Proceedings of the meeting of the Association of British Neurologists held in Newcastle upon Tyne, 3–4 April 1987

DEFECTS OF FATTY ACID OXIDATION IN SKELETAL MUSCLE
DM Turnbull, B Ashworth, K Bartlett, I Shepherd. Departments of Neurology and Child Health, University of Newcastle upon Tyne and Department of Neurology, Northern General Hospital, Edinburgh

Fatty acids are important substrates for both exercising and resting skeletal muscle. Impaired fatty acid oxidation in human skeletal muscle causes weakness and/or pain associated with lipid accumulation in muscle fibres. Fatty acid oxidation is a complicated process involving at least 12 enzymes and there are many potential sites at which a defect may occur. Many cases of lipid storage myopathy were thought to be due to carnitine deficiency although this is now thought to be unlikely in the majority of cases. The most probable site of the enzyme abnormality in these patients is a defect of one of the three acyl-CoA dehydrogenases, the group of enzymes at the beginning of the B-oxidation sequence. We describe a 38 year old male who presented with a painful proximal myopathy whose muscle contained an abnormal accumulation of lipid. The activity of both short- and medium-chain dehydrogenase was low in this biopsy. The patient improved clinically and electrophysiologically with the administration of riboflavin, and a repeat muscle biopsy revealed only a minor morphological abnormality as well as improved activity of the acyl-CoA dehydrogenases. This unique case highlights the importance of comprehensive investigation of patients with lipid storage myopathies, since these disorders are potentially treatable.

THE ANALYSIS OF NEUROMUSCULAR TRANSMISSION IN MOTOR NEURON DISEASE
TJ Walls, CR Slater, PRW Fawcett, IS Schofield. Muscular Dystrophy Laboratories, Newcastle General Hospital, Newcastle upon Tyne

Single fibre EMG reveals defects of neuromuscular transmission in several neuromuscular diseases where the principal abnormality is not at the neuromuscular junction. These include motor neuron disease, spinal muscular atrophy and the muscular dystrophies. The pathophysiology of these transmission defects is unknown. To examine their cellular basis, we have developed procedures for studying the structure and function of motor innervation in motor point biopsies from the vastus lateralis.

In addition to routine histological and histochemical examination, quantitative morphological studies of the intramuscular nerves and neuromuscular junctions are made. To study function, nerve-muscle preparations are obtained from portions of the biopsy and intracellular recording techniques are used to study transmitter release and action.

We have investigated 21 patients with a variety of myopathic and neurogenic diseases so the number of patients with any given condition is still small. However, our results from patients with motor neuron disease already suggest that in this condition there is a reduction in the amount of transmitter released from the nerve terminals at some neuromuscular junctions. If this occurs in vivo, it would reduce the safety factor at these junctions and might account for the increased jitter and impulse blocking on single fibre EMG.

MYOTOXIC EFFECTS OF KRAIT VENOMS
BA Summers, JB Harris. Muscular Dystrophy Group Research Laboratories, Department of Neurology, University of Newcastle, Newcastle upon Tyne

Snake bite is a common cause of distress. Although krait venom is generally considered purely neurotoxic, a clinical report of five bites by the Malayan krait, *Bungarus candidus*, included a case with generalised muscle tenderness and pain on passive movement. This raised the possibility of myotoxicity which was assessed using the rat soleus muscle. Crude venoms from four krait species were injected subcutaneously into hind limbs of anaesthetised rats. Soleus muscles were removed between 1 hour and 7 days later and frozen in Arcton. Polyvalent and monovalent antivenoms were examined. The venom of *Bungarus candidus* caused a dose dependent muscle necrosis with more than 75% of muscle fibres destroyed by 0.4 mg/kg body weight. Muscle fibre degeneration and infiltration by inflammatory cells was seen at 6 hours and appeared maximal 24 hours after injection. Muscles sampled at 1 week showed muscle fibre regeneration. Comparable results were obtained using *B. fasciatus* venom, but no such effect was seen with venoms of *B caeruleus* or *B multi- cinctus*. Calculations based on venom yields suggest some relevance for human toxico- nology; an average adult specimen of *B fasciatus* yields 25–50 mg venom. Inoculation of 25 mg into a 60 kg man is equivalent to a dose of 0.41 mg crude venom/kg body weight delivered locally.

