the soft palate, and the posterior third of the tongue. For patients refractory to medical treatment several surgical options are available including extracranial avulsion, intracranial preganglionic root section, trigeminal tractotomy, either open³ or percutaneous CT guided, and microvascular decompression. As mentioned at the outset, intracranial root section has been the most often employed and is generally regarded as curative. It was, however, realised early that section of the upper vagal rootlets is important in that some cases without the additional section were either not relieved or experienced early recurrence.² More recently microvascular decompression has been employed, particularly by Jannetta *et al*, with complete relief of pain in 76% and substantial improvement in a further 16% in the largest series, with a mean follow up of 48 months.⁴ As with trigeminal neuralgia, the actual incidence of presumed causative "neurovascular conflict" and, indeed, the exact mechanism of causation are as yet unresolved questions.

The particular dilemma posed by the present case had both a diagnostic and a therapeutic arm, referable in each case ultimately to mechanism. The only reported cases of recurrence after preganglionic section are the small group, referred to above, in whom only the IXth nerve root had been cut and who subsequently responded to section of the upper vagal rootlets and one patient who had had both a IXth and partial Xth rhizotomy and who later responded to a trigeminal nerve procedure. In these cases failure was typically either immediate or not long delayed. In the largest series reporting the results of treatment⁵ and in a smaller series with long follow up⁶ there were no recurrences after preganglionic section of the IXth and upper Xth roots. Likewise, after total sensory root section via the posterior fossa (Dandy procedure) trigeminal neuralgia does not recur.

In our case, assuming completeness of the initial section, there seemed to be, essentially, three possible explanations for the recurrent pain. Firstly, that the pain was due to involvement of the remaining non-trigeminal somatic afferent components of the spinal trigeminal nucleus (in the VIIth and the remainder of the Xth cranial nerves); secondly, that it was some form of postdenervation pain akin to the anaesthesia dolorosa described after Vth nerve section⁷ and in one instance after IXth nerve section; and, thirdly, it was a form of trigeminal neuralgia, there being a reported coincidence of the two forms of neuralgia in a few cases.² The close similarity of the recurrent to the initial pain, both in nature and site, the long period since the initial pain, and the response to carbamazepine all favoured the first possibility. On the basis of this diagnosis, coupled with the patient's relative youth and, it must be said, her strong insistence, re-exploration was undertaken as described above. Whatever one's position on the vascular compression theory of the cause of cranial nerve neuralgias the findings were impressive and, in conjunction with the undesirability of further nerve section, encouraged treatment by microvascular decompression alone. The immediacy of pain relief, sustained now for 18 months, supports this decision. It might be argued that the presumed vascular compression was overlooked at the first procedure but there are several points against this. Firstly, both procedures were performed by the same surgeon, experienced in posterior fossa surgery,

and the area of compression was in the same place as the initial section. Secondly, the young age at first presentation is against a vascular pathology, particularly where the vertebral artery is causative; and thirdly, there is a reported incidence of new vascular compression in re-exploration for recurrent trigeminal neuralgia.

In conclusion, the salient points to emerge from this brief report are that vagoglossopharyngeal neuralgia can recur after IXth and partial Xth nerve section and that this patient provides evidence for a pure vagal neuralgia. This supposition is supported by the finding that even the most caudal vagal rootlets may carry general somatic afferent fibres to the spinal trigeminal tract.¹ In addition, the two separate episodes with differing pathologies raise the interesting question of whether there is a particular propensity for neuralgia which may or may not require a vascular trigger. This bears on the point raised by Adams *et al* as to why there are so many possibly causative vessels and so few neuralgias.⁶

BKO and IJ are supported by the Sydney University Medical Foundation Wood Grant and by the Madeline Foundation for Neurosurgical Research.

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- 1 White JC, Sweet WH. *Pain and the neurosurgeon: a 40 year experience*. Springfield, Illinois: CC Thomas, 1969.
- 2 Rushton JG, Stevens C, Miller RH. Glossopharyngeal (vagoglossopharyngeal) neuralgia. A study of 217 cases. *Arch Neurol* 1981;38:201-5.
- 3 Kunc Z. Treatment of essential neuralgia of the 9th nerve by selective tractotomy. *J Neurosurg* 1965;23:494-500.
- 4 Resnick DK, Jannetta PJ, Bissonnette D, *et al*. Microvascular decompression for glossopharyngeal neuralgia. *Neurosurgery* 1995;36:64-9.
- 5 Taha JM, Tew JM. Long term results of surgical treatment of idiopathic neuralgias of the glossopharyngeal and vagal nerves. *Neurosurgery* 1995;36:926-31.
- 6 Adams CTB, Kaye AH, Teddy PJ. The treatment of trigeminal neuralgia by posterior fossa microsurgery. *J Neurol Neurosurg Psychiatry* 1982;45:1020-6.

