J R Coll Physicians Edinb 2007; **37**:352–356
© 2007 Royal College of Physicians of Edinburgh

Neurology symposium report

K Taylor
Clinical Lecturer in Neurology, Institute of Neurological Sciences, Southern General Hospital, Glasgow, Scotland, UK

ABSTRACT The Royal College of Physicians of Edinburgh held its latest Neurology Symposium on 9 November 2006. The topics, summarised in this report, included useful clinical approaches to some common neurological problems (blackouts, dizziness, headache, and functional symptoms), original basic and clinical research on subarachnoid haemorrhage, a discussion of exciting new advances made in multiple sclerosis over the last 10 years, and current thinking on the management of Parkinson's disease. Finally, a debate on the controversial issue of the role of NICE in neurology concluded that NICE had not enhanced the care of neurological patients in the UK. However, there was a general consensus that there is an important role for an organisation to appraise neurological healthcare interventions.

KEYWORDS Multiple sclerosis, neurology, NICE, Parkinson's disease, subarachnoid haemorrhage, symposium

LIST OF ABBREVIATIONS Experimental autoimmune encephalomyelitis (EAE), Epstein Barr virus (EBV), multiple sclerosis (MS), National Institute for Clinical Excellence (NICE), Parkinson's disease (PD), quality adjusted life year (QALY), subarachnoid haemorrhage (SAH), single photon emission computed tomography (SPECT), vestibulo-ocular reflex (VOR)

DECLARATION OF INTERESTS No conflict of interests declared.

Published online ***December 2007***

Correspondence to ***K Taylor, Clinical Lecturer in Neurology, Institute of Neurological Sciences, Southern General Hospital, 1345 Govan Road, Glasgow G51 4TF, Scotland, UK***

tel. ***+44 (0)141 423 2564***

e-mail ***katetaylor2@nhs.net***

CME

The Royal College of Physicians of Edinburgh held its latest Neurology symposium on 9 November 2006. The event was very well attended by a cross-section of interested medical personnel, including medical students, junior doctors, consultants, professors of neurology, and a single brave orthopaedic surgeon.

Topics included useful clinical approaches to four common neurological problems (blackouts, dizziness, headache and functional symptoms), original basic and clinical research on subarachnoid haemorrhage, a discussion of exciting new advances made in MS over the last ten years, and current thinking on the management of Parkinson's disease. Finally, a debate on the controversial issue of the role of NICE in neurology concluded that NICE had not enhanced the care of neurological patients in the UK. However, there was a general consensus that there is an important role for an organisation to appraise neurological healthcare interventions.

A NO-NONSENSE APPROACH TO SOME COMMON NEUROLOGICAL PROBLEMS

Chairman: Dr Richard Davenport, Consultant Neurologist, Western General Hospital, Edinburgh, Scotland

Dr Geraint Fuller (Consultant Neurologist at the Gloucestershire Royal Hospital) set the scene with a very practical session on 'Blackouts', concentrating on how to distinguish between the three common categories of blackout: fits, faints and functional seizures. He advised characterising the three phases of the blackout (the prodrome, the blackout itself, and the post-ictal phase), with the help of three forms of witnesses (the patient, eye witnesses, and the so-called 'silent witnesses').

The differentiation between fits and faints can be difficult, and many of the factors traditionally associated with seizures have been shown (in a study of German medical students) to occur also during syncope.[1] The time course can, however, be revealing, in that the prodrome in syncope is often longer than in a seizure, whereas the recovery in syncope is usually quicker. Silent witnesses include clues that may be available after blackouts, even unwitnessed ones. Of these, urinary incontinence is a poor witness, as it can occur in any form of blackout. Evidence of tongue biting, however, is a useful clue; in particular, biting of the lateral border of the tongue is very suggestive of a seizure. Vertebral fracture and bilateral posterior shoulder dislocation are also both very suggestive of seizure when they do occur, but they are rare.

Dr Fuller stressed the importance of correct diagnosis for patients with non-epileptic attacks, many of whom are initially diagnosed with epilepsy and therefore incorrectly managed. He emphasised that where the situation is unclear, premature diagnosis should be avoided.

Professor Alfonso Bronstein (Professor of Clinical Neuro-otology at Imperial College London) spoke on 'The dizzy patient', using video examples to illustrate clinical points.

