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Platform Presentations

LOWER CRANIAL NERVE COMPRESSION SYNDROMES
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Objectives—To validate the causal significance of compression and the effectiveness and safety of microvascular decompression (MVD) in syndromes of the V, VII, VIII, IX and Xth cranial nerves.

Design—Clinical, neurological, and imaging assessment, including magnetic resonance tomo-angiography (MRTA),1 followed by MVD during continuous brainstem (auditory) monitoring.

Patients—110 patients with trigeminal neuralgia (TGN); 25 patients with hemifacial spasm (HFS); two patients with tinnitus; six patients with IX or X neuralgia; six patients with systemic hypertension (HBP).

Outcome—The quantitative effectiveness of MVD including morbidity data, has been established by questionnaire and interview over the 15 year study.

Results—6% of TGN recurred; 20% HFS was unrelieved or recurred; the two patients with tinnitus were satisfactorily relieved; five of the six patients with IX/X neuralgia were cured, and three of the six patients with HBP seemed improved.

Conclusions—Microvascular decompression is more effective than other existing methods in relieving symptoms and signs of lower cranial nerve compression syndromes with acceptable safety using diagnostic imaging and interoperative monitoring. Outcome measurement supports the compression as being significantly involved in achieving relief rather than this being simply due to nerve injury.

[SBNS]

RISK OF ACCIDENTS IN DRIVERS WITH EPILEPSY
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Between June 1992 and May 1993 a survey was undertaken of driving and accident experience in people with a history of epilepsy communicating with the DVLA. 24 000 questionnaires were issued as part of the routine relicensing of drivers at three year intervals, of which just over 17 000 were returned (response rate of 71%). In addition, 468 questionnaires were issued to drivers reporting recent seizures at the DVLA of which 291 were returned (response rate of 62%). The questionnaire used identical methods to a cohort of non-epileptic drivers carried out between 1990 and 1991 by the Transport and Road Research Laboratory (8888 drivers). Both surveys were retrospective and collected clinical data for three years before the survey.

The relative risk for involvement in any accident during this period was 0.95 (95% CI 0.88–1.02). However, the adjusted relative risk for involvement in an injury producing accident was somewhat raised in the epilepsy group 1.1 (0.91–1.3). The adjusted odds ratio for serious physical injury was 1.37 (1.02–1.84). In the epilepsy group there were 12 drivers involved in an accident resulting in a fatality, but none in the TRL group.

The factors that influenced the risk of accident rates were not dissimilar in the two groups, age, driving experience, and mileage being the most important. The absence of any seizure within the three year period of the survey halved the risk of involvement in an accident producing some form of serious physical injury or fatality. No other clinical factors in the epilepsy group seemed to influence accident rates. [ABN]

NEURAL TRANSPLANTATION BY ER HITCHCOCK: TREATING PARKINSON’S DISEASE BY GRAFTS OF FOETAL MESENCEPHALON AND STRIATUM
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Objectives—Experimental neurosurgical treatment of Parkinson’s disease.

Design—Since 1988, 55 patients with severe Parkinson’s disease (Hoehn and Yahr stage IV, V) have been treated at the Midlands Centre for Neurology and Neurosurgery by stereotactic implantation of brain tissue from spontaneously aborted human foetuses. Each implantation used a single cohort of second trimester (11–20 weeks post-gestational); grafts dissected 5–12 hours after foetal expulsion, disaggregated mechanically, and implanted as clumps (not as cell suspensions); there was no immuno-suppressive therapy.

Consecutive patients formed five series differing in site of implantation (caudate or putamen, unilateral or bilateral) and in nature of graft (foetal mesencephalon alone or with striatum).

In the final series (described here) grafts of foetal mesencephalon and striatum were implanted bilaterally into the head of the caudate nucleus.

Patients—Seven patients (Hoehn and Yahr stage IV, V) aged 46–62 years.

Results—All seven patients improved. There were very good group improvements, statistically significant (Wilcoxon), in a wide range of activities of daily living measures, clinical neurological, and timed motor tasks sustained throughout 18 months follow-up—with substantial reduction in need for dopaminergic medication.

Conclusions—Results were strikingly better than those of all four previous series, which used foetal mesencephalon alone. This experimental technique shows promise for treating Parkinson’s disease. [SBNS]

EN BLOC TEMPORAL LOBECTOMY V SELECTIVE AMYGDALOIDHIPPOCAMPECTOMY AS TREATMENTS FOR INTRACTABLE EPILEPSY DUE TO HIPPOCAMPAL SCLEROSIS
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Various surgical treatments for intractable epilepsy due to hippocampal sclerosis are recommended. It is uncertain which is most effective. Sixty nine patients with this condition were treated—50 by Falconer type en bloc temporal lobectomy (TL), 19 by selective amygdalohippocampectomy (AH). The two methods are compared. Of particular concern was seizure outcome and verbal memory loss after left operations. Eleven AH were transcortical via the middle temporal gyrus, and eight were trans-sylvian. Two years after operation 54% had not had any seizure since surgery; 23% had experienced only very occasional seizures (77% in Engel grades I + II). Thirty of 41 cases (73%) were seizure free five years after operation. Neither seizure outcome nor serious unwanted effects differed significantly according to type of surgery.

Two years after operation showed less verbal memory decline after left AH than after left TL. Left AH, but not left TL gave significant improvements in verbal IQ and non-verbal memory. Performance IQ improved in both groups. Postoperative MRI showed less temporal lobe white matter disruption after trans-sylvian AH than after the transcortical approach.

It is concluded that trans-sylvian AH is preferable to TL as a treatment for most cases of intractable epilepsy due to left hippocampal sclerosis and probably also that due to right hippocampal sclerosis. [ABN]

VOLUMETRIC MAGNETIC RESONANCE IMAGING (MRI) IN CHRONIC EPILEPSY
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Volumetric MRI enables detailed examination of cortical anatomy. An investigation into chronic epilepsy using MRI and post-processing techniques is being carried out.

Scanning patients with primary generalised epilepsy showed underlying structural abnormalities in six cases. Three had subependymal heterotopia and three hippo-campal asymmetry: one of these improved after temporal lobectomy. Reconstruction of
a three dimensional image of the cerebral hemispheres and comparison of the gyral patterns demonstrated with control subjects showed gyral abnormalities in 16 of 30 patients with normal MRI on inspection of routine two dimensional images, and additional gyral abnormalities in three of 18 patients with cortical dysgenesis observed on routine images. Analysis of the distribution of cerebral grey/white matter, by division of reconstructed objects into coronal 10ths, allows measurement of cerebral structure. The existence of structural abnormality beyond the visualised lesion was shown in 15 of 18 patients with cortical dysgenesis on routine imaging and in nine of 14 patients with lesions demonstrated only on reconstructed images. This supports the hypothesis that cortical dysgenesis is an extensive disorder. Block analysis has also shown structural disruption in patients with mental retardation and epilepsy with normal imaging and reconstruction.

Volumetric MRI is important in the investigation of epilepsy. Visual inspection of data alone is not adequate in cases where no lesion is found. [ABN]

IMPROVEMENT OF EPILEPSY AFTER STEREOTACTIC RADIOSURGERY FOR ARTERIOVENOUS MALFORMATIONS
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Objectives—Stereotactic radiosurgery (STRS) is primarily aimed at achieving thromboobliteration of arteriovenous malformations (AVMs). This study was carried out to evaluate the degree of amelioration in seizure activity observed clinically as an additional benefit after STRS.

Design—Telephone interview with patients and analysis of the prospectively maintained departmental database.

Patients—From over 1500 patients 269 had epilepsy; 149 were included in the analysis who fulfilled the following criteria: active epilepsy before STRS; follow up longer than two years; angiographic control.

Outcome measures—The patients classified the severity and frequency of their seizures subjectively into improved/no change/worse. A category of “no fits” was assigned to those with no seizures for a year.

Results—Fifty four per cent of patients became fit free and 29% had subjective improvement. The size of the AVM nidus and the radicality of the treatment plan affected the change in epilepsy. More than 50% of those whose AVMs were not obliterated reported worthwhile improvement in their epilepsy.

Conclusion—Improvement after STRS in epilepsy is a realistic expectation in most patients with AVM.

[SBNS]

11C-FLUMAZENIL PET AND VOLUMETRIC MRI IN MESIAL TEMPORAL LOBE EPILEPSY
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11C-Flumazenil PET has been used to compare extent of loss of benzodiazepine receptor density with volumetric MRI in patients with epilepsy due to mesial temporal sclerosis (MTS). 11C-Flumazenil binding has been shown to be reduced in MTS. To date, no studies have formally compared extent of loss of density with volumetric MRI and 3D 11C-Flumazenil PET changes. It is hypothesised that the reduction of hippocampal BZ/GABA-A receptor density in patients with MTS is over and above the loss of hippocampal volume.

Ten patients with MTS and pronounced unilateral hippocampal sclerosis were studied. 11C-Flumazenil PET Vd images were produced. These scans were co-registered with high resolution MRI. The hippocampus and neighbouring gyri were delineated on coronal MRI sections. Asymmetry indices were compared with 10 age matched normal controls. In all patients reduction of 11C-Flumazenil Vd correlated with the side of hippocampal sclerosis. On average 11C-Flumazenil Vd was reduced in the smaller hippocampus by 20%. Changes of BZ/GABA-A receptor density in the other hippocampus lay within normal limits.

In conclusion, there is a reduction of BZ/GABA-A receptor density in the hippocampus of patients with mesial temporal lobe epilepsy and above and over loss of hippocampal volume. This may be of importance in planning the extent of resection in patients with MTLE.

[ABN]

SEIZURE FUNCTIONAL OUTCOME ONE YEAR AFTER HEMISPHERECTOMY
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One year outcome data after hemispherectomy in 20 paediatric patients with severe medically intractable seizures is presented. Their average age at the time of surgery was 4.7 years (range 0.5 to 16) with an equal number of boys and girls. All patients had a preoperative hemi-inapropsia but they varied widely in their neurological disability. Two patients presented with episodic partialis continua. Preoperative electroencephalography and MRI localised the abnormality to a single hemisphere in all cases (9L, 11R).

A functional hemispherectomy was the preferred operation, but anatomic hemispherectomy was performed in three cases. Most had hemimegacephaly (five) or cortical dysplasia (six); the rest had a porencephalic cyst (four), Rasmussen’s encephalitis (two), Sturge-Weber syndrome (two), and a large extradural cyst (one). All patients tolerated their operation well, with no complications in the immediate perioperative period.

All of the patients have had at least a 75% reduction in seizure frequency and 16 are seizure free at 1 year (range 0 to 3.5 years). Three patients (15%) have required the placement of a ventriculoperitoneal shunt. There was worsening of motor function in two patients. The striking feature in most cases was the developmental improvement that occurred after surgery.

[SBNS]

SUBARACHNOID HAEMORRHAGE AND THE INFLAMMATORY CYTOKINE RESPONSE
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Introduction—There is evidence that the immune system is activated after aneurysmal subarachnoid haemorrhage (SAH). The proinflammatory cytokines IL-1α, IL-6 and TNF-α were measured in 10 patients who had had SAH.

Method—The in vivo cytokine response was monitored in eight patients by daily measurements of systemic concentrations in serum during their hospital stay. A whole blood endotoxin stimulation assay was also used for in vitro assay of cytokine in the same blood samples. This gave a measure of each patient’s total capacity to produce cytokines in response to a stimulus.

Results—All patients underwent craniotomy with clipping of the aneurysm. No systemic cytokine release was seen among this group, but the in vitro cytokine pattern during the postoperative period showed an upward trend in two patients, a downward trend in three, and a consistent oscillation of cytokine over several days in the remaining three patients. Interestingly, all patients showed a significant decrease in their ability to secrete TNF-α after operation (P < 0.05) with a highly significant corresponding increase in the two types of soluble TNF receptors TNFrp55 and TNFrp75 (P < 0.001). Similar findings were not seen for either IL-1α or IL-6.

Conclusions—These preliminary findings highlight an alteration of the physiological production of TNF-α and its receptors p55 and p75 after SAH.

[SBNS]

THE EFFECT OF CSF PROTEIN CONCENTRATION ON SUBSEQUENT SHUNT COMPLICATIONS: A PROSPECTIVE STUDY
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Objective—to assess the effect of the CSF protein concentration on subsequent shunt complications.

Design—a prospective clinical study comparing complications arising within two months of surgery to the peroperative CSF protein concentration.

Subjects—Ninety five patients undergoing shunt surgery (new insertion or revision) during a 15 month period. In total, 132 definitive shunt operations were performed. Most had meningitis (50) or cortical dysplasia (30); the rest had a porencephalic cyst (four), Rasmussen’s encephalitis (two), Sturge-Weber syndrome (two), and a large extradural cyst (one). All patients tolerated their operation well, with no complications in the immediate perioperative period.

All of the patients have had at least a 75% reduction in seizure frequency and 16 are seizure free at 1 year (range 0 to 3.5 years). Three patients (15%) have required the placement of a ventriculoperitoneal shunt. There was worsening of motor function in two patients. The striking feature in most cases was the developmental improvement that occurred after surgery.

[SBNS]
Assessment—Evidence of posterior column involvement, cord signals in MRI and/or severe compression in CT myelogram, and evidence of pathological lesions. Results—Numb-clumsy hand was associated with no objective posterior column involvement (clinical or EMG/NC study), with seven sensory findings on T2-weighted myelogram/MRI and cord signal on MRI and with pathological lesions: C3/4 spondylosis (19), C1/2 rheumatoid subluxation (five), tumours (two), and others (four).

Conclusion—Numb-clumsy hand was associated with high cervical (C1-4) lesions causing severe anterior central compression of cord and intrinsic cord signal on MRI, but minimal objective neurological signs. Pathogenic mechanisms are probably related to compression and disconnection of spino-cerebellar tracts.1,2


[SBNS]

FAMILIAL NON-SPECIFIC DEMENTIA MAPS TO CHROMOSOME 3

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A substantial minority of patients with presenile dementias lack distinctive inclusion bodies, plaques or tangles on pathological examination. Such dementias typically present with evidence of frontal lobe dysfunction and are probably the commonest cause of frontal lobe dementia. These dementias have been termed non-specific dementias (NSD). Cerebroplaque and spongiform change have a positive family history of dementia. Clinical and molecular genetic studies on the largest published family with NSD have been conducted. There are 20 affected patients in three generations. The disease is inherited in an autosomal dominant fashion. After running over 170 microsatellite probes and excluding 75% of the genome the disease locus has now been assigned to the pericentromeric region of chromosome 3.

