

LETTERS TO THE EDITOR

Central neurocytoma of the cervical spinal cord

The World Health Organisation (WHO) classification of brain tumours now includes the entity central neurocytoma as originally defined by Hassoun *et al* in 1982.¹ Typically the tumour occurs in a supratentorial location in or around the lateral ventricles. Six cases of central neurocytoma of the spinal cord have been reported to date.²⁻⁴ We report a further case to highlight the importance of recognising this lesion at this site because the prognosis, as with central neurocytomas elsewhere, seems to be highly favourable.

A 12 year old boy presented with an eight week history of interscapular pain at night, after a fall. This was accompanied by numbness of the left arm and paraesthesiae of both hands coupled with fatigue in the legs. There had been no sphincteric symptoms. There had been no perinatal difficulties and he had reached his developmental milestones appropriately. On examination there was a symmetric proximal grade 4/5 weakness of the upper limbs and a reduction in sensation in both arms corresponding to the C5, C6, and C7 root distributions.

Brain MRI (fig 1) showed a well defined, partially cystic, intramedullary mass with areas of gadolinium enhancement extending from the level of C4 to T1. He underwent a



Figure 1 T1 weighted sagittal MRI showing an intramedullary mass between C4 and T1 which seems to be a well defined, partially cystic lesion with areas of enhancement after administration of gadolinium.

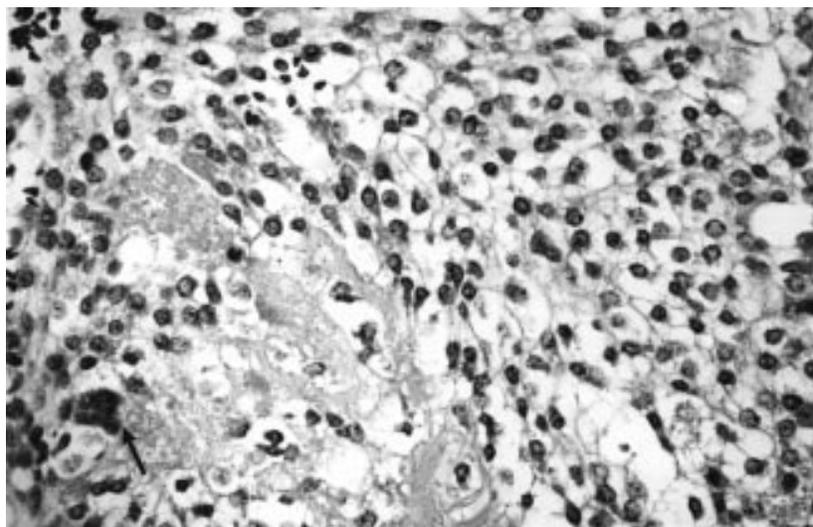


Figure 2 Histologically there are sheets of uniform tumour cells with round nuclei, delicate chromatin, and prominent perinuclear halos as well as an occasional ganglion cell (arrow; haematoxylin and eosin, original magnification $\times 440$). The tumour cells are positive for synaptophysin, PGP 9.5, and neuron specific enolase (NSE) but negative for glial fibrillary acidic protein (GFAP).

lower cervical laminotomy and complete resection of the tumour. His postoperative course was complicated only by transient left arm pain which responded to carbamazepine. He remains well with no neurological deficits at 24 months of follow up.

Histologically the tumour comprised sheets of uniform polygonal cells entrapped in a highly collagenised vascular network. Tumour cells had small round nuclei and delicate stippled chromatin, their cytoplasm contained a small eosinophilic crescent, or more often formed a perinuclear halo. A few cells with larger vesicular nuclei, prominent nucleoli, and more copious cytoplasm with Nissl substance suggested ganglionic differentiation (fig 2). Occasional foci of eosinophilic fibrillary tissue were scattered among the tumour cells. Mitotic activity and necrosis were not seen.

Immunohistochemically the tumour cells were negative for glial fibrillary acidic protein (GFAP) but strongly positive for synaptophysin, protein gene product 9.5 (PGP 9.5), and neuron specific enolase (NSE). These morphological and immunohistological features suggested the diagnosis of central neurocytoma.

Although the term central neurocytoma is generally restricted to tumours of the supratentorial ventricular system several reports of this tumour occurring in extraventricular sites have appeared.⁵ Seven cases of "central neurocytoma" have now been described occurring in the spinal cord.²⁻⁴ Such a diagnosis is based on the immunohistochemical profile of the lesions showing neuronal differentiation. The principal differential diagnoses in our case, ependymoma and oligodendroglioma, are excluded by virtue of their immunohistochemical profile.

It has been suggested that the cell of origin of the central neurocytoma arises in the periventricular germinal matrix⁶ and this may account for the finding of these tumours in the spinal cord, arising from the region of the central canal.

Most reported cases of central neurocytoma occur in adolescents or young adults. A review of the cases occurring in the spinal cord shows a wide range of ages (12-67 years). The numbers are too few to draw any

firm conclusions but several cases have occurred at a young age.

As with supratentorial examples of central neurocytoma, the clinical behaviour seems to run a benign course in cases involving the spinal cord. The two cases reported by Tatter *et al*³ received radiotherapy; however, it remains to be seen whether or not this is necessary in most cases. In view of the benign histological appearances (unless there are malignant histological features or aggressive tumour behaviour making the diagnosis of central neurocytoma less likely) we think that postoperative adjuvant radiotherapy should be avoided, particularly in the younger age group with a still growing skeleton.

This case is documented to highlight the importance of recognising central neurocytoma in extraventricular sites as it carries a good prognosis.

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- Hassoun J, Gambarelli D, Grisoli F, Pellet W, Salamon G, Pellissier JF, Toga M. Central neurocytoma. An electron-microscopic study of two cases. *Acta Neuropathol (Berl)* 1982;56:151-6.
- Miller DC, Kim R, Zagzag D. Neurocytomas: non-classical sites and mixed elements. *J Neuropathol Exp Neurol* 1992;51:364.
- Tatter SB, Borges LF, Louis DN. Central neurocytomas of the cervical spinal cord. *J Neurosurg* 1994;81:288-93.
- Coca S, Moreno M, Martos JA, Rodriguez J, Barcena A, Vaguero J. Neurocytoma of spinal cord. *Acta Neuropathol (Berl)* 1994;87:537-40.
- Hassoun J, Soyomezoglu F, Gambarelli D, Figarella-Branger D, von Ammon K, Kleihues P. Central neurocytoma: a synopsis of clinical and histological features. *Brain Pathol* 1993;3:297-306.
- von Deimling A, Kleihues P, Saremaslani P, Yasargil MG, Spoerri O, Sudhof TC, Wiestler OD. Histogenesis and differentiation potential of central neurocytomas. *Lab Invest* 1991;64:585-91.

Cenesthetic hallucinations in a patient with Parkinson's disease

Hallucinations are a side effect of treatment with levodopa and dopamine agonists. They are more common in patients with Parkinson's disease with advanced age and cognitive impairment.¹⁻³ Hallucinations secondary to dopaminergic drugs are usually visual, and less often, auditory.⁴ We describe a patient who developed cenesthetic hallucinations during pergolide and levodopa treatment.

A 66 year old woman with Parkinson's disease, predominantly rigid akinetic, had been treated with carbidopa-levodopa since the age of 55 in 1984. When she was evaluated for the first time in our hospital in 1991, she was treated with 62.5/625 mg/day of carbidopa/levodopa divided into five doses, 5 mg/day selegiline, and 7.5 mg/day bromocriptine. She had motor fluctuations and mild peak dose dyskinesias. Pergolide was introduced in gradually increasing doses up to 3 mg/day as replacement for bromocriptine, with a good initial response. However, in 1992, the parkinsonian symptoms had worsened progressively, and she spent around 60% of the day in "off" periods. Pergolide was increased up to 5 mg/day with a good response. In October 1993, standard levodopa was changed to a controlled release preparation of carbidopa/levodopa, up to 1400 mg/day divided into seven doses, and pergolide was reduced to 3 mg/day because of dyskinesias. On this combination, the parkinsonian symptoms remained stabilised until July 1995, the "off" time being about 20% of the day. At that time, controlled release carbidopa/levodopa needed to be increased up to 450/1800 mg/day and pergolide up to 3.5 mg/day. In September 1995, the patient developed somatic hallucinations that she described as feeling as if her bowels and bladder extruded from the distal parts of her upper limbs. She tried to avoid the extrusion of these organs by compulsively scratching her arms, up to the point of inducing erosions. Reduction of pergolide to 2.5 mg/day and of controlled release carbidopa/levodopa to 350/1400 mg/day did not control the hallucinations, but they improved greatly with clozapine in gradually increasing doses up to 150 mg/day. The somatic hallucinations remained stabilised until November 1996. At that time the dose of clozapine needed to be increased up to 200 mg/day because of worsening. In January 1997, these symptoms are again well controlled.

Somatic hallucinations are defined as false sensations of things occurring in or to the body. When they are visceral in origin they are named cenesthetic hallucinations.⁵ Our patient developed cenesthetic hallucinations that were likely to be related to the antiparkinsonian treatment and were controlled adequately with clozapine. To our knowledge, cenesthetic hallucinations had not been described in this situation previously, and should be added to the range of psychiatric side effects of antiparkinsonian drugs.

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- Meco G, Bonifati V, Cusimano G, Fabrizio E, Vanacore N. Hallucinations in Parkinson disease: neuropsychological study. *Ital J Neurol Sci* 1990;11:373-9.
- Friedman A, Sienkiewicz J. Psychotic complications of long-term levodopa treatment of Parkinson's disease. *Acta Neurol Scand* 1991;84:111-3.
- Saint-Cyr JA, Taylor AE, Lang AE. Neuropsychological and psychiatric side effects in the treatment of Parkinson's disease. *Neurology* 1993;43(suppl 6):S47-52.
- Kippervasser S, Inzelberg R, Korczyn AD. Auditory hallucinations (AH) in Parkinson's disease (PD) [abstract]. IVth international congress of movement disorders. Vienna, Austria, June 17-21, 1996; poster 727. *Mov Disord* 1996;11(suppl 1):194.
- Kaplan HI, Sadock BJ. *Comprehensive textbook of psychiatry*. 5th ed. Baltimore: Williams and Wilkins, 1989:474.

Neuroleptic malignant syndrome-like condition in multiple system atrophy

Neuroleptic malignant syndrome (NMS) usually occurs during treatment with neuroleptic drugs, but a similar condition may occur after a sudden withdrawal of antiparkinsonian drugs or an imbalance of the monoaminergic systems in the brain. On the other hand, extrapyramidal symptoms and dysautonomia are common in multiple system atrophy, which is a disorder of the monoaminergic system, affecting dopamine, noradrenaline, and serotonin. Catecholaminergic agents are sometimes used to treat multiple system atrophy, and NMS-like conditions may also occur in patients with multiple system atrophy.^{1,2} We found six episodes of an NMS-like condition in three out of 14 patients with multiple system atrophy over a one year period (table).

Patient 1 was a 47 year old man who had been receiving antiparkinsonian drugs from the age of 45. Because the drugs did not cause much response, he needed an increasing dosage. On 12 October 1995, the daily dosage of bromocriptine was decreased from 26 mg to 8.6 mg and he was also given 6 mg trihexiphenidyl HCl.

After four days, he developed myalgia, hallucination, hyperhidrosis, and severe bradycardia. On 19 October his body temperature

was 37.7°C. He had high serum creatine kinase (5264 IU (normal <180 IU/l)) and was admitted.

Bromocriptine (26 mg/day) and dantrolene sodium produced an immediate response, but also urinary retention and orthostatic hypotension. Brain MRI suggested a diagnosis of multiple system atrophy. In February 1996, the addition of 50 mg/day trazodone HCl induced bradykinesia and rigidity. Serum creatine kinase was 2560 IU/l. Discontinuation of trazodone HCl and administration of 75 mg dantrolene sodium produced an improvement.

