidation of etiological factors in MS, therefore, the differences in frequency and nature of the disease in India (and Asia) should be taken into consideration. (Mathew et al., J. Neurol. Sci. 13, 27, 1971; Singhal & Wadia, J. Neurol. Sci. 26, 259, 1975; Chopra et al., Acta neurol. scandinav. 62, 312, 1980).

Heron J.R. (introduced) & Jones R.E. (introduced) (University of Keele, Keele ST5 5BG)

**Paroxysmal events in multiple sclerosis**

Brief, repetitive, paroxysmal symptoms may occur in multiple sclerosis (MS) either as presenting symptoms or during the course of the disease. These include paroxysmal dysarthria, ataxia, visual symptoms, akinesia, sensory disorders and tonic seizures. The mechanism of these is uncertain. Demyelination of nerve fibres causes conduction delay, increased refractoriness and conduction block. It has been suggested that ephaptic transmission may be a significant factor in paroxysmal symptoms (Ostermann et al., Brain 98, 189, 1975) and in luminance-dependent variability in visual thresholds in MS (Patterson et al., Brain 103, 139, 1980). Bostock et al. (Nature 274, 385, 1978) suggested that drugs which prolong action potentials may overcome conduction block in demyelinated nerves and be of therapeutic value in MS. They showed that 4-aminopyridine, which blocks voltage dependent potassium currents, prolongs the action potential in demyelinated rat nerve and facilitates transmission. Preliminary clinical studies with 4-aminopyridine in patients with MS have not shown significant benefit.

**FRIDAY 26 JUNE**

Thomas M., Brown I.L. (introduced) & Graham D.I. (Institute of Neurological Sciences, and the Western Infirmary, Glasgow)

**Lymphoma of the central nervous system: a review of 32 cases. 1. Clinical and radiological findings**

Large series of lymphoma of the nervous system are rarely reviewed, therefore we took the opportunity to review 32 cases clinically, radiologically and pathologically. In the absence of systemic lymphoma there are no specific clinical features suggesting lymphoma. Cranial nerve palsies or a confusional state, however, are frequently present. Post-mortem examination of twenty-six cases were compared to the sometimes distinctive CT scan appearance. The poor prognosis of lymphoma of the nervous system in comparison with systemic lymphoma is noted. One patient (with a renal transplant) had no neurological symptoms and it is possible that here the 'microgliomatous' appearance of the brain is reactive and not malignant.

Brown I.L. (introduced), Graham D.I. & Thomas M. (Western Infirmary and the Institute of Neurological Sciences, Glasgow)

**Lymphoma of the central nervous system: a review of thirty-two cases. 2. Combined histological and immunocytological studies**

The biopsy and autopsy material from thirty-two patients have been reviewed to determine whether microgliomatosis is a specific primary CNS tumour or a manifestation of lymphoid neoplasia. The British National Lymphoma Investigation Classification of non-Hodgkin's lymphoma has been used in
this morphological classification since it does not require supplementary specialized haematological techniques. The immunoperoxidase technique for immunoglobulin light chains and markers for histiocytic cells have also been used. The results indicate that the microgliomas are indeed CNS representatives of the non-Hodgkin's lymphomas, that many contain immunoglobulin, and that the usual ratio of $\kappa$ to $\lambda$ light chain production is reversed with the $\lambda$ light chain being detected in excess.

McCormick D., Wallace I. (introduced) & Kirk J. (Institute of Pathology (Neuropathology), Queen's University, Belfast)

A biochemical and morphological study of the C-6 glioma cell line in vivo and in vitro

Athymic mice were inoculated with aliquots of the C-6 glioma cell line. Four subcutaneous injections of $10^6$ cells were made in separate sites into 10 mice. The tumour 'take' rate was 100% and the latent period before appearance of the tumours was 11.6 ± 6.6 days. Subsequent growth was rapid and animals were killed at intervals between 10 and 30 days after inoculation. Although the tumours were frequently found to invade abdominal muscles, remote metastases were not seen. Biochemical, immunocytochemical and ultrastructural properties of these tumours were described and compared with those of C-6 cells in vitro.

