

# PostScript

## CORRESPONDENCE

### Anti-GQ1b IgG antibody syndrome: clinical and immunological range

We read with interest the article by Odaka *et al.*<sup>1</sup> In this article, the authors attempted to establish a nosological relation between Miller Fisher syndrome, Guillain-Barré syndrome with ophthalmoplegia, Bickerstaff's brain stem encephalitis, and acute ophthalmoparesis without ataxia on the basis of anti-GQ1b IgG antibody. The retrospective study included only those patients who were positive for anti-GQ1b IgG antibody, whose clinical range was subsequently evaluated. This introduces a selection bias, as there was no reference to those patients who may have had these diseases with ophthalmoparesis and yet do not have this particular antibody in their serum. Thus, this inherently flaws the attempt to establish these entities as a clinical range, as there may be other antibodies detected in these other patients.

Because there is no specific diagnostic criteria established for Miller Fisher syndrome, Bickerstaff's brain stem encephalitis, and acute ophthalmoparesis, the authors have used their own diagnostic criteria for the purpose of the study to classify the patients. The criteria set down for diagnosis do satisfy the minimum prerequisites required to diagnose the conditions as defined in previous reports on these clinical entities.<sup>2,3</sup> However, the inclusion of the presence of anti-GQ1b IgG antibody as a supportive feature for diagnosis is the authors' bias in these criteria.

It has been established in previous immunological studies that the patients with anti-GQ1b IgG antibody presented with varying combinations of ophthalmoparesis, ataxia, areflexia, or altered sensorium.<sup>4</sup> However, without studying the clinical and immunological profile of other patients with Miller Fisher syndrome, Bickerstaff's brain stem encephalitis, and Guillain-Barré syndrome with ophthalmoplegia and acute ophthalmoparesis without ataxia who do not demonstrate anti-GQ1b IgG antibody in the serum, it would be fallacious to use the term "anti-GQ1b IgG antibody syndrome". The association of anti-GQ1b IgG antibody has been established with 88%–89% concordance in those with Miller Fisher syndrome,<sup>5</sup> but whether patients with Miller Fisher syndrome, Guillain-Barré syndrome with ophthalmoplegia, acute ophthalmoparesis without ataxia, and Bickerstaff's brain stem encephalitis without anti-GQ1b antibody have a similar or different clinical profile and other associated antibodies needs to be evaluated. Only then can the knowledge of association of anti-GQ1b IgG antibody be extrapolated to the clinical range.

Grouping these patients into an antibody syndrome also does not help in deciding therapy as patients without this antibody may respond equally well to plasmapheresis, due to the presence of other recognised or unrecognised antibodies. Therefore, patients presenting with Miller Fisher syndrome, Bickerstaff's brain stem encephalitis or Guillain-Barré syndrome should be given the

benefit of plasmapheresis and intravenous immunoglobulins, irrespective of the presence of anti-GQ1b IgG antibody in the serum.

In conclusion, although the authors have probed an important association of anti-GQ1b IgG antibody with some cases of Miller Fisher syndrome, Guillain-Barré syndrome with ophthalmoplegia, Bickerstaff's brain stem encephalitis, and acute ophthalmoparesis without ataxia, it cannot lead us to make a syndromic diagnosis clinically and infer about therapy.

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### Authors' reply

Those patients showing either consciousness disturbance (coma, semicomatose, or stupor) or pyramidal signs (hyperreflexia or pathological reflexes) were diagnosed as "Bickerstaff's brain stem encephalitis" in our article.<sup>1</sup> One of the authors, however, has proposed that "brain stem encephalopathy of Bickerstaff type" or "Bickerstaff's encephalopathy" is an appropriate diagnosis for such patients.<sup>2</sup> The lack of definite inflammatory changes in the brain stem in two necropsied cases reported by Bickerstaff's group suggests the term *encephalopathy*, not *encephalitis*. We therefore use the term "Bickerstaff's encephalopathy" in this reply.

Panda and Tripathi misunderstand what we described. We did not intend the term "anti-GQ1b IgG antibody syndrome" to be used as a clinical diagnosis, which was clearly stated in the conclusion of the abstract of our article.<sup>1</sup> We mentioned that recognition of this syndrome is useful for understanding the aetiological relation among Miller Fisher syndrome, Guillain-Barré syndrome, Bickerstaff encephalopathy, and acute ophthalmoparesis without ataxia. Willison's group have shown the pathogenic effects of anti-GQ1b IgG antibody in an *ex vivo* model.<sup>3</sup> Their excellent studies provide us with theoretical backing that the removal of anti-GQ1b antibodies is reasonable. Recognition of the anti-GQ1b IgG antibody syndrome, therefore, is useful for introducing the established treatments of Guillain-Barré syndrome

(plasma exchange and intravenous immunoglobulins) for use with the other conditions. Although acute paresis of extraocular muscles is a cardinal sign among each condition, the reason why the clinical presentations differ remains to be elucidated.