Patient 2 was a 58 year old man who had developed gait disturbance with parkinsonism at the age of 51 and was taking antiparkinsonian drugs. In July 1991, he received low temperature burning on his abdominal skin. After 10 days, he developed rigidity and was admitted to hospital. He had severe rigidity, pyrexia with high serum concentrations of creatine kinase (34 080 IU/l), blood urea nitrogen (51 mg/dl), and creatinine (10 mg/dl), urinary myoglobin (600 mg/day), and showed oliguria. He was diagnosed as having acute renal failure caused by myoglobinuria, and haemodialysis resulted in recovery. In January 1992, he was transferred to our hospital. In June 1993, he developed pneumonia and received antibiotics with a continuation of antiparkinsonian drugs. After recovery from pneumonia, he continued to have a pyrexia, increased rigidity, tremor, and bradykinesia. On 12 July, his temperature was 39.8°C with high serum creatine kinase (2418 IU/l). Discontinuation of L-threo-DOPS and an increase in bromocriptine (17.2 mg to 26 mg) with intravenous dantrolene sodium (40 mg/day) therapy produced improvement. Discontinuation of dantrolene led to a relapse. Increased dosage of levodopa/dopa-decarboxylase inhibitor (300/75 mg to 900/225 mg/day) produced a response. In August 1995, he had a body temperature of 40.3°C and raised creatine kinase (1200 IU/l) with no inflammation or altered medication. Treatment with intravenous dantrolene sodium (40 mg/day) induced recovery within three days.

Patient 3 was a 56 year old woman with a six year history of dysautonomia. At the age of 52, she was pyrexial in the summer. Four years later, she had severe ataxia with hypotonia and no involuntary movements. On 10 July 1987 L-threo-DOPS (600 mg/day) was added to the previous drugs to decrease

Description of patients

Patient	Illness	Sex	Age	Duration of illness	Month of NMS-like episode	Maximum body temp (°C)	Maximum serum CK (IU/l)	Cause	Course
1	SND	M	47	3	October	37.7	5264	Decrease of bromocriptine	Recovery by bromocriptine and dantrolene
				4	February	37.4	2560		
2	SND	M	54	3	July	>39.0	34081	Low temperature burning	Renal failure. Recovery by dialysis
				5	July	39.8	2518		
3	OPCA	F	56	58	August	40.3	1200	Pyrexia + L-threo-DOPS	Recovery by dantrolene
				6	July	42.0	1500		

SND=Striatonigral degeneration; OPCA=olivopontocerebellar atrophy; CK=creatinine kinase.

autonomic failure. On 21 July, she had a low grade fever, and was transferred to Kishiwada Hospital. Her temperature was 37.5°C and she had a normal serum creatine kinase concentration. Five days later, she developed a pyrexia of 42°C with high serum creatine kinase (1500 IU/l). Intravenous dantrolene therapy produced no response and she died of disseminated intravascular coagulation two days later.

In these six episodes of an NMS-like condition, one was caused by decreased antiparkinson medication, one by an antidepressant drug, two by complications, one by hyperthermia from environmental origin, and one by hyperthermia with L-threo-DOPS. Five episodes occurred in the hot season. In Japan, we had hot days in October 1995. Two cases had multiple episodes.

A putative mechanism of pyrexia in an NMS-like condition is dopamine depletion in the extrapyramidal system causing severe rigidity, resulting in high fever and creatine kinase leakage from the muscle to the blood.¹ With antipsychotic drugs, the stronger the affinity to the D₂ receptor, the more often NMS occurs. On the other hand, some agents which do not influence the dopaminergic system also produce an NMS-like condition. An abnormal mechanism in the monoaminergic system is thought to alter the function of the thermal centre of the hypothalamus.³ The setting of body temperature becomes higher by activation of the noradrenergic system, and lower by the dopaminergic or serotonergic systems in the thermal centre.⁴ An imbalance of these systems via medication or other causes may trigger an NMS-like condition. In patient 1, an antidepressant, which influences serotonergic and noradrenergic activities, caused the second episode.

It is characteristic that five episodes were caused by somatic stresses such as infection or hyperthermia of various origins. This condition occurred during the hot season in patients with or without antiparkinson drugs. In a patient with vascular parkinsonism not receiving antiparkinsonian drugs, an NMS-like condition after typical hyperthermia³ was reported to be immediately alleviated by intravenous levodopa therapy. This suggests that activation of the dopaminergic system was important in the NMS-like condition even when dopamine depletion was not its cause. In patient 3, treatment of pyrexia with L-threo-DOPS, a precursor of noradrenaline, caused a further increase in body temperature and development of an NMS-like condition. This substance is effective for akinesia in Parkinson's disease and dysautonomia, and is reported to provoke an NMS-like condition by causing monoaminergic imbalance in the CNS.² A change in hypothalamic noradrenergic activity caused by L-threo-DOPS seems to precipitate an NMS-like condition.

Besides withdrawal of dopaminergic agents, administration of agents which alter monoaminergic neuron activities, stresses to the body, and heat increase from various causes tend to be triggers of an NMS-like condition. Patients with multiple system atrophy, which usually affects thermal regulation, are particularly at risk of developing the condition.

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- 1 Gibb WRG. Neuroleptic malignant syndrome in striatonigral degeneration. *Br J Psychiatry* 1988;153:254-5.
- 2 Murano S, Ogawa N, Ishibe Y, Yamana S. Neuroleptic malignant syndrome associated with droxydopa in a patient with striatonigral degeneration. *Research Communications in Psychology, Psychiatry and Behavior* 1993;18:13-8.
- 3 Kish SJ, Kleinert R, Minauf M, Gilbert J, Walter GF, Slimovitch C, et al. Brain neurotransmitter changes in three patients who had a fatal hyperthermia syndrome. *Am J Psychiatry* 1990;147:1358-63.
- 4 Hori T, Kiyohara T, Nakashima T. Thermosensitive neurons in the brain; role in homeostatic functions. In: JB Mercer ed. *Thermal physiology*. Amsterdam: Excerpta Medica, 1989:3-12.
- 5 Saito T, Honma M, Akanuma J, Shimizu S, Yamamoto T. A classic heat stroke complicated by malignant syndrome. A case improved by intravenous L-dopa. *Neurol Med Chir (Tokyo)* 1996;44:167-72.

Non-Hodgkin's lymphoma as a new cause of non-thrombotic superior sagittal sinus occlusion

The syndrome of non-thrombotic superior sagittal sinus occlusion is an uncommon complication of local neoplastic disease which presents clinically as chronic intracranial hypertension without focal signs.¹ A few cases have been reported as complications of midline tumours involving the occipital region such as Ewing's sarcoma, plasmocytoma, neuroblastoma, and disseminated carcinoma of the breast.¹⁻⁴

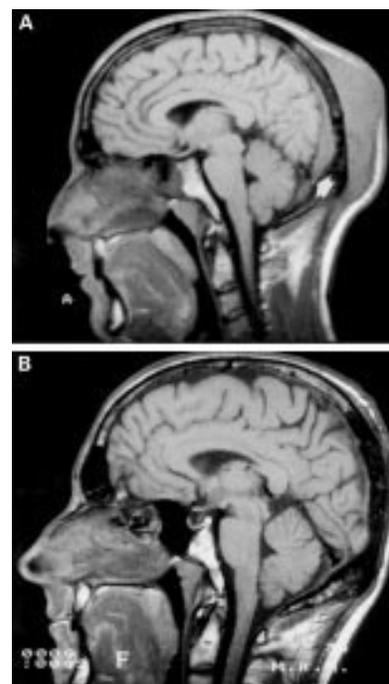
To our knowledge, this is the first case report in which this complication appeared secondary to a non-Hodgkin's lymphoma.

A 36 year old man presented with a subcutaneous mass in the occipital region of the scalp which had increased in size during the past year. His medical history was unremarkable.

The tumour was painless, hard, and fixed to underlying tissue. Neurological examination was normal, except for bilateral papilloedema. Visual acuity was normal. Cranial MRI disclosed an occipital subcutaneous tumour 10×8×3 cm in diameter. Surrounding bone was thickened, and part of the mass extended extradurally, causing displacement of the venous sinuses. Normal signal void in the superior sagittal sinus in T1 weighted images was replaced by a hyperintense signal (figure, A). Complete coagulation studies were normal. The tumour biopsy disclosed a non-Hodgkin's lymphoma and extension study showed a metastatic lesion in the right femur, confirmed by biopsy.

The patient was treated with local radiotherapy and chemotherapy (six sessions CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)).

The subcutaneous mass had disappeared two months later. At one year follow up the patient did not complain of neurological or ophthalmological symptoms, and recent MRI and magnetic resonance angiography showed the absence of occipital tumour and superior sagittal sinus occlusion (figure, B).



(A) Sagittal cerebral T1 weighted (TR 441, TE 15) MRI (1 tesla) showing an occipital subcutaneous tumour infiltrating bone and extending extradurally causing occlusion of superior sagittal sinus (arrow); note a retention cyst in sphenoid sinus. (B) Sagittal cerebral T1 weighted (TR 600, TE 15) MRI (1.5 tesla) one year after local radiotherapy and chemotherapy: the mass has disappeared and superior sagittal sinus has returned to normal.

The syndrome of non-thrombotic occlusion of the superior sagittal sinus, first described by Plant *et al.*,¹ consists of compressive occlusion of dural venous sinuses secondary to midline tumours in the occipital region of the skull. The clinically distinctive feature is the lack of focal signs in the course of chronic intracranial hypertension.

The most common thrombotic occlusion of the superior sagittal sinus is an acute disorder, usually with disturbance of consciousness and focal signs, including seizures and paresis.⁵ Reported cases of occlusion of the superior sagittal sinus associated with neoplastic disease have usually been examples of thrombotic complications secondary to hypercoagulability states.

The syndrome of non-thrombotic occlusion of the superior sagittal sinus occurs when a tumour produces an extradural tissue mass beneath the inner table of the skull, and it is difficult to differentiate between compressive occlusion of the superior sagittal sinus or tumour invasion of the dura and sinus. Cerebral angiography may help in such differentiation, but unfortunately, this examination was not performed in our patient.

This complication has not been described in tumours that commonly give rise to bone metastases such as carcinoma of the bronchus, which develop expanding lytic lesions in the skull with minimal soft tissue involvement. Previous cases of non-thrombotic occlusion of the superior sagittal sinus have been reported secondary to solitary plasmocytoma, Ewing's sarcoma, disseminated carcinoma of the breast, and neuroblastoma,¹⁻⁴ which, as in our case, all present significant involvement of soft tissue.

It is also worthy of mention that the site of first clinical manifestation in our patient, the skull, is suggestive of metastases rather than that of a primary intracranial neoplasm as confirmed on further scanning. Moreover, the excellent response to standard chemotherapy suggests a systemic vascularisation of this tumour.

The site of compression of the superior sagittal sinus in nearly all the reported cases, including the present patient, is the terminal portion of the superior sagittal sinus and the torcular herophili.¹ The chronic course of the sinus compression allows the formation of good colateral venous return, making this process clinically silent.

In conclusion, we report a new cause of non-thrombotic occlusion of the superior

sagittal sinus, and emphasise that this syndrome should be considered in cases of mid-line occipital neoplasms presenting with raised intracranial pressure without focal signs.

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- 1 Plant GT, Donald JJ, Jackowsky A, et al. Partial, non-thrombotic, superior sagittal sinus occlusion due to occipital skull tumors. *J Neurol Neurosurg Psychiatry* 1991;**54**:20–23.
- 2 Korenmna G, Mones RJ. Carcinomatous involvement of the superior sagittal sinus. *Transactions of the American Neurological Association* 1970;**95**:271–2.
- 3 Jakubowski J, Kendall BE, Symon L. Primary plasmocytomas of the cranial vault. *Acta Neurochir (Wien)* 1980;**55**:117–34.
- 4 Mones RJ. Increased intracranial pressure due to metastatic disease of the venous sinuses. A report of six cases. *Neurology (Minneapolis)* 1965;**15**:1000–7.
- 5 Bousser MG, Chiras J, Bories J, Castaigne P. Cerebral venous thrombosis: a review of 38 cases. *Stroke* 1985;**16**:199–213.