IMMUNOLOGICAL OBSERVATIONS ON PARANEOPLASTIC SENSORY NEUROPATHY
DJ Dick, JB Harris, JB Foster. Muscular Dystrophy Sensory Neuropathy, Newcastle General Hospital, Newcastle upon Tyne

We have identified three patients with paraneoplastic sensory neuropathy associated with a small cell carcinoma of lung. Two were plasmaphoresed but showed no clinical improvement. Serum from all three patients contained an IgG antibody which bound to neuronal nuclei in dorsal root ganglia, spinal cord and cerebral cortex. Nuclei in non-neural tissues were negative. The IgG contained both kappa and lambda light chains and could fix complement. The antibody also reacted with dorsal root ganglia from rodents. Western blotting techniques have demonstrated antibody binding to a constant and specific band.

A passive transfer of the neuropathy was attempted by injecting a cohort of mice with plasma from an affected patient for 100 days. No clinical or morphological effect was observed and no human immunoglobulin was found in the mouse dorsal root ganglia.

We have however demonstrated that the antibody can enter neurons and bind to neuronal nuclei culture although it does not appear to alter their viability. It is still unclear from these results whether the antibody is directly involved in the pathogenesis of this disease.

1716
SHORT TERM STABILITY OF SINGLE MOTOR UNIT RECORDINGS IN MOTORNEURONE DISEASE. A MACRO EMG STUDY

RJ Guiloff, H Modarres-Sadeghi, H Rogers. Department of Neurology, Westminster Hospital, Charing Cross and Westminster Medical School, London

We have previously shown an acute 25–30% increase in mean corrected fibre density and in mean Macro EMG median amplitude and area of brachial biceps in 29 patients with MND receiving a TRH analogue (RX77368).

Baseline Macro EMG recordings of seventeen voluntarily activated single motor units and five fasciculations in nine MND patients showed a small mean % standard error for both mean amplitude (2.38%, range 0.58–8.84 %) and mean area (2.62%, range 0.25–5.95 %). Recordings every 15 minutes for 2 hours of single motor units, with (11 units) and without (11 control units) intravenous infusion of 0.2 mg/kg of RX77368, showed no significant change in amplitude nor area with the drug.

The findings suggest that with this technique, over short periods, no gross change in the functional peripheral territory of individual motor units in the muscles studied can be detected during drug administration. The results are consistent with the hypothesis that the effect on fibre density and Macro EMG previously found may relate to direct or indirect action of RX77368 on anterior horn cells.

A NEW PORTABLE UNIT FOR THE ASSESSMENT OF THERMAL SENSATION PATHWAY IN MAN

GA Jamal, S Hansen, Al Weir, JP Ballantyne. Department of Neurological Sciences, St. Bartholomew’s Hospital, London and Institute of Neurological Sciences, Glasgow

A new microprocessor controlled, self contained, portable and easy to operate unit for the assessment of the small diameter afferent thermal pathways with high sensitivity and reproducible is described. The technique uses the Pelletier effect, the two alternative forced-choice method of psychophysical analysis, the up-and-down transform rule of mathematical assessment and standardises all other sources of variability.

The method tests the functional integrity of the thinly myelinated (AΔ) and unmyelinated (C) fibres which cannot be assessed by conventional nerve conduction and EMG and somatosensory evoked potential studies. From the application of the technique to a large group of patients with peripheral neuropathy of various aetiology, it is concluded that it is of value in (a) the early detection of subclinical and serial assessment of ongoing neuropathy, (b) reliable diagnosis of selective small fibre neuropathy, (c) serial monitoring of the effect of therapy on neuropathy, (d) the assessment of neuromotoxifying effects of various industrial products and pharmaceutical agents, and (e) detection of subtle sensory dysfunction in other complications.

