was found to be highly effective in inducing changes in the intraocular pressure (IOP) and vasodilatation in the uvea in the rabbit; the reaction seems to have much in common with an axon reflex mediated by the peripheral branches of the nerve, at the endings of which some active histamine-like substance is liberated, causing pupillary contraction and intense intraocular vasodilatation.³

Can mechanical activation of iris trigeminal nerve terminals develop naturally and contribute to meiosis seen during and between migraine attacks? Acute elevations in the IOP have been shown to discharge impulses in iris nerve fibres (and whole nerve and corneo-scleral fibres) probably due to mechanical distortion of the iris and the chamber angle⁴ which suggests the production of painful impulses described in experimental animals.^{3,4} An association between migraine and low-tension glaucoma (LTG) has been suggested recently;⁵ the differential diagnosis of LTG should include wide diurnal fluctuations in which high pressures are occurring at times when they are not being recorded. Given the central importance of autonomic effects on aqueous dynamics, autonomic hypofunction in those with migraine during headache-free intervals⁶ allow development of a relatively higher IOP in response to a variety of stimuli and situations, thereby resulting in exaggerated fluctuations in the pressure that possibly contributes both to visual field loss and mechanical activation of iris nerve fibres.

The results of studies of autonomic nervous system dysfunction in migraine have been contradictory.⁶ Besides wide normal inter- and intra-individual variations in the reactions of the autonomic nervous system, it may be useful (and not necessarily simplistic) to view autonomic hyperfunction during migraine attacks as an adaptive (secondary stress) response liable to "fatigue" variably in the later stages of severe headache, one function of which may serve to limit the effects of vasodilatation (of intraocular and cranial blood vessels) resulting from antidromic discharge from trigeminal nerve fibres.

VK GUPTA
PO Box 12005,
Jumeirah, Dubai, UAE

- 1 Drummond PD. Disturbances in ocular sympathetic function and facial blood flow in unilateral migraine headache. *J Neurol Neurosurg Psychiatry* 1990;53:121-5.
- 2 Fanciullacci M, Fusco BM, Alessandri M, Campagnolo V, Sicuteri F. Unilateral impairment of pupillary response to trigeminal nerve stimulation in cluster headache. *Pain* 1989;36:185-91.
- 3 Duke-Elder S. The Physiology of the Eye and of Vision. *System of ophthalmology*, vol 4. London: Henry Kimpton, 1968:300-30.
- 4 Zuazo A, Obanez J, Belmonte C. Sensory nerve responses elicited by experimental ocular hypertension. *Exp Eye Res* 1986;43:759-69.
- 5 Phelps CD, Corbett JJ. Migraine and low-tension glaucoma. *Invest Ophthalmol Vis Sci* 1985;26:1105-8.
- 6 Havanka-Kanninen H, Tolonen U, Myllyla VV. Autonomic dysfunction in migraine: A survey of 188 patients. *Headache* 1988;28:465-70.

Drummond replies:

I thank Dr Gupta for his comments and for the opportunity to clarify a point which may not be clear in my paper.¹ In 62 patients with headache on the usually-affected side the pupil was smaller, on average, and eyelid separation greater, on the symptomatic side.

These autonomic disturbances, however, were not normally observed in the same

patients. In fact, miosis was usually associated with ptosis on the symptomatic side during attacks of migraine (in darkness, $r = 0.38$, $p < 0.001$, see table 4). Since miosis persisted during the headache-free interval^{1,2} it seems likely that, in some cases, permanent ocular sympathetic deficit prevented greater eyelid separation on the affected side during attacks of migraine.

Discharge of the trigeminal nerve could have contributed to miosis during migraine, but this is unlikely to be the mechanism of miosis during the headache-free interval.^{1,2} On the other hand, thermoregulatory flushing is reduced on the usual side of migraine headache,³ consistent with a decrease in cervical sympathetic outflow.^{4,5} Intraocular pressure does not increase on the symptomatic side during attacks of migraine,⁶ which argues against the idea that autonomic disturbances are due solely to trigeminal discharge.