PROCEEDINGS

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INTRACRANIAL PRESSURE GRADIENTS IN PATIENTS WITH UNILATERAL MASS LESIONS: THEIR IMPORTANCE IN DEFINING THE SEVERITY OF SECONDARY INSULTS

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In patients who have an unrelieved mass lesion or unilateral swelling there may be pressure gradients throughout the cranial cavity and if the severity of secondary insults is to be accurately determined it is important to ensure that the intracranial pressure (ICP) level is correctly known. Depending on the relative positions of the ICP sensor and the lesion the pressure readings may produce clinically significant pressures.

Ten patients whose intracranial pathology was either a non-evacuated unilateral mass lesion or unilateral hemispheric swelling with midline shift had bilateral frontal Camino ICP monitors inserted. Data were recorded and continuously averaged electronically every two minutes and monitoring was continued while clinically indicated. After removal of the catheters the atmospheric pressure reading of each pressure monitor was recorded to ensure that the readings were not biased by drift.

The recordings ranged in duration from 8.8 to 53.3 (average 33.9) hours and there was a wide range in the ICP levels of the patients, up to a maximum of 127 mm Hg. The recordings could be divided into two groups; those who had sustained differences (>10 minutes) of over 10 mm Hg (group 1) and those in which the readings remained within 10 mm Hg (group 2). The patients in group 1 all had a non-evacuated subdural haematoma whereas the patients in group 2 had sustained either temporal contusions (five) or an intracerebral haematoma (two). The recordings of the patients in group 1 showed differences between the ipsilateral and contralateral recordings. In comparison the recordings from the patients in group two did not show any great discrepancy over time.

The data suggest that there may be differences in the levels of ICP which are obtained from each hemisphere in patients with an unrelieved subdural haematoma. In a total of 10 171 readings the difference exceeded 10 mm Hg on 1391 occasions. With a greater emphasis on the detection and prevention of secondary insults it is important to recognise that these differences exist. There may also be more localised pressure gradients which have yet to be determined. Nevertheless, differences seldom exceeded 10 mm Hg unless an acute subdural haematoma was present so

that practically the data suggest that monitoring can be conducted on either side except with an unrelieved subdural haematoma.

APOLIPOPROTEIN E AND OUTCOME OF HEAD INJURY

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Much of the variation in outcome after head injury remains unexplained. Polymorphism of the apolipoprotein E (ApoE) influences neuropathology of fatal head injury—the $\epsilon 4$ allele being associated with amyloid β protein deposits.¹ Experimental studies indicate that ApoE has an active role in response to acute brain injury, and $\epsilon 4$ status is a risk factor for Alzheimer's disease. A prospective study was therefore conducted to determine the influence of ApoE status on clinical outcome. A pilot series of 100 patients was identified in the acute stage after injury after admission to the neurosurgical unit. Survivors have been followed up and outcome determined at six months. The ApoE genotype was determined by polymerase chain reaction (PCR). Data on outcome are available on 82 subjects. In the group of 28 with an ApoE $\epsilon 4$ allele (34%) outcome was worse, with 61% being dead/vegetative or severely disabled compared with 30% of the other 54 subjects ($\chi^2=7.4$ 1 df, $P=0.006$). The groups of subjects with ApoE $\epsilon 4$ tended to have a lower Glasgow coma score but they were younger and had fewer mass lesions; adjustment for these factors indicated that ApoE status remained associated with poor outcome. Further studies are needed to confirm the influence of ApoE status on outcome, if there are interactions with type of injury, and to determine if its influence on the biology of recovery from head injury is amenable to modification.

1 Nicoll JAR, Roberts GW, Graham DI. *Nature* 1995;1:135-7.

CEREBRAL HAEMODYNAMICS (CH) IN CHRONIC SUBDURAL HAEMATOMA

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The purpose of this study was to establish (a) CH status in chronic subdural haematoma (CSDH), (b) changes induced by surgery, (c) possible clinical relevance.

Of 28 surgical patients, 21 had uneventful postoperative courses (group 1), seven (group 2) developed complications. Serial middle cerebral artery blood flow velocities (FV) and transient hyperaemic response (THR) on both sides were assessed by transcranial Doppler (TCD), and FV ratio

(affected: normal) calculated (FVR). Intracranial pressure (ICP) was assessed at operation.

Admission clinical neurology and CT assessment were similar in both groups. With one young exception initial TCD disclosed reduced systolic and average FVs on the affected side. Group 1 PVRs improved on the first postoperative day, reaching significance (compared with group 2) on the second ($P<0.05$). ICP ($r=+0.66$) and FVR ($r=-0.77$) correlated with midline shift, as did ICP with FVR ($r=-0.83$). Affected side THR was significantly lower ($P<0.05$). Dense hemiplegia was associated with a low THR but not inevitably low FV. THR return preceded recovery. Low postoperative FVR indicated likely recollection and persisting deficit.

1 Giller CA. *Acta Neurochir* (Wien) 1991;108:7-14.

COMPOUND FRACTURES OF THE ANTERIOR CRANIAL BASE: A NEW CLASSIFICATION AND ITS IMPLICATIONS FOR SURGICAL MANAGEMENT

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The risk of post-traumatic meningitis after cranial base fractures is difficult to determine and current management is primarily guided by the fractures' association with CSF rhinorrhoea. It is likely, however, that the location and size of the cranial disruption are important predisposing factors to intracranial infection; despite this, the effect of these variables has not been investigated.

To determine whether the relative risk of post-traumatic meningitis is related to the location and size of cranial base disruption, a classification of compound anterior cranial base fractures has been developed which incorporates both location and size; these criteria were used in addition to other variables (duration of rhinorrhoea, aerocele, brain herniation in cranial defects, episodes of infection, or neurological state) to decide whether a patient should be treated by surgical or conservative means.

With the aid of high resolution thin section coronal CT, these fractures were classified into four major types: (1): cribriform, (2): frontoethmoidal, (3): lateral frontal, and (4): complex, and depending on their size as "large" and "small".

Forty eight patients who were treated by conservative (n=20) or surgical (n=28) means were studied. The number of patients in each fracture type was as follows: seven in 1, 12 in 2, 13 in 3, and 16 in 4. Nineteen fractures were small and 29 were large. At surgery, the dural defect was found to be adjacent to and larger than the fracture in all patients. None of the surgically treated

patients developed recurrence of rhinorrhoea or intracranial infection.

In the early post-traumatic stage (three months), high resolution CT is a sufficiently sensitive investigative technique and the indications for contrast cisternography are limited. Anterior cranial base microsurgical repair has a minimal complication rate. This classification can improve the management of post-traumatic "CSF fistulas" of the anterior cranial base and may provide insights into the mechanisms underlying their spontaneous repair and susceptibility to meningitis.

HOSPITALISED HEAD INJURIES: SEQUELAE, REHABILITATION SERVICES, AND OUTCOME
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The study, funded by the Chief Scientist, Scottish Health Department, aims to provide the first fully representative picture of the problems and needs of an adult head injured population after discharge from hospital, how these are being managed, and how they should be met. In the first phase of the study 3005 adults (over 14 years of age) admitted to hospital in Glasgow over a one year period were identified. To provide a comprehensive picture, patients with previous medical or social problems, neurological illness, psychiatric history, or alcohol misuse were included, although they are often excluded from neuropsychological studies.

Categorised according to Glasgow coma scale on arrival at hospital: mild 92%, moderate 5%, and severe 3%. There was a record of previous head injury, in 25% of a previous neurological illness in 10% and of preceding physical limitations in 29%. Excessive/problem drinking was recorded in 33%. Patients are followed up by a combination of questionnaire, telephone interview, and in person assessment at one, three, six, and 12 months postinjury. The instruments used are the DRS, modified Brook McKinlay relative questionnaire, functional assessment scale, and a general health status questionnaire – Short form 36, Glasgow outcome scale. Medical therapeutic and social services post discharge were documented.

One year after injury information is being obtained from 80% of patients. Data from the first 100 patients show a high rate of flexibility—moderate disability as classified by Glasgow outcome scale in 30% of patients, severe disability in 26%, 1% in vegetative state. Even in mild/minor injuries only 29% made a good recovery. This reflected a high proportion of patients reporting problems in behaviour, relations, and cognition. Furthermore 32% of patients were reporting that they were not coping with problems, 7% were overwhelmed and depressed. The data indicate a lack of initial planning and minimal contact with rehabilitation/support services and medical outpatient clinics after discharge from hospital.

A COMPARATIVE STUDY OF SPONTANEOUS AND TRAUMATIC INTRACEREBRAL HAEMORRHAGE
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Spontaneous intracerebral haemorrhage is associated in most cases with structural

abnormalities of the small arteries of the brain. Much work has been done on the pathology, natural history, treatment options, and prognostic indicators in patients with spontaneous intracerebral haemorrhage. Traumatic intracerebral haematomas, on the other hand, are aetiopathologically different and less well understood. These two pathophysiologically different varieties of intracerebral haemorrhage have been compared to find out the similarities and differences between the natural history, clinical behaviour, and outcome. This is a prospective study comprising 259 patients in the spontaneous group and 102 patients in the traumatic group. The two groups of patients are matched according to location, size of haematoma, and level of consciousness on admission. The demographic data were similar in both the groups. The age and sex distribution does not differ significantly in either of the groups. The most important predictor of the outcome was the Glasgow coma scale score on admission in both the groups ($P < 0.01$). Age of the patient was important in predicting the outcome in the traumatic group. The size of the haematoma was a strong predictor of the outcome in the spontaneous haematomas ($P = 0.006$) although it was less significant in the traumatic group. Evacuation of haematomas was carried out in 31% of the traumatic versus 13% of spontaneous haematomas. The evacuated traumatic haematomas fared well compared with the non-evacuated group (mortality 15% and 37% respectively). With spontaneous haematomas on the other hand the mortality was similar in the evacuated and non-evacuated groups. The overall outcome was better in the traumatic haematomas with the mortality of 18% and a favourable outcome (good recovery and moderate disability on Glasgow outcome scale) of 52%. The spontaneous haematomas on the other hand had an overall mortality of 43% and a favourable outcome in only 33% of patients at the end of six months.

DISRUPTION OF THE DENDRITIC AND AXONAL CYTOSKELETON AFTER ACUTE SUBDURAL HAEMATOMA IN THE RAT
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Ischaemic brain damage is the most important secondary pathophysiological process after acute subdural haematoma. Breakdown of the cytoskeleton and alterations in microtubule associated proteins may play an important part in this process.

Acute subdural haematoma was created by the injection of 0.4 ml venous blood into the subdural space. Sham controls had needle insertion only. After 30 minutes, two hours, and four hours the brains were perfused fixed and processed for MAP 2 and tau-1 immunohistochemistry. Electron microscopy was performed in a group of four hour survival animals.

In the ipsilateral cortex there was loss of MAP 2 immunostaining indicating disruption of dendrites. Ultrastructural analysis showed misalignment of dendritic microtubules with the formation of an abnormal helically oriented pattern rather than the linear arrangement identified in controls. In the corpus callosum and white matter tracts underlying the haematoma there was an abnormal punctate, granular pattern of tau-1 immunoreactivity compared with the smooth

pattern of staining in controls. Electron microscopy showed loss of microtubules and compaction of neurofilaments in axons of reduced calibre.

Cytoskeletal breakdown occurs in dendrites and axons after acute subdural haematoma. Abnormalities of the neuronal cytoskeleton may play an important part in the pathobiology of acute subdural haematoma.

CONSERVATIVE MANAGEMENT OF CAVERNOUS ANGIOMAS: REVIEW OF NINE CASES
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Nine patients with cerebral cavernous angiomas treated conservatively in the department were reviewed. Five presented with epilepsy and four presented with focal neurological deficits (one case presented with a spontaneous intracerebral haematoma).