The VOR allows the eyes to remain fixed when the head moves, and when disrupted causes complaints of movement or blurring of the visual image on moving the head. This can be demonstrated on clinical examination by measuring the visual acuity using a Snellen chart when the patient's head is still, then again whilst moving their head from side-to-side, with a reduction in acuity signifying impairment of the VOR. Alternatively, the head thrust manoeuvre can be used whereby the examiner observes the eyes whilst moving the patient's head briskly to one side. The eyes should remain fixed on the examiner's nose, and the presence of corrective saccades signifies impairment of the VOR. Professor Bronstein described the main causes of loss of the VOR as cranial neuropathies with damage to the vestibular nerves, ototoxicity (particularly due to gentamicin), and autoimmune causes, although about one third remain idiopathic.

The differentiation between central and peripheral causes of nystagmus can cause clinicians considerable difficulty. Professor Bronstein suggested that nystagmus is always central in origin if it is pendular (with no fast and slow phase), if it is vertical, or if it beats in at least two directions. The use of the Hallpike and Semont manoeuvres respectively in the diagnosis and treatment of benign positional paroxysmal vertigo were described.[2] The audience were urged to perform the head thrust test and Hallpike manoeuvre in all dizzy patients.

Dr Giles Elrington (Honorary Consultant Neurologist at the Barts and London NHS trust) spoke entertainingly on 'Headache'. He emphasised that headache is very common in the general population,[3] and that when considering the cause clinicians should take account of the context in which the patient is being seen. Patients who present to accident and emergency with headache are more likely to have a serious cause than those who present to their general practitioner.[4]

Dr Elrington highlighted two treatable forms of chronic headache which are important to recognise: medication overuse headache and *hemicrania continua*. Medication overuse headache is a very common complication of primary headaches, and responds to withdrawing the causative drugs.[5, 6] *Hemicrania continua* is not an uncommon cause of chronic unilateral headache[7] which responds so reliably and specifically to indomethacin that response to this drug is included in its diagnostic criteria.[8, 9] A trial of indomethacin should therefore be considered in any case of unilateral chronic daily headache.[7] Dr Elrington went on to emphasise some of the features that may flag up a serious cause of headache, such as the 'first or worst headache', new headache in older people, headaches exacerbated by straining or stooping, and of course headaches accompanied by abnormal physical signs such as papilloedema.

Dr Jon Stone (Consultant Neurologist at the Western General Hospital in Edinburgh) discussed 'When weakness, fatigue and other symptoms are not explained by disease'. The problem is certainly common, as around one third of new neurology outpatients have symptoms which are not at all or only somewhat explained by disease, and these people are just as disabled but more distressed than those with physical disease [unpublished data from the Scottish Neurological Symptoms Study]. Dr Stone gave a practical approach to dealing with such patients in the thirty minutes allotted in most neurology clinics.

He suggested beginning by eliciting a list of all the patient's symptoms (although not necessarily covering each individual symptom in detail), and finding out the patient's own thoughts about the cause and potential treatment. When addressing the psychological state of the patient he suggesting asking 'Do your symptoms get you down?' which may be more acceptable to a patient presenting with physical symptoms than 'Are you feeling depressed?' which may alienate them. He emphasised the importance of finding positive features to confirm the diagnosis of functional problems such as Hoover's sign rather than purely relying on the absence of disease.[10]

Dr Stone drew attention to two of his review articles, which summarise the diagnosis and management of functional symptoms in neurology.[10, 11]

The Stanley Davidson Lecturer, Professor Gabriel Rinkel (Professor of Neurology from the University Medical Centre in Utrecht, the Netherlands) focused on 'Intracranial aneurysms and subarachnoid haemorrhage'.

Traditional teaching has suggested that aneurysms are congenital, and once they have been successfully clipped, patients have no further risk of SAH. However, the known risk factors (particularly smoking, hypertension and excess alcohol) are not really compatible with a congenital origin.[12, 13] Additionally, patients have been reported with second episodes of SAH due to newly developed aneurysms. Professor Rinkel's talk concentrated on these recurrent episodes of SAH, and the potential use of screening to prevent them.

Professor Rinkel's team have identified a group of patients with a second SAH due to a new aneurysm not present on the original angiogram, confirming that second

CME

© 2007 RCPE

episodes can be due to newly developed aneurysms, and supporting the idea that aneurysm development occurs as an expression of the underlying abnormality of patients' vessels.[14] The frequency of second SAH from *de novo* aneurysms was investigated, and found to occur with a cumulative incidence of 3·2% in the ten years following the index SAH.[15] The frequency of the development of *de novo* aneurysms was then investigated by screening patients with previous SAH. Sixteen percent were found to have a further aneurysm (20% at the clip site and 80% at a new site), of which about one third were truly new, and two thirds had been previously missed.[16]

In light of these data, Professor Rinkel then presented a decision analytical model used to determine whether screening should be proposed in clinical practice. The model showed that screening resulted in only a very small increase in life expectancy, and actually reduced QALYs. He concluded therefore that screening in general is not beneficial, but suggested that if patients could be identified who are at high risk of new aneurysm development and subsequent rupture, targeted screening may be appropriate.