INVESTIGATION OF DEFECTS OF FATTY ACID OXIDATION IN SKELETAL MUSCLE

DM Turnbull, K Bartlett, A Aynsley-Green, HSA Sherratt, NJ Watmough, I Shepherd, AKMJ Bhuiany. Departments of Neurology, Child Health and Pharmacological Sciences, University of Newcastle upon Tyne

Myopathies due to defective fatty acid oxidation are potentially treatable by dietary manipulation and/or drug therapy. It is therefore important that this group of disorders is properly investigated so that the site of the enzyme abnormality can be detected and appropriate treatment instituted. Many previous cases of lipid storage myopathy have only been studied by morphological examination of the muscle biopsy and determination of the carnitine concentration. Carnitine deficiency is a secondary biochemical change in the majority of patients. Our approach involves investigating the possibility of other organ involvement by measuring blood and urine metabolites during a prolonged fast. We determine the concentration of individual acyl carnitine esters in the blood and urine by hplc and this often suggests the site of the defect. We have shown that the radiochemical measurement of fatty acid oxidation in skeletal muscle is adequately assessed by measuring radioactive CO2 release alone. We have developed a radio-hplc method to show that the majority of the reaction product is in the acid soluble fraction and is either citric acid cycle intermediates or acylcarnitine. Assay of the individual enzymes of B-oxidation, in particular the acyl-CoA dehydrogenases, requires sensitive methods. Using an ETF-linked assay we can measure the activity of the three acyl-CoA dehydrogenases in 10 mg of muscle. These techniques allow accurate assessment of fatty acid oxidation in skeletal muscle and help in the diagnosis of this important group of muscle diseases.

NORMAL AND PHYSIOLOGICAL VARIATIONS IN CRANIAL CSF VOLUME MEASURED BY MAGNETIC RESONANCE IMAGING

R Grant, B Condon, A Lawrence, D Hadley, J Patterson, I Bone, GM Teasdale. Institute of Neurological Sciences, Glasgow

We have developed a method of measuring CSF volumes, using a new MRI sequence. The relationships between CSF volume, age, sex, difference, skull circumference and the menstrual cycle have been assessed.

Sixty-four normal subjects between the ages of 18–64 were studied. The pulse sequence used (IRCP 300/440/5000) provides a sagittal image of cranial CSF only. Total cranial, cortical sulcal, ventricular and posterior fossa CSF volumes were calculated.

Total cranial and ventricular CSF volumes ranged from 57.1–286.5 mls and 6.8–30 mls respectively (male mean 146 mls, female mean 114 mls). Total and cortical sulcal volumes increased steeply with age in males and females while ventricular and posterior fossa CSF volumes showed a less marked increase with age and wide variation. There was no association between skull circumference and total cranial CSF volume. Immediate reproducibility studies in 25 subjects demonstrated a median difference in ventricular and cortical sulcal volume of 0.2 mls and 2.1 mls respectively. Of 20 women with a normal menstrual cycle, 19 had more total cranial CSF pre-menstrually than at mid cycle.

The validation of this technique allows the future study of CSF volumes in neurological and neurosurgical conditions and assessment of medical or surgical treatment.

TRANSIENT FEELINGS OF COMpULSion CAUSED BY HEMISPHERic LESIONS: THREE CASES

CD Ward. Southampton University, Southampton

Feelings of compulsion are described in post-encephalitic states—where the pathology is poorly localised—and in Gilles de la Tourette syndrome, in which the pathological basis is poorly understood. In both conditions the ensuing involuntary movement generally overcomes internal resistance and seems to be the primary phenomenon, whereas it has been suggested that in obsession-compulsion disorder the reverse is true. Three patients with no previous psychiatric history described feelings of compulsion which were clearly associated with hemispheric lesions and which must have been primary since no movement occurred. A woman of 59 presented with an attack in which she successfully resisted a compulsion to walk to the left. A man of 43 repeatedly experienced a transient compulsion to move the right arm and to shout. These patients had hemispheric gliomas. A
right-handed woman of 62 had an episode of dysphasia which resolved within a few minutes. In the next few weeks she felt the need on 3 or 4 occasions to prevent her right arm from moving against her will. The only abnormality on CT scan was a dubious lucency in the left basal ganglia. These cases show that feelings of compulsion may arise as primary neurological disturbances rather than as epiphenomena of movement disorders.