These were four female and five male patients, two lesions were found in the brainstem, one in the cerebellum, and six were supratentorial (one in the basal ganglia). The patients who presented with epilepsy had good control of their seizures during the follow up period. Only one developed an episode of status epilepticus, which was successfully treated. In the follow up period (6 months-10 years), the remainder of the patients had a favourable outcome, including the two cases with brain stem lesions who showed progressive improvement of their neurological deficits. No patient had a further haemorrhage. Our results in this small series of patients indicate that surgical treatment may not always be necessary for the treatment of cavernous angiomas, as good results can be achieved with conservative management only.

It is suggested that randomised controlled trials be considered to compare the results of surgical and conservative management strategies, because both seem to yield good results.

STRESS HMPAO CEREBRAL PERFUSION IMAGING USING ACETAZOLAMIDE IN CEREBROVASCULAR DISEASE: THE EFFECT OF DIASCHISIS ON IMAGE QUANTIFICATION
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Stress/rest cerebral perfusion imaging may identify patients with transient ischaemic attacks (TIAs) who may benefit from surgery. This study assessed 20 patients having HMPAO SPECT and transcranial Doppler flow measurements before (rest) and after (stress) acetazolamide. The SPECT images were registered to a common template. Regions of interest (ROIs) were drawn over RIL cerebral cortex and cerebellum and asymmetry indices calculated. Of the 20 patients, 19 had clinical signs localising to a particular hemisphere (13 TIAs, six CVAs); this was correctly identified in 16/19 on rest studies and in 18/19 on stress studies.

The resting asymmetry as measured by SPECT correlated significantly with the degree of carotid stenosis. There was a significant inverse correlation between LIR cerebral perfusion ratios and LIR cerebellar ratios as a result of diaschisis. The differences in stress/rest cortical asymmetries also correlated significantly with the change in trans-

cranial Doppler flow velocities. However, this relation did not hold if the cortical counts were normalised to the cerebellum. This seems to be a consequence of diaschisis and, in this situation shows the potential limitations of using the cerebellum as the denominator in ROI analysis.

VASCULAR REACTIVITY OF RAT MIDDLE CEREBRAL ARTERIES TO NIMODIPINE IN ACUTE EXPERIMENTAL SUBARACHNOID HAEMORRHAGE
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Nimodipine (calcium channel blocker) is recognised as a cell protecting agent. It is also widely considered to be a vasodilator for cerebral vessels. The aim was to evaluate the action of nimodipine on rat middle cerebral arteries, *in vitro*, in normal, and after SAH of varying severity. The Sheffield rat model was used to produce SAH. The animals were killed three hours after the haemorrhage or if their blood pressure dropped to below 50 mm Hg systolic. Brain was removed and both middle cerebral arteries harvested and mounted on a Mulvany small vessel myograph. The viability of the vessels was assessed by using known vasoconstrictors and vasodilators. Subsequently the response to nimodipine in increasing concentration (2-20 µg) was tested.

Twenty four rats were divided into the following groups: group I: (n=9) No SAH; group II: (n=9) SAH and occlusion of ipsilateral carotid artery; group III: (n=6) SAH and reperfusion of ipsilateral carotid artery. Group III represents the greater severity of SAH. Mean maximum response (mN/mm) to nimodipine, of vessels precontracted with prostaglandins: Prostaglandin, group I-2.59, group II-1.2, group III-0.89; nimodipine 2 µg, group I-1.08, group II 0.99, group III -0.73; nimodipine 6 µg, group I-2.75, group II-2.35, group III-1.54; nimodipine 12 µg, group I-4.95, group II-3.64, group III-3.02; nimodipine 20 µg, group I-6.47, group II-5.01, group III-4.19. These results show that nimodipine produces a significant dose related vasoconstriction in cerebral vessels, both in normal rats and after SAH. The constriction was less pronounced with increasing severity of the bleed.

TRANSFORMING GROWTH FACTOR β1 CONCENTRATIONS IN CSF FROM PATIENTS WITH SUBARACHNOID HAEMORRHAGE
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Cytokines are important regulators of tissue wounding responses, and have previously shown that transforming growth factor-β1 (TGF-β1) is a major fibrotic factor within CNS wounds. Manipulation of its action in a rat model of CNS injury can prevent scar formation. Previous work has shown that TGF-β1 can be detected in human CSF, and therefore TGF-β1 concentrations were measured in CSF samples from patients who have sustained a form of CNS injury (subarachnoid haemorrhage-SAH) and in samples from a CSF bank, using an enzyme linked immunosorbent assay kit (Promega). Results indicate that the concentration of total TGF-β1 in patients with CNS injury is indeed higher than in control subjects with idiopathic hydrocephalus. In controls TGF-1 was generally below 270 pg/ml. In patients

with SAH the concentration was raised to above 420 pg/ml, and up to as high as 2000 pg/ml. The highest concentrations were detectable in the first days post-SAH, thereafter concentrations decline towards those seen in controls. Establishing that TGF-β1 concentrations rise after injury is the first step towards utilising a TGF-β related antifibrotic strategy in the injured human CNS. The ultimate goal of this research is to work towards pharmacological manipulation of endogenous trophic growth factors.

THE ROLE OF ENDOTHELIN IN THE DEVELOPMENT OF DELAYED PERILESIONAL ISCHAEMIA AFTER INTRACEREBRAL HAEMORRHAGE IN DIABETIC AND NON-DIABETIC RATS

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The role of endothelin (ET) in the evolution of delayed perilesional ischaemia, and the contribution to final outcome of the chronic cerebrovascular dysfunction associated with diabetes mellitus¹ were studied in a rodent model of intracerebral haemorrhage.

During a brief period of anaesthesia, 50 µl of arterial blood was injected into the striatum of spontaneously diabetic insulin treated BB rats and non-diabetic controls. Groups of diabetic and non-diabetic animals received either the ET antagonist SB209670² (10mg.kg⁻¹ intraperitoneally) every 6 hours, starting 30 minutes before the induction of the haematoma or saline injection. After 24 hours local cerebral blood flow (LCBF) was measured using [¹⁴C]-iodoantipyrine autoradiography.¹ Results are presented as mean (SD) (n=6 in each group)

MABP in SB209670 treated diabetic rats (103 (6 mm Hg)) was significantly lower than in those treated with saline (121 (12 mm Hg)), but there was no difference in the non-diabetics. In non-diabetic rats, SB209670 treatment significantly reduced the volume of striatal ischaemia by 85% (0.1 (0.1) v 0.68 (0.42) mm³) but it failed to reduce the volume of ischaemia in the diabetic animals (5.64 (3.86) v 4.89 (3.14) mm³). In the contralateral striatum SB209670 increased LCBF significantly in the diabetic rats (from 89 (14) to 121 (12) ml. 100 g⁻¹.min⁻¹), whereas it had no effect in the non-diabetic group.

These results indicate that in normal rats ET may contribute to the development of delayed perilesional ischaemia after intracerebral haemorrhage. The increases in contralateral striatal blood flow and the reduction in MABP in diabetic rats after SB209670, is consistent with an increased basal ET production in these rats. However, ET does not seem to be involved in the increased vulnerability to cerebral ischaemia associated with diabetes mellitus.

- 1 Fouyas IP, Kelly PAT, Ritchie IM, *et al.* *Br J Pharmacol* 1996;118: 243-8.
- 2 Barone FC, White RF, Elliot JD, *et al.* *J Cardiovasc Pharmacol* 1995; 26: S404-7.

FUNCTIONAL ASPECTS OF THE IMMEDIATE EARLY GENE RESPONSE TO CEREBRAL ISCHAEMIA: AN ANTISENSE APPROACH

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The expression of various immediate early genes (IEGs) has been shown after cerebral

ischaemia and head injury.¹ The role of these factors *in vivo* remains unresolved.

The expression of several IEGs after experimental cerebral ischaemia with reperfusion has been studied. The induction patterns show a relation between junB expression and delayed neuronal death after global ischaemia, and between c-jun expression and neuronal survival after global and focal ischaemia. Specific antisense oligonucleotide treatments offer a promising means of examining the consequences of inhibiting IEG responses. However, the IEG responses to ischaemia were not attenuated using this approach. Marker studies suggested that intraventricular antisense treatments were not taken up by neurons. In hippocampal cell cultures, treatment with junB antisense enhanced neuronal survival after N-methyl-D-aspartate administration (P = 0.01), whereas c-jun antisense showed no protection.

The IEG response to cerebral ischaemia seems to be involved in both protective and toxic pathways. However, pharmacokinetic factors significantly hamper the applicability of the antisense approach in unravelling unanswered questions.

- 1 Whitfield PC, Woodburn VL, Pickard JD. *J Neurol Neurosurg Psychiatry* 1996;61: 550.

ARTERIOVENOUS MALFORMATIONS AND SEIZURES: TREATMENT OUTCOMES

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17%-40% of arteriovenous malformations (AVMs) present with a seizure disorder. Treatment is indicated to eliminate the risk of haemorrhage but may affect the seizure pattern. The purpose of the study is to determine the outcome in such a group of patients and serve as a pilot for a larger multicentre project.

Sixteen patients (12 male, 4 female; ages 14-59) with AVMs presenting with seizures without haemorrhage between 1990-1996 were reviewed retrospectively. Most were AVMs in the frontal and temporal lobes. Seizure type depended upon location. All patients were on antiepileptic drugs, five being seizure free; five patients had one to four seizures/month. Neurological examination was normal in nine, others had deficits dependent on location. Angiographic, CT, and MRI features were discussed. Seven patients had surgery alone; surgery with preoperative embolisation in three; stereotactic radiosurgery (STRS) alone in three; embolisation + STRS in one; surgery + STRS in one; embolisation alone in one.

Twelve patients were seizure free post-treatment. In one, there has been no change; one has improved seizure control and one patient (STRS alone), deteriorated. Pretreatment neurological deficits resolved in five patients and only one mild and one moderate permanent neurological deficit occurred as a result of treatment. Treatment complications were presented. The pathophysiology of seizures secondary to AVMs were discussed. Treatment of AVMs presenting with seizure disorders is beneficial.

ASSESSMENT OF ACETAZOLAMIDE CEREBROVASCULAR REACTIVITY TESTING USING NEAR INFRARED SPECTROSCOPY (NIRS) AND TRANSCRANIAL DOPPLER (TCD)

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Cerebrovascular reactivity is predictive of stroke risk in patients with carotid disease. However, the use of CO₂ as a cerebrovascular stimulant alters arterial blood pressure (ABP) which confounds estimations of reactivity. In addition, accompanying changes in extracranial cutaneous blood flow interferes with reactivity measurements using near infrared spectroscopy (NIRS). The use of acetazolamide, a traditional specific cerebrovasodilator, has been explored, and the effects of this agent on ABP and cutaneous blood flow determined.

Twenty eight patients with symptomatic carotid disease were investigated. Middle cerebral artery flow velocity (FV) was measured using transcranial Doppler, and NIRS measurements of oxy (HbO₂) and deoxyhaemoglobin (Hb) were obtained from ipsilateral frontal optodes. Cutaneous blood flow was surveyed between the optodes using a laser Doppler probe (LDF). ABP was measured continuously (Finapres). Stable baseline recordings were collected for 15 minutes before intravenous injection of 1g acetazolamide. FV and HbO₂ increased to a new steady state level after 6.4 minutes (range 4.5-11.5 minutes). Five minute epochs for baseline and hyperaemic stages were calculated.

FV increased 32.3% ($P < 0.001$), HbO₂ increased (mean 2.27 (0.398) $\mu\text{mol/l}$, $P < 0.001$), and Hb decreased (mean 0.427 (0.182) $\mu\text{mol/l}$, $P < 0.001$). The change in NIRS variables showed significant correlation with FV (v HbO₂; $P = 0.0087$, $r = 0.485$). After acetazolamide, ABP variation was not significant (+0.06% (SEM 1.58)). However, changes in LDF were seen which were highly variable (7.6% (SEM 7.5)).

Acetazolamide is not associated with significant changes in ABP allowing a stable environment for calculation of cerebrovascular reactivity. However, significant extracranial cutaneous flow changes do occur which contaminate the calculation of NIRS-reactivity indices.