CME

WHAT'S NEW IN ...?

Dr Alasdair Coles (Consultant Neurologist at the University of Cambridge), summarised what we have learnt about MS in the last ten years.

He described advances in understanding of the aetiology, including the demonstration that EBV infection in young adulthood is a risk factor, associated with an eight-fold risk of later MS.[17] This may be explained by molecular mimicry, as there is a structural similarity between part of the virus and myelin basic protein. Additionally, we now understand that the regulatory T cell (which can prevent an abnormal immune response by inhibiting other T cells) functions abnormally in MS.[18] *In vitro*, vitamin D restores normal function to these cells, which means that exposure to sunlight may partially explain the well-known geographical variation in MS.

He then described a new hypothesis which may explain why demyelination early in MS leads later to axonal degeneration, and the gradual accumulation of irreversible disability. Recent studies have implicated the sodium channels in this process, with a redistribution of sodium channels along the demyelinated axons causing a high metabolic load and axonal injury.[19–22] This has lead to the suggestion that manipulation of these channels may limit the progression of disability.[20] In EAE in animals, the sodium channel blockers phenytoin and lamotrigine have been shown to protect axons against degeneration.[23, 24] However, there is controversy as to whether EAE is a valid model of MS.[25] A clinical trial looking at the possibility of preventing neurodegeneration with lamotrigine is currently under way.[26]

With regard to new treatments, Dr Coles discussed Nataluzimab, a monoclonal antibody that prevents T cells entering brain, and reduces relapse rate by 60%; however, the effect on long-term disability is unknown. It also has a risk of causing progressive multifocal leucoencephalopathy in about one in 1,000 patients treated.[27] Interim results on another monoclonal antibody, Campath, suggest it may reduce relapse rate by 75%, and reduce disability after two years.[28] Dr Coles concluded by suggesting that in the future early aggressive treatment is likely to be the goal in MS, a view supported by three recent early treatment trials.[29]

Professor Ralph Gregory (Consultant Neurologist at the Radcliffe Infirmary in Oxford), gave a practical talk on current guidelines for the management of PD.[30]

At the time of diagnosis, FP-CIT SPECT scans can help to distinguish PD from essential tremor, drug-induced parkinsonism and vascular parkinsonism, but not from other degenerative parkinsonian disorders such as progressive supranuclear palsy or multiple system atrophy.[31]

Although there remains broad opinion as to the first line treatment in PD, Professor Gregory described evidence that dopamine agonists are less likely to cause motor complications such as fluctuations and dyskinesia, and are therefore probably the best choice in patients with a life expectancy of more than a few years. However, he did remind the audience that agonists are less dopaminergic than levodopa, and can cause serious side-effects such as fibrotic reactions and compulsive gambling. When patients develop complicated PD, with unpredictable response to medication, 'on-off' fluctuations and dyskinesia, it is useful to involve the PD specialist nurse to provide support and advice. Amantadine can be antidyskinetic so may be useful at this stage, and subcutaneous apomorphine has a role as it avoids the variable absorption that comes with the oral route. Neurosurgical techniques seem to mimic the effect of levodopa, and so are useful only if the patient's problematic symptoms are predominantly motor, and if they achieve a good 'on' state with levodopa.[32] Once patients develop problematic hallucinations and dementia, the best strategy is to simplify their dopaminergic medication to levodopa alone, and consider using cholinesterase inhibitors.

NICE for Neurology: Debate on the motion 'The existence of NICE has enhanced the care of neurological patients in the UK'.

Chairman: Dr Richard Metcalfe, Consultant Neurologist, Southern General Hospital, Glasgow, Scotland.

Professor Peter Littlejohns (Clinical and Public Health Director of NICE), spoke first for the motion, giving a

J R Coll Physicians Edinb 2007; **37**:352–356
© 2007 RCPE

broad perspective of the purpose of NICE. He emphasised that healthcare has to be prioritised. By balancing benefits and their costs, using a process involving all those affected (including patients, healthcare professionals and drug companies) NICE decides which new healthcare interventions should go ahead in a fair and transparent way. He urged the audience to consider 'If not NICE then what?'