Immunohistochemistry distinguishes between Pick's disease and corticobasal degeneration

The clinical syndrome of frontotemporal dementia is associated with several neurodegenerative disorders: Pick's disease, corticobasal degeneration, motor neuron disease-associated dementia (MND-dementia), frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDP-17), and frontal lobe degeneration (FLD). These disorders, although they do not match the frequency of Alzheimer's disease, are far from uncommon, and present clinicians and neuropathologists with formidable, if not insurmountable diagnostic difficulties. However, recent advances in cellular and molecular pathology, biochemistry, and molecular genetics have been instrumental in their nosological definition. The discovery of a mutation in the tau protein gene on chromosome 17 in

1998 has established that several phenotypically heterogeneous familial dementias with a confusing variety of names all belong to FTDP-17.^{1,2} Most but not all frontotemporal dementias are characterised by intracellular inclusions formed by abnormal cytoskeletal components, both in neurons and in glial cells. Pick's disease, corticobasal degeneration, and FTDP-17 belong to the larger group of tauopathies, as their hallmark lesions contain tau protein, distinguishing them from MND-dementia and FLD, two disorders without tau pathology. Of the three tauopathies, FTDP-17 can be defined by its genetic abnormality, whereas the differential diagnosis of Pick's disease and corticobasal degeneration remains difficult and controversial.

Clinically Pick's disease is characterised by frontal and anterior temporal lobe dysfunction and progressive dementia, whereas neuropathologically the underlying frontotemporal atrophy is complemented histologically by the presence of large, swollen, achromatic neurons, the Pick cells, and by tau positive intraneuronal inclusions, the Pick bodies. The clinical features of corticobasal degeneration include asymmetric extrapyramidal signs, parkinsonism, and the "alien limb" phenomenon (apparent purposeful movements which are not under voluntary control) followed by cognitive impairment. Histologically there is neuronal loss, astrogliosis, and tau positive neuronal and glial inclusions, but the most prominent feature is the presence of large, swollen neurons, morphologically indistinguishable from Pick cells. It is the occurrence of these cells in both disorders which causes most of the differential diagnostic problems.

In the human central CNS six tau isoforms are generated by alternative splicing and these are then posttranslationally phosphorylated. At molecular level the electrophoretic profiles of aggregated tau proteins in these neurodegenerative disorders are disease specific. For example, although both Pick's disease and corticobasal degeneration are tauopathies, characterised by tau positive cellular inclusions, their tau profile is apparently different: the tau doublet is 64 and 69 kDa in corticobasal degeneration, but 55 and 64 kDa in Pick's disease.³ Here we report the use of tau antibodies which, exploiting the different phosphorylation patterns of these two disorders, has made a more accurate neuropathological diagnosis possible.

Sections from the frontal lobe and the temporal lobe (including the hippocampus) from 10 cases of corticobasal degeneration and 10 cases of Pick's disease were examined by immunohistochemistry, using phosphorylation independent (SMI51, TP007, TP70, 304, 189) and phosphorylation dependent (AT180, AT270, AT8, 12E8) anti-tau antibodies. All sections were immunostained according to a standardised protocol using the avidin-biotin complex (DAKO) with appropriate positive and negative controls. All the swollen neurons and neuronal and glial inclusions were positively immunostained with all the anti-tau antibodies in corticobasal degeneration. However, in Pick's disease all the antibodies but one immunostained the Pick bodies and the large swollen Pick cells: antibody 12E8 gave negative results (figure A and B).

Phosphorylation at the site of Ser262/Ser356 is thought to be one of the most prominent factors affecting the biological activity of tau.³ In corticobasal degeneration antibody 12E8 detected the phosphorylated epitopes Ser262 and/or Ser356, whereas in

Positive and negative immunostaining in large, swollen neurons by anti-tau antibody 12E8 in corticobasal degeneration (A) and in Pick's disease (B), respectively. ABC method (DAKO).

Pick's disease these sites remain unphosphorylated and consequently this antibody did not label any of the Pick bodies or Pick cells.⁴ These findings are important both from a practical and from a theoretical point of view. The immediate practical implication is a more accurate neuropathological diagnosis, enabling Pick's disease to be distinguished from corticobasal degeneration; this, in turn, is essential for improving clinical investigations. In addition, new insights into the molecular pathology of these disorders contribute to the nosological definition and better understanding of a complex group of neurodegenerative diseases.

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- 1 Lantos PL. Cracking an enigma: the puzzle of unusual dementias. In: Iqbal K, Swaab DF, Winblad B, et al, eds. *Alzheimer's disease and related disorders*. Chichester: John Wiley, 1999:509-22.
- 2 Spillantini MG, Goedert M. Tau mutations in familial frontotemporal dementia. *Brain* 2000;123:857-9.
- 3 Haque N, Tanaka T, Iqbal K, et al. Regulation of expression, phosphorylation and biological activity of tau during differentiation in SY5Y cells. *Brain Res* 1999;838:69-77.
- 4 Delacourte A, Sergeant N, Wattez A, et al. Vulnerable neuronal subsets in Alzheimer's and Pick's disease are distinguished by their tau isoform distribution and phosphorylation. *Ann Neurol* 1998;43:193-204.

CORRESPONDENCE

Neurological emergencies: acute stroke

We greatly enjoyed reading the recently published review on acute stroke by Davenport and Dennis.¹ Their didactic approach and strict compromise to distinguishing between evidence based approaches and their personal beliefs deserve compliment. We would like to contribute by clarifying some information on two topics.