Haplotype analysis shows a common region shared between all affected patients. The maximum pairwise lod score obtained was +4.2, multipoint analyses increased this to +5.8. The clinical studies show that paterally inherited cases develop the disease at a significantly lower age than their affected parent. This anticipation of the disease onset with paternal transmission suggests that the disease is produced by a trinucleotide repeat expansion mutation. Some other neurogenic diseases, including Huntington's disease, have now been related to such mutations. [ABN]

NEUROPSYCHOLOGY AND SPECT IN DIAGNOSIS AND STAGING OF ALZHEIMER'S DISEASE

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Given the advent of drug treatments for dementia of the Alzheimer type (DAT), it is important to develop more secure methods for diagnosis and staging. The role of neuropsychology and SPECT imaging in diagnosis and staging DAT in 33 patients with mild disease and 30 matched controls was studied. Working, episodic, remote, and semantic memory were assessed. Tc-HMPOA SPECT was analysed quantitatively to obtain measures of regional cerebral blood flow.

For diagnosis, the memory tests were highly discriminatory, with a canonical correlation coefficient of 0.975. The most useful test was delayed verbal recall; SPECT data were, by contrast, less useful. The group membership; 33% of patients had normal SPECT scans.

For staging, stepwise regression analysis using all memory tests could predict 79% of the variance in mini mental state examination scores. The measures most useful for staging were immediate, recognition, semantic, and autobiographical memory. SPECT data were again of less use in modelling severity of dementia. In a group of patients who used SPECT scans could be predicted from SPECT data.

Neuropsychology has been shown to be superior to SPECT both in diagnosis and staging DAT. Different memory tests are useful for diagnosis and staging: delayed verbal recall is the best discriminator, whereas immediate, recognition, autobiographical, and semantic memory, are of most use in staging severity. [ABN]

MITOCONDRIAL ENCEPHALOMYOPATHY WITH MULTIPLE MITOCHONDRIAL DNA DELETIONS: A REPORT OF TWO FAMILIES AND TWO SPORADIC CASES WITH UNUSUAL CLINICAL AND NEUROPATHOLOGICAL FEATURES


Most diseases associated with abnormalities of human mitochondrial DNA (mtDNA) occur either sporadically or show maternal inheritance. Recently, a mitochondrial myopathy associated with multiple deletions of mtDNA has been identified in pedigrees that show an autosomal dominant mode of inheritance. In this syndrome the mtDNA defect is presumed secondary to a nuclear gene mutation.

The first two British kindreds with this disorder and two sporadic cases, are reported. All patients had adult onset progressive external ophthalmoplegia and muscle weakness, with muscle biopsy appearances of a mitochondrial myopathy. Southern blot analysis of mtDNA digested with appropriate restriction enzymes shows a pattern consistent with multiple populations of mtDNA.

The cases exhibit, in addition, some unusual clinical features. They include pigmentary retinopathy and tremor; the last was levodopa responsive and associated with rigidity and micrographia in one family. One family and both sporadic cases have a neuropathy and nerve biopsy confirms the indication of an axonal neuropathy suggested from nerve conduction studies. Postmortem examination of one patient showed pronounced nigral degeneration, which is of interest in relation to the parkinsonism seen and the evidence of mitochondrial chain dysfunction in Parkinson's disease. [ABN]

OCCULOMOTOR FUNCTION IN MOTOR NEURODISEASE

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Although it is generally held that the oculomotor system is spared in motor neurodisease (MND), several recent oculographic studies of reflexive saccades and smooth pursuit in MND have yielded conflicting results. Oculomotor function was therefore studied in a range of paradigms, some of which are considered to involve the frontal lobes in their execution.

Eye movements in 17 patients with MND and 11 age matched normal controls were recorded with the scleral search coil technique. Smooth pursuit, fixation, and reflexive, remembered, and antisaccade paradigms were studied. Results were analysed for saccadic latency, peak velocity, gain, final eye position (FEP), antisaccade/remembered saccade error rates, pursuit peak velocity gain, and square wave jerk frequency. Reflexive saccades were unimpaired in patients with MND compared with controls. Error rates for both antisaccades and remembered saccades were elevated in the MND group (antisaccades: MND 31.9 (24-9)% control 10-3 (9-6)%, P = 0.004; remembered saccades: MND 30-8 (24-6)%, control 12-4 (14-4)% P = 0.02). Antisaccade and remembered saccade latencies were also prolonged (antisaccades: MND 376-9 (87-9) ms, control 30-3 (53-9) ms, P = 0.01; remembered saccades: MND 318-1 (74-9) ms, control 258-3 (43-76) ms, P = 0.02). Square wave jerk frequency was increased in patients with MND (MND 32-9 (18-0) ms, control 15-9 (6-0) ms, P = 0.007), but smooth pursuit showed no impairment.

These findings of prolonged volitional saccade latency and high distractability with greatest prefrontal impairment in MND, and are consistent with the results of recent neurophysiological, pathological, and PET studies. [ABN]
A STUDY OF THE CAUSES OF LATE FUNCTIONAL DETERIORATION AFTER PREVIOUS POLYOMIELITIS

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Many patients with previous poliomyelitis develop "postpolio syndrome" (PPS) in which late functional deterioration follows a period of relative stability. The frequency with which PPS can be attributed to clearly defined causes remains uncertain. A review of newly referred patients with previous poliomyelitis seen consecutively over a three year period was undertaken. There were 156 patients (51 men, 105 women, mean age 52 (range 17-80) years who had developed acute paralytic poliomyelitis at a mean age of 6 (0-5-42) years. Eighteen patients had been ventilated, and 124 had severe weakness during the acute illness. After recovery, 22 were wheelchair bound and 31 mobile with severe disability. 140 patients (90%) developed symptoms of functional deterioration at a mean time interval of 42 (17-76) years after the paralytic illness. Functional deterioration was associated with orthopaedic disorders in 125 cases, neurological disorders in 16, respiratory disorders in 12, and others in 13. Treatment of bone and joint abnormalities including surgery (26 cases) and provision of orthotic appliances (70 cases) with physiotherapy, was associated with functional improvement in 90% of those followed up. Other treatments included weight loss, ventilatory support, and pain relief. In this series progressive postpolio muscular atrophy was not noted. Functional deterioration was common and associated with orthopaedic, neurological, respiratory, and general medical factors which are potentially treatable.

[ABN]

A COMPREHENSIVE CLINICO-EPIDEMIOLOGICAL STUDY OF IDIOPATHIC GENERALISED EPILEPSIES WITH ABSENSES IN ADULTS

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Eighty five patients over 16 years of age with typical absences (TAs) were studied. All had EEG confirmation, and 47% had additional video-EEG documentation of TAs. Prevalence of TAs was similar among adults with epilalesies and 63% among idiopathic generalised epilepsies (IGE).

The clinico-EEG manifestations of absences were syndrome related. 30 patients had juvenile myoclonic epilepsy; all had mild absences and myoclonic jerks on awakening, and all but two had generalised tonic-clonic seizures (GTCS). 10 patients had juvenile absence epilepsy; all had severe absences and all but one GTCS. 11 patients had epilepsy myoclonia with absences, a syndrome characterised by eyelid myoclonia with absences, and photosensitivity. Seven patients had parietal myoclonia with absences, a syndrome characterised by TAs associated with atypical rhythmic perioral myoclonia. Four patients had predominantly photo or pattern induced TAs. Twelve of the remaining patients, showed remarkably similar clinicosepolar patterns, which were not fortuitous. A new syndrome characterised by "phantom absences" and GTCS, is proposed. The name "phantom absences" has been coined to denote TAs that are so mild that they are inapposusive to the patient and invisible to the observer. Absences in adults constitute a diagnostic challenge to physicians and have important implications in the syndromic classification and management of patients.

[ABN]

EFFECT OF SURGICAL REPAIR ON PAIN RELIEF AFTER BRACHIAL PLEXUS INJURY IN ADULTS

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The characteristic pain after root avulsion begins within weeks of brachial plexus injury in adults, and persists for many years, still being severe in 25% of patients after four years. Surgical treatment of avulsion injuries led to preliminary observations that the surgery accelerated resolution of pain. This study examined the effect of surgery—nerve grafts and anastomoses—on the duration and severity of root avulsion pain. 487 patients were studied prospectively over 10 years with preganglionic root avulsions alone or in combination with postganglionic ruptures or lesions in continuity (LIC). They were compared with pure ruptures and pure LIC. In the avulsion group, pain was reduced substantially at an average time of 175 days, after grafting or of orthotic appliances (70 cases with 68 days for the pure rupture group and 58 days for the pure LIC group. Of the 39 pure avulsion patients, only three reported no improvement in their pain 20 months after surgery, and several had median times for improvement being 120 days. These findings support the view that nerve repair accelerates pain amelioration after brachial plexus injury. Pain resolution usually preceded recovery of motor or sensory function.

[ABN]

REGIONAL CEREBRAL BLOOD FLOW DURING POSTERIOR SEIZURES: AN HMPAO SPECT STUDY

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Ictal HMPAO SPECT was used to study five patients whose clinical and surface video EEG data indicated seizure origin in the area of the temporoparieto-occipital junction (TPOJ). Three patients had structural lesions in the area of TPOJ, and HMPAO injection was carried out from 30-120 seconds from clinical seizure onset. Acquisition was carried out with a Strichmann 810 dedicated head imager.

Ictal SPECT showed perfusion deficits in keeping with anatomical lesions in three patients, hemispheric hyperperfusion on the side of electrical seizure origin in a fourth, and was normal in a fifth. Ictal images showed hyperperfusion in the area of the TPOJ in all five patients. This hyperperfusion extended anteriorly into the ipsilateral lateral temporal cortex and pole, with hyperperfusion of a lesser degree in the ipsilateral mesial temporal cortex, and ipsilateral hyperperfusion of the basal ganglia in two patients. In two patients there was ictal hypoperfusion of the rest of the ipsilateral hemisphere. Measured as a change in asymmetry index with respect to the ictal image, ictal hyperperfusion was most pronounced at the TPOJ in all five cases.

It is concluded that ictal SPECT shows distinct patterns of perfusion in TPOJ seizures, and can distinguish them from mesial temporal seizures.

[ABN]

EYELID MYOCLOMIA WITH ABSENSES: A CLINICAL AND VIDEO-EEG STUDY IN ADULTS

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Eyelid myoclonia with absences (EMA) is an idiopathic generalised epilepsy (IGE) syndrome, manifested by eyelid myoclonia associated with brief absences (AEDs) 98% of whom had refractory seizures, and those who had not received treatment (n = 140).

The overall mideagnosis rate was 26-1% (46/184) with inadequate history taking and misinterpretation of EEG equally responsible, 19/40 reported side effects from AEDs while unnecessary driving restrictions and employment difficulties were encountered by 12/33 and 5/33 respectively. Of those labelled "refractory epilepsy", 12 did not have epilepsy and 41 were rendered seizure free by significantly improved by optimal use of AEDs or surgery. Diagnosis of "funny turns" was usually achieved on clinical grounds alone except in patients with pseudoseizures. AEDs and in whom required investigation to refute the diagnosis of epilepsy. These data show suboptimal diagnostic and management services for patients with "funny turns" and epilepsy respectively and provides a strong case for expansion of specialist services and open access to multidisciplinary epilepsy clinics.

[ABN]

DIAGNOSIS AND MANAGEMENT OF EPILEPSY AND "FUNNY TURNS" IN A SPECIALIST CLINIC

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Patients with "funny turns" are often referred to neurologists with a previous or possible diagnosis of epilepsy. This study was designed to assess the frequency of factors contributing to and the consequences of an erroneous diagnosis of epilepsy, the outcome of patients referred with "refractory seizures", and the relative roles of clinical acumen and investigations in establishing the cause.

A retrospective analysis of the case records of 324 patients was conducted. The sample was divided into those exposed to antiepileptic drugs (AEDs) (n = 184), and those who were seizure free or refractory seizures, and those who had not received treatment (n = 140).

The overall mideagnosis rate was 26-1% (46/184) with inadequate history taking and misinterpretation of EEG equally responsible, 19/40 reported side effects from AEDs while unnecessary driving restrictions and
IGE with absences. There were 11 patients with EMA, all female, with a mean age of 30-9 years. Reported onset of absences was at a mean age of 7-8 years. Eyelid myoclonia with absences was confirmed with video-EEG in 10 patients. The seizures consisted of eyelid myoclonia alone or preceding brief (3-6s) absences. Ictal clinical and EGG manifestations occurred mainly after eye closure and were inhibited by total darkness. Only five patients showed photoparoxysmal responses as adults, although all had a previous clinical and/or EGG documentation of photosensitivity. None of the patients had self-induced seizures. Infrequent generalised tonic-clonic seizures occurred in 10 patients, and were precipitated mainly by lights, sleep deprivation, fatigue, and menstruation. Mild myoclonic jerks of the upper limbs occurred in six patients. Eyelid monoclona with absences is often resistant to medication and persists into adult life.

[ABN]

MEDULLOBLASTOMA: HAS THERE BEEN ANY IMPROVEMENT IN FIVE YEAR SURVIVAL OVER THE PAST 20 YEARS?
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The large number of cases of medulloblastoma seen at Great Ormond Street allows a unique opportunity to view longitudinally the effect that modern methods of investigation and treatment have on the prognosis. A cohort of cases treated over a 10 year period for whom a five year follow up was available (1980-9) have been analysed. Eighty children were admitted during this time, of whom 75 went on to receive radiotherapy and/or chemotherapy (operative mortality 5%). Forty patients were alive and 38 disease free at five years after diagnosis—90% of those with favourable prognostic features (no peripheroperative spinal metastases, radical surgery) and 10% of those without. Comparison with an earlier cohort of cases from this institution (1965-74) gives the following information.

1 Modern methods of investigation and treatment have clearly improved the outlook for patients with medulloblastoma—but the greatest advance remains the changes to radiotherapy regimes introduced in the 1960s. It is suggested that there is unlikely to be any further dramatic improvement until radical changes can be made in either the chemotherapy regimes (for example, high dose chemotherapy with bone marrow rescue) or in immunological or gene mediated therapies.