THE NEUROLOGICAL CONSEQUENCES OF HUMAN IMMUNODEFICIENCY VIRUS INFECTION

M Johnson, R Clifford Jones, SM Forster, AJ Pinching, JRW Harris. St. Mary's Hospital, Praed Street, London

Reports from USA indicate that as many as 30% of patients with human immunodeficiency virus (HIV) infection may have neurological problems in life, and that 80% have neuropathological abnormalities at autopsy. There are reasons to expect that the manifestations of this infection may differ from country to country, depending for example on the prevalence of local endemic infections. At St. Mary's Hospital, where the largest group of HIV+ve patients in this country have been cared for, we are rapidly accumulating cases in which neurological disturbances complicate this disease, and here report the salient features in the first 40 patients with neurological abnormalities. The pattern broadly follows that described from the USA with the majority showing encephalopathic features. Our patients showed insidiously progressive dementia which has to be distinguished from other encephalopathies which may be reversible and from the effects of opportunistic infection. We have also studied a group with a painful, symmetrical, sensorimotor neuropathy, and describe one patient with proximal myopathy. The commonest opportunistic infections of the CNS have been toxoplasmosis (eight cases) and cryptococcosis (eight cases). The advent of treatment trials for HIV infection will demand reliable assessment of neurological involvement, and we will describe psychometric and electrophysiological approaches to this problem.

MAGNETIC RESONANCE IMAGING AND ELECTROPHYSIOLOGICAL STUDIES OF THE OPTIC NERVE IN OPTIC NEURITIS

DH Miller (introduced), MR Newton (introduced), JC van der Poel (introduced), G Johnson (introduced), DG MacManus (introduced), AM Halliday, WI McDonald. Institute of Neurology, Queen Square, London

Using a newly introduced magnetic resonance imaging (MRI) sequence (STIR) we have studied the optic nerves in 33 patients aged 7-44 years with optic neuritis. Visual evoked potentials (VEP) were recorded in all cases. Twenty seven had had unilateral optic neuritis and six bilateral. Of the 39 optic nerves clinically affected, MRI was abnormal in 33 and VEP in 38. Of 27 asymptomatic optic nerves, MRI was abnormal in three and VEP in four. The MRI lesions were in the anterior part of the nerve in 18 (50%), in the middle in 25 (72%), and in the posterior part in 25 (25%). Nine of 10 with disc swelling had a lesion visible at MRI; the lesion was anterior within the nerve in five, in the mid portion in three and posterior in one. All 15 with clinical evidence of optic atrophy had a positive MRI.

The mean length of lesions in patients with poor visual recovery (VA > 6/9) was 18.6 mm, and in those with a good recovery, 10.0 mm. The six nerves where no abnormality was seen all had a good visual recovery.

There was no correlation of visual prognosis with the site of the lesion along the nerve. There were no particular VEP correlates with the site and length of MRI lesions.

VISUAL FUNCTION AND CEREBROSPINAL FLUID IMMUNOGLOBULINS IN EARLY MULTIPLE SCLEROSIS

WP Honan, JR Heron, DH Foster, MO Scase, GK Edgar. Department of Postgraduate Medicine, University of Keele, Department of Communication and Neuroscience, University of Keele

We report the initial findings in a longitudinal study of visual function and cerebrospinal fluid (CSF) immunoglobulins in multiple sclerosis. Cases were studied as near as possible to the time of clinical onset of the disease.

Visual function was assessed clinically and by visual fields, visual evoked potentials (VEP) and psychophysical measures of luminance and chromatic thresholds and the de Lange attenuation characteristic. CSF immunoglobulins were estimated using IgG levels, IgG synthesis and agar-gel electrophoresis.