IMPAIRED AUTOREGULATION DURING CAROTID ENDARTERECTOMY: AN EARLY INDICATOR OF CEREBRAL ISCHAEMIA

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The decision to shunt during carotid endarterectomy is based on indicators of cerebral ischaemia during internal carotid artery (ICA) clamping. A new technique is described to identify patients who exhibit impaired cerebral autoregulation before clamping, who are at risk of developing cerebral ischaemia during clamping. This would facilitate preparation for shunting.

Seventy five carotid endarterectomies were performed under general anaesthesia. Shunting criteria were: contralateral ICA occlusion, clamp stump pressure of < 50 mm Hg or $> 2/3$ reduction, or clamp MCA-V of < 30 cm/s, or $> 60\%$ reduction. Mean arterial blood pressure (MAP) and middle cerebral artery flow velocity (MCA-V) were continuously monitored by transcranial Doppler. A close correlation between MAP and MCA-V, defined by a regression correlation of > 0.75 , was taken to indicate impairment of cerebral autoregulation.

Thirty five patients were shunted. MAP/MCA-V correlation before clamping corre-

lated with shunting criteria with a sensitivity of 89% (32/35) and a specificity of 92.5% (37/40). It is concluded that this method identifies patients at risk of cerebral ischaemia, allowing early shunt preparation and decreased clamp time, when there is the greatest risk of cerebral ischaemia. False negatives would be detected by shunting criteria, and therefore all patients at risk would be detected.

A DIFFERENTIAL RESPONSE OF THE CRITIKON NEAR INFRARED SPECTROSCOPIC DEVICE IN NORMAL SUBJECTS DURING MENTAL ACTIVATION TASKS

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Previous studies using near infrared spectroscopy (NIRS) during reactivity or mental activation tasks have shown some correlation with regional brain perfusion. This study set out to evaluate the Critikon device in its ability to detect similar changes in brain oxidative state during controlled mental activation tasks.

Twelve normal volunteers had two standard NIRS probes placed bilaterally over the frontal region. Standard NIRS derived indices including regional saturation and total haemoglobin were sampled continuously. After a two minute baseline resting phase, subjects were given a three minute encoding task which consisted of memorising a set of word pairs read to them by a neuropsychologist. This was followed by a retrieval phase in which subjects were asked to remember the matching word when prompted with the first word of the word pair.

Individual patients showed subtle increases ($< 2 \mu\text{M}$) in total haemoglobin (tHB) during the encoding task when compared with the baseline resting phase. However, there was a wide variation in response to this task with 7/12 subjects showing an increase in tHB (range 0.20 $> 1.10 \mu\text{M}$, median 0.58 μM) whereas the remaining subjects showed a similar range of decrease in tHB during the encoding phase (range 0.11 > 1.04 , median 3.8 μM). Grouped analysis of variance (ANOVA) comparing the change in tHB between baseline and the encoding phase showed no significant difference ($P = 0.419$) either within each monitored hemisphere or between hemispheres.

This study provides no evidence that this device detects changes in brain perfusion during mental activation tasks. It is interesting that some patients show an increase whereas others show a decrease in tHB during activation. It is possible that these changes may be following extracranial changes in perfusion brought on by stress effects or is linked to within subject variability to brain activation tasks. Work is in progress, using measures of task effort employed and monitoring of the extracranial perfusion, to investigate this phenomenon further.

AN INCREASE IN TRANSCRANIAL DOPPLER PULSALITY INDEX DOES NOT INDICATE THE LOWER LIMIT OF CEREBRAL AUTOREGULATION
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Transcranial Doppler pulsatility index has been reported clinically to increase when cerebral perfusion pressure decreases, hypothetically marking the lower limit of cerebral autoregulation. To clarify these findings, the relation was investigated between pulsatility index, cerebrovascular resistance, and cerebral perfusion pressure in various states of autoregulation in an animal model of moderate intracranial hypertension.

Experiments were performed in eight anaesthetised and ventilated New Zealand white rabbits. Basilar artery blood flow velocity (ultrasound Doppler) and cortical blood flow (laser Doppler) were monitored continuously during slow subarachnoid saline infusion to cause a moderate increase in intracranial pressure. During this infusion, four animals showed a stable cortical blood flow, and four showed decreasing blood flow when cerebral perfusion pressure decreased.

In all rabbits, the pulsatility index showed an increase when cerebral perfusion pressure decreased, whether cortical blood flow was stable or falling. Furthermore, the percentage rate of increase in the pulsatility index was not different in autoregulating and non-autoregulating animals. However, the rate of decrease in cerebrovascular resistance was significantly lower in non-autoregulating than in autoregulating animals ($P < 0.05$).

The increase in transcranial Doppler pulsatility index when cerebral perfusion pressure falls cannot be interpreted as a phenomenon able to mark the lower limit of cerebral autoregulation

THE ROLE OF PROTEOLYTIC ENZYMES IN ISCHAEMIC NEURONAL INJURY

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Proteolytic enzymes are involved in intracellular protein degradation and neuropeptide metabolism in normal brain, and have been implicated in the pathogenesis of tissue damage in various neurodegenerative disorders. Enzyme activation might also contribute to ischaemic neuronal injury, thereby providing a potential site for therapeutic intervention in human stroke. Proteolysis was therefore evaluated after induction of a focal cerebral ischaemic lesion in aged rodent brains and the influence of established neuroprotective therapy with NMDA receptor antagonism was assessed.

Aged (30 months) male Wistar rats were randomly allocated to treated (the non-competitive NMDA receptor antagonist D-CPP-ene) and untreated (saline) groups. Focal cerebral ischaemia was induced by proximal thermocoagulation of the left middle cerebral artery according to the technique of Tamura. After six hours, the brains were removed, the cerebral hemispheres were separated, and protease activities were assessed in ischaemic (left hemisphere) and non-ischaemic (right hemisphere) brain tissue of both groups. After repeated cycles of homogenisation, centrifugation, and resuspension of tissue samples, various neutral, acidic and alkaline peptidase activities were assayed using a previously established technique.¹

All enzyme activities were significantly reduced in ischaemic brain—for example, the mean activity of the calcium regulated neutral peptidase alanine aminopeptidase (ala AP) in

ischaemic and non-ischaemic brain tissue (n=10 in both groups) was 433 (93) and 816 (122) respectively ($P<0.05$), with respective mean activities of proline endopeptidase (proEp) of 162 (30) and 422 (43) nmol substrate/hour/ml brain extract ($P<0.0005$). D-CPP-ene moderated the reduction in proEp activity, with mean values of 314 (40) and 137 (54) in the ischaemic tissue of treated and untreated aged rats respectively ($P<0.05$).

Ischaemic neuronal injury does not result from the activation of endogenous proteolytic enzymes and so therapeutic strategies based on the administration of protease inhibitors are unlikely to be of benefit in human stroke. The reduction in enzyme activity in infarcted brain tissue may represent inhibition of cellular protein synthesis and the moderation of enzyme inhibition in treated animals might therefore merely reflect the reduction in cerebral infarct volume that has previously been documented with D-CPP-ene.

1 Shaw P, Ince P, Falcous G, Mantle D. *J Neurol Sci* 1996;139:71-5.

ASSESSMENT OF COMPLIANCE OF LARGE CEREBRAL ARTERIES

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Previous studies^{1, 2} have indicated that pulsations of intracranial pressure (ICP) are derived from the blood pressure (ABP) pulse by transmission through compliant arterial walls (C_a) to the compliant compartment of cerebrospinal space (C_s).

Therefore the ICP pulse can be expressed as $ABP_{pulse} \cdot C_s / (C_a + C_s)$. Measuring the value of C_s by continuous CSF infusion, and recording ICP_{pulse} and ABP_{pulse}, it was aimed to establish the relation between C_s , arterial CO_2 concentration, and cerebral perfusion pressure (CPP).

Twelve New Zealand White rabbits were studied under the UK Animal (Scientific Procedures) Act, 1986. Arterial blood pressure (ABP), intracranial pressure (ICP), basilar artery flow velocity, and laser Doppler cortical blood flux were recorded continuously. In six rabbits a series of three subdural infusions of saline (0.1 ml/min) were performed on three different levels of arterial CO_2 (hypocapnic, normocapnic, and hypercapnic). In the remaining six animals infusion was repeated on two different levels of ABP: baseline (mean 92 mm Hg) and reduced (mean 71 mm Hg).

Both resistance to CSF outflow and compliance C_s were independent of CO_2 . ICP_{pulse} amplitude had a slight but significant tendency to rise with CO_2 ($P<0.05$). The impact of CPP on ICP pulsatility was clearly much greater, showing an inverse relation ($P<0.001$). Similarly, the relation between C_s and CPP was inverse, with only a slight modulation by CO_2 . This method for the evaluation of compliance in big cerebral arteries provides reproducible data that shows differential dependence of C_s on arterial CO_2 and CPP.

1 Piper I, Miller JD, Dearden M, et al. *J Neurosurg* 1990;73: 871-80.

2 Czosnyka M, Guazzo E, Whitehouse H, et al. *Acta Neurochir* 1996;138:531-42.

CSF FROM PATIENTS WITH SUBARACHNOID HAEMORRHAGE ACCELERATES VASCULAR SMOOTH

MUSCLE OXIDATIVE METABOLISM

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The aim was to determine whether CSF from patients with SAH had an effect on vascular smooth muscle oxidative metabolism in excess of tension development in vitro. The oxidative metabolism findings were compared with the predicted risk of vasospasm (using Fisher grade) and the presence of angiographic vasospasm.

Samples of CSF were obtained from 32 patients, mean age 54, with SAH. Lengths of porcine carotid artery were incubated in an oxygen electrode chamber and exposed to the patients' CSF. Of the 20 patients with vasospasm or at risk of spasm (Fisher grade 3/4), the CSF of 16 elicited more than a fivefold increase in the O_2 consumption whereas this only occurred in two of the 12 patients of low risk ($X^2 = 0.0003$). Of these two, only one, with a basilar aneurysm, developed angiographic vasospasm.

The porcine carotid arteries were treated with various compounds to determine how the CSF accelerated O_2 consumption in excess of tension development. A protein kinase C and protein kinase A inhibitor, and an endothelin antagonist were not able to prevent the stimulation of oxidative metabolism by the CSF. The increase in O_2 consumption has so far, proved to be irreversible. Compounds acting through α_1 receptors, such as dobutamine and noradrenalin, reduced this rise in oxidative metabolism in vitro.

MAGNETIC RESONANCE ANGIOGRAPHY AFTER SUBARACHNOID HAEMORRHAGE

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Negative digital subtraction angiography (DSA) after established subarachnoid haemorrhage (SAH) is well recognised. Generally it is held to augur well for the patient. However, over the past year (1996) a policy has been adopted of following up patients after proved SAH and negative DSA with a magnetic resonance angiogram (MRA).

The results have been surprising. Out of 22 such patients, five have been shown to have been harbouring aneurysms on the MRA study. These aneurysms were not visible on a conventional DSA. It must be emphasised that all the initial DSA studies were technically good, with multiple views taken of all the vessels: importantly, no arterial spasm was seen in any of these studies.

The MR angiograms have shown four anterior communicating aneurysms, and one true anterior choroidal aneurysm. Even in retrospect, these aneurysms were not visible on the original DSA studies.

The DSA angiograms were repeated, showing the aneurysms in every case.

All these patients went on to have successful clipping of their aneurysms, and none—fortunately—rebled during the interval between their original subarachnoid haemorrhage and surgery.

It is not clear why good quality initial digital subtraction angiograms failed to show these aneurysms. It is proposed that magnetic resonance angiography may be a useful

adjunct to conventional DSA, in patients in whom there is a very strong suspicion of an underlying aneurysm.

DEMANDS FOR NEUROINTENSIVE CARE (“TRIPLE H”) SUPPORT IN PATIENTS UNDERGOING EARLY ANTERIOR CIRCULATION ANEURYSM SURGERY
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The concern that early surgery for aneurysmal subarachnoid haemorrhage (SAH) may result in greater demand for neurointensive care during the peri-operative period has been examined. The clinical and intensive care records of 110 consecutive SAH patients (WFNS grade I-III after resuscitation) undergoing anterior circulation aneurysm surgery were examined and recorded on a standard proforma. A policy for surgery within four days was pursued. Activity while resident on the intensive care unit (ICU) was specifically considered, including the need for hypervolaemia, hypertension, and haemodilution (“triple H” treatment).