Several groups, including ours, have reported that some patients with Miller Fisher syndrome, Guillain-Barré syndrome with ophthalmoplegia, Bickerstaff's encephalopathy, and acute ophthalmoparesis have anti-GQ1b IgG antibody during the acute phase of the illness. Not all the patients with each condition have this autoantibody, even those with Miller Fisher syndrome. The presence of seronegative patients indicates that pathogenesis of each condition (even Miller Fisher syndrome) is heterogeneous. Because the purpose of our study was to clarify the nosological relation among each condition, we reviewed medical records of 194 patients with anti-GQ1b IgG antibody, and diagnosed them.<sup>1</sup> This step enabled each condition to be more homogenous, then it became more easy to judge whether a clinical and immunological continuity exists among those conditions. That is one way to elucidate the nosological relation among each condition which has heterogeneous pathogenesis, although Panda and Tripathi thought that selection bias existed in our study. As disclosed in patients with myasthenia gravis without antiacetylcholine receptor antibody,<sup>4</sup> novel autoantibodies may be found in seronegative patients with Miller Fisher syndrome. If the novel autoantibodies are detected in the other conditions as well, our hypothesis that each condition forms a continuous range will be supported.

Another way to clarify the nosological relation is shown. Irrespective of the presence or the absence of the anti-GQ1b IgG antibody, for example, we investigated clinical and immunological continuity of 62 patients with Bickerstaff's encephalopathy with (n=37) and without (n=25) limb weakness.<sup>5</sup> There was no significant difference in the clinical features except limb weakness between Bickerstaff's encephalopathy with and without limb weakness. Both conditions therefore may be closely related, and form a continuous range. The results give further support to the idea that Bickerstaff's encephalopathy and Guillain-Barré syndrome form a continuous range. In a large series, moreover, we will report whether clinical and immunological continuity exists among Fisher syndrome, Bickerstaff's encephalopathy, and Guillain-Barré syndrome. In these studies, we will analyze whether clinical presentations differ between seropositive and seronegative patients in each condition. Here we show the preliminary results obtained in Bickerstaff's encephalopathy (table 1). Anti-GQ1b IgG antibody was present in 15 (60%) of the 25 patients with Bickerstaff's encephalopathy. There was no significant difference in the clinical features including the presence of antecedent infections between the seropositive and seronegative patients (p=0.8; post hoc test). These results suggest that an autoimmune mechanism may function in the development of seronegative Bickerstaff's encephalopathy as well.

Panda and Tripathi also misunderstand the point of treatment. We insisted that established treatment for Guillain-Barré syndrome might be more readily introduced as

**Table 1** Clinical profiles in patients with Bickerstaff's encephalopathy with or without anti-GQ1b IgG antibody

	Anti-GQ1b IgG			
	Positive		Negative	
Number of patients	15		10	
Sex (M/F)	10/5		7/3	
Median age (range)	52 (17–63)		48 (3–91)	
	n	%	n	%
Antecedent illness:				
Upper respiratory infection	8	53	7	70
Diarrhoea	2	13	0	0
Initial symptoms:				
Diplopia	8	53	5	50
Consciousness disturbance	4	27	2	20
Gait disturbance	3	20	4	40
Blepharoptosis	2	13	0	0
Photophobia	1	7	0	0
Dysesthesia	0	0	2	20
Dysarthria	0	0	1	10
Neurological signs during the course of the illness:				
Consciousness disturbance				
Drowsiness	4	27	9	90
Stupor, semicoma, or coma	3	20	1	10
Blepharoptosis	4	27	4	40
External ophthalmoplegia	15	100	10	100
Internal ophthalmoplegia	6	40	1	10
Nystagmus	8	53	3	30
Facial weakness	5	33	2	20
Bulbar palsy	2	13	2	20
Tendon reflex				
Brisk	7	46	3	30
Normal	1	7	3	30
Decreased	3	20	1	10
Absent	4	27	3	30
Babinski's sign	4	27	3	30
Ataxia	15	100	10	100
Deep sense impairment	0	0	1	10
Superficial sense impairment	1	7	2	20

the treatment for anti-GQ1b IgG antibody syndrome.<sup>1</sup> We think that the treatment should be given for seronegative patients with Fisher syndrome and Bickerstaff's encephalopathy, although we should rule out similar conditions