Thirty years ago, Walsh and O'Doherty⁷ suggested that swelling of the internal carotid artery during migraine could cause ophthalmoplegia, either by direct pressure on nerves in the cavernous sinus, or by interfering with the local circulation of the involved nerves. Narrowing of the internal carotid artery, presumably due to oedema, was demonstrated by arteriography in two of three selected cases. This same process could cause cervical sympathetic deficit in migraine, because sympathetic fibres supplying the eye and skin of the forehead form a plexus around the internal carotid artery.

PD DRUMMOND
Psychology Section,
Murdoch University,
Murdoch,
Western Australia

- 1 Drummond PD. Disturbances in ocular sympathetic function and facial blood flow in unilateral migraine headache. *J Neurol Neurosurg Psychiatry* 1990;53:121-5.
- 2 Drummond PD. Pupil diameter in migraine and tension headache. *J Neurol Neurosurg Psychiatry* 1987;50:228-30.
- 3 Drummond PD. Effect of body heating and mental arithmetic on facial sweating and blood flow in unilateral migraine headache. *Psychophysiology* 1990; (in press).
- 4 Drummond PD, Lance JW. Facial flushing and sweating mediated by the sympathetic nervous system. *Brain* 1987;110:793-803.
- 5 Drummond PD, Finch PM. Reflex control of facial flushing during body heating in man. *Brain* 1989;112:1351-8.
- 6 Hovran I, Sjaastad O. Cluster headache syndrome and migraine: ophthalmological support for a two-entity theory. *Acta Ophthalmol* 1977;55:35-51.
- 7 Walsh JP, O'Doherty DS. A possible explanation of the mechanism of ophthalmoplegic migraine. *Neurology* 1960;10:1079-84.

Increased risk of multiple sclerosis among nurses and doctors

A recent study concluded that the multiple sclerosis (MS) death rates in British nurses and qualified medical practitioners was not greater than expected.¹ However, as part of a population-based prevalence study of MS in North East Scotland,² the occupation of all economically-active patients over 15 years of age was classified at the time of onset of the disease³ and compared with the distribution of economically-active males and females in North East Scotland based on the 1961 Census.⁴ Fifteen female nurses (occupational

group 282) had MS (expected 6.2) and four male medical practitioners (occupational group 280) were affected whilst 0.8 were expected (both $p < 0.001$).⁵

Whilst the actual numbers involved were small, particularly for medical practitioners, an analysis of occupation at the time of onset of MS will nevertheless, produce a less biased assessment than analysis of occupation at the time of death, given the well-recognised downward occupational drift in chronic disabling diseases such as MS and accepted by Dean and Gray.¹ I conclude that, at least in North East Scotland in 1970, there was an excess risk of MS among female nurses and possibly among male doctors.

DAVID I SHEPHERD
Department of Neurology,
North Manchester General Hospital,
Manchester, UK

- 1 Dean D, Gray R. Do nurses or doctors have an increased risk of developing multiple sclerosis? *J Neurol Neurosurg Psychiatry* 1990;53:899-902.
- 2 Shepherd DI, Downie AW. Prevalence of multiple sclerosis in north-east Scotland. *BMJ* 1978;2:314-16.
- 3 General register office. *Classification of occupations 1960*. London: HMSO, 1960.
- 4 General register office. *Census 1961 Scotland Occupation and Industry. County tables, Aberdeen City and Counties of Banff, Kincardine, Moray, Nairn and Aberdeen*. Edinburgh: HMSO, 1966.
- 5 Shepherd DI. *Multiple sclerosis in North-East Scotland*. (MD Thesis). University of Aberdeen 1976.

Gray and Dean reply:

We are grateful for Dr Shepherd's comments on our study of mortality from multiple sclerosis (MS) among doctors and nurses¹ and for his interesting data suggesting an excess incidence of MS among doctors and nurses in North East Scotland.

Dr Shepherd suggests that downward occupational drift by the time of death could explain the lack of any excess of MS deaths among doctors and nurses in our study. However, we believe this to be unlikely—particularly for medical practitioners. The British doctors study was a prospective study and the occupation of medical practitioner was (by definition!) the necessary prerequisite to be included. Occupation was determined from the 1951 British Medical Register and not from the death certificates.