[SBNS]

BLOOD TRANSFUSION AND SURVIVAL FROM INTRINSIC SUPRAVENTRICAL HIGH GRADE GLIOMAS
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Objectives—To measure the influence of blood transfusion on survival in patients with intracranial gliomas.

Design—Prospective data were examined from 175 patients who had entered EORTC glioma studies. Transfusion data were collected retrospectively from case records. Patients—All patients were over 16 years old, steroids had been stopped by the 10th postoperative day, survival was expected for more than eight weeks, and all had similar courses of radiotherapy.

Outcome measures—Survival was established by telephone interview of the next of kin.

Results—Hazard ratios of factors affecting survival were calculated by a series of Cox regression models. Variables significantly affecting survival were age (P = 0.0016), pathology (P = 0.0075), and tumour location (P = 0.0075). After adjustment, Karnovsky index, tumour resection, or adjuvant treatment had no significant effect on survival. Blood transfusion was a significant protective factor for glioblastoma with a hazard ratio of 0.38 (95% confidence intervals 0.22-0.67), had no effect for anaplastic astrocytoma 1.70 (0.54-9.4), and was a risk factor for other pathologies 4.56 (0.97-21.35). The different risk between these groups is highly statistically significant (P = 0.0003).

Conclusions—In this group of patients transfusion improved survival from glioblastoma. Suppression of cell mediated immunity is known to occur in patients with glioblastoma similar to that seen in AIDS; further modulation by transfusion may play a part in improving survival.

[SBNS]

AN ECONOMIC ARGUMENT IN FAVOUR OF ENDOSCOPIC THIRD VENTRICULOSTOMY AS A TREATMENT FOR OBSTRUCTIVE HYDROCEPHALUS
HS Ching, P Barlow. Southern General Hospital, Glasgow, UK

Objectives—To examine the health resource implications of performing endoscopic third ventriculostomy as an alternative to CSP shunting in appropriate patients.

Design—A retrospective study of case records and radiographs of patients shunted de novo at the Institute of Neurological Sciences, Glasgow for the two year period 1990-1.

Outcome measures—The number of repeat operations and extra days in hospital required due to shunt complications compared with the predicted extra operations and days in hospital for patients suitable for endoscopic third ventriculostomy.

Results—One hundred and fifty new shunts were inserted in the two years. Of these, 23 patients (15%) were judged suitable for endoscopic third ventriculostomy as an alternative to CSP shunting. Eight out of 23 patients required a total of 29 repeat operations and an extra 230 days in hospital due to shunt complications. Assuming an 80% success (shunt free) rate for endoscopic third ventriculostomy, nine operations and 74 bed days per year could be saved by using this technique.

Conclusions—In units undertaking a large number of CSF shunt insertions, investment in neuroendoscopic equipment has the potential to release significant resources for other uses.

[SBNS]

VINCISTINE AND CARBOPLATIN TREATMENT FOR PROGRESSIVE LOW GRADE ASTROCYTOMA OF BRAIN
MS Ashraf, P May, H McDowell. Royal Liverpool Children's Hospital, Liverpool, UK

Five children (age range 4 months to 8 years and 4 months), with progressive low grade astrocytoma (grades I and II) were treated with weekly vincristine (1-5 mg/m²) and carboxplatin (500 mg/m²), every 3-4 weeks. Response in terms of either reduction in tumour size or progression of disease, was achieved in all cases. The follow up period is 20 to 10 months (mean seven months). Initial response suggests combination chemotherapy with vincristine and carboxplatin is effective in holding the disease and delaying the use of radiotherapy particularly in younger children.

[SBNS]

EVALUATION OF MICROENVIRONMENTAL HYPOXIA OF BRAIN TUMOURS: MODIFYING FACTORS
GS Cruickshank, R Duckworth. Institute of Neurological Sciences, Glasgow, UK

Objectives—To assess the impact of PaCO₂ and blood pressure on oxygenation of human brain tumours at operation measured by dynamic stepping microphotography and microelectrode Doppler.

Design—The stratification of patients based on the oxygen profile of their intracranial
tumours may allow assessment of the impact of chemical modifiers on radiation sensitivity.1 Characterisation of factors that influence intracranial tumour hypoxia, is therefore important. The question is whether the effect of altered arterial PaCO₂ and blood pressure on cerebral blood flow and brain oxygenation devalue the significant level of hypoxia recorded in these tumours at operation.

Subjects—Twenty anesthetised animals were ventilated at an FiO₂ of 0.25-0.3, and end tidal CO₂ and PaCO₂ were monitored. The Eppendorf PO₂ histogram probe was used to measure PO₂ profiles in tumours in these patients. Concurrently, microdoppler Doppler flow measurements were made from brain, brain around tumour and tumour.

Conclusions and results—Alteration in PO₂ indices and variations in erythrocyte flux were assessed in response to a fixed change in PaCO₂ or mean arterial blood pressure; for reproducibility and reversibility of effect, altering the PaCO₂ from 37 mm Hg to 31 mm Hg and back resulted in a reversible fall in median tumour PO₂ of 4-2 (0-4) mm Hg, and in PO₂ levels less than 2-5 mm Hg from 26-3% to 46-5%. Changes in micro-regional blood flow (erythrocyte flux) recorded in the tumour, peritumoural area, and distant brain illustrate a pronounced impairment of reactivity in the peritumoural area. Conclusions—Altering PaCO₂ has a reproducible impact on tumour PO₂ that may be due to direct or shunting effects on cerebral circulation. The tumour ApO₂/PaCO₂ seen is less than that for normal brain and does not overlap with tumour PO₂ data from extracranial tumours, suggesting that hypoxia in intracranial tumours may be an important factor in their resistance to treatment. Multichannel microdoppler techniques used in conjunction with tissue oxygen measurement allows the factors controlling tumour hypoxia to be evaluated and possibly manipulated therapeutically.


SAFE NEUROSURGERY? AN AUDIT OF ACOUTIC NEUROMA SURGERY IN A SMALL NEUROSURGICAL UNIT

PJ Kane, B Gendeb, M Hawthorne, FP Nait, Middlesbrough General Hospital and North Riding Infarmary, Middlesbrough, UK

Aims—to audit the results of acoustic neuroma surgery in a neurosurgical unit with small caseload and compare and publish outcomes to compare with published standards of outcome.

Design—Retrospective study of 64 patients with acoustic neuroma operated on by a single neurosurgeon and neurootologist in the period 1986–94. All patients were operated on by the suboccipital retromastoid approach. Peroperative facial nerve monitoring became available in 1992. Specific audit protocol was kept, mortality, postoperative CSF leak; postoperative facial nerve function at six months; and hearing preservation.

Results—Nine per cent of patients were referred by otorlogists, the remainder from neurologists, general physicians, or general practitioners. Two patients (3%) died after surgery. Both had large tumours (>5.5 cm).

Five patients (8%) developed CSF leak that was treated operatively in four and by spinal drainage in one. All patients with small tumours (<10 mm) had good recovery of facial nerve function (House-Brackmann grade I/II). 27% of patients with medium sized tumours (11–25 mm) and 33% of patients with large tumours (>26 mm) had a facial palsy. Ten patients had some preserved hearing on the affected side at the time of their presentation. Postoperatively four were deaf, three had retained non-useful hearing, and three had retained useful hearing.

Conclusions—Five patients compare favourably with published data. Acoustic neuroma surgery can be performed safely in a small neurosurgical unit. [SBNS]

COMPLICATIONS OF SKULL BASE GLOMUS TUMOR SURGERY: 10 YEARS OF OTONEUROSURGICAL EXPERIENCE

PC Whitfield, DA Moffat, DG Hardy, Addenbrooke's Hospital, Cambridge, UK

Objectives—to review and evaluate the management and outcome in patients undergoing surgery for skull base glomus tumours.

Design—Retrospective analysis of all patients with large skull base glomus tumours treated by combined otoneurosurgery during a 10 year period.

Subjects—Fifteen patients with glomus jugulare tumours, three patients with glomus vagale tumours, and one patient with a glomus hypoglossus.

Outcome measures—(a) Performance of additional procedures and complications. (b) Functional outcome on a disability scale at long term follow up.

Results—An infra/transtemporal approach (n = 15) for Fisch grade C and D tumours, or a tympanomastoid approach (n = 4) for Fisch grade B tumours was performed. The facial nerve was transposed in 12 patients (63%). Cranial nerves were necessarily transected in eight cases (42%); in six of these preoperative signs of cranial nerve involvement were evident. Ten patients (53%) underwent surgery to treat complications; teflon injection of vocal cord (n = 5), tarsorrhaphy (n = 3), and one patient who underwent re-exploration (n = 3), surgery for facial palsy (n = 2), thyroplasty (n = 2), ventriculoperitoneal shunt (n = 1), and squint surgery (n = 1). At long term follow up (mean 3-24 years) 68% of patients had an excellent functional outcome, 11% a good outcome, and 21% a fair outcome.

Conclusions—Most patients with a pre-existing lower cranial nerve palsy adapt to intraoperative cranial nerve transection extremely well. A multidisciplinary team is required to achieve optimal results in patients with these complex skull base tumours. [SBNS]

RADIO-SURGERY / STEREOTACTIC RADIOTHERAPY FOR SOLITARY BRAIN METASTASES: A NON-INVASIVE ALTERNATIVE TO SURGERY

M Bradfield, RE Wurm, AP Warrington, RW Laing, S Sardelli, F Hines, JD Graham. Royal Marsden Hospital and Institute of Cancer Research, London, UK

Fifty two patients with 57 solitary brain metastases (one to two lesions) were treated with stereotactic radiotherapy/radiosurgery (SRT) with or without whole brain irradiation (WBRT). Twenty nine patients received SRT as primary treatment. Twenty three patients were treated for recurrence after surgery and WBRT and after WBRT alone. The SRT dose was 20 Gy in two fractions in most patients prescribed to the 90% isodose. The target volume encompassed the enhancing tumour and a 2 mm margin.

Local progression free survival (PFS) was 61% at one year (27 months median PFS) and the median survival was seven months. Most patients had a functional improvement as measured by the Barthel index. Neurological deterioration was noted in two patients within one month of SRT.

The results of SRT in patients with solitary brain metastases in terms of local control and survival seem equivalent to neurosurgical excision; SRT is a useful palliative treatment—it is well tolerated, non-invasive, and outpatient based and is particularly of value in patients whose survival is determined by the systemic course of disease. The role of WBRT in combination with SRT remains to be defined. [SBNS]

INCIDENCE OF BRAIN METASTASES AND RELATION TO SYSTEMIC TUMOUR SITES

R Grant, D Collie. Western General Hospital, Edinburgh, UK

There are no good epidemiological studies of brain metastases in the United Kingdom. The incidence of brain metastases in the Lothian region, the frequency of single metastasis and metastases of unknown primary, and the clinical relations with primary site were examined.

Frequency of intracranial tumour (1989–1990) in the Lothian region, identified by examining all CT reports from the three scanners that cover SE Scotland, supplemented by multiple cross referenced cancer registration and neurological databases. Case records were retrieved and patient data analysed.

One hundred and eighty four people with brain metastases were identified (incidence: 12-6/100 000 pop/year). Brain metastases accounted for 46.5% of all intracranial tumours; 37% of brain metastases were single; 34% of patients had no history of systemic malignancy at neurological presentation and no systemic treatment was ever identified in 15% (27). Lung (104), breast (22), melanoma (14), GI tract (seven) and renal (four) were the most commonly identified primary sites. All patients with brain metastases from breast and GI tumours and 13 with melanoma, had a history of malignancy before neurological presentation. This provides useful clinical information for investigating patients with brain metastases. [ABN]

EFFECTS OF ARTERIOVENOUS MALFORMATIONS ON CORTICAL ORGANISATION: IMPLICATIONS FOR SAFETY OF REXFUSION

GM McKhann II, JM Eskridge, DL Silbergeld, AB Harris, GA Ojemann, HR Winn. University of Washington, Seattle, USA

Objectives—Preoperative and intraoperative functional mapping can be used to identify the Rolandic and language cortex in patients
with arteriovenous malformations (AVMs) near essential cortex. Using these techniques to facilitate safe excision of AVMs, the impact that these lesions have on cortical organisation has been studied.

**Design**—Utilising preoperative superselective amobarbital (WADA) testing and intraoperative stimulation mapping, the topographical organisation of functional cortex in patients with AVMs was investigated.

**Patients**—Thirty-eight consecutive patients with AVMs near essential functional cortex were evaluated.

**Results**—Individual variability exists in the topographical location of sensory and motor cortex, and variability may be essential for language function in patients with AVMs. Most patients with AVMs reorganise functional cortex into atypical topographical configurations by displacing Rolandic and/or language cortex. Two patients were found to have motor cortex located within AVMs.

**Conclusions**—There are variations and plasticity of human cortical organisation in patients with AVMs. Most AVMs displace functional cortex and can potentially be safely resected. Preoperative superselective WADA testing and/or intraoperative stimulation mapping are recommended for lesions near eloquent cortex to determine those that may be resectable.

**“DYNAMICS” OF INTRACRANIAL ANEURYSMS DEMONSTRATED BY COLOUR TRANSCRANIAL DOPPLER ULTRASOUND**

J M Wardlaw, J Cannon. University of Edinburgh, Edinburgh, UK

It is possible to demonstrate intracranial aneurysms and AVMs using directionally sensitive conventional colour transcranial Doppler ultrasound (CDU), which has been available for several years. A recent development of colour Doppler technology “colour Doppler energy” (CDE) or “power Doppler” is considerably more sensitive to flowing blood. This technique has been applied to the detection of intracranial aneurysms in patients presenting with subarachnoid haemorrhage (SAH).

As many patients as possible presenting to our regional neurosurgical service with recent SAH (either CT or LP proved) were assessed by colour transcranial Doppler, using the temporal bone windows, blind to the result of angiography although not to the distribution of blood on CT.