Firstly, the authors make a brief comment on the use of anticoagulants in the treatment of cerebral venous thrombosis (CVT) indicating that a recent randomised trial showed a non-significant favourable effect.² This may lead to a misinterpretation. Most experts currently agree that anticoagulation should be used in the acute treatment of CVT based on the available evidence. In 1991, Einhaupl et al³ published the results of their randomised double blind prospective study comparing heparin and placebo. This study was prematurely interrupted after enrolling 20 patients because of the dramatic differences noted in outcome in favour of the heparin group (basically eight patients recovered fully and no deaths occurred in the heparin arm whereas only one patient recovered completely and three others died in the placebo group). Concerns about possible methodological flaws in this German trial fueled some controversy about its results. This led to a new trial by the Cerebral Venous Sinus Study Group³ which randomised 60 patients with CVT to receive nadroparin or placebo for 3 weeks. Poor outcome was defined as death, Barthel index of less than 15 at 3 weeks or Oxford handicap score equal or greater than 3 at 12 weeks. The results showed poor outcome in six of 30 patients (20%) in the nadroparin arm and seven of 29 (24%) in the placebo group at 3 weeks and four of 30 (13%) in the nadroparin treated patients versus six of 29 (21%) in the placebo group (absolute risk reduction of 7% and relative risk reduction of 38% for a non-statistically significant difference). But also very remarkably, there were no new symptomatic cerebral haemorrhages even among the 15 patients treated with anticoagulation who had haemorrhagic lesions on the initial CT. Finally, the same authors performed a meta-analysis combining the results of the two available trials^{2,3} which showed a "modest but clinically important" (although not statistically significant) benefit in the use of anticoagulation (absolute risk reduction of 14% in mortality and 15% in death or dependency, with relative risk reductions of 70% and 56% respectively). When combined with the proved safety of anticoagulation even in the setting of pre-existent haemorrhagic infarct and the highly unpredictable course of patients with CVT, these results should encourage the use of anticoagulation in the treatment of CVT.

Secondly, Davenport and Dennis mentioned the use of decompressive craniectomy as one of the interventions that may be used

in patients with stroke who are rapidly deteriorating from raised intracranial pressure. However, they questioned whether this aggressive approach was associated with "improved survival with acceptable quality of life".¹ Growing experience with our patients as well as the available literature seems to indicate that it does, especially when decompressive surgery is performed early. Schwab et al⁴ studied 63 patients with complete middle cerebral artery (MCA) infarctions and evidence of increased intracranial pressure treated with either early (within 24 hours of symptom onset) or late craniectomy. Mortality was 27% (compared with 78% in historical controls) and all survivors were reported to be able to walk short distances without assistance and none were left with global aphasia. Mean Barthel index scores were 68.8 in the early hemispheric resection group, 62.6 in the late hemispheric resection group, and 60 in historical controls (but the very high mortality in this last group may account for a less dramatic difference in functional outcome). Similar favourable results were reported by Carter et al⁵ in their retrospective analysis of 14 patients treated with decompressive surgery after massive non-dominant hemispheric infarctions. Eight of their 11 surviving patients were able to function with minimal to moderate assistance (Barthel index >60) 1 year after the surgery. Depression and failure to reintegrate socially were often found in this group of patients³ as opposed to the experience reported by Schwab et al.⁴

In conclusion, decompressive craniectomy seems a valuable treatment option in cases of malignant MCA infarction, especially when involving the non-dominant hemisphere. This surgery is potentially lifesaving and reported functional outcomes are encouraging. Therefore, it needs to be considered early in every patient with complete MCA strokes showing incipient signs of increased intracranial pressure.

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- 1 Davenport R, Dennis M. Neurological emergencies: acute stroke. *J Neurol Neurosurg Psychiatry* 2000;68:277-88.
- 2 Einhaupl KM, Villringer A, Meister W, et al. Heparin treatment in sinus venous thrombosis. *Lancet* 1991;338:597-600.
- 3 De Bruijn SFTM, Stam J, for the Cerebral Venous Sinus Thrombosis Group. Randomised placebo controlled trial of anticoagulant treatment with low molecular weight heparin for cerebral sinus thrombosis. *Stroke* 1999;30:484-8.
- 4 Schwab S, Steiner T, Aschoff A, et al. Early hemispheric resection in patients with complete middle cerebral artery infarction. *Stroke* 1998;29:1888-93.
- 5 Carter BS, Ogilvy CS, Candia GJ, et al. One-year outcome after decompressive surgery for massive nondominant hemispheric infarction. *Neurosurgery* 1997;40:1168-75.

Davenport and Dennis reply:

We are grateful for Rabinstein's interest and comments. Although our interpretation of the available data may be more conservative, we do indeed consider anticoagulation for CVT, but do not think that it is appropriate in all cases. Similarly, we have considered craniectomy for "malignant" MCA occlusion, but so far we have not thought it appropriate to proceed. We note the good outcomes from the published case series and await the results of randomised trials with interest. However, many of the case series have involved rather younger than average