Dr Carl Counsell (Clinical Senior Lecturer at the University of Aberdeen), spoke against the motion. He acknowledged the important and difficult job done by NICE. However, he used a series of examples (the MS risk-sharing scheme, cholinesterase inhibitors in Alzheimer's disease, and patent *foramen ovale* closure in stroke) to illustrate limitations that he saw in the recommendations made by NICE in the field of neurology. These included compromised assessment of the evidence, over reliance on cost effectiveness, and inappropriate research recommendations. He concluded that NICE has promoted widespread use of treatments with unclear long-term clinical benefits, distorted research agendas, and diverted resources from other clinical needs. He felt that the way forward is to make expensive new interventions available in the NHS only in the context of nationally co-ordinated independent trials.

Professor David Chadwick (Liverpool Walton Centre for Neurology and Neurosurgery) seconded the motion. He described NICE as fundamental to promoting equitable health care provision, but acknowledged that it has to work with imperfect data. Using examples (riluzole in motor neurone disease, cholinesterase inhibitors in Alzheimer's disease, and the new anti-epilepsy drugs), he demonstrated how NICE has focused on the paucity of clinically relevant data, emphasised the importance of specialist care, and prevented inappropriate use of some treatments.

Professor Keith Wheatley (Professor of Medical Statistics at the University of Birmingham Clinical Trials Unit) seconded the opposition to the motion. He described NICE as a good idea in principle, but with room for improvement. He gave examples of how NICE made conclusions which were too definite in the absence of adequate data (deep brain stimulation for dystonia), and where guidance was issued on the basis of results from trials with flawed designs, and where an ongoing trial (AD 2000) was damaged by the issuing of NICE guidance (cholinesterase inhibitors in Alzheimer's disease). He also described how decisions are influenced by groups with vested interests using the example of riluzole in motor neurone disease, where an independent report did not support its use because of uncertainty in the evidence, but company and patient groups were in favour and NICE recommended it.

In the final vote, 79% of the audience disagreed with the motion that '[t]he existence of NICE has enhanced the care of neurological patients in the UK'. However, there was a general consensus amongst all the speakers (both for and against) that there is an important role for an organisation to appraise neurological healthcare interventions, and ensure equitable provision across the NHS, but that the evidence available for this purpose is currently often inadequate. Perhaps this gives an important message to those of us in the neurology community.

CONCLUSION

I was once told to judge an educational programme by whether I learnt three things that would change my clinical practice for the better. I am sure that most of the attendees found more than three things to remember, making the symposium a most successful day.

CME

REFERENCES

1 Lempert T. Recognising syncope: pitfalls and surprises. *J R Soc Med* 1996; **89:**372–5.
2 Bronstein AM. Vestibular reflexes and positional manoeuvres. *J Neurol Neurosurg Psychiatry* 2003; **74:**289–3.
3 Stovner LJ, Zwart J-A, Hagen K, Terwindt GM, Pascual J. Epidemiology of headache in Europe. *Eur J Neurol* 2006; **13:**333–45.
4 Craig JJ, Patterson VH. Headaches in the accident and emergency department. *Br J Hosp Med* 1997; **57:**202–6.
5 Silberstein SD, Olesen J, Bousser M-G *et al.* The International classification of headache disorders (2nd edition) (ICHD-II) – revision of criteria for 8·2 medication-overuse headache. *Cephalgia* 2005; **25:**460–5.
6 Dodick D, Freitag F. Evidence-based understanding of medication – overuse headache: clinical implications. *Headache* 2006; **46 (Suppl 4):**S202–S211.
7 Peres MFP, Silberstein SD, Nahmias S *et al. Hemicrania continua* is not that rare. *Neurology* 2001; **57:**948–51.
8 Sjaastad O, Spierings E. *Hemicrania continua:* another headache absolutely responsive to indomethacin. *Cephalgia* 1984; **4:**65–70.
9 International Headache Society Classification Subcommittee. International Classification of Headache Disorders (2nd edition). *Cephalgia* 2004; **24(Suppl 1):**1–160.
10 Stone J, Carson A, Sharpe M. Functional symptoms and signs in neurology: assessment and diagnosis. *J Neurol Neurosurg Psychiatry* 2005; **76(Suppl 1):**i2–i12.
11 Stone J, Carson A, Sharpe M. Functional symptoms in neurology: management. *J Neurol Neurosurg Psychiatry* 2005; **76(Suppl 1):**i13–i21.
12 Ruigrok YM, Rinkel GJE, Buskens E. Attributable risks of common and rare determinants of aneurysmal subarachnoid haemorrhage. *Stroke* 2001; **332:**1173–5.
13 Ruigrok YM, Rinkel GJE, Wijmenga TN. Genetics of intracranial aneurysms. *Lancet Neurology* 2005; **4:**179–89.