Thirty-nine patients have been examined so far (mean age 50), the first nine with CDE and the last 30 patients with CDE. Aneurysms were recognised as an area of colour where no normal artery was expected, and on CDE by apparently greater “pulsatility” than normal arteries during the cardiac cycle. CDE reduced the proportion of patients with a poor bone window (10% with CDE and 33% with CDU) and CDE detected 26 of 29 aneurysms demonstrated angiographically (90%), whereas CDI only detected 55%. In five patients who underwent aneurysm coiling it was possible to see the coil being inserted into the aneurysm and to measure the residual neck with CDE. The mean change in aneurysm cross sectional area between systole and diastole was 49% (± 2.4 cm²) and in the cross sectional area of an adjacent normal artery was 18% (± 2.20); mean of difference —30.8%, 99% CI —60 to —2%. CDE is an appreciable improve ment in colour TCD technology. Further evaluation is required to see whether aneurysm “pulsatility” could be used as an indicator of impending rupture. [ABN]

**SERUM LIPOPROTEIN (A) CONCENTRATIONS IN FAMILIAL CEREBROVASCULAR ANEURYSM C Bolger, JP Phillips, Beaumont Hospital, Dublin, Eire and Walton Hospital, Liverpool, UK

Objectives—To investigate serum lipoprotein (A) (Lp(a)) concentrations in patients with familial cerebrovascular saccular aneurysms.

**Design**—Case identification from family history of patients admitted with proven subarachnoid haemorrhage. In the secondary to saccular cerebrovascular aneurysm. Patients with two or more first degree relatives with proved aneurysmal subarachnoid haemorrhage were recruited. They were screened with cerebral angiography and fasting serum Lp(a) was measured.

**Patients**—To date 15 patients (siblings) from two families had been identified (eight males and seven females, mean age 37 (10.2) years.

**Outcome measures**—Serum Lp(a) concentrations in relation to the presence or absence of saccular aneurysm.

**Results**—Four patients died from subarachnoid haemorrhage before enrolment into the study; one patient refused investigation. Of the remaining 10 patients: seven had asymptomatic aneurysms identified on cerebral angiography. Six of these patients had serum Lp(a) concentrations above normal (> 30 mg/dl; mean SD) 54.7 (11.8 mg/dl). Two patients had normal cerebral angiograms and the Lp(a) in both patients was normal (10 and 25 mg/dl). In the remaining patient (with an Lp(a) concentration of 64 mg/dl) angiography was incomplete.

**Conclusions**—There is evidence of an association between raised serum concentration of Lp(a) and cerebral aneurysms.

**A MAGNETIC RESONANCE SPECTROSCOPIC STUDY OF PARKINSONISM RELATED TO BOXING**


Proton magnetic resonance spectroscopy, localised to the lentiform nucleus, was carried out in three ex professional boxers who developed a parkinsonian syndrome, six patients with idiopathic Parkinson's disease and in six age matched controls. The three boxers all showed a pronounced reduction in the absolute concentration of N-acetyl aspartate (NAA), compared with the patients with Parkinson's disease and the control group. This reduction is likely to reflect neuronal loss occurring in the putamen and globus pallidus, and supports the hypothesis that the extra pyramidal syndrome, which occurs in ex boxers, is distinct from idiopathic Parkinson's disease. These findings will be related to the existing literature on post traumatic Parkinson's syndrome. [ABN]

**IMPLEMENTATION OF HEAD INJURY GUIDELINES: WHERE ARE WE AFTER TWO CYCLES OF A REGIONAL GUIDELINE**
P Pickard, S Jackson, J Addison, P Smielewski, HK Richards. University of Cambridge, Cambridge, UK

Guidelines for the management of head injuries have been widely adopted but may not be followed in practice.1 A criterion based audit was conducted in the eight district general hospitals in our region to assess the quality of documentation, investigation, and care of patients with head injury. First cycle (1 October 1992–31 March 1993)—4789 patients’ notes (1458 admitted) were examined and those that did not meet the guidelines were peer reviewed anonymously in each hospital. Documentation was poor (no record of GCS 52%, BP 37%, or skull radiograph 75%). Failure at peer review for skull radiograph, admission and/or CT criteria was 12% (range 8–15% between hospitals); under investigation 10%, over investigation 2.4%. Second cycle (1 December 1993–28 February 1994)—a structured head injury head proforma was introduced in October 1993.1 A total of 2718 notes (786 admissions) were audited and peer reviewed. Documentation improved by 37% to 90% (P < 0.001). Overall failure for skull radiograph, admission, and/or CT criteria was not significantly reduced (13%; range 10–19%). Over-investigation was reduced from 11% to 1% (P < 0.001). Failure at peer investigation increased from 10% to 12% (P < 0.001).

**Conclusion**—Improvement in documentation and provision of a “structured” proforma have not yet improved the implementation of guidelines agreed by regional consensus.

1 Suggestions from a group of neurosurgeons.


**ASSESSMENT OF THE GLASGOW HEAD INJURY OUTCOME PREDICTION PROGRAM**

JJ Nissen, PA Jones, DF Signorini, JD Miller. Western General Hospital, Edinburgh, UK

Objectives—To compare the predicted actual outcome after head injury using the Glasgow head injury prediction program,3 and to determine how often predictions were available.

**Design**—Retrospective data (1989-94) from 325 patients with severe head injury, haematoma requiring evacuation and/or coma >6 hours, were collected to the Glasgow outcome scale (GOS) scores at six to 24 months follow up. The program calculates the probabilities of death/vegetative state (GOS 1 or 2), severe disability (GOS 3 or 4) and disabled recovery (GOS 4 or 5) on admission after severe injury, before evacuation of acute haematoma, or at 24 hours, three days, or seven days after coma. Results: predictions were possible in 77%, 19%, 19%, 34%, and 53% of “suitable” patients at admission, operation, 24 hours, three days, and seven days respectively. Paralysis/ventilation meant that predictions were often unattainable and only from 15% of those “suitable” at admission, to 76% at 24
hours. Seventy four per cent of predictions were correct (highest probability), 16% pessimistic, and 10% optimistic. Of those patients whose eventual outcome was either GOS 4/5 or GOS 1, 84% were correct; for those GOS 3, only 12% were correctly predicted. Of 64 pessimistic predictions, 48% were predicted to die or be vegetative, but actually achieved a moderate or good outcome.

Conclusion—The Glasgow head injury prediction program can be a useful adjunct in clinical decision making in some head injured patients.


[SBNS]

OUTCOME IN CHILDREN WITH SEVERE HEAD INJURY: IMPORTANCE OF CEREBRAL PERFUSION PRESSURE
PJ Kane, IR Chambers, A Davidson, L Treadwell, N Tod, A Jenkins, PJ Crawford, RP Sengupta, AD Mendelow, Newcaste General Hospital, Newcastle-upon-Tyne, UK

Objectives—To determine what factors may be important in predicting outcome after severe head injury in children.

Design—Retrospective study of 50 children (age ≤16) with a severe head injury (Glasgow coma score on admission to the neurosurgical unit ≤8) who required intracranial pressure (ICP) monitoring as a routine part of their management. Mean arterial blood pressure, ICP, and cerebral perfusion pressure (CPP) were measured continuously. Outcome was determined at six months with the Glasgow outcome scale. Independent outcome is defined as those children who made a good recovery or were moderately disabled.

Results—Nine patients died. In the remainder the outcome scores at six months after injury were: seven severely disabled; 12 moderately disabled; 22 good recoveries. Glasgow coma score on admission, injury severity score, and average maximum ICP were not reliable predictors of outcome. As with a previous study,1 higher values of average minimum CPP were associated with a better outcome: good recovery 58.5 ± 3.9 mm Hg; moderately disabled 58.4 ± 2.5 mm Hg; severely disabled 44.5 ± 4.3 mm Hg; dead 45.3 ± 16.2 mm Hg. Average minimum CPP values >50 mm Hg were associated with a significantly greater chance of independent outcome (2P < 0.05).

Conclusion—This study points to the importance of CPP as a determinant of outcome after severe head injury in children.


[SBNS]

LABORATORY TESTING OF THREE INTRACRANIAL PRESSURE MICROTRANSUDERS
M Czosnyka, Z Czosnyka, JD Pickard.
University of Cambridge, Cambridge, UK

Three comparably priced ICP microtransducers have become available on the United Kingdom market, each characterised by their manufacturer as having very low zero drift over long periods, an excellent frequency response, and a low measurement error. The three microtransducers, coded A, B, and C, were examined in the pressure flow test rig designed for assessment of hydrocephalus transducers, all manufactured with their manufacturer’s specifications, giving high quality readings under test conditions. Some differences were noted, however, at 24 months where transducer A had 6 mm Hg and C had the lowest. The temperature drift was very low in B and C but A had a drift of 0.27 mm Hg°C; A had a static error of less than 0.3 mm Hg, B of less than 2 mm Hg, and C had an error of 0.6 mm Hg. The limits of the frequency response were not detectable in A and B (band width wider than 50 Hz), whereas C had a band width limited to 18 Hz.

Conclusion—Transducer B scored the best overall but all three behave satisfactorily on bench testing. The use of each transducer in everyday clinical practice requires evaluation.

[SBNS]

A PROSPECTIVE COMPARISON OF SUBDURAL FIBROEPITIC AND FLUID FILLED SINGLE LUMINUM BOLT PRESSURE TRANSUDERS IN VENTILATED PATIENTS
S Bavetta, JC Sutcliffe, P Chumans, OCE Sparrow, PJ Hamlyn. The Royal London Hospital and St Bartholomew’s Hospital, London, UK

A clinical comparison was made between subdural fibroepithelial and fluid filled subdural pressure transducers in ventilated patients with head injury. Twelve patients had both devices inserted in neighbouring sites. In two patients there were obvious technical problems with the fibroepithetic system and the results were therefore excluded from further analysis. In the remaining 10 patients 2167 pairs of simultaneous recordings were made for up to nine days and the degree of correspondence studied. A quarter of paired readings differed by more than 5 mm Hg. Neither device showed a predisposition to reading either higher or lower than the other, but in individual patients there was often a consistent bias. The proportion of closely corresponding readings tended to diminish after four days, and when either device registered a very high or low value. Clinically relevant episodes, defined as a reading of over 20 mm Hg by only one of the two monitors, occurred 221 times with both systems equally likely to produce higher readings. Differences in treatment would be likelier if such values occurred on consecutive occasions, which happened, on averaged age, about every 30 hours. The relative accuracy of the two devices remains uncertain, but there is evidence suggesting that both are prone to errors.

[SBNS]

EVIDENCE OF SMALL VESSEL CHANGES CAUSING ISCHAEMIA AFTER SUBARACHNOID HAEMORRHAGE
JG Rowe, N Soper, R Ouwerkerk, RSC Kerr, B Rajagopalan. MRC Spectroscopy Unit and the Radcliffe Infirmary, Oxford, UK

Objective—To follow cerebral blood flow (CBF) with single photon emission computed tomography (SPECT), metabolism with phosphorus magnetic resonance spectroscopy, and vasospasm with angiography and transcranial Doppler (TCD), in a 62 year old woman with subarachnoid haemorrhage from a right middle cerebral artery (MCA) aneurysm.

Results—On day 3, she was well. Spectroscopy on the right showed acidosis (pH 6.5–5) suggesting anaerobic metabolism, but was normal contralaterally (pH 7.01, control mean 7.02 (SD 0.01). On day 6, she became drowsy and confused. Spectroscopy showed decreased high energy phosphates, suggesting cell death. SPECT showed pronounced hypoperfusion of the right frontal lobe (CBV relative to cerebellum 0.58 (SD 0.03 right), 0.87 (SD 0.02) left). There was no TCD evidence of vasospasm (right MCA velocity 49 (SD 1) cm/s, left 35 (SD 2), controls 58 (SD 2). Angiography (day 7) did not show vasospasm.

Aneurysm clipping was complicated by rebleeding, and postoperatively by vasospasm (MCA velocity >120 cm/s). A recoup SPECT (day 25) showed hyperaemia (0.98 (SD 0.03) in the right frontal lobe.

Conclusions—Angiography and TCD only examine large and medium sized arteries. The SPECT study provided insight into perfusion, reperfusion, and reverse angiographic vasospasms, suggests that there may be changes in small vessels beyond angiographic resolution. The existence of such changes could explain discrepancies between ischaemia and angiographic vasospasm complicating subarachnoid haemorrhage.

[SBNS]

FAMILIAL HEMIPLEGIC MIGRAINE AND THE AGE RELATED SPECTRUM OF CEREBRAL AUTOSONAL DOMINANT ARTERIOPATHY LINKED TO CHROMOSOME 19
M Hutchinson, J O’Riordan, J Maved, E Quin, T Willcox, N Parfrey, D Macerlaine, TG Nagy, E Tournier-Lasserve. St Vincent’s Hospital, Dublin, Eire, and Inserm U25, Paris, France

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy (CADASIL) is a recently described familial cerebrovascular disorder whose phenotype has been shown to be a result of a single point mutation in the CHD7 gene. At least 19q12. Familial hemiplegic migraine has also been shown to be linked to chromosome 19 close to the CADASIL locus. The CADASIL phenotype is defined, as a mimimum, by brain MRI abnormalities in an at risk family member. By this criterion 10 of 15 fully investigated members of a large Irish family had CADASIL. Brain MRI showed a leucoencephalopathy of varying severity. The spectrum of presenting features included familial hemiplegic migraine, common and classical migraine, transient cerebral ischaemic attacks, recurrent strokes, and spinal cord infarction. One family member was asymptomatic; two members developed a pseudobulbar palsy and subcortical dementia. In five familial hemiplegic migraine started in childhood and four of these had subsequent developed the features of CADASIL. Familial hemiplegic migraine has not been reported in association with CADASIL. Linkage analysis showed a significant lod score (3.91 with D19S226) with markers close to the locus for the CADASIL gene. We postulate that familial hemiplegic migraine is, in this
In future, non-invasive techniques will obviate the need for carotid subtraction angiography (DSA) in the assessment of extracranial internal carotid artery stenosis. There is currently much debate concerning which measuring technique to adopt when assessing calipers, the ECST and the common carotid stenosis from angiograms. Using both DSA's and magnetic resonance angiograms (MRAs), four different methods—the "ECST", the "NASCET", the "common carotid artery as denominator" and the visual impression ("eyeballing") methods—were assessed and their reproducibility determined. One hundred and ten DSA's and 74 MRAs were assessed using all four methods by two independent observers in two separate occasions. Measurements were made using vernier scale calipers. The mean (SD) of the differences were calculated for each method (the smaller the SD the better the agreement). For DSA, the mean (SD) of the differences between observers were: ECST, 6.4 (8.9); NASCET, 9.6 (21.3); common carotid, 6.5 (13.8); eyeballing, 0.1 (10.7) respectively. The consistency improved by each technique as the degree of stenosis increased. Similar results were obtained for MRA and intraobserver agreement.