Thirty two cases were included with an average symptom duration of 7-6 months, range 0-25-14 months. The series was subdivided into two groups: A: without optic neuritis and B: with optic neuritis. Abnormalities of at least one measure of visual function were detected in 26/32 (81%) cases; CSF immunoglobulins were abnormal in 19/31 (61%) cases. Analysis of the subgroups revealed abnormalities of visual function in 13/18 (72%) cases in group A and 13/14 (93%) cases in group B. CSF immunoglobulins were abnormal in 8/17 (47%) cases in group A and 11/14 (79%) cases in group B.

VISUAL FUNCTION IN PATIENTS WITH MULTIPLE SCLEROSIS AND NORMAL VISUAL ACUITY

B Ashworth, PA Aspinall, JD Mitchell. Department of Clinical Neurosciences, University of Edinburgh

Eighty nine patients with multiple sclerosis and normal visual acuity have been submitted to a battery of test of visual function. The tests included the visual evoked potential, tests of colour vision and lightness discrimination, and spatial contrast sensitivity. The Posner diagnostic classification was used. This group of controls and patients forms the basis of a continuing serial study over five years.

Results show significant difference between the clinical and normal groups in yellow-blue, lightness discrimination, and at several frequencies of spatial contrast sensitivity in the range 0.3 to 10 cycles/degree. Abnormalities of these measures were demonstrated in patients with no history of acute optic neuritis. Further, more significant differences between the clinically defined groups and probable groups were found in red-green discrimination and contrast sensitivity.

LAMBERT-EATON MYASTHENIC SYNDROME: CLINICAL FEATURES AND RESPONSE TO TREATMENT IN 50 CASES

JN O'Neill (introduced), NM Murray, J Newson-Davis. Institute of Neurology, Queen Square, London

The Lambert-Eaton myasthenic syndrome is a rare pre-synaptic disorder of neuromuscular transmission, often associated with carcinoma of the lung, in which the number of acetylcholine packages released by a nerve impulse is reduced. Recent experimental studies have shown that it has an autoimmune basis in both its cancer-associated and non-cancer-associated forms, the disorder of transmission being due to an IgG antibody that interferes with the function of voltage-dependent calcium channels at motor nerve terminals. No large clinical series has been reported apart from the description of electromyographic findings in 17 cases by Lambert et al in 1961.

The 50 consecutive cases seen by one of us (JND) over the last eight years formed the basis for this study. Electromyographic and autoantibody studies were undertaken in all
patients. The disease was associated with overt malignancy in 23 cases, histologically proven to be small cell lung carcinoma in 20; disease duration in the remaining 27 cases ranged from one to twelve years. We have analysed the clinical features, course (monitored clinically and electromyographically) and response to treatment that included 3,4-diaminopyridine, immunosuppressive drugs, plasma exchange and, in cancer cases, chemotherapy.

MYELOGRAPHY IN A REGIONAL NEUROLOGY UNIT; USE, MISUSE AND COSTS
PAG Sandercok, LD Blumhardt, MA Roberts. Department of Neurology, Walton Hospital, Liverpool

The number of myelograms performed each year in our unit has increased steadily from 289 in 1972 to 612 in 1985. We have audited our use of myelography over 6 months. We present data on the first 318 myelograms performed on 311 patients. The indication (some patients had more than one) for myelography was: lumbar or cervical radiculopathy in 170 (55%), spinal cord lesion for >1 month in 85 (27%), spinal cord lesion <1 month in 27 (9%), suspected Arnold-Chiari malformation in 22 (7%), suspected spinal dysraphism 9 (3%), other 85 (27%). Ancillary investigations performed were: visual evoked potentials performed before the myelogram in 15 cases (five were abnormal), CT of the spine in 44 and CT of the head in 96. Myelography had to be repeated in 25 patients (often because the test, performed elsewhere, was inadequate). Clinical information on X-ray request forms was inadequate or misleading in many cases. The radiology department costs were small in comparison to the hospital cost of £130 per bed day. The mean time from admission to myelography was 2.98 days. Several areas where our use of this test might be improved have been identified.