© 2007 RCPE

14 Wermer MJH, Rinkel GJE, Greebe P *et al.* Late recurrence of subarachnoid haemorrhage after treatment for ruptured aneurysms: patient characteristics and outcomes. *Neurosurgery* 2005; **56:**197–204.

15 Wermer MJH, Greebe P, Algra A, Rinkel GJE. Incidence of recurrent subarachnoid haemorrhage after clipping for ruptured intracranial aneurysms. *Stroke* 2005; **36:**2394–9.

16 Wermer MJH, Van der Schaaf IC, Velthuis BK *et al* for the ASTRA study group. Follow-up screening after subarachnoid haemorrhage: frequency and determinants of new aneurysms and enlargement of existing aneurysms. *Brain* 2005; **128:**2421–9.

17 Lang HL, Jacobsen H, Ikemizu S *et al.* A functional and structural basis for TCR cross-reactivity in multiple sclerosis. *Nature Immunol* 2002; **3:**940–3.

18 Viglietta V, Baecher-Allan C, Weiner HL, Hafler DA. Loss of functional suppression by CD4+CD25+ regulatory T cells in patients with multiple sclerosis. *J Exp Med* 2004; **199:**971–9.

19 Frohman EM, Filippi M, Stuve O *et al.* Characterizing the mechanisms of progression in multiple sclerosis. *Arch Neurol* 2005; **62:**1345–56.

20 Waxman SG. Axonal conduction and injury in multiple sclerosis: the role of sodium channels. *Nature Reviews Neuroscience* 2006; **7:**932–41.

21 Wada A. Roles of voltage-dependent sodium channels in neuronal development, pain, and neurodegeneration. *J Pharmacol Sci* 2006; **102:**253–68.

22 Coman I, Aigrot MS, Seilhean D *et al.* Nodal, paranodal and juxtaparanodal axonal proteins during demyelination and remyelination in multiple sclerosis. *Brain* 2006; **129:**3186–95.

23 Black JA, Liu S, Hains BC *et al.* Long-term protection of central axons with phenytoin in monophasic and chronic-relapsing EAE. *Brain* 2006; **129:**3196–208.

24 Bechtold DA, Miller SJ, Dawson AC *et al.* Axonal protection achieved in a model of multiple sclerosis using lamotrigine. *J Neurol* 2006; **253:**1542–51.

25 Sriram S, Steiner I. Experimental allergic encephalomyelitis: a misleading model of multiple sclerosis. *Ann Neurol* 2005; **58:**939–45.

26 Kapoor R. Neuroprotection in multiple sclerosis: therapeutic strategies and clinical trial design. *Current Opinion in Neurology* 2006; **19:**255–9.

27 Langer-Gould A, Atlas SW, Green AJ *et al.* Progressive multifocal leukoencephalopathy in a patient treated with natalizumab. *N Engl J Med* 2005; **353:**375–81.

28 Coles AJ, Cox A, Le Page E *et al.* The window of therapeutic opportunity in multiple sclerosis; evidence from monoclonal antibody therapy. *J Neurol* 2006; **253:**98–108.

29 Frohman EM, Stüve O, Havrdova E *et al.* Therapeutic considerations for disease progression in multiple sclerosis. *Arch Neurol* 2005; **62:**1519–30.

30 Parkinson's disease National Clinical Guideline. Royal College of Physicians CODE 15116006; June 2006.

31 Marshall V, Grosset D. Role of dopamine transporter imaging in routine clinical practice. *Movement Disorders* 2003; **18:**1415–23.

32 Gregory R. Surgery for movement disorders. *J Neurol Neurosurg Psychiatry* 2002; **72(Suppl 1):**32–5.

CME

Royal Medical Benevolent Fund
Tod Endowment Trust

Suitable applications are invited for the Tod Endowment Trust, which provides financial help for members of the medical profession, their spouses, partners and dependents (up to age 18, or 25 if in full-time education) who are in need of rest and recouperation in Scotland. This could include respite care, if appropriate, or a holiday in Scotland that would not normally be affordable.

Beneficiaries must have been in medical practice in Scotland for a minimum of two years. Widows/widowers and their dependents who are financially eligible can apply.

If you know of anyone who might benefit from this Trust, please contact the Royal Medical Benevolent Fund.

Further information and application forms can be obtained from:

Case Workers,
Royal Medical Benevolent Fund,
24 King's Road,
Wimbledon,
London SW19 8QN

E-mail: caseworkeradmin@rmbf.org

Tel: 020 8540 9194

© 2007 RCPE