Eighty (73%) patients underwent surgery within four days (mean time 2.3 days). The remaining 30 (27%) underwent later surgery (mean time 11.9 days) due to delays in presentation or management. There was no significant difference between the SAH grade of the early and late group and no difference in the three and six month Glasgow outcome scores (favourable GOS 4,5 in 85% v 87% and 84% v 83% respectively). Each group received similar volume expansion, and there was no difference between the groups in the percentage of patients receiving inotropic support. However, a larger number of early operated patients were monitored using a PAWP catheter. The mean length of ICU stay was 4.7 days for the early group and 5.9 days for the late group.

The data does not support the concern that early surgery offers a greater demand for “triple H” treatment, and therefore for ICU facilities. Early anterior circulation aneurysm surgery can be considered for all patients presenting with grade I-III SAH.

CEREBRAL ANEURYSM FORMATION IN AUTOSOMAL POLYCYSTIC KIDNEY DISEASE

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Between 5% and 22% of patients with autosomal dominant polycystic kidney disease (ADPKD) harbour a cerebral aneurysm.¹ Rupture leads to death in 10% and severe disablement in a further 38%. Screening using magnetic resonance angiography (MRA) detects asymptomatic aneurysms allowing preventative therapy. Previous aneurysm incidence studies in ADPKD have suffered from significant ascertainment bias towards families with cerebral aneurysm formation. The role of environmental and genetic factors in familial clustering of cerebral aneurysms in ADPKD is unknown.

One hundred unselected patients with ADPKD will be screened for asymptomatic cerebral aneurysm, using MRA. The i antitrypsin phenotypes of these patients and also of all patients with ADPKD referred with a history of cerebral aneurysm will be documented. The role of environmental factors such as smoking in familial clustering of aneurysms in ADPKD will be investigated. To

date 38 patients have been recruited to the trial and investigations are ongoing. The putative underlying genetic mechanisms and the potential for intervention was discussed.

1 Huston J III, Torres VE, Sullivan PP, *et al.* *J Am Soc Nephrol* 1993;3:1871-7.

GENE-ENVIRONMENT INTERACTIONS IN FAMILIAL CLUSTERING OF CEREBRAL ANEURYSM FORMATION

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Familial clustering of cerebral aneurysms is well documented. Previous reports of affected pedigrees have not systematically excluded hereditary diseases associated with cerebral aneurysm formation. The interaction of genetic and environmental factors in familial clustering is uncertain.

The incidence of asymptomatic cerebral aneurysm among first degree relatives of probands was compared with the general population incidence. Hereditary diseases known to be associated with cerebral aneurysm formation were excluded by clinical examination, abdominal ultrasound, and linkage analysis. Environmental risk factors were documented. One pedigree had unrecognised polycystic kidney disease; 75 asymptomatic first degree relatives from 11 pedigrees were screened for cerebral aneurysm.

The incidence of asymptomatic cerebral aneurysm among relatives was 10%. The heritability is 81(14.5)% in keeping with multifactorial inheritance. A greater proportion of aneurysm patients smoked (66% compared with 45% of unaffected relatives ($X^2=4.6, 1 \text{ df}, P=0.03$)). The incidence of hypertension was higher among aneurysm patients: 39% and 13% respectively ($X^2=8.3, 1 \text{ df}, P=0.004$).

These data support the presence of a genetic susceptibility to cerebral aneurysm formation the expression of which is modified by smoking. Hereditary diseases associated with cerebral aneurysms—for example, polycystic kidney disease may be otherwise asymptomatic and should be systematically excluded.

IN VITRO RESPONSES OF RAT MIDDLE CEREBRAL ARTERIES TO PHARMACOLOGICAL AGENTS IN THE ACUTE PHASE OF EXPERIMENTAL SUBARACHNOID HAEMORRHAGE

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It has been assumed that the reactivity of the cerebral vessels alters after SAH. The Sheffield model of subarachnoid haemorrhage in rats has been used to evaluate the reactivity of the middle cerebral artery to known pharmacological agents after SAH of varying severity. Twenty four animals were divided into the following groups: group I (n=9) no SAH (control); group II (n=9) SAH and occlusion of proximal ipsilateral carotid artery; group III (n=8) SAH and reperfusion of ipsilateral carotid artery. Animals were anaesthetised using intraperitoneal urethane. Physiological variables are monitored Right common carotid bifurcation exposed in the neck. SAH was produced by passing a 3/0 prolene suture rostrally through the internal carotid artery and intracranial pressure was monitored. Animals were killed three hours after the

haemorrhage or if the systolic blood pressure fell below 50 mm Hg. Both middle cerebral arteries were harvested and mounted and the vascular reactivity was tested to vasoconstrictors potassium, prostaglandin, and serotonin and vasodilators papaverine, L-arginine, histamine, and sodium nitroprusside. Group III represented a greater severity of bleed. Intracranial pressure rose to an average mean of 32 mm/Hg. The reactivity to vasoconstrictors such as potassium and PG₂ was significantly affected and the mean maximum response reduced. This was more pronounced in the third group with more severe bleeds. The response to vasodilators did not alter.

MOOD DISTURBANCE IN PATIENTS WITH AN INTRACRANIAL NEOPLASM

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Few studies have previously investigated anxiety or depression in patients with an intracranial neoplasm. This study was therefore set up (1) to identify and describe mood changes in such patients and (2) to determine whether relations exist between mood disturbance and side of lesion or patient gender, as have been shown in several stroke studies. It was hoped that some insight might be obtained into the emotions accompanying brain tumour.

The hospital anxiety and depression scale (HAD) was used to evaluate mood. Three score ranges indicate the probable absence, the possible presence, and the probable presence of anxiety or depression. Questionnaires were completed by patients before and after biopsy or resection. A control group provided a measure of psychological reaction to surgery by completing the HAD before and after lumbar spinal surgery. Statistical analysis was by paired and unpaired *t* test as appropriate.

Fifty six patients with a left and 49 patients with a right hemispheric tumour completed the HAD before biopsy or resection. Sixty one patients were male. The scores obtained by most patients for anxiety and depression were within normal limits (70% and 84% respectively), reflecting the probable absence of psychological disturbance. The difference in mean scores between male and female patients was highly significant ($P<0.001$). There was no demonstrable difference in affective status between patients with a left or right hemisphere tumour. The differences in mean scores obtained by the tumour patients and control group (n=20) were not significant. Changes in scores after surgery were not significant in either group.

This study shows that (1) emotional disturbance is surprisingly uncommon in patients with a brain tumour despite the severity of the condition; (2) levels of anxiety and depression do not differ significantly from a surgical control group; and (3) there is no identifiable relation between mood disturbance and side of lesion. These results are unexpected and contradict some of the findings of stroke studies.

RADIOIMMUNODETECTION OF MALIGNANT GLIOBLASTOMA WITH THE HUMAN ANTITUMOUR MONOCLONAL ANTIBODY MAB BT32/A6

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Tumour reactive monoclonal antibodies (MAbs) have been shown to be important diagnostic and therapeutic tools in the clinical management of cancer. The human monoclonal IgM antibody MAb BT32/A6 was developed for the treatment of malignant gliomas. This MAb specifically reacts with glioma, neuroblastoma, and melanoma tumour types, but does not react with normal human tissues.^{1,2} The low immunogenicity of a human MAb, combined with tumour specific reactivity makes MAb BT32/A6 an ideal candidate for radioimmunotherapy of glioma. A patient with a recurrent right frontal glioblastoma was administered a single intravenous dose of 1 mg MAb BT32/A6 labelled with 10 mCi ¹³¹I. Using imaging scintigraphy, an image of the tumour was obtained 72 hours after administration of the antibody. Pharmacokinetic data indicated that ¹³¹I-MAB BT32/A6 has a serum half life of about 24 hours; structural stability of MAb BT32/A6 in circulation was observed up to 49 hours postadministration. Favourable pharmacokinetics and tumour localisation, coupled with no observable toxicity, indicates the potential use of MAb BT32/A6 in cancer therapy.

1 Dan MD, Earley EM, Griffin MC, *et al.* *J Neurosurg* 1992;76:660-9.

2 Dan, MD, Schlachta CM, Guy T, *et al.* *J Neurosurg* 1993;82:475-80.

P53 AND P-GLYCOPROTEIN EXPRESSION IN HUMAN GLIOMAS

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P-glycoprotein (Pgp), product of the multi-drug resistance gene (MDR) has a regulatory role in uptake of chemotherapeutic agents by tumour cells. It is well known that the expression of Pgp in tumours may be regulated by the product of the tumour suppressor gene p53. To determine this possible relation in human brain tumours, expression of Pgp and p53 was assessed in a series of 55 paraffin embedded astrocytic gliomas of various degrees of malignancy. Monoclonal antibodies JSB-i and DO-7 were used for immunohistochemical detection.

In peritumorous normal tissue and low grade astrocytomas P glycoprotein staining was clearly detected in capillary endothelia as a component of the blood brain barrier function. However, frequent loss of endothelial staining and intense immunoreactivity in tumour cells was seen in malignant astrocytomas and glioblastomas. Positivity of p53 showed a relation to the malignancy degree of astrocytic gliomas and it was often associated with overexpression of Pgp in neoplastic cells.

The present results show the close relation between p53 and Pgp overexpression in malignant astrocytomas and confirm that alterations in p53 protein have an influence in tumour aggressiveness and drug resistance.

A LIGHT DELIVERY SYSTEM FOR ADJUNCTIVE INTRAOPERATIVE PHOTODYNAMIC THERAPY OF PITUITARY TUMOURS

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A phase I/II study has been designed to evaluate the use of photodynamic therapy

(PDT) as an adjunct to surgery in the treatment of pituitary tumours. Photofrin 11 (2 mg kg⁻¹ body weight) is injected 48 hours before transphenoidal hypophysectomy. Immediately after the operation the tumour bed is illuminated with 630 nm laser light. A method of transphenoidal light delivery that comprises a simplastic catheter (Rusch, UK) modified so that the standard end is replaced by a latex balloon was described. A 600 µm core optical fibre with a spherical diffusing tip is passed through the central channel of the catheter so that a 1 cm length of fibre projects from the distal end into the balloon. Inflation of the balloon with light scattering solution (0.25% Intralipid) ensures a spherical geometry of defined dimension and imposes a near isotropic light distribution over the balloon surface. Miniature fibre optic light detectors, located at the outer surface of the balloon, are forced into contact with the target tissue upon inflation. This allows continual monitoring of the intracavity fluence rate and hence the delivery of a prescribed light dose.

CAPILLARY PERMEABILITY MODULATION IN RAT GLIOMA MODEL WITH L-NAME SIN-1, BRADYKININ AND HOE-140
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Experimental intracerebral glioma express nitric oxide synthase (NOS) abundantly. Modulation of the NOS system alters tumour blood flow but the effects on tumour capillary permeability are uncertain. In this study the effects of NOS inhibitors (L-NAME) and NO donors or stimulators (SIN-1, bradykinin, and HOE) were evaluated in an experimental glioma model. Adult male Wistar rats (n=23) with implantation C6 glioma (day 14-17) were given a single injection of saline (n=5), L-NAME (30 mg.kg⁻¹.n=4) or HOE (0.1 mg.kg⁻¹ n=4), an intravenous infusion of SIN-1 (1.8 mg.kg⁻¹.h⁻¹ n=5) or bradykinin (0.9 mg.kg⁻¹.h⁻¹, n=5). Capillary permeability was measured within the tumour (confirmed by histology of adjacent sections) and correspondingly in the contralateral hemisphere, using the [¹⁴C] aminoisobutyric acid technique. Mean arterial blood pressure, blood gases, and pH were monitored before and during measurement procedures. Data were analysed using a modified *t* test for multiple pairwise comparisons. Acceptable levels of significance were set at P<0.05.