There may be three explanations for the excess incidence seen among doctors and nurses in Dr Shepherd's study. First, the methods of identifying patients² are likely to have resulted in over-representation of doctors and nurses. To supplement the original register of patients with MS further patients were identified by visits to local hospitals and extensive surveillance of their records. A further 73 cases in this study were then identified by asking the region's GPs to note any additional cases that they knew of. As a result, nurses and doctors with MS seem more likely to be identified than those in non-medical professions.

Second, using the 1961 census data to estimate the proportion of economically active males and females who are doctors or nurses in 1970 may have introduced some bias if the proportion who were doctors and nurses had increased over the intervening period.

Finally, doctors and nurses may have MS diagnosed earlier in the disease than other MS sufferers. Again, this "lead time" bias is likely to suggest—artefactually—that there is

an excess incidence among doctors and nurses.

The sharply conflicting data from the two studies suggests that one may be biased. The lack of any excess of MS among spouses of MS patients³ indicates that MS is not (or is very rarely) a transmissible disease among adults. This observation, as well as our study, and the potential biases outlined above suggest that the incidence and mortality of MS among doctors and nurses is likely to be close to that in the general population.

RICHARD GRAY

Clinical Trial Service Unit and ICRF Cancer Studies Unit,
Radcliffe Infirmary,
Oxford, UK

- 1 Dean G, Gray R. Do nurses or doctors have an increased risk of developing multiple sclerosis? *J Neurol Neurosurg Psychiatry* 1990;53:899-902.
- 2 Shepherd DJ, Downie AW. Prevalence of multiple sclerosis in north-east Scotland. *BMJ* 1978;2:314-16.
- 3 Editorial. Risk factors for multiple sclerosis: race or place? *J Neurol Neurosurg Psychiatry* 1990;53:821-3.

Evaluation of vigabatrin in refractory epilepsy

We were interested to read the report by Sander *et al* of their experience of vigabatrin in 128 patients with severe medically refractory epilepsy, and in particular their comments on neurotropic side effects.¹ We began using vigabatrin at the beginning of 1990 and were struck by the high incidence of such side effects. We therefore recorded the effects of vigabatrin therapy in 30 sequential patients.

All the patients had localisation related seizures intractable to conventional medical therapy. The seizures were complex partial in 24, focal motor in five, and secondary generalised in one patient. Eleven patients had secondary generalised seizures in addition to focal seizures. The average age was 33.9 years with an average duration of seizure disorder of 17.8 years. The first 10 patients were started on a dose of 2000 mg/day, the rest on 1000 mg/day (see below). The maximum dose used was 4000 mg/day. The patients were started on vigabatrin between January and August 1990, and all are still being followed up. Side effects permitting, all had a minimum three month trial of therapy.

Of the 30 patients started on vigabatrin only seven remain on it. The drug was withdrawn in 10 patients because of lack of effect, in four patients who relapsed following an initially good response (all the relapses have occurred within three months of starting therapy), in two patients whose seizures appeared to become worse on vigabatrin, and in seven patients because of neurotropic side effects. This type of side effect was most common in the group as a whole, and included drowsiness (five), irritability (three), anxiety (one), depression (two), emotional lability (two), confusion (one) and psychosis (one). Other side effects included weight gain (two patients) and headache (one patient).

The seven (23%) patients remaining on vigabatrin therapy have all had either a useful reduction (> 30%) in seizure frequency, and/

or significant amelioration of seizure manifestations, but none is seizure free.

The starting dose of vigabatrin was reduced after the first 10 patients because seven of these patients suffered neurotropic side effects, in two cases severe. There were no severe neurotropic side effects in patients started on the lower dose of 1000 mg/day. All of our patients who showed a therapeutic response did so at a dose of 2000 mg/day or less, and there were no patients in whom increasing the dose beyond this produced any further response.

Our group of patients was different from that of Sander *et al*, in the type of epilepsy, and in being composed entirely of outpatients who may have less severe disease. We have found its therapeutic effect less good, but our experience of the neurotropic adverse effects associated with vigabatrin is similar, and we too have seen tolerance develop in a significant number of patients. A response rate of 23% in patients refractory to first line anticonvulsant agents is certainly worthwhile, but careful supervision is required in the early stages of therapy, and we agree with Sander *et al* that vigabatrin should be used with particular caution in those with a previous history of psychological problems.