ILLNESS BEHAVIOUR AND PSYCHIATRIC DISEASE IN NEUROLOGICAL PATIENTS
RA Metcalfe, D Firth, SS Pollock, M Timol, F Creed. Departments of Neurology and Psychiatry, Manchester Royal Infirmary

The relationship between neurological and psychiatric illness has previously been studied in those selected patients who have been referred to a psychiatrist. We have assessed a consecutive series of female patients admitted to a neurological investigation unit, to examine the likelihood that the patients' symptoms were explicable in terms of neurological and/or psychiatric illness. Of 93 patients 54 were thought by the neurologist to have symptoms that were entirely explicable in terms of organic disease (group 1). Twenty two had symptoms that were less clearly organic in origin (group 2), and in 17 the neurologist was sure that the symptoms could not be due to organic disease (group 3). The median total psychiatric score according to the Clinical Interview Schedule, was 13 for group 1, 25 for group 2 and 30 for group 3 (p >0.001). But the hypochondriasis score of the Illness Behaviour Questionnaire (phobic concern about health) was 0-5, 1 and 5 for the three groups (p >0.001) indicating that illness behaviour was far more evident in group 3. Psychiatric illness could entirely explain the symptoms in only 2 of the group 2 patients and 8/17 of the group 3 patients. It is suggested that this method of evaluation could indicate which patients with "functional" symptoms require psychiatric treatment and which require further investigation.

SUBACUTE ADMINISTRATION OF A TRH ANALOGUE (RX 77368) IN MOTOR NEURON DISEASE (MND). OPEN STUDY
H Modarres-Sadeghi (introduced), RJ Guiloff. Department of Neurology, Westminster Hospital, Charing Cross and Westminster Medical School, London

A controlled acute trial of a single i.v. dose of 0-3 mg/kg has previously been reported. Longer term effects are unknown.

Twelve MND patients aged 34-66 years were infused 0-1-0-35 mg/kg i.v. over 2-6 hours daily or at longer intervals for up to ten weeks, after baseline assessments. Eight patients with bulbar symptoms showed improvement in speech with objective changes in tongue, lip and jaw movements, lasting about one week after cessation of therapy. Five had improvement in vital capacity and four in maximal respiratory pressures. Two had moderate improvement in swallowing. Two further cases showed deterioration in respiratory parameters, one had significant side effects, the other was asthmatic. Dyanometry in eighty-five muscles showed improvement in ten in five patients and deterioration in eleven in five patients for up to five days after cessation of therapy. Some activities of daily living improved in three of six tested patients. Cramps improved for up to eight weeks in five patients. The drug was useful for bulbar symptoms but its effect on muscle force was not predictable. Careful individual adjustment of the dose was required. Long term studies are indicated.

THERMAL THRESHOLD TESTING IN DIABETIC NEUROPATHY
Al Weir, G Jamal, S Hansen, JP Ballantyne. Institute of Neurological Sciences, Glasgow

The criteria for diagnosis of diabetic peripheral neuropathy are not universally agreed. Dyck1 has sought to investigate this problem using a combination of clinical scoring methods, automated sensory testing, electrophysiology and neuropathology. We have also completed a comprehensive study of 73 diabetics in whom neuropathy was diagnosed or suspected clinically.

Dyck detected abnormalities of thermal cooling in 13/23 (56%) using his computer assisted sensory examination and concluded that thermal sensation was the least sensitive in the detection of abnormality when compared with touch/pressure and vibration. We have used the Glasgow designed thermal threshold testing technique and detected abnormality in 69/73 (95%) of our patients. There is therefore a considerable discrepancy between the techniques.

We have compared published results from the two techniques for absolute values and intra-individual variability. Secondly, we have modified our equipment to simulate the method and procedure used by Dyck and other groups to determine thermal thresholds. In each case our technique produced a lower absolute thresholds and proportionally much smaller standard deviations. This decreases the overlap between the abnormal and normal populations to a minimum.

We conclude that dramatic statements about the usefulness of testing certain modalities of sensation in detection of neuropathy must be qualified by the type of technique used. With our technique thermal threshold testing detects abnormality in 95% of diabetics in whom neuropathy is suspected.