Mitchell J., Mather K. & Weller R.O. (Departments of Pathology (Neuropathology) and Human Morphology, University of Southampton)

Astrocyte reactions associated with gliomas in cold lesions in the rat cortex. Observations on the origin of microglia in human brain

Immunoperoxidase (PAP) techniques for glial fibrillary acidic protein (GFAP) and serum proteins (IgG and albumin) were applied to formalin-fixed paraffin sections of cold lesions in rat cortex and to sections of ethyl nitrosourea induced gliomas. Astrocytes in mitosis were observed near the 2–5 day cold lesions but astrocyte hypertrophy with a marked increase in GFAP was seen in the brain well beyond the region of serum protein exudation and remote from cold lesions. Astrocyte hypertrophy in and around rat gliomas was mainly restricted to the region of serum protein exudation. These findings suggest that different mechanisms, including serum protein exudation, may stimulate astrocyte hypertrophy. Microglial cells in intact cortex around the cold lesions contained serum protein and on occasion were seen in mitosis. The origin of microglial cells was further investigated in normal and infarcted human brain. A blood monocyte marker, alpha 1-antichymotrypsin, was present not only in foamy phagocytic macrophages but also in rod-shaped microglia in infarcted tissue and around the blood vessels in intact and normal cerebral cortex. These observations suggest that resting and activated microglia together with brain macrophages, are derived originally from blood monocytes.

Scott G. (introduced), Adams J.H., Graham D.I., Murray L.S. (introduced) & Doyle D. (Institute of Neurological Sciences, Glasgow)

Diffuse axonal injury in non-missile head injury: an analysis of forty-five cases

Diffuse axonal injury is an important form of brain damage in non-missile head injury and is characterized by focal lesions in the corpus callosum and rostral brain stem, and histological evidence of widespread axonal damage. A detailed neuropathological and statistical study has been undertaken on 45 cases and the results compared with a series of 132 non-missile head injuries without diffuse axonal injury. Patients with diffuse axonal injury most frequently receive their injury in road traffic accidents, they never experience a lucid interval and their median survival is longer than that of controls. There is a statistically significant lower incidence of fraction of the skull, intracranial haematoma, cerebral contusions and raised intracranial pressure compared with the controls, and there is a higher incidence of hypoxic brain damage in arterial boundary zones. Diffuse axonal injury is a distinct clinico-pathological entity, and the available evi-
dence points to its being an immediate impact phenomenon.

Allen I.V., Scott R. (introduced), Tanner J.A. (introduced) & Shillington R.K.A. (introduced) (Institute of Pathology (Neuropathology), Queen's University, Belfast)

**Experimental high velocity missile head injury**

A standardized penetrating head injury was produced in anaesthetized rhesus monkeys. The trans-frontal wound resulted from the passage of a 1/8 in. (3.2 mm) steel sphere at an impact velocity of approximately 1000 m/s. There was comparatively little tissue destruction in the direct pathway of the missile. Bone fragments were found in the wound of twenty of the twenty-one experimental animals. Subarachnoid, perivascular and intraventricular haemorrhage and ependymal disruption were constant features in all brains. The subarachnoid haemorrhage and the perivascular parenchymatous lesions were frequently dissociated from the primary wound tract: particularly vulnerable regions were hypothalamus, midbrain, pons and cerebellum. Three kinds of perivascular lesion were seen: (a) classical 'ring' haemorrhages, (b) haemorrhage with surrounding decreased staining intensity (c) increased staining intensity. In nineteen of the twenty-one experimental animals areas of decreased staining intensity were present, apparently dissociated from areas of haemorrhage. Comparison of nuclear counts in areas of decreased staining intensity with counts in surrounding normally stained tissue showed significantly lower counts in pale areas in cerebral cortex ($P < 0.0005$), deep white matter ($P < 0.005$) but not in brain stem ($P > 0.3$).

Heath J.W. (introduced), Ueda S. (introduced), Raine C.S., Bornstein M.B. (introduced) (Albert Einstein College of Medicine, The Bronx, NY) & Daves G.D. (introduced) (Oregon Graduate Center, Beaverton, OR, USA)

**Buckthorn neurotoxins in vitro: evidence for a primary neuronal effect**

The peripheral demyelinating neuropathy resulting from exposure to toxins of the buckthorn *Karwinskia humboldtiana* affects many species including man. Animal studies have implicated a primary metabolic effect upon the Schwann cell. The present study has examined buckthorn neuropathy *in vitro* to dissect chronologically the pathological events in this disease. Myelinated organotypic cultures of mouse spinal cord and dorsal root ganglia were exposed for 20 h to 14 days to toxins T496 or T544 (1–5 µg/ml, dissolved in 0.1% ethanol). Control cultures were grown with or without ethanol. The earliest, perhaps most profound changes selectively affected axons, both myelinated and unmyelinated, and included peripheral relocation of microtubules, alignment of microtubules with SER to form stacks, and vacuolation. Other prominent features, previously reported following intoxication *in vivo*, included Schwann cell and myelin sheath abnormalities, axonal degeneration and chromatolysis. The present culture system indicates that buckthorn neuropathy might arise from axonal abnormalities, possibly through a deficit in transport mechanisms.