Using calipers, the ECST and the common carotid techniques show least variation in reporting. The NASCET technique seems the least reproducible. Interestingly, eyeballing is a highly reproducible technique.

ACE GENE POLYMORPHISM, CEREBROVASCULAR DISEASE, AND CAROTID ATHEROMA

H Markus, J Barley, S Jeffery, R Lunt, JM Bland, N Carter, MM Brown. King's College School of Medicine and Dentistry and St. George's Hospital Medical School, London, UK

The molecular basis of the genetic predisposition to stroke is largely unknown. A deletion polymorphism in intron 16 of the ACE gene has been reported as an independent risk factor for myocardial infarction although the mechanism of this effect remains unknown.

With the polymerase chain reaction the insertion-deletion polymorphism was determined in 101 white patients (mean age 64-8) and 137 age matched controls (mean age 63-9). All were presented with a carotid territory acute ischaemic event and carotid duplex was performed to assess degree of internal carotid artery stenosis and common carotid artery intima-media (IM) thickness. Plasma ACE concentrations were measured.

The DD genotype was common in patients with cerebral vascular disease than in controls (36/101 v 30/137, P = 0.02). D/I allele frequency was 0.59:0.41 in cases and 0.48:0.52 in controls (P = 0.01). The DD genotype conferred a relative risk of cerebrovascular disease of 2.4 (95% CI 1.14-5.01; P = 0.02). The relation was independent of age, sex, smoking history, diabetes, or cholesterol but seemed to be mediated at least in part through hyper tension. Neither the DD genotype nor the D allele were positively associated with carotid stenosis or intima-media thickness.

The DD genotype is a new risk factor for cerebrovascular disease. It seems to exert its action at least partly through hypertension in this age group, although not via extracranial large vessel disease. In view of the lack of association with carotid artery wall thickness and stenosis it may act via small vessel disease, altered functional vessel responses, or by predisposing to cardiac disease.

CONTINUED ISCHAEMIC DAMAGE AFTER CEREBRAL INFARCTION IN HUMANS

DE Saunders, FA Howe, A van den Boogaart, MA McLean, JR Griffiths, MM Brown. St. George's Hospital Medical School, London, UK

The aim was to study the ischaemic penumbra in humans, by measuring metabolic changes after middle cerebral artery occlusion (MCA) infarction using proton magnetic resonance spectroscopy ('H-MRS; 1.5T system). Localised 'H-MRS was carried out within the area of infarction and contralateral hemisphere. Peak areas were obtained by variable projection time domain fitting analysis. The unsuppressed water signal was used as internal concentration standard. Ten patients with acute MCA territory infarction were studied within 28 hours of stroke and for three months. Significant changes were seen in the initial infarct spectra compared with the contralateral spectra (table 1). Lactate, a marker of anaerobic metabolism, was detected within the infarct but not in the contralateral hemisphere. N-acetyl aspartate (NAA), a neuronal marker, and total creatine (Cr/PCr) were significantly reduced. Further reductions in NAA and Cr/PCr occurred within the first week (table 2). A fall in lactate was seen within the infarct core over the first seven to 10 days.

In conclusion, neuronal loss is detected non-invasively by 'H-MRS within 28 hours of stroke onset. The continuing loss of neurons may represent continued ischaemic damage after MCA infarction.

Table 1

<table>
<thead>
<tr>
<th>Initial data (day 1)</th>
<th>Contralateral (n=7)</th>
<th>Infarct (n=10)</th>
<th>P value (t test)</th>
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<tr>
<td>NAA (mmol/l)</td>
<td>14.7 (1.6)</td>
<td>8.8 (4.3)</td>
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<td>Cr/PCr (mmol/l)</td>
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<td>9.4 (2.9)</td>
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<td>Cho (mmol/l)</td>
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<td>Lactate (mmol/l)</td>
<td>0</td>
<td>19.2 (5.5)</td>
<td>&lt;0.001</td>
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Table 2

<table>
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<tr>
<th>Infarct</th>
<th>Value day 1 (n=7)</th>
<th>Value 7 days (n=7)</th>
<th>P value (t test)</th>
</tr>
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<tbody>
<tr>
<td>NAA (mmol/l)</td>
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<td>6.1 (4.1)</td>
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<td>Cho (mmol/l)</td>
<td>1.8 (0.6)</td>
<td>1.7 (0.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Lactate (mmol/l)</td>
<td>16.9 (9.3)</td>
<td>11.4 (7.2)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values for tables 1 and 2 are means (SD).

STATUS DYSTONICUS ET RIGIDITUS: A REPORT OF 10 CASES

H Manji, RS Howard, NP Hirsch, DH Miller, L Carr, NP Quinn, CD Marsden. National Hospital for Neurology and Neurosurgery and Great Ormond Street Hospital for Sick Children, London, UK

Patients with primary and secondary dystonic syndromes may develop increasingly frequent and severe episodes of generalised dystonia and rigidity, which may be refractory to conventional drugs and, in severe cases, result in bulbar and ventilatory compromise.

Ten cases (mean age 21-4 (range 6-39) years) are presented. The diagnoses were athetoid cerebral palsy (three), post-traumatic dystonia (three), postencephalitic hemiplegia (one), Huntington's disease-parkinsonism (one), infantile striatal necrosis (one), and myoclonic dystonia (one). Possible precipitating factors included infection (one) and starting clonazepam (two). Eight patients were ventilated for a mean period of 61 days (range 7-300) days. The indications for ventilation were bulbar (four), respiratory (five), exhaustion (eight), and metabolic disturbance as a result of rhabdomyolysis (two).

Drug treatment used included benzhexol, tetrabenazine, pimozide, baclofen (oral and intrathecal), chlorpromazine, and carbamazepine. One patient improved with benzhexol and another with tetrabenazine. Two patients underwent thalamotomy—bilateral (no improvement); unilateral (improved). Two patients died, four returned to their prestatus condition, two improved partially, and two eventually recovered.

Thus patients with status dystonicus et rigiditius should be managed in intensive care units; standard drug treatment may be beneficial, but ventilatory and ventilation may be of benefit and the prognosis is guarded, partly depending on the underlying condition.

ABNORMAL MOTOR UNIT SYNCHRONISATION BETWEEN ANTAGONIST MUSCLES IN DYSTONIA

SF Farmer, G Shean, JC Rothwell, CD Marsden. Institute of Neurology, London, UK

Activity in networks of neurons that provide common presynaptic input to motoneurons produces synchronisation of motor unit discharges. Cross correlation of EMGs from pairs of synergistic muscles in humans may
show motor unit synchronisation and thus common presynaptic input. By contrast, antagonist motor units—for example, flexor and extensor carpi radialis (FCR/ECR)—do not produce synchronised discharges even when a subject deliberately cocontracts the muscles.

Dystonia is characterised by involuntary cocontraction of antagonist muscles. One hypothesis concerning abnormal muscle cocontraction in dystonia is that it is produced by abnormal common presynaptic input to motor units of antagonist muscles. Five patients with dystonia were studied (two idiopathic, two post-traumatic, during which their ages 17–60). Simultaneous multunit EMGs were recorded using concentric needle electrodes inserted into FCR and ECR, while patients cocontracted the muscles. For comparison, identical recordings were obtained from four healthy subjects (three men, ages 28–33). The times of motor unit occurrence from FCR and ECR were cross correlated. Cross correlations of the healthy subjects were flat. Traces of dystonic subjects contained a peak at time zero (median size k = 1.6; median duration = 38 ms), indicating abnormal motor unit synchronisation.

Dystonia and dystonia antagonist motor units share abnormal common presynaptic inputs. Activity of these inputs may produce abnormal muscle cocontraction. [ABN]


The role of EMG in selection and placement of injections of botulinum toxin (BTX-A) in the management of dystonia was defined. EMG guided injections of Dysport® BTX-A were used to treat 37 patients with task specific dystonia, 30 with writer’s cramp (14 simple, 16 dystonic), five with primary writing tremor. After clinical inspection during the relevant task, likely active muscles were sampled with a teflon coated, 23G monopolar needle which allowed simultaneous EMG recording and injection. Usually two or three, but up to six, muscles were treated in each session. Commonly injected muscles included the wrist flexors/extensors, thumb and deep finger flexors, and index finger extensors. Initial doses ranged from 20–80 MU and follow up was from 1–60 months. Initial evaluation and treatment generally took 45–60 minutes and up to 30 minutes at follow up. Subjective improvement occurred in 86% of patients (good to excellent in 76%). Four showed no benefit. Significant weakness developed in nine and involved an adjacent, non-injected muscle in one case. EMG is essential for accurate identification of target muscles (both before and after BTX-A) and is particularly important for muscle selection in tremor. [ABN]

PRIMARY WRITING TREMOR
PG Bain, LJ Findley, TC Britton, MA Oresty, JC Rothwell, PD Thompson, CD Marsden. MRC Human Movement and Balance Unit, London, UK

The clinical and neurophysiological features of 21 patients with primary writing tremor (PWT) were described. This was first described by Rothwell, et al (1979). Subsequently there has been controversy as to whether PWT is a forme fruste of essential tremor or a variant of writer’s cramp.

Twenty one patients with PWT were studied using surface polyomography and accelerometer. Seven had a family history of PWT. In 11 patients the forearm reciprocal inhibition curve of the median nerve H reflex was also examined. The results of reciprocal inhibition were compared with those of 10 normal controls and to those obtained from patients with essential tremor.

The median frequency of PWT was 5.5 Hz (range 4.1–7.3 Hz). Segregated EMG activity was typically alternating in forearm flexor/extensor pairs but co-contraction, extensor activation alone and varying EMG patterns were also recorded. Forearm reciprocal inhibition was normal in PWT. The patients were subclassified on clinical grounds into type A (task induced) and type B (positionally sensitive) PWT. The only differences between these two groups were that cocontracting tremor and tremor induced by tendon taps to the volar aspect of the wrist occurred in type B but not type A cases. Dominant hand writing speed was significantly reduced in PWT compared with age matched controls (PWT 73.1 letters/min; controls 136.9 letters/min (P < 0.001))

It is concluded that patients with PWT can be distinguished from writer’s cramp as both the dysynaptic and presynaptic phases of reciprocal inhibition are normal in PWT whereas the amount of presynaptic inhibition is decreased in writer’s cramp; PWT can also be differentiated from hereditary essential tremor on clinical criteria. [ABN]

ADHESION MOLECULES IN AXO-GLIAL INTERACTIONS
CE Shaw, R Milner, C french-constant, DAS Compston. University of Cambridge, Cambridge, UK

With recent advances in immunotherapy for multiple sclerosis (MS) the possibility exists for promoting remyelination by endogenous or transplanted oligodendrocytes. The molecular mechanisms regulating axo-glial interaction in developmental myelination and repair are largely unknown. To study the role of the adhesion molecules, myelin associated glycoprotein (MAG), and integrins in mediating this interaction an in vitro model of myelination co-culturing rodent sensory neurons and glia has been used. The regional expression of MAG by oligodendrocytes is under axonal influence and MAG protein binds to axons confirming a specific ligand interaction. MAG expression occurs after the initial recognition and enhancement takes place and blocking antibodies do not inhibit myelin formation, suggesting that MAG plays only a minor part in myelination. Integrins are heterodimeric adhesion molecules, and about half of the molecules in the extracellular matrix. With immunoprecipitation of cross species co-cultures of6A9/1 and 49/9 were greatly upregulated during myelination, suggesting that they may have a role in mediating this event. With a better understanding of the molecular mechanisms that control myelination it is hoped that treatments can be developed which enhance endogenous or transplanted oligodendrocyte repair. [ABN]

IS THE VARIATION IN PREVALENCE OF MULTIPLE SCLEROSIS WITHIN THE UNITED KINGDOM DUE TO MIGRATION, LATITUDE, OR GENES?
PM Rothwell. Western General Hospital, Edinburgh, UK

There is debate about the extent to which the worldwide latitudinal gradient in the prevalence of multiple sclerosis is due to genetic or environmental factors. Northern Scotland has the highest prevalence in the world. Recent findings of a low rate in southern England, however, have cast doubt on the assumption of a latitudinal gradient within the United Kingdom. To assess this a prevalence study was performed in south east Scotland. In addition, as susceptibility to multiple sclerosis seems to be either inherited or determined in childhood, mortality from multiple sclerosis within England and Wales was analysed by place of birth as well as place of death to detect any confounding due to migration.