None of the four agents tested significantly altered permeability in host brain (1.6 (1) ml g⁻¹. min⁻¹.10³). Within the glioma, tumour capillary permeability was considerably higher than in the host (21.2 (2.6)), but only L-NAME (13.9 (1.8)), had any significant effect, resulting in a 34% reduction from control. As L-NAME also significantly (by 40%) reduces tumour blood flow the reduction of tumour capillary permeability may be an epiphenomenon. Overall the results from this study suggest that agents that modulate the NOS system do not have significant direct effects on either TCP or blood brain barrier integrity.

REPLICATION COMPETENT MUTANT AVIRULENT HERPES VIRUS (HSV1 1716): A PHASE 1 PROTOCOL FOR VIRAL GENE THERAPY OF MALIGNANT BRAIN TUMOURS
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HSV1 1716 is an avirulent mutant capable of replicating only in growing cells. In mitotic adult human brain, HSV1 1716 will divide only in growing tumour cells, and previous work has shown that this will kill glioma cells in culture.¹ Replication competent virus has a greater potential to spread and impact on the tumour mass, whereas replication incompetent viruses do not spread.

A phase I trial of HSV 1716 has been licensed to commence early in 1997. In this report the protocol is described with particular reference to the evaluation of safety and toxicity and also to maximising the understanding of the behaviour of the virus in vivo. Patients with recurrent malignant glioma implied by thallium SPECT or MRI gadolinium imaging proved response to surgery and radiotherapy, will undergo confirmatory stereotactic biopsy and injection of graded doses of HSV1 1716 at a starting titre of 10² cfu in 1 ml. Patients will be extensively monitored but nursed on an open ward. Patients will be treated in groups of three at each dose level in accordance with standard Phase I toxicity programmes up to a dose of 10⁶ cfu. A number of patients will require subsequent tumour resection at which time in situ vector activity can be assessed.

If safety criteria are satisfied, it is proposed that tumour will be injected with HSV1 at open operation when tumour responsiveness is likely to be greater.

Patients who have malignant brain tumours have a very poor life expectancy. The use of replication competent viral vectors offers a new departure in the treatment of these highly resistant tumours. Open analysis of the safety, protocols, and mechanisms behind the introduction of such new techniques is fundamental in ensuring their rational appraisal and development.

1 McKie EA, MacLean AR, Lewis AD, et al. *Br J Cancer* 1996;74:745-52.

IMPROVED IDENTIFICATION OF TRAUMATIC INTRACRANIAL HAEMATOMAS: THE IMPACT OF PATIENT MANAGEMENT GUIDELINES FOR HEAD INJURY (1987-95)
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Patient management guidelines have been used as a tool to decrease the morbidity and mortality in patients with head injury. Their distribution in the Northern Region has been reported previously¹ and has been satisfactory. However, implementation of the criteria for skull radiography and admission was disappointing as judged by handwritten accident and emergency records.² The objective of these guidelines has been the early identification and prompt treatment of traumatic intracranial haematomas. This study effectively documents the usefulness of clinical guidelines in identification of intracranial haematomas. Over the period of study there was a significant and well documented increase in the identification of traumatic haematomas in head injury admissions to the Newcastle General Hospital. Since the introduction of the guidelines there was a minimal increase in the regional referral of head injury patients reflected by only a 14% increase

(486 to 558) in the total number of admissions with head injury. At the same time the identification of intracranial haematomas more than doubled after implementation of guidelines (53 to 117). This study spanning over eight years, emphasises the role of clinical guidelines in improving the identification of intracranial haematomas; an effect which occurs despite poor implementation of specific written criteria.

- 1 Madhok R, Thomson RG, Mordue A, Mendelow A D, Barker J. *Quality in Health Care* 1993;2:27-30.
- 2 Thomson RG, Gray J, Madhok R, Mordue A, Mendelow A D. *Quality in Health Care*. 1994;3: 86-91.

IMMUNOHISTOCHEMISTRY OF VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) AND PLATELET DERIVED GROWTH FACTOR RECEPTOR (PDGFR) IN HUMAN GLIOMAS RELATED TO PROLIFERATING ACTIVITY
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The growth of gliomas depends on angiogenesis induced in tumour microenvironment. Vascular endothelial growth factor (VEGF) and platelet derived growth factor receptor (PDGFR) are involved in angiogenesis process. Upregulation of PDGFR-β expression is associated with a malignant phenotype. To elucidate the relation among angiogenic promoters and proliferation, immunohistochemical detection of VEGF, PDGFR-β, PCNA, and Ki-67 was assessed in 56 human astrocytic gliomas. Vascular abnormalities of glioblastoma exhibited remarkable positivity for VEGF, in perivascular areas foci of VEGF rich cells were found.

Endothelium in low grade astrocytomas was stained by PDGFR-β. Intense immunoreactivity was found in vessels between peritumoral and malignant areas. PDGFR-β positive tumour cells showed aberrant differentiation features. PCNA or Ki-67 stained rarely endothelium and only in highly proliferant tumours with outstanding immunoreactivity for VEGF and PDGFR-β.

VEGF expression correlates to malignancy degree and topographically to histological changes such as oedema or necrosis. Expression of PDGFR-β in clusters of tumour cells shows a close relation to cell proliferation and differentiation. Immunohistochemistry of VEGF and PDGFR-β provides information about the invasive potential of gliomas. Inhibition of these factors and their receptors may have therapeutic applications.

ASSESSMENT OF PROGRESSIVE NEUROLOGICAL DYSFUNCTION AFTER EXPERIMENTAL IMPLANTATION GLIOMA
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Mechanisms by which intracranial tumours induce peritumoural brain dysfunction are poorly understood. One of the difficulties in understanding this phenomenon is the lack of defined clinical dysfunction in experimental models of brain tumours. In this study progressive focal neurological dysfunction was studied using the staircase test in the rodents after implantation of C6 glioma cells into the striatum

Eleven adult black hooded Lister rats were trained to retrieve food pellets using the stair-

case test. Six then had stereotactic intrastriatal implantation of C6 glioma cells whereas five had innoculums of culture media. Performance of each forelimb was assessed on the staircase test over the subsequent 22 days. At the end of the study neuropathological and comprehensive volumetric tumour analysis was performed. Analysis of variance and post hoc analysis of significant interactions were performed using Tukey's protected *t* test.

Both groups showed almost identical patterns of forelimb function before implantation, and thereafter none of the animals exhibited any abnormality of feeding, grooming, or locomotion. However, in the glioma implanted animals, all of which had striatal tumours varying in volume from 93 to 140 mm³ (median 125), contralateral forelimb function was significantly worse than preoperatively by day 7 ($P < 0.01$) and worse than sham implanted animals by day 12 ($P < 0.01$). Ipsilateral forepaw function was also impaired from day 12. Sham implanted animals showed mild, transient postimplant contralateral forepaw dysfunction and at postmortem had foci of encephalomalacia along the needle tract.

The staircase test can be used to measure progressive focal neurological deficits attributable to a growing glioma. This experimental paradigm can be used to evaluate both the mechanisms of and therapies for peritumorous brain dysfunction.

“RESPIRATORY BURST” OF SUPEROXIDE RADICALS IN PRIMARY CORTICAL NEURONAL CULTURES
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Involvement of oxygen free radicals (OFRs) in brain cell death has been extensively investigated. Both superoxide (O₂⁻) and nitric oxide (NO) seem to play a vital but as yet unidentified part in the cascade of events leading to cell death. The main research tools to date can measure OFRs indirectly by using either byproducts of their action or spin traps. This has led to significant controversy in the interpretation of their action.

New data are presented utilising a novel electrochemical, real time, reagentless method of detection of OFRs. For the first time, detection of O₂⁻ radicals immediately on stimulation by phorbol myristate acetate (PMA) of primary rat cortical neurons in culture is reported. The mode of O₂⁻ production closely resembles the “respiratory burst” of neutrophils during phagocytosis. Furthermore, it is followed by NO⁻ production and is protein kinase C (PKC) independent.

The results are thought to indicate a previously unsuspected pathway of O₂⁻ production in neurons and will lead to a better understanding of the pathophysiology of OFRs in brain cell death.

1 McNeil CJ, Greenough KR, Weeks PA, Self CH, Cooper JM. *Free Radic Res Commun* 1992; 17:399-406.

TRANSGENIC EMBRYONIC NEURAL TISSUE IS A POTENTIAL DONOR FOR INTRASTRIATAL TRANSPLANTATION
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Huntington's disease is an incurable progressive neurodegenerative disorder characterised pathologically by the loss of intrinsic neurons from the basal ganglia which manifests clinically as cognitive, psychiatric, and motor dysfunction.

Neuronal replacement using intrastriatal transplantation of embryonic neural tissue is being actively investigated as a possible therapeutic strategy. Indeed, human clinical trials have already begun in the United States. The ethical and moral issues surrounding the use of human foetal tissue mean that it will probably never be widely available. Consequently alternative sources of donor tissue are being sought.

One possible source is from pigs genetically engineered to prevent hyperacute, complement mediated rejection (Immutran Ltd). Before the transgene can be properly evaluated in animal models the optimal donor age must be determined. Embryonic porcine tissue of 24, 28, 31, 35, and 40 days gestation was stereotactically implanted into a rat model of Huntington's disease. After eight weeks survival, during which the animals were immunosuppressed with cyclosporin A, the rats were killed.

Preliminary results confirm surviving striatal grafts were present in about 50% of the animals. Grafts were significantly larger from donors over 28 days gestation. These results suggest that good sized grafts can be obtained from transgenic porcine embryos of 31 to 35 days gestation.

VALIDATION OF A TREMOR RATING SCALE TO DETERMINE THE EFFECTS OF THALAMIC DEEP BRAIN STIMULATION FOR MOVEMENT DISORDERS IN PATIENTS WITH MULTIPLE SCLEROSIS
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A study to evaluate the effects of thalamic deep brain stimulation (DBS) on movement disorders in patients with multiple sclerosis (MS) is currently being performed. Measuring the effects of treatment presents a challenge because, it is often difficult to differentiate between cerebellar ataxia and tremor in patients with MS. The effect of reducing the movement disorder is also important. One of the most important aspects of the study is therefore to determine the reliability and sensitivity of the chosen tests, in particular Fahn's tremor rating scale (TRS).¹

The intrarater and interrater reliability of Fahn's TRS is currently being assessed by measuring Cohen's κ coefficient of categorical data obtained from assessments of tremor severity for the head, trunk and limbs for rest postural and action/intention tremor. The six raters observe standardised videotaped assessments of 10 patients. Qualitative spirometry, a volumetric test (pouring water from cup to cup), timed functional tasks (60s sitting balance, 10 s standing balance, 10 metre walk) and the Jebsen test of hand function² (recognised as a reliable and valid measure of hand function in neurological patients) are also included.

Preliminary results and validation of the TRS were presented. A comprehensive assessment battery is required to establish the effects of thalamic DBS in the management of movement disorders in patients with MS. Once validated such an approach could be adopted by all centres performing such

surgery so that results of studies can be interpreted monitored and reported consistently.

1 Fahn S. *Curr Opin Neurol Neurosurg* 1988;1:338-40.
2 Jebsen R, et al. *Arch Phys Med Rehabil* 1969;50: 311-19.

WHAT IS THE ROLE OF MOTOR EVOKED POTENTIALS (MEPs) IN THE EVALUATION OF NEUROSURGICAL PATIENTS?
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If MEPs are to be a useful tool in neurosurgical practice, then they must accurately correlate with clinical examination. The purpose was to investigate the hypothesis that an abnormality of the MEP correlates accurately with clinical assessment of corticospinal tract function: assessment of motor function, using the MRC power grading system, supplemented by the Babiniski response, was compared with examination of MEPs from 77 patients (age range, 16-76 years: mean age 47.9 years) with surgical pathology causing a corticospinal tract disturbance. Surgical pathology of the corticospinal tract that had caused abnormal motor signs on clinical examination usually resulted in abnormality of MEP conduction time. Sensitivity of MEPs in detecting a clinically proved motor deficit was only 6% in the upper limbs and 73% in the lower limbs. The specificity of MEPs in detecting a clinically proved motor deficit was only 68% in the upper limbs and 73% in the lower limbs. Greater abnormality of motor power was usually positively associated with greater disturbance of MEP conduction, but this correlation only had a P value of 0.04 in the lower limbs and 0.002 in the upper limbs. These results raise doubts as to the value of MEPs as a diagnostic adjunct in neurosurgical practice.