SPINAL CORD STIMULATION AND THE RELIEF OF CHRONIC PAIN
TH Koeze, AC deC Williams, S Reiman, ES Watkins. The London Hospital Medical College, London

Spinal cord stimulation has been used for the relief of chronic pain for nearly twenty years. Long term results have not been encouraging. However, many early studies included patients with a history of drug abuse and psychiatric illness. Most were done by postal surveys or retrospective data collection from
clinical records. We studied 26 patients with chronic intractable pain without a history of drug abuse or psychic illness who received spinal cord stimulation for a median period of 28 months. The patients were evaluated by structured videotaped interviews with psychologists not involved in the patients' care. In addition estimates of pain relief were obtained from clinicians involved in the patient's care and from close relatives or friends. Information about general activities and drug usage was also collected. At the time of the interview of the half of the patients were receiving 50% or better relief of their pain. There was a decrease in the use of analgesic medication and increased domestic and leisure activity. The "costs" of this result included repeated visits to outpatient clinics for detection and repair of stimulator faults.

RADIOLICAL SUPPORT FOR THE PRIMARY ROLE OF OCCIPITAL DYSPLASIA IN THE ADULT CHIARI MALFORMATION

W Schady, RA Metcalfe, P Butler. Departments of Neurology and Neuroradiology, Manchester Royal Infirmary, Manchester

The reason for cerebellar herniation in the adult Chiari type I malformation (ACM 1) is not known. It has been postulated that it is secondary to a reduction in size of the bony posterior fossa, although the reported incidence of platybasia and basilar invagination in ACM 1 is only 20-30%. In order to test this hypothesis detailed surface area, angular and linear measurements were undertaken on plain radiographs of 32 symptomatic patients (mean age 39 years) with myelographically proven primary ACM 1.

Basal and Bogard's angles were significantly larger in patients than in controls. The clivus was shorter, Klaus' level index was smaller and the area of the bony posterior fossa in the sagittal plane was reduced in patients compared with controls, even after correction for unequal total skull size. By the use of discriminant analysis 68% of patients were accurately predicted to belong to the patient group and 94% of controls were identified as such.

These results show that over two-thirds of patients with ACM 1 have recognisable occipital dysplasia. Furthermore, there was an inverse relationship between the size of the posterior fossa and the degree of cerebellar herniation. This suggests that the bony anomaly is primary and that tonsillar descent occurs as a result of crowding out of the cerebellum.

PRE-BY PASS HYPOCAPNIA IS CORRELATED WITH THE POST-OPERATIVE APPEARANCE OF SIGNS OF OCULAR HYPERPERFUSION IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS SURGERY

M Nevin, A Colchester, J Pepper, S Adams, R Humphrey, A Davies. St George's Hospital, London

Thirty patients undergoing coronary artery bypass surgery had detailed neurological, ophthalmological and psychometric assessment pre-operatively and again on the third and seventh post-operative day. Pre-operatively arterial and jugular bulb venous pressures and gas tensions were monitored frequently but the surgeon and anaesthetist were not informed of these results.

In 15 patients (Group I) expired CO₂ monitoring was not used by the anaesthetist who referred to intermittent blood gas samples according to routine practice. Seven of the patients developed new eye signs post-operatively (Group Ia): five had retinal changes consistent with ocular hyperperfusion and two showed a reduction in visual acuity without retinal changes. For Group Ia the mean PaCO₂ immediately prior to bypass was 27.1 mm/Hg. A significant psychometric deficit was found in five patients.

The other eight patients in Group I did not have eye signs (Group Ib). They had a mean PaCO₂ prior to bypass of 36.0 mm/Hg and only three showed a significant psychometric deficit post-operatively.

In the remaining 15 patients (Group II) the anaesthetist used end-tidal CO₂ monitoring and took special care to maintain normocapnia. The only post-operative eye signs observed were glaucomatous changes in the one patient, although six Group II patients developed a psychometric deficit. The mean PaCO₂ prior to bypass was 37.4 mm/Hg.

Statistical analysis showed a highly significant difference (p < 0.001) between the pre-bypass PaCO₂ values in the patients with eye signs (Group Ia) and those without eye signs (Groups Ib and II combined). There was no evidence in any of the patients of retinal microembolisation.