Between 1969 and 1974 all deaths registered in England and Wales were linked with birth records. Records of deaths before age 10 and 10-34 years were obtained for 3151 deaths in which multiple sclerosis was a cause and analysed within the nine standard regions. There was no latitudinal gradient by place of death, but the proportion of patients born outside the region in which they died was higher in southern regions (41%–63%) than northern regions (8%–18%). Reanalysis by place of birth, however, still failed to show a latitudinal gradient within England. There were fewer than expected deaths of people born in Wales (observed/expected = 0.64, 95% CI = 0.54–0.75). The preliminary prevalence rate of multiple sclerosis in the Lothian and Border regions of Scotland (population 850 000) was in excess of 200/100 000. This is similar to rates in northern Scotland and significantly higher than the rates in southern England. These data suggest that there is no latitudinal gradient within either England or Scotland, but that there are differences in the prevalence of multiple sclerosis between England, Scotland, and Wales. This most probably reflects the genetic susceptibility of the respective populations. [ABN]

SERIAL BRAIN AND SPINAL CORD MRI IN MULTIPLE SCLEROSIS
JW Thorpe, D Kidd, IF Moseley, BE Kendall, WI McDonald, DH Miller. Institute of Neurology, London, UK

The dynamics of multiple sclerosis have been extensively studied by serial MRI of the brain and spinal cord. Monthly gadolinium-enhanced brain and spinal cord MRI over a period of one year were carried out in 10 patients with relapsing-remitting multiple sclerosis. Six patients had a total of 11 clinical relapses of which eight implicated the spinal cord. One hundred and sixty seven active (enhancing or new non-enhancing) lesions were detected in...
The excretion of neopterin, ratios progressive, immuno
logography by in found activity.

trigger for disease activity. Higher fluctuations with average (119 controls, eight patients who relapsed. Both cord and brain lesions found were symptomatic; conversely six of the 19 active spinal patients. The personal details and disease status have been systematically recorded for more than 11 000 relatives of 650 probands with probable or definite disease listed on the Cambridgeshire Multiple Sclerosis Register and prevalent on 1 July 1993 to provide crude and age adjusted recurrence risks for first, second, and third degree relatives. Maximal crude risks were found for sisters of female probands (5%) and age adjusted risks for female offspring of male probands (7%). Risk was found to fall proportionately with genetic distance from the proband but was still significantly raised in first cousins (1-0%) compared with background prevalence (132 × 10−3) suggesting that the phenomenon of familial aggregation in multiple sclerosis is likely to depend on genetic factors. [ABN]

The excretion of neopterin, a marker of macrophage activity in patients with multiple sclerosis. Daily urinary neopterin/creatinine ratios (UNCR) were measured by high performance liquid chromatography for a 12 week period in eight controls, eight patients with non-relapsing progressive, and nine patients with relapsing multiple sclerosis. Infection, relapses, day to day fluctuations in neurological function and Gd enhanced MRI were monitored.

The mean UNCR was significantly higher in patients with non-relapsing progressive (191 (86) µmol/mol) and relapsing disease (558 (562) µmol/mol) compared with controls (119 (28) µmol/mol, P = 0.001). One asymptomatic patient in the serial UNCR was found in one control subject compared with an average 2-2 (2-3) peaks/patient/month in non-relapsing progressive and 3-2 (1-3) peaks/patient/month in patients with relapsing multiple sclerosis (P = 0.002). Two peaks were temporally associated with a clinical relapse and clearly defined peaks and elevations in the baseline were noted around 21 days after an upper respiratory tract infection in three patients. Patients with day to day fluctuations in neurological function had higher mean UNCR than patients without (526 (624) × 182 (69) µmol/mol, P = 0.05).

Mean UNCRs tended to be higher in patients with MRI activity than patients without activity (512 (631) × 203 (84) µmol/mol, NS).

Neopterin seems to be a promising immunological marker that can detect sub-clinical inflammation in patients with multiple sclerosis. [ABN]

Multiple sclerosis: recurrence risks for relatives

N Robertson, J Deans, M Fraser, DAS Compton. University of Cambridge, Cambridge, UK.

Familial recurrence risks in multiple sclerosis are becoming of increasing interest to geneticists in search of disease susceptibility genes and to clinicians who counsel patients. Little contemporary information is available for the United Kingdom, the population of which continues to exhibit an overall trend of increasing prevalence and incidence; rates derived from genetically and geographically distant populations may not be relevant. In addition crude risks, which have previously been used, may be misleading in younger populations because of the widely distributed age at onset profile of multiple sclerosis. The personal details and disease status have been systematically recorded for more than 11 000 relatives of 650 probands with probable or definite disease listed on the Cambridgeshire Multiple Sclerosis Register and prevalent on 1 July 1993 to provide crude and age adjusted recurrence risks for first, second, and third degree relatives. Maximal crude risks were found for sisters of female probands (5%) and age adjusted risks for female offspring of male probands (7%). Risk was found to fall proportionately with genetic distance from the proband but was still significantly raised in first cousins (1-0%) compared with background prevalence (132 × 10−3) suggesting that the phenomenon of familial aggregation in multiple sclerosis is likely to depend on genetic factors. [ABN]
but the most common adverse event has been the formation of thromboemboli. As a result anticoagulants are now given during and for up to 48 hours after treatment.

**Subjects**—Twenty one neuropeptide concentrations were significantly higher in the middle cerebral artery compared with the posterior cerebral artery (NPY 13:53 (2:85) P = 0.005; VIP 17:32 (2:95) P = 0.034 (77), P < 0.01; SP 8:83 (1:43) < 1.0 (46), P < 0.001; CGRP 26:93 (3:02) < 2.12 (3:02), P < 0.001). There was no difference between the concentrations in the middle cerebral artery compared with its trifurcation. There was no correlation between neuropeptide concentrations and either age or postmortem delay.

**Conclusion**—Neuropeptide concentrations are consistently higher in the middle cerebral artery than in the posterior cerebral artery in humans. The concentrations are stable and independent of postmortem delay. Postmortem cerebral vessels are thus suitable for comparative studies of neuropeptide concentrations in disease.

**PEROPERATIVE MEASUREMENT OF JUGULAR VENOUS OXIMETRY DURING CAROTID ENDARTERECTOMY**

AJ Davidson, AD Mendelow, IR Chambers.
Newcastle General Hospital, Newcastle-upon-Tyne, UK

**Objective**—To measure jugular bulb oxygen saturation during carotid endarterectomy.

**Design**—Prospective observational study. This was performed by means of a 40 cm 4 FG Optical fiberoptic catheter connected to an Oximetric 3 computer and recorded continuously on a paper hard copy and a Pison computer. The fibroptic catheter was positioned by the surgeon under direct vision via a facial vein tributary into the jugular bulb on the operative side and removed at the end of the procedure. Other monitoring included ECG, invasive blood pressure, central venous pressure, pulse oximetry, and tidal capnography.

**Patients**—Twenty patients undergoing carotid endarterectomy under either local or general anaesthesia depending on the preference of the patient and surgeon.

**Outcome**—Assessed correlation of peroperative monitoring with neurological outcome.

**Results**—The system provided a reliable, continuous, real time monitor of jugular bulb saturation during surgery. Observation of changes in jugular bulb saturation and correlation with neurological deficits in those patients under local anaesthesia alone greatly aided in blood pressure manipulation and in the decision as to the need to insert temporary bypass shunts. Typical patterns seen included falls in jugular saturation associated with hypotension and hence inadequate cerebral perfusion and profound falls in saturation on carotid cross clamping relieved by insertion of temporary shunts. Equally useful were stable readings obtained during general anaesthesia or cross clamping, thus avoiding the potentially deleterious side effects that might occur with shunt insertion, fluid loading, or isotropic drug treatment given in an attempt to raise blood pressure.

**Conclusion**—Jugular venous oximetry is a valuable monitor to aid in the peroperative care of patients undergoing carotid endarterectomy.

**PROJECTED COMPARATIVE STUDY ON 110 PATIENTS OPERATED ON FOR CEREBRAL DISC DISEASE**

AA Madawi, M Powell, HA Crockard. The National Hospital for Neurology and Neurosurgery, London, UK

**Design**—A total of 18 patients with suspected aneurysmal subarachnoid haemorrhage (SAH) had intracranial pressure (ICP) monitoring during measured transfemoral digital subtraction angiography under local anaesthesia. Five of these also had their ICP monitored during anaesthesia and operation. ICP was measured with a Camino pressure transducer. Simultaneously, blood pressure was measured either with a cuff or arterial line.

**Results**—Angiography raised the ICP in all patients. Preangiographic ICP was 11.59 (1.54) mm Hg, whereas perangiographic peak ICP was 23.61 (4.68) mm Hg. Intubation during anaesthesia was the most important variable affecting ICP, which rose from between 3 and 87 mm Hg (average rise 15.9 ± 5.9 mm Hg). A corresponding rise in MAP, however, ensured a relatively stable CPP.

**Conclusion**—These findings suggest that the use of haemodynamic monitoring during angiography in patients with subarachnoid haemorrhage occurs during intubation. This strengthens the case for performing angiography under local anaesthesia.

**EXPERIENCES WITH AN ARTIFICIAL CERVICAL JOINT**

BH Cummins. Frenchay Hospital, Bristol, UK

Most surgical procedures on the cervical spine include fusion by bone, metal, or both. Over the years such fusion at one or more levels may be associated with osteophytic degeneration at the adjacent levels, causing radiculopathy or myelopathy. In 10 “last ditch” spaces of such disorder accompanying multiple levels of congenital or surgical fusion, an artificial joint designed by the author and made by the engineering department of the hospital has been inserted to provide some degree of flexibility at that level. The joint is of stainless steel in two pieces, the upper with a downward facing dome slightly smaller in radius than the shallower saucer of the upper face of the lower piece. This allows rotation, limited flexion, and extension and glide. Locking screws maintain the joint in position.

**Conclusion**—This has proved satisfactory and nine of the 10 joints have provided resolution of symptoms in these difficult cases.

**BIOCOMPATIBLE OSTECONDUCTIVE POLYMER V/ILAC GRAFT IN ANTERIOR CERVICAL DISC DISEASE: A PROSPECTIVE COMPARATIVE STUDY ON 110 PATIENTS OPERATED ON FOR CERVICAL DISC DISEASE**

AA Madawi, M Powell, HA Crockard. The National Hospital for Neurology and Neurosurgery, London, UK

**Donor site morbidity is a significant problem in anterior cervical fusion. A biocompatible
Materials and methods—One hundred and ten patients, 50 for iliac graft (IG) and 60 for BOP were recruited into this study. 72 patients were radiculopathic, 20 myelopathic, and 18 had radiculomyelopathy. The mean duration of symptoms was 20-3 months. The Smith Robinson technique was used in 70, and the Cloward technique in 40 patients; 80 patients had one level, 30 had two level surgery. Patients were followed up routinely at three to six month intervals (range 3-24, mean 11 months) at which time clinical and radiological assessment were made, including CT and MRI.

Results—The mean hospital stay was 5-9 days for those with IG, and 5-1 days for BOP. Complications were recorded as two neck haematomas required evacuation, one ileac wound haematoma was managed conservatively, two graft non-unions with kyphus (IG) required revision and plating, two complete graft extrusions (one IG, one BOP) required revision. Partial graft extrusion occurred in 18 IG (2-5 mm, mean 3 mm) and seven BOP (2-4 mm, mean 2-6 mm). Kyphus was found in 13 IG (3-30, mean 12-3 degrees) and in four BOP (mean 3-15, 10-3 degrees). The BOP sank into the adjacent endplates and the space collapsed after Smith Robinson procedures. Also scle- rosis was found around BOP within one to two months, but even by 18 months there was no incorporation or degradation. Osseous union was seen to begin within one to two months and had finished by one year in 48 cases after IG.

Conclusions—BOP can act as a good spacer after anterior cervical fusion, with evidence of incorporation or degradation through the period of follow up.

A RANDOMISED CONTROLLED TRIAL COMPARING AUTOMATED PERCUTANEOUS LUMBAR DISCECTOMY AND LUMBAR MICRODISCECTOMY
G Findlay, S Chatterjee, P Foy, Walton Centre for Neurology and Neurosurgery, Liverpool, UK

Much interest has been created by the advent of automated percutaneous lumbar discectomy (APLD) in the management of contained lumbar disc herniation. Several papers have reported encouraging results but to date attempts to perform controlled studies of APLD have been hampered by numbers too small to be statistically significant. We designed a randomised study with a separate blinded subgroup to compare the results of APLD with conventional lumbar microdiscectomy. It was planned to recruit 180 patients to the study and to complete a two year follow up in all cases. During the study it became apparent to the non-blind participants that the results of APLD were much worse than surgery and it was decided to analyse the results at that stage.

This produced 70 patients who had small contained disc herniation proved by MRI (all other types were excluded from the study). In the APLD group only eight of 30 (26-7%) achieved excellent or good results, whereas the corresponding figure for the microdiscectomy group was 32 of 40 (80%). Moreover for patients in the APLD group who had unsatisfactory results and opted for subsequent microdiscectomy (20 of 22 patients), the success rate was only 13 of 20 (65%). Thus the eventual success rate of those treated by APLD alone or APLD and microdiscectomy was 21 of 30 (70%).

A recent controlled study comparing APLD to conventional microdiscectomy also showed poor results for APLD. Our study shows that in the chosen group of patients APLD is ineffective. Our success rate for microsurgery for all types of disc herniations was found to be 91% and better than the 80% we found for the selected group in our study.

It is considered that a trial is needed to compare the results of APLD with conservative treatment and that a third control group of patients who had neither surgery nor APLD would have been valuable in this study.

A SPINAL MENINGIOMAS: A 20 YEAR REVIEW
AT King, B Doshi, RW Gullan, MM Sharr, JR Bartlett. Brook General Hospital, London, UK

This is a retrospective study of 78 patients with spinal meningiomas operated on over 20 years at the Brook Neurosurgical Unit. The age range was 22-91 (mean 61-5) years, with 12 men (15%) and 66 women (85%), followed up for a mean of 10-5 years. The clinical history was of less than one year in 55 patients and less than six months in 26 patients. There was poor correlation between the duration of symptoms and the relation to the spinal cord: 15 lay anteriorly, 15 anterolaterally, 23 laterally, 17 posterolater- ally, and eight posteriorly. Plain radiology was normal in the entire intradural group (74 patients) with only one example of tumour calcification. Three out of the four extra- dural group showed abnormalities on plain radiology. Two tumours were purely extra- dural and a further two both intradural and extradural. The dural attachment was ex- cised in 20 cases. Full recovery of function was achieved in 57 patients (73%), and a further 17 (22%) were improved to independent mobility. There was one recurrence, at 14 years after operation. By contrast with previous series, histology showed no striking predominance of psammomatous meningiomas.

TRANSDURAL MICroneurosurgical EXCISION OF PROLAPSED DORSAL DISCS
JM Rice Edwards, D Peterson. Charing Cross Hospital, London, UK

A tenet of neurosurgical practice is that a lamincotomy should not be done for the removal of dorsal discs. This belief is based on historical evidence of operations performed with rongeurs and of impossible attempts to remove anterior lesions extra- durally.

An operation is described which involves careful removal of laminae with a drill and a transdural microapproach to the dorsal disc.

After removing the lamina the spinal cord is not usually displaced against the dorsal dura and a very adequate view of the anterior disc can be obtained laterally without signifi- cant retraction of the spinal cord. It has been possible to completely remove the hard disc prolapse in the 10 cases where this approach has been used.