A CLINICAL ASSESSMENT OF THE CODMAN MICROSENSOR FOR THE MEASUREMENT OF INTRACRANIAL PRESSURE
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The Camino fiberoptic pressure transducer has been shown to correlate well with the intraventricular fluid filled catheter for the measurement of intracranial pressure (ICP).¹ After this work, its use has become standard in the clinical monitoring of ICP in patients. More recently, the Codman Microsensor ICP transducer has shown consistently good performance in laboratory studies.² This study was designed to compare the in vivo performance of the Codman transducer with the Camino fiberoptic transducer in patients.

Eight patients were studied over extensive periods, five had intracerebral haematoma, and three were head injured patients. Each patient had a Codman microsensor inserted along with a Camino transducer immediately adjacent to it. A computerised system was used to record paired ICP readings at 10 second intervals for the duration of ICP monitoring of each patient.

A total of 140 323 paired measurements were obtained over a wide range of ICP values, with recording periods ranging from three hours to five days. In one patient the Codman transducer tracing failed after several days. This was probably due to fracture

of the electrical cable close to the interface box. In another patient, the Camino tracing failed after the patient pulled at the fiberoptic cable. The paired ICP readings were compared using time series, linear regression, and Altman-Bland plots. In two patients there was a drift of the pressure recorded by the Codman microsensor, one in a positive going direction (maximum deviation 30 mm Hg) and one in a negative going direction (maximum deviation -15 mm Hg). In both cases the Camino reading seemed relatively stable. In a third patient the Codman reading was stable whereas the Camino reading drifted. The mean difference between the Codman and the Camino pressure readings was 6 mm Hg. The difference in pressure readings was >5 mm Hg in 30% of the recordings with the Codman tending to read higher than the Camino and was >10 mm Hg in 12% of the recordings. Clinically relevant episodes, defined as a reading of over 20 mm Hg by only one of the transducers, occurred in 12% of the readings with the preponderance of these produced by the Codman.

Although the two traces tended to show very good agreement in terms of the timing of any changes, there was often a significant offset between the two measurements. In some cases this could be explained by an offset of the Codman transducer as described previously. However, continuous monitoring of the two pressures has shown that the difference between the measurements may vary with time. Further investigation of the device is required.

- 1 Chambers IR, Mendelow AD, Sinar EJ, *et al.* *Neurosurgery* 1990;26:421-3.
- 2 Gopinath SP, Cherian L, Robertson CS, *et al.*, *J Neuroscience Methods* 1993;49:11-15.

INTRAOPERATIVE NEUROPHYSIOLOGICAL STUDIES OF THE TRIGEMINAL NERVE

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The objective of the study was to make intraoperative recordings from the trigeminal nerve, to investigate neurophysiological changes during microvascular compression, and locate the trigeminal somatosensory area.

Stimulation of the trigeminal nerve was performed electrically to its three peripheral divisions; recordings were made directly from the nerve root using a custom built electrode; further recordings were made from the exposed cortex of the brain, and from scalp.

Patients were undergoing microvascular decompression for trigeminal neuralgia and temporal lobectomy for epilepsy. Informed consent was obtained.

Excellent recordings can be obtained from the nerve root allowing the differing divisions to be mapped. Most fibres are of the second division. In some cases abnormal waveforms are seen both in respect of direct recordings and scalp far field potentials. After microvascular decompression both abnormal waveforms are almost immediately corrected. This result is in keeping with the restitution of sensory abnormalities seen after microvascular decompression, which we have previously reported.

Direct recordings from the cortex during epilepsy surgery indicate that the somatosensory area for the trigeminal nerve is located within the sylvian fissure, explaining the difficulty of obtaining direct scalp recordings

similar to those obtained with median nerve stimulation.

BRAIN STEM MECHANISMS OF AKINESIA IN THE PRIMATE

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Parkinsonian akinesia is probably due to excessive pallidal inhibition of the pedunculo-pontine nucleus (PPN) in the upper brain stem. If so, lesioning it should generate akinesia in the normal behaving primate. Understanding the mechanism of the most disabling symptom of this condition may lead to more effective surgical means of alleviation.

Preliminary results of a study of the effects of lesioning the PPN in the normal rhesus monkey are presented. The activity counts of three unrestrained monkeys were monitored for a week before and after stereotactically lesioning the PPN bilaterally. Surgery was performed using intravenous anaesthesia and contrast ventriculography used to localise the nucleus (2.0 mm lateral 6.0 mm below the posterior commissure). A 2.0 mm exposed, 1.0 mm diameter electrode was used to make a 70°C, 60 second thermolitic lesion bilaterally. Accuracy of lesion placement was confirmed histologically in the first monkey.

The activity counts decreased from 1936.7 (857.7)/24 hours preoperatively to 923.4 (541.4)/24 hours postoperatively with obvious slowing of movements. Although preliminary, these results support the role of the pedunculopontine nucleus in the facilitation of movement.

NOTICE

Announcement from the British Neuropsychiatry Association: 1997 summer meeting

The 1997 summer meeting of the BNPA will be held jointly with the American Neuropsychiatry Association on 20-22 July at Robinson College, Cambridge, UK. It will include half day sessions on Frontosubcortical circuits and emotion/reward/violence, and the presentation of short scientific papers, posters, and single case videos by members. The winner of the 1997 BNPA Prize will be announced. Two prizes of £200 each will be given to the best paper/poster presentations by junior members. The AGM of the BNPA will be held on 21 July.

For further details of this meeting please contact Suzanne Miller, 44 Roan Street, London SE10 9JT. Telephone 0181 858 2699; fax 0181 853 4416; e-mail wight@compuserve.com.

For details of the BNPA, which is open to psychiatrists, psychologists, neurologists, and those in related fields, please contact Dr Jonathan Bird, Secretary BNPA, Burden Neurological Hospital, Stoke Lane, Stapleton, Bristol BS16 1QT.

BOOK REVIEWS

Cerebral Gliomas. Bailliere's Clinical Neurology. International Practice and Research. Vol 5 No 2. Edited by W K A YUNG (Pp 251-445; price £30). London: Bailliere Tindall, 1996. ISBN 07020 20745.

This monograph presents a useful review of a difficult area of clinical neurology. Primary brain tumours are fortunately fairly rare with about 2500 new cases a year being recorded in the United Kingdom. The term "cerebral gliomas", by custom, encompasses all tumours of central neuroepithelial origin. This is a rather more general definition than limiting it to those clearly arising from the neuroglia. It is a useful approximation as the treatments vary little. The complexities of pathological classification are well summarised in a chapter by Collins. This well indicates the evolving nature of cell type identification as new immunocytochemical techniques are developed but some more detailed indication of the sensitivity of such techniques to tissue fixation would have been useful.

There is little definite known about epidemiological links apart from certain rare genetic predispositions and a few environmental risk factors such as ionising radiation. Of current interest is the public health concern about electromagnetic fields from power lines and mobile phones. These are all usefully discussed in the opening chapter but without definitive conclusions.

Related advances in molecular and cell biology are well covered in two chapters largely devoted to relevant tumour suppressor genes and growth factors. These and a further chapter on gene therapy provide hope rather than promise for useful new therapies. In particular strategies to block angiogenesis and the development of antisense oligonucleotides which will selectively block RNA transcription are being investigated. However, the same problems remain, as with techniques based on gene transfection by various virus vectors, of ensuring adequate exposure of all viable tumour cells to the agents. Despite this some promising initial studies are recorded.

The more conventional therapies of surgery, radiotherapy, and chemotherapy are covered in three comprehensive chapters which well summarise the current situation. Whereas the usefulness of surgery and radiotherapy is established, there is still a lack of really effective agents for chemotherapy. It is sad to relate that even in this decade it is clear that much more definitive assessments of efficacy could be made if there was more general participation in randomised multicentre studies such as those of the MRC, EORTC and RTOG.

The final chapter discusses the assessment of quality of life. For some patients treatment may be successful, but for others it may be just an additional terminal burden for them and their families. Progressive disease and treatment may produce focal and diffuse defects which are both functional and neurobehavioural. Careful assessments of these changes by established instruments is important, particularly in the context of clinical trial. This chapter presents a useful introduction to the subject.

This small volume contains a wealth of relevant information. It is extensively referenced and although multiauthored, maintains a high standard throughout. It is strongly recommended.

NORMAN M BLEEHEEN

Atlas of Cerebrovascular Disease. Edited by PHILIP B GORELICK (price £90.00). Edinburgh: Churchill Livingstone, 1996. ISBN 01878132164.

This is an impressive book, indeed one of my colleagues referred to it as "Cerebrovascular Disease meets Paris Match". There are certainly a vast number of high quality illustrations but this is a serious textbook which Dr Gorelick hopes "addresses all of the facets and complexities of stroke risk factors, diagnosis, and treatment in the 1990s in an easily digestible format that emphasises illustrative displays with brief, understandable textual commentary". To do this 39 authors have contributed to 23 chapters which cover the gamut of cerebrovascular disease. In all of these the text supports the illustrations rather than vice versa but the reference lists are extensive and commendably up to date. One might wonder whether imaging stroke with SPECT deserved an entire chapter particularly since I could not find any discussion of carotid or trans-cranial ultrasound techniques but otherwise there is comprehensive coverage of the topic including a chapter on vascular dementia and three chapters on aspects of rehabilitation.

For those vascular neurologists whose shelves contain well thumbed copies of Barnett *et al*, this book will not be a replacement. I suspect, however, that the highly visual format will find favour with junior members of the medical and possibly paramedical staff and if it promotes an interest in cerebrovascular disease so much the better. Nevertheless, unless the book is rapidly followed by an accompanying slide atlas, I suspect it will spend a good deal of its time in medical illustration departments!

JOHN BAMFORD

Neurosurgery of Complex Tumors and Vascular Lesions. Edited by SHIGEAKI KOBAYASHI, ATUL GOEL, AND KAZUHIRO HONGO (Pp480; price £130.00). Edinburgh: Churchill Livingstone, 1996. ISBN 044307870X.

The sale of cookery books is now one of the most active and lucrative areas of publishing. The purchasers of such books, which are usually lavishly illustrated and always expensive, are apparently almost all already expert cooks who buy the books not so much to employ the recipes but as light and enjoyable bedside reading. A recent subcategory are the books providing a "travel guide" to regional cuisine—for example, *Thai Regional Cookery*. In the realm of medical publishing, the equivalent niche is occupied by the *Operative Surgical Guide* which, like the cookery book, sets down in usually lavishly illustrated form various surgical approaches, the equivalent of the "travel guide" cookery book being in this case the particular surgical "Region" which is the subject of the book. This type of medical niche publishing is at its most active in the surgery of the skull base, - perhaps the surgical equivalent of "Thai Regional Cookery".

This book is the latest in a number of such texts published within the past five years or so. Like the cookery book, its appeal is not so much to the tyro but to the already established expert in the field who will buy and enjoy the book largely for its excellent presentation and lavish illustrations. They may even find the occasional "recipe" helpful. However, for the trainee neurosurgeon the value of the book is less certain. Like the tyro cook, he may become the victim of overambition and may be seduced into tackling procedures which are better left to those who are already expert in skull base surgery. Although the book is well written, with a good range of chapter topics and excellently illustrated, it deals with difficult and complex surgery often in brief and rather superficially written chapters. The book undoubtedly deserves a place in the specialist ear, nose, and throat or neurosurgical library but for the individual trainee—at whom the book is no doubt targeted—it might be wise for it to have carried a health warning: "use only sparingly and after considerable preliminary training".

The cost of the volume may be rather too high for the limited market it is aimed at. As a manual for "how to do it", Fisch's book *Microsurgery of the Skull Base* would perhaps represent a better buy.

DAVID HARDY