Kirk J. & Dermott E. (introduced) (Departments of Pathology, and Microbiology and Immunobiology, Queen's University, Belfast)

**Criteria for the ultrastructural recognition of paramyxoviridae (morbillivirus) in CNS and tissue culture**

The morphogenesis of the morbillivirus genus, and in particular measles virus, by electron microscopy has been extensively documented. However, there continue to be reports in the pathological literature in which unknown tubular and lamellar structures are interpreted as 'paramyxovirus-like' despite their failure to exhibit the morphological characteristics and intracellular location of the virus group concerned. The essential features of morbillivirus morphogenesis were presented and comparisons were made with inclusions which have been described as morbillivirus-like in tissue from multiple sclerosis and other pathological conditions.

Nevin N.C. & Hughes A.E. (both introduced)
Feto-specific proteins in the prenatal detection of neural tube defects

Neural tube defects (anencephaly and/or spina bifida) have a high incidence in the north-west of the British Isles, particularly in Northern Ireland (8.7 per 1000 newborn). The discovery of elevated levels of alphafetoprotein (AFP) in the amniotic fluid in cases of fetal neural tube defects provided a major advance in the avoidance of these disorders, and is useful in the detection of the majority of 'open' neural tube defects. However, in some cases of spina bifida the amniotic fluid AFP elevation may be marginal, and in such circumstances other parameters may be helpful. Amniotic fluid from fetuses with an open neural tube defect contains a high proportion of cells which adhere to glass and recently the application of immunocytological methods had demonstrated that many are of neural origin. The use of amniotic fluid acetylcholinesterase levels and isoenzyme patterns has also provided valuable parameters in the recognition of those cases of open neural tube defect with normal amniotic fluid AFP levels.

Mullan S. (introduced) (University of Chicago, Chicago, Ill, USA)

In vitro studies of cerebrovascular spasm

A variety of in vitro studies on cerebrovascular spasm were presented with particular reference to spasmogenic factors. The clinical implications for these studies were discussed.

Dinn J.J. (St James's Hospital, Dublin, Eire)

Subacute combined degeneration—the pathogenesis demonstrated in an animal model

Monkeys exposed to N₂O develop neurological and pathological abnormalities which are indistinguishable from SCD that occurs in humans due to vitamin B₁₂ deficiency (Lancet ii, 1154, 1978). Based on the known biochemical pathways of vitamin B₁₂ metabolism, a hypothesis was formulated (Ir. J. Med. Sc. 149, 1, 1980) suggesting that the neurotoxicity of N₂O resulted from inactivation of the methionine synthetase reaction, thus block- ing the production of methionine and creating a 'methyl group deficiency' in nerve tissue. This became manifested pathologically by defective myelin maintenance. To investigate this theory, we have recently examined four further pairs of monkeys—all exposed to similar concentrations of N₂O but one of each pair receiving a methionine supplemented diet. The results of the experiments reveal that the monkeys receiving methionine were protected from the effects of N₂O exposure and demonstrate the site of the biochemical lesion in SCD.

Crockard A. (introduced), Bhakoo K. (introduced), Lascelles P.T. (introduced) & Russell R.R. (The National Hospital for Nervous Diseases, Queen Square, London)

Prostaglandins and ischaemic oedema

In gerbils, unilateral or bilateral extracranial carotid occlusion leads to reproducible cerebral ischaemia, and with this model, studies have been made of focal cerebral blood flow, brain water and brain tissue prostaglandin levels. Brain oedema begins when the cerebral blood flow is less than 20 ml/100 g/min reaching maximal levels at 5–7 ml/100 g/ml. Prostaglandin F₂ and E₂ rise to 10–20-fold in the ischaemic area. Pretreatment of the animal with prostaglandin inhibitors reduces significantly the tissue prostaglandin levels and the amount of oedema without affecting blood flow. It is suggested that prostaglandins released from ischaemic tissue are involved in the pathogenesis of this type of brain oedema.