The technique has the following advantages: the approach is familiar to neuro- surgeons whereas the anterolateral and transantrhmoric approaches can be difficult unless practised often, the spinal cord can be inspected for adhesions to the dura (which occurred in two cases with associated arach- noiditis), it is safe provided that the disc protrusion is not of an extreme size. This can be judged from MRI.

Poster Presentations
ASYMPTOMATIC CNS ABNORMALITIES IN BEHÇET’S DISEASE: A MAGNETIC RESONANCE STUDY
F Ahmed, JM Bamford, KS Blanshard, BA Noble. St James’s University Hospital, and the General Infirmary, Leeds, UK

Involvement of the CNS occurs in up to one third of patients with Behçet’s disease, desig- nated as neuro-Behçet’s disease. Clinical features are either due to cerebral venous thrombosis or parenchymal pathology.
A SURVEY OF THE USE OF LAMOTRIGINE AND VIGABATRIN IN CLINICAL PRACTICE
D Chadwick, G Schapel. University of Liverpool, Liverpool, UK

A survey was undertaken between September 1993 and February 1994 that identified 356 patients who had been prescribed either vigabatrin or lamotrigine since the licensing of these compounds from a comprehensive database of just over 2200 patients with epilepsy attending the Mersey Regional Epilepsy Clinic since 1989. The lamotrigine group had a chronic refractory epilepsy, 90% were having more than one seizure per week and two thirds were receiving one drug.

Two hundred and twenty three patients were taking lamotrigine for up to 56 months and 217 patients to vigabatrin for up to 72 months. The median maximum dose of lamotrigine achieved was 400 mg per day and that for vigabatrin was 2 g per day.

Kaplan-Meier survival curves were plotted for time to withdrawal of the new drug. The probability of continuing on lamotrigine at 40 months was 57% compared with 43% for vigabatrin. The commonest adverse event causing withdrawal of lamotrigine was skin rash (5% of patients exposed), whereas adverse psychiatric consequences were the commonest reason for withdrawal of vigabatrin (8% of cases). Ten per cent of patients exposed to lamotrigine became seizure free compared with 6% exposed to vigabatrin. Most of the patients becoming seizure free on lamotrigine were those with generalised epilepsies and there was little difference between the outcomes for the new drugs in partial epilepsies.

This survey indicates that there is little difference in the efficacy of these two novel drugs in the partial epilepsies. The side effect profile of the drugs seems radically different as does the range of activity, lamotrigine exhibiting a broad range of activity, and particular effectiveness in more resistant forms of idiopathic generalised epilepsy. [ABN]

A COMPREHENSIVE ELECTROPHYSIOLOGICAL EVALUATION OF PHRENIC NERVE INJURY RELATED TO OPEN HEART SURGERY
E Chroni, RL Patel, N Taub, GE Venn, RS Howard, CP Panayiotopoulos. St Thomas' Hospital, London, UK

Phrenic nerve damage is a widely recognised complication of open heart surgery. A prospective electrophysiological study of phrenic nerve function was conducted in 50 patients undergoing cardiopulmonary bypass. The right and left phrenic nerves were stimulated percutaneously at the neck and the diaphragmatic responses were recorded with surface electrodes placed over the 8th intercostal space. The latency, amplitude, duration, and area of the evoked responses were measured before and after the operation. Postoperatively no responses were elicited in two patients (4%), in five from the left, and in two from the right phrenic nerve. Comparison of the postoperative with the preoperative group values in the remaining patients showed that the amplitude and area of the left phrenic nerve were lower in the postoperative study, indicating that some of the nerve fibres were not conducting. There were no statistically significant differences between pre and postoperative values of latency or duration on the left or any of the parameters on the right.

Follow-up studies showed that in eight of nine survivors with unobtainable responses postoperatively, the conduction returned in four to seven weeks. The findings suggested that the amplitude and area of the diaphragmatic response are more sensitive than latency in detecting phrenic nerve paresis associated with open heart surgery. [ABN]

AN INVESTIGATION OF DIFFUSE AXONAL INJURY OCCURRING AFTER CLOSED HEAD TRAUMA
CA Davie, R Greenwood, IF Moseley, WI McDonald, DH Miller. Institute of Neurology, London, UK

Pathological studies in patients with severe head injury often show changes of diffuse axonal shearing. The abnormalities detected by MRI are often insufficient to explain the deficits of memory or changes in personality that can occur. Proton magnetic resonance spectroscopy (MRS) may be useful in assessing the presence of axonal loss or dysfunction by observing changes in N-acetylaspartate (NAA)—a neuronal marker. MRI and MRS have been carried out in 10 patients with severe head injury and 10 age-matched controls.

The patients who had sustained diffuse axonal injury showed decreased NAA/Cr values in the parietal and prefrontal regions in all cases. In controls the NAA/Cr values were higher compared with patients and only in one case was there a decrease in these regions. The patients with diffuse axonal injury showed a significant decrease in NAA/Cr compared with controls in the parietal region (20%) and in the prefrontal region (40%). The NAA/Cr values in the cerebellum were lower in patients with diffuse axonal injury compared with controls. The NAA/Cr values in the cerebellum were lower in patients with diffuse axonal injury compared with controls.

There was a significant decrease in NAA/Cr in the parietal and prefrontal regions in patients with diffuse axonal injury compared with controls. The decrease in NAA/Cr was in the range of 20% to 40%.

The findings suggest that the diffuse axonal injury observed in patients with severe head injury is associated with a decrease in NAA/Cr in the parietal and prefrontal regions. Further studies are needed to determine the clinical significance of these findings.
out in six patients with a history of severe head trauma and in eight healthy controls. MR images of the brain were collected followed by long echo proton MRS from a localised volume of normal appearing white matter (NAWM) in the left frontal lobe. In five patients there was mild cerebral atrophy with ventricular dilatation and in one patient, more severe cerebral atrophy. There was a significant reduction in the concentration of NAA (median 8.22 mM, range 6.5-8.8 mM) from frontal NAWM in the patient group compared with healthy controls (median 10.44 mM, range 8.76-10.81 mM, P < 0.006). There was no significant difference in the concentrations of creatine and choline containing compounds between the two groups. Proton MRS may be useful in measuring the extent and degree of axonal loss and/or dysfunction occurring after closed head injury. [ABN]

AUTOSOMAL DOMINANT DESMINOPATHY WITH A DISTAL MYOPATHY AND HEART BLOCK
DJ Dick, JR Anderson. Norfolk and Norwich Hospital, Norwich, and Addenbrooke’s Hospital, Cambridge, UK

Three members of one family over two generations were found to have heart block and a distal myopathy. Neurological examination of the index case showed a distal pattern of muscle weakness with preserved reflexes and normal sensation. Electromyography, ECG, serum creatine kinase, and an ischaemic lactate test were normal. A muscle biopsy showed selective type 2 atrophy and mainly subsarcoclemmal eosinophilic plaques of cytoplasm. Immunohistochemical staining showed that these deposits stained positively for desmin and to a lesser extent for ubiquitin, actin, and glycogen. Electron microscopy of the deposits showed the presence of glycogen granules and electron dense granular material, which was often closely associated with a smoothened Z band.

These are the muscle biopsy features of a desminopathy, which in this family is inherited as an autosomal dominant trait. This is a rare disorder in which there is accumulation of desmin in the muscle and presumably there are similar abnormalities to be found in cardiac muscle or the conducting system. Desmin is one of the intermediate neurofilaments and is a structural component of the cytoskeleton of mature muscle. It anchors myofibrils in the transverse plane and to the sarclemma. The mechanism by which desmin accumulates in this condition is not clear;

Previously reported cases have been mainly sporadic and if cardiac involvement occurred, it took the form of cardiomyopathy. [ABN]

A METHOD OF CHARACTERISING CEREBRAL ATROPHY
M Doran, N Roberts, RHT Edwards. University of Liverpool, Liverpool, UK

The aim was to evaluate the patterns and morphological characteristics of cortical atrophy using volumetric MRI. Volumetric MRI was obtained from patients with focal aphasic syndromes. The images were analysed with stereological grids to determine the cross sectional area (A) and cortical boundary length (B) on each image. Profile plots of the cross sectional areas (A) and the complexity parameter B/A of individual lobes of each hemisphere were obtained.

The data for patients with focal aphasic syndromes show distinct anterior or posterior patterns of morphological change in the temporal lobe. The profiles show that significant quantitative changes can occur to be determined within a period of one year. The pattern of the changes has been related to the evolving pattern of neuro-psychological deficit.

It is concluded that stereology represents a rapid and efficient method of determining morphological data to characterise the pattern of atrophic change in cortical disease. [ABN]

INCREASED SOLUBLE VCAM-1 CONCENTRATIONS IN CSF OF PATIENTS WITH MULTIPLE SCLEROSIS
AG Droogan, SA McMillan, JP Douglas, SA Hawkins. Royal Victoria Hospital, Belfast and Belfast City Hospital, Belfast, UK

Factors determining the composition and temporal evolution of the inflammatory infiltrate in multiple sclerosis are unknown, but the profile of adhesion molecule expression at the site of the lesion may play a part. Activated cerebral vascular endothelial cells express leucocytes, vascular cell, and intracellular adhesion molecules (E-selectin, VCAM-1, and ICAM-1), which facilitate leucocyte adherence to endothelium and migration into inflammatory lesions. Serum and CSF concentrations of soluble (s) E-selectin, sVCAM-1, sICAM-1 were determined by enzyme linked immunosorbent assay in 51 patients with clinically definite multiple sclerosis, 28 patients with inflammatory neurological disease (IND), and 39 patients with non-inflammatory neurological disease (NIND). Concentrations of sVCAM-1 in CSF were significantly increased in multiple sclerosis (mean, SD), 18.3 (9.9) ng/ml compared with IND (11.3 (7.3) ng/ml, P < 0.001) and NIND (10.6 (5.3) ng/ml, P < 0.001). Serum and CSF concentrations of sICAM-1 were normal in each group. Serum sE-selectin was decreased in multiple sclerosis compared with IND (45.5 (23.9) ng/ml v 55.0 (19.9) ng/ml, P = 0.03). In multiple sclerosis, high CSF concentrations of sVCAM-1 and sICAM-1 correlated with the presence of CSF oligoclonal bands (P = 0.004 and P = 0.001 respectively). Measurement of soluble VCAM-1 in CSF therefore seems to provide a marker of disease activity in multiple sclerosis. [ABN]

PERIPHERAL NERVE BLOCKADE WITH PHENOL IN SPASTICITY: A MYOMETRIC AND FUNCTIONAL ASSESSMENT
S Duckworth, N Johnson. Hunters Moor Regional Rehabilitation Centre, Newcastle-upon-Tyne, UK

Spasticity remains a significant cause of neurological disability. Oral pharmacological treatment is associated with unwanted side effects. Selective tone management is of value. Peripheral nerve phenol injections have been shown to produce tone changes. This effect may be of functional value in the management of spasticity. A myometric paradigm was employed alongside standard measures of disability. The definition of local phenol injection into different sites in 23 patients with spasticity. The amount of force required to move the selected joint through a predetermined range was made before and after injection and at one and 21 days after injection. Results showed significant tone reduction in ankle plantarflexion (n = 14, P < 0.001), knee flexion (n = 14, P < 0.01), leg adduction (n = 9, P < 0.01), elbow flexion (n = 9, P < 0.05), and ankle extension (n = 2, P < 0.01). The effect was maintained at one month after injection at the ankle (n = 7, P < 0.001), knee (n = 14, P < 0.05), leg adduction (n = 9, P < 0.01), and fingers (n = 2, P < 0.05) but not at the elbow (n = 7, P = 0.51). Overall activities of daily living scores improved significantly after injection (n = 23, P < 0.01). This study confirms the usefulness of peripheral nerve blockade with phenol in the management of spasticity using a myometric paradigm and standard measures of overall function. [ABN]

INTEROBERVER VARIATION IN CLASSIFYING MULTIPLE SCLEROSIS
HL Ford, MH Johnson, AS Rygo. St James’s University Hospital, Leeds, UK

With the advent of new treatments for multiple sclerosis, clinicians must be able to use diagnostic criteria reliably and to define the course of multiple sclerosis. The aim was to determine if the Poser diagnostic criteria could be applied consistently in practice and the course of multiple sclerosis defined.

The case records of 85 consecutive outpatient with multiple sclerosis were retrospectively analysed by two independent observers. The cases were classified: clinically definite multiple sclerosis, laboratory supported definite multiple sclerosis, clinically probable multiple sclerosis, laboratory supported probable multiple sclerosis, suspected multiple sclerosis, and unable to classify; the course was defined as early relapsing-remitting, benign, secondary progressive, primary progressive, and unable to classify.

The statistical agreement between the two observers was measured by calculating the κ statistic. There was substantial agreement in classifying the cases (κ = 0.65, 95% CI 0.52-0.78). The main disagreement lay in defining attacks of multiple sclerosis (κ = 0.50, 95% CI 0.35-0.65). There was moderate agreement for determining the course of multiple sclerosis (κ = 0.57, 95% CI 0.43-0.71). The observers differed in their definition of primary progressive and secondary progressive cases. These may be due to the poor documentation of relapses and remissions early in the disease course.

The efficacy of new treatments is being judged on relapse rate. Coexistence of an attack of multiple sclerosis is therefore essential. Each attack should be well documented, as should subsequent clinical improvement. The definition is rigorously adhered to allow consistent application of diagnostic criteria in practice. [ABN]
ANTI-PURKINJE CELL CYTOPLASMIC ANTI-BODIES. ARE THEY NON-SPECIFIC MARKERS OF CEREBELLAR CELL DAMAGE?
A Gibson, M Hadivassilou, A Milford-Ward, GAB Davies-Jones. Royal Hallamshire and Northern General Hospitals, Sheffield, UK

Anti-Purkinje cell antibodies that recognise discrete antigenic components within Purkinje cell cytoplasm have been designated "anti-Yo" and shown by some authors to be strongly associated with paraneoplastic cerebellar degeneration. The association is not universally accepted and may merely reflect Purkinje cell damage.

We have used an immunofluorescent method, with monkey cerebellar slices as substrate, to detect the presence of a Purkinje cell cytoplasmic antibody in patients with and without cerebellar signs as well as a group of age and sex matched healthy controls.