ILONKA KRUTSCHMANN

RODERICK DUNCAN

Institute of Neurological Sciences,
Southern General Hospital,
Glasgow, UK

- 1 Sander JWAS, Trevisol-Bittencourt PC, Hart YM, Shorvon SD. Evaluation of vigabatrin as an add-on drug in the management of severe epilepsy. *J Neurol Neurosurg Psychiatry* 1990;53:1008-10.

BOOK REVIEWS

Handbook of Sleep Disorders. (Neurological Disease and Therapy Series/6). Edited by M THORPY. (Pp 817 Illustrated; Price US & Canada \$165.00; All Others \$198.00.) New York, Marcel Dekker Inc, 1990. ISBN 0 8247 8295 X.

This is a new and attractive book about sleep disorders. The stated aim is to be a comprehensive summary of knowledge in nearly all aspects of human sleep. Under the able editorship of Michael Thorpy the book substantially but not completely fulfils this claim. About a third of the book covers the physiology and anatomy of sleep mechanisms and the pharmacology of sleeping and waking. The remainder is concerned with clinical sleep medicine. The code of practice of American sleep disorders centres is amply covered, and reflects the very high ratio of North American authors. There are two starting points for this approach. The first is the chapter by Lemmi on sleep disorders centres and polysomnographic evaluation, and the second is the recent American-inspired, international classification of sleep disorders. This system may result in a primary focus on the sleep laboratory rather than on the patient.

The coverage of primary and secondary sleep disorders as well as circadian rhythm problems is wide. Some might argue at the

use of the term "dyssomnia" to cover narcolepsy, obstructive sleep apnoea and other hypersomnias, but this classification is clinically relevant. Many of the sections on insomnia are particularly good, notably those by the Italian school, led by Lugaresi in his description of fatal familial insomnia. The discussion of parasomnias and secondary sleep disorders is thorough but I wonder if a disproportionate amount of the book is devoted to these topics. For example, the detailed focus on sleep disorders in many degenerative neurological disorders seems excessive. However the book is essential reading for European as well as American polysomnographers and contains outstanding sections on narcolepsy from Broughton and Honda, despite some apparent contradictions. Thus Broughton reports that monozygotic twins may be concordant for narcolepsy and cites three references in favour of this; in the next chapter the same references are cited by Honda to support the statement that no examples of complete concordance are known. The book is well produced, with good illustrations and figures and adequate references. It is however far too expensive.

MERYL DAHLITZ

Positron Emission Tomography in Dementia. Frontiers of Clinical Neuroscience Vol 10. Edited by RANJAN DUARA. (Pp 186; Price: US\$ 89.95). New York: Wiley-Liss, 1990. ISBN 0 471 56804 X.

This is an elegantly bound volume in the Wiley-Liss series of Frontiers of Clinical Neuroscience. It reviews our current understanding of dementia using Positron Emission Tomography. At \$89, I picked up this book excited as if I had been invited to eat at an exclusive restaurant by a selection of famous transatlantic chefs.

The first course, which explained the methodology behind PET was excellent. Despite the risk of being a rather indigestible topic, it combined sufficient spices to make a most agreeable *hors d'oeuvre*. To the non expert this section was refreshingly easy to read and understand.

The main course in contrast, which tackled the metabolic deficit found in Alzheimer's disease, was rather disappointing. One of the reasons for this was the tone set by a prefacing chapter on cerebral atrophy. This was the wrong accompaniment for a review of the PET findings and the savoury topic of atrophy should have been reserved for after dinner. An opportunity was missed to provide an elegant meta-analysis of PET results. The presentation was not as good as I expected and the chef must have been disappointed with the quality of the plates. However the chapter on Huntington's chorea was excellent.

For dessert there was a wide range of topics, including, ligands and PET, activation paradigms, and SPECT. It was a little over-ambitious, since it failed to mention a number of important findings. For example the studies of 18F Dopa in Alzheimer's Disease, and some of the case reports of PET in the rarer dementing syndromes, were absent. Work from Mesulam and others from this side of the Atlantic on focal degeneration were omitted. The foreword expressed a