Gessaga E.C. (Department of Neuropathology, Cantonal Hospital, CH-5001 Aarau, Switzerland)

Dissecting aneurysm of cerebral arteries. Report of three cases

Three young adults died with massive infarcts of one hemisphere due to spontaneous dissecting aneurysms of one internal carotid artery. The dissection had occurred between the internal elastic lamina and the media and extended into the major intracranial branches. The false channels contained thrombus and had collapsed the original lumina. The patients, two females, 25 and 31
years old, and a male, 15 years-of-age, were previously healthy. Autopsy did not reveal obvious vascular or other underlying disease. From the literature it is apparent that this type of lesion occurs mainly in young patients. Although dissecting aneurysm of cerebral blood vessels is usually a post mortem finding, the diagnosis is made angiographically with increasing frequency, and early treatment may be lifesaving. It appears that this type of lesion is more common than previous reports suggest (Grosman et al., J. Neurosurg. 53, 693, 1980).

Ekström von Lubitz D.K.J. (introduced & Diemer N. (University of Copenhagen, Copenhagen 2100, Denmark)

Ultrastructure of the hippocampal CA-1 region in rats after cerebral ischaemia

To anaesthetized rats given curare a neck cuff and hypovolemic hypotension were applied to induce 10 min of complete cerebral ischaemia causing loss of CA-1 and Purkinje cells. Ten and 60 min after the restitution of the cerebral blood flow, a 20-min systemic perfusion with 3-aldehyde was made (Kalt & Tandler, J. ultrast. Res. 36, 633–645, 1971). The brains were then processed for TEM. 10-min reflow: The neuronal processes of the stratum radiatum showed only slightly dilated ER and a few swollen mitochondria. Initial signs of synaptic degeneration (change in the curvature of the synaptic membranes, reduction in the number of synaptic vesicles, beginning separation between the presynaptic membrane and the vesicle pool) were also present. Swollen end-feet occurred in the astrocytes. 60-min reflow: EM changes in CA-1 neurons were pronounced, namely loss of ribosomes along considerable stretches of RER, vacuolization of ER and extensively swollen and disrupted mitochondria. Synapses had strongly modified membrane shape and there was a considerable loss of both pre- and post-synaptic densities. Total disruption or disappearance of the vesicle pool was common. Astrocytes had intensely swollen end-feet, aggregations of a strongly argyrophilic substance, slightly dilated mitochondria. The early changes in the synapses show that the area of synapse transmission is among the most vulnerable to ischaemia.

Larroche J.C. (Hôpital Port-Royal, Paris, France)

Neocorticogenesis in the human embryo: an electron microscopic study of the plexiform layer

Ultrastructural study of the plexiform (molecular, subpial layer) of a 7-week-old human embryo confirms recent observations from various laboratory animals and revises some classical concepts of corticogenesis. At 7 weeks, the telencephalic vesicle is made of two layers, the ventricular layer or matrix and the plexiform layer. The first cells found in the plexiform layer have the morphological attributes of the Cajal–Retzius cells. They have already migrated, before any cortical plate can be identified. In this primitive layer are the first synapses to be described indicating the precocity of an elaborate circuitry at this level.

Cole G (introduced) (The Midland Centre for Neurosurgery and Neurology, Smethwick)

Organic disease of the brain in mental hospital patients: an autopsy study

The pathological findings at autopsy were studied in a sample mental hospital population in the Transvaal, South Africa. Autopsies were carried out on 200 patients, and the percentage autopsy rate was 57%. The opportunity existed to compare the findings in two racial groups: namely South African Black and White patients. Attention is confined to cerebral pathology. It was found that 66% of the patients had a pathological abnormality of some kind in the brain. Senile, and less commonly arteriosclerotic brain disease was present in 25% of the cases. The incidence of intracranial space-occupying masses was 13.5% (Cole J., Neurol. Neurosurg., Psychiat. 41, 730, 1978), and these included cerebral tumours, subdural haematomas, parasitic (tapeworm) cysts, tuberculomas and cerebral abscesses. In most cases it was possible to decide whether pathological lesions had developed before or after admission to hospital. Error in antemortem diagnosis was highest in
the group of patients with intracranial space-occupying masses.

Cumming W.J.K. (Department of Neurology, Withington Hospital, Manchester)

Neurogenic scapuloperoneal syndrome

Since its original description in 1886, there have been frequent reports of the syndrome of scapuloperoneal muscle disease. There has, however, been very little agreement as to the aetiology and subdivision of this syndrome. This report dealt with the pathological and morphometric assessments of quadriiceps muscle biopsies in twelve patients with the scapuloperoneal syndrome, all of whom had a common neurogenic aetiology.