[ABN]

EVALUATION OF A COMPUTER ASSISTED QUANTIFICATION OF MULTIPLE SCLEROSIS LESIONS IN CRANIAL MRI

Several computer assisted techniques for measuring multiple sclerosis lesion volume on MRI have been developed to provide an objective, quantitative, and sensitive means for monitoring disease activity, particularly in the context of treatment trials. We have evaluated three techniques: manual tracing (similar to that of the North American IF interferon trial), automated lesion contouring (focal lesion based threshold) and intensity based thresholding for the whole brain. Contiguous 5 mm thick axial proton density images of the brain were obtained on a 1.5 T MR imager in eight patients with definite multiple sclerosis. Analysis of the scans were performed twice, independently by three operators, using the three different techniques.

The table shows the results. The automated lesion contouring technique was the most reproducible and should therefore be considered for use in treatment trials. Further studies are needed to assess sensitiv-

[ABN]

LNK, A NEW CLASS OF PROTEIN KINASE: HIGH EXPRESSION LEVELS IN GLIOMAS AND DURING HUMAN NERVOUS SYSTEM DEVELOPMENT

Protein kinases that include growth factor receptors are central in mediating division and differentiation in the nervous system and may also be important as cell lineage markers.

From the cDNA library of a human glioblastoma multi form cell line of the oligodendrocyte type 2 astrocyte (0-2A) lineage a new protein kinase LNK was cloned.

LNK represents a new class of protein kinase. Although it contains all conserved motifs in the kinase domain it has low overall amino acid homology to other kinases in this domain. It also has two LIM domains in the amino terminal region possibly indicating a transcriptional role. By northern analysis on total RNA, the LNK 3-3 kb band has been found to be upregulated in many glioblastoma primary cell populations. In the mouse the highest expression of murine LNK is found in the nervous system. Expression of LNK has been found in the developing human nervous system by in situ hybridisation.

These findings may be consistent with LNK having a regulatory role in human CNS development, in gliomas, and also as a cell lineage marker.

[ABN]

UPKEEP OF SERVICES FOR EPILEPSY AND THE COSTS OF CARE
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Epilepsy is a common neurological condition and it is estimated that in the United Kingdom there are presently around 300,000 people with active epilepsy. The resource implications of caring for these patients are likely, therefore, to be significant. A recent community study in one health region in the United Kingdom has examined the uptake of medical services among people with epilepsy and calculated the direct and indirect costs of their care. Patients included in the study were identified through the medical records of a random sample of general practitioners in the region. The pattern of care was very different for adults and children, reflecting in part the natural history of epilepsy: thus 86% of children had a hospital outpatient attendance in the past year compared with only 31% of adults; children were also significantly more likely to have had diagnostic investigations.

The largest single cost to the health service was the drug cost, representing around 40% of the total; inpatient costs also accounted for a sizeable proportion of costs. Uptake of medical services was significantly higher among patients with frequent seizures—for example, mean number of inpatient admissions was 1-6 among adults with frequent seizures, compared with 0-01 among those seizure free. People with frequent seizures also had a much higher uptake of state benefits. Improvements in the management of epilepsy may improve seizure control, which is the key to reducing the direct and indirect costs of this condition.

[ABN]

WEAKLY r MONTHLY BRAIN MRI FOR DETECTION OF DISEASE ACTIVITY IN MULTIPLE SCLEROSIS

In therapeutic trials, MRI at monthly intervals is often used to evaluate efficacy. At such an interval, 80% of new lesions on T2 weighted images enhance, and conversely, about 50% of new gadolinium enhancing lesions are not associated with clear changes on the T2 weighted image. Weekly T2 and gadolinium enhanced brain MRI were performed for three months in three patients with clinically active relapsing progressive multiple sclerosis.

On weekly MRI 38 new enhancing lesions were seen. On monthly scans there were 33 new enhancing lesions but only 13 new T2 lesions. Twenty five lesions were followed up from when they first enhanced until they had stopped enhancing. Of these 11 (44%) enhanced for less than four weeks (one to three weekly scans). All new T2 lesions showed initial enhancement.

Monthly gadolinium enhanced MRI is only slightly less sensitive than weekly scanning for detecting disease activity, and is still the preferred frequency for monitoring treatment as it is easier to perform. It seems from weekly studies that virtually all new T2 lesions undergo an initial phase of enhancement—this may occasionally be as short as one to two weeks, it is sometimes missed on monthly studies.

[ABN]

X LINKED DOMINANT HEREDITARY MOTOR AND SENSORY NEUROPATHY WITH CX32 MUTATION
BRF Mackay, PK Thomas, S Malcolm. Walton Centre for Neurology and Neurosurgery, Liverpool, Royal Free Hospital School of Medicine, and Institute of Child Health, London, UK

Three generations of a family are described with hereditary motor and sensory neuropathy (HMSN). Inheritance is consistent with X linked dominant transmission and is also suggested by the more severe clinical involvement of affected males. The onset of symptoms is in early adolescence with distal

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Coefficients of variation of the measurement techniques (0-0 = perfect reproducibility).

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Patient 1, aged 47 had 18 months pain and wiggling of the right little toe. Injection of 150–250 MU Dystrop three monthly into adductor digitii quarti and the fourth interosseous muscle has greatly improved involuntary movements and pain since 1989. Patient 2 aged 50 had five years of wiggling movements of all toes and severe pain in the left foot and lower leg. Infiltration of 500 MU Dystrop through the plantar fascia controlled movements for six months. Pain cleared for one month, and for a further year was reduced with an additional transcutaneous nerve stimulator. Further BTx-A injections controlled the movements but not the pain.

Patient 3, aged 37 had 18 years of pain and movements of all toes and both feet. Dystrop (250 MU) infiltrated into each foot as for patient 2 suppressed the movements, but gave only two weeks of pain relief, and adjunctive measures were unsuccessful. Booster doses of 300 MU/foot added no benefit.

More studies are needed, but BTx-A may control the movements and sometimes the pain in patients with this syndrome. [ABN]

A prospective study was conducted on all patients presenting to the accident and emergency department with a primary complaint of headache. They were followed up after three months to reach a final diagnosis.

In three months, there were 93 cases out of 21 187 attendances (0.44%). Serious pathology was found in 10 patients: three subarachnoid haemorrhages (3.2%), one intracerebral haemorrhage, three meningeitis, and three cerebral neoplasms. 48 patients (52%) were seen acutely by a neurologist, 31 being admitted. This included all cases of serious pathology except for one neoplasm. 39 patients (42%) described a headache of sudden onset, the remaining having a headache of gradual onset. Of the first, six had serious pathology: the three subarachnoid haemorrhages, one intracerebral haemorrhage, one meningeitis, and one neoplasm. They were among the 18 (46%) patients admitted from this group. Forty-five patients (48%) were referred by their general practitioner. Serious pathology was found in two of the 18 describing a sudden headache (one neoplasm and one subarachnoid haemorrhage) and two of the 27 with a headache of gradual onset (both neoplasms). In all, 30 (32%) had a head CT, eight in the acute phase. There were seven other subarachnoid haemorrhages presenting differently during the study period.

The results highlight suboptimal use of resources. Is there a case for headache cards similar to head injury cards used in the accident and emergency department? [ABN]

TREATMENT OF PAINFUL FEET AND MOVING TOES WITH BOTULINUM TOXIN A

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Treatment of an underlying cause may help in the syndrome of painful feet and moving toes, but conventional treatment is often ineffective in ideopathic cases. Treatment with botulinum toxin A (BTx-A) has not been previously reported. We describe three women with painful feet and moving toes unresponsive to conventional treatment, and treated with local injections of BTx-A.
Hhal polymorphism in the CYP2D6 gene is not associated with Parkinson's disease in Caucasians
DJ Nicholl, AC Williams, P Bennett, SL Ho, DB Rapee, and University of Birmingham, Birmingham, UK

A genetic association between mutant alleles of the cytochrome P-450 (CYP2D6) gene and idiopathic Parkinson's disease has been reported. Polymorphisms in this gene, situated on chromosome 22, give rise to the autosomal recessive, poor debrisoquin metaboliser phenotype. More than twofold increased risk of developing Parkinson's disease in Caucasian populations. Recently, a novel mutation, an Hhal polymorphism in CYP2D6 exon 6, was shown to confer a five-fold increased risk of Parkinson's disease in Japanese; we have studied this further in a Caucasian population where Parkinson's disease is more common.

DNA was analysed by the polymerase chain reaction (PCR) in 96 patients with sporadic Parkinson's disease and 60 controls, the products digested with Hhal restriction endonuclease, and the digest patterns studied after gel electrophoresis. Although the overall prevalence of this mutant allele was significantly higher in this population than in Japanese (36% vs 12%, \( \chi^2 = 63.2, P < 0.001 \)), there was no statistically significant difference in the distribution of the alleles between the patients with Parkinson's disease and controls (Parkinson's disease: 42% wild type (wt), 41% heterozygotes (he), 13% mutant homozygotes (mu); controls:23 wt, 30 he, 7 mu) (\( \chi^2 (3 \times 2 \text{ table}) = 0.79; P = 0.68 \)). Therefore, it seems that the Hhal polymorphism is not, by itself, of major significance to the aetiology of Parkinson's disease in Caucasians. [ABN]

FUNCTIONAL INTEGRITY OF CORTICAL DYSPLASIA
MP Richardson, MJ Koepp, DJ Brooks, DR Fish, JS Duncan. Institute of Neurology and MRC Cyclotron Unit, London, UK

The extent of altered benzoazepine receptor density in focal cortical dysgenesis was determined. It was hypothesised that the area of functional cortical abnormality in cortical dysgenesis exceeds the structural abnormality seen on MRI.

1C-Flumazenil PET was performed to determine volume of distribution (1C-FMZ-Vd) in four patients. These scans were co-registered with high resolution MRI pixel by pixel. The extent of dysplasia was defined on the MRI and regions of interest placed on the abnormality, surrounding cortex, distant cortex, and in corresponding areas in the opposite hemisphere. The same set of regions of interest was applied to the PET and 1C-FMZ-Vd determined. The results were compared with 10 normal controls and expressed as asymmetry indices. Additionally, each of these same four patients' 1C-FMZ-Vd scans were analysed by Statistical Parametric Mapping (SPM) via automated volumetric normalisation, analysis of covariance (ANCOVA), and pixel-by-pixel t test in comparison with 24 normal controls.

The regions of interest based approach showed significant differences between asymmetry indices in patients and controls for the lesion region (P < 0.01) and for the surrounding cortex (P > 0.02) but not for distant cortex. These findings were confirmed at the P < 0.001 level in SPM, which additionally showed the anatomical extent of changes in detail. It was concluded that the existence of a widespread functional, compared with structural abnormality may in part explain the poor outcome of focal resections in patients with focal dysplasia. [ABN]

EUROPEAN COMMUNITY STROKE PROJECT: RESOURCE USE, COSTS, AND OUTCOME OF DIFFERENT CARE PACKAGES FOR STROKE
J Stewart, R Howard, R Ross Russell, A Rudd, C Wolfe. St Thomas' Hospital, London, UK

Stroke imposes a major burden on health resources worldwide; in the United Kingdom acute stroke care alone costs 4.6% of the NHS budget. There is a 10-fold variation in age standardised mortality for stroke in people under 65 years across Europe, which is not reflected in the incidence rates and therefore may be related to different patterns of care for stroke patients.

The EC stroke project has been established to explore the relation between resource use, costs, and outcome of stroke. The study involves 24 hospitals from nine European countries, commenced on 1 January 1993. Methodology has been developed to enable standardised data collection to describe stroke care in terms of type and severity of treatment, hospital admission rates, bed type, duration of stay, use of tests, amount of rehabilitation, and outcome at one year. Initial resource data on 2438 stroke patients are reported for the first year. In two Spanish centres, 81% of patients were admitted to neurology beds compared with 0% in two British centres. In one German...
centre, 94% of patients received brain imaging, 80% carotid Dopplers, and 36% cerebral angiography, compared with 30%, 0%, and 1% respectively in one British centre. It will be interesting to correlate this wide variation in resource use with outcome at one year.

[ABN]

Although MRI detects the white matter lesions of multiple sclerosis within the brain with high sensitivity, a minority of patients have normal brain imaging. Nineteen patients are described, selected from over 170 who had undergone brain and spinal cord imaging, in whom minimal (n = 9) or no (n = 10) brain abnormalities were found. Eleven had clinically definite or laboratory supported definite multiple sclerosis according to the Poser criteria; four had clinically probable disease, and four had progressive isolated myelopathy. All had presented with symptoms and signs referable to the spinal cord or optic nerves. Eleven had a primary progressive course, seven relapsing-remitting and only one secondary progressive. Moderate or severe disability was the rule in the primary progressive patients whereas the relapsing remitting patients were minimally disabled. All had at least one lesion visible in the spinal cord. In patients in whom the diagnosis of multiple sclerosis is not supported by abnormalities on brain MRI, imaging of the spinal cord can be of considerable value.

[ABN]

"PURE" AUTOSOMAL DOMINANT SPASTIC PARAPLEGIA WITH LATE ONSET DEMENTIA: A FAMILY STUDY
S Webb, J Hutchinson, M Hutchinson. St Vincent's Hospital, Dublin, Eire

The phenotype of "pure" forms of hereditary spastic paraplegia (HSP) is highly variable. Familial dementia has not been reported in either the pure or complicated forms of HSP. A family with autosomal dominant HSP is presented. Thirty eight of the 54 living members of the family were examined; there were 11 affected persons of the 26 members over the age of 30. Both the severity of the paraplegia and the age of onset (20-50 years) varied considerably, with one asymptomatic person at the age of 62 years.

One member died of a four year dementing illness at the age of 62. Four other members of this sibship aged 62-70 had neuropsychological examination; all showed evidence of a dementia. Vocabulary, reading, and computational abilities were relatively preserved by contrast with a pronounced deficit in perceptual and constructional ability. Verbal learning and memory were below expectation but not as dramatically impoverished as visual recall. All four profiles were remarkably similar, worsened with age, and all four tended to use overt compensatory verbal analysis in visuoconstructive tasks. Magnetic resonance imaging showed a generalised atrophy. This dementia differs from Alzheimer's disease in having intact reasoning and relatively preserved verbal skills and is characterised by a progressive predominantly partial cognitive loss in the seventh decade.

[ABN]