BRADYKINESIA IN PARKINSON'S DISEASE AND PSYCHOMOTOR RETARDATION IN DEPRESSION: AN EXPERIMENTAL STUDY


Thirty newly diagnosed patients with Parkinson's disease showed motor and cognitive slowing, or bradyphrenia, on a computerised digit symbol substitution test, related to motor and cognitive impairment. Thirty patients with primary depressive illness showed comparable deficits, related to motor impairment. Retesting 12 of the Parkinsonian patients after treatment with dopaminergic agonists, and 12 of the depressed patients showed improvement in affective impairment. It is suggested that bradyphrenia in Parkinson's disease and psychomotor retardation in depressive illness are closely related and that impairment of dopaminergic systems may be involved in both.

BRADYKINESIA—A FAILURE OF COROLLARY DISCHARGES?

AP Moore. Institute of Neurological Sciences, Glasgow

The pathophysiological mechanism of bradykinesia is unclear. It is thought to be due to a failure of the basal ganglia to "execute" learned motor plans. This may be a purely motor abnormality but many authors have suggested that sensory features are important. This experiment was an attempt to distinguish between the two possibilities.

With eyes closed, patients with asymptomatic bradykinesia (1) matched the movements of one (guide) arm with the other arm and (2) matched the movements of both arms in self-guided actions.

Movements were active not passive, and were not rapid. Controls accurately performed both tasks. Patients regularly failed to match formal bradykinesia reference arm movements, even when the good arm was matching the more bradykinetic reference arm. The accuracy of matching was correlated with the symmetry of bradykinesia. Patients thus thought the bradykinetic limb moved further than it had.

Parkinsonian patients with drug induced unilateral dyskinesia, patients with idiopathic unilateral dystonia, and patients with weakness of one arm moved the abnormal limb further.

It is suggested that bradykinesia could be caused by reduction in corollary discharges, and dyskinesia and dystonia result from exaggeration of corollary discharges.

DYKINESIA IN MPTP-TREATED PRIMATES ON LONGTERM LEVODOPA THERAPY

CE Clarke, S Boyce, AR Crossman, MA Sambrook. Experimental Neurology Group, Medical School, Manchester

The administration of MPTP to non-human primates produces a Parkinsonian syndrome...
comparable to idiopathic Parkinson's disease in man. Using this animal model the effect of long-term levodopa administration has been examined, and, in particular, whether the complications of such treatment in Parkinson's disease can be reproduced. After 4-8 weeks treatment with therapeutic doses of levodopa all animals developed peak-dose choreiform movements affecting the lower limbs. Despite a constant dose regime over a further 6 months, the dyskinesia became more severe and extensive involving the upper limbs and face. A second group of MPTP-treated animals did not receive regular levodopa therapy and the severity of the Parkinsonian features remained stable over at least 6 months.

Since the Parkinsonian syndrome remained constant in the non-levodopa-treated animals, the onset and progress of dyskinesia in the treated animals must relate to levodopa treatment rather than disease progression. This confirms the results of clinical trials which suggest that the introduction of levodopa therapy in Parkinson's disease should be delayed and used at the lowest possible dose.

THE NATURAL HISTORY OF UNTREATED EPILEPSY
RDC Elwes, AL Johnson, EH Reynolds.
Department of Neurology, Kings College Hospital, London and MRC Biostatistics Unit, Cambridge

Recent studies suggest that the prognosis for newly referred epileptic patients treated with carefully monitored monotherapy is very good. What is lacking is any information about the natural history and prognosis of untreated epilepsy as, for ethical reasons, such studies have never been undertaken. A limited view of natural history can be obtained by detailed retrospective analysis of untreated seizures in patients referred for the first time to a hospital clinic. Of 281 patients with 2-5 untreated tonic clonic seizures the attacks can be accurately dated in 183 patients. Overall there was a progressive decline in seizure intervals between successive seizures. In only 20% of instances did the interval between any successive seizures increase. Our observations provide some support for Gowers' view that seizures may beget further seizures and for the need for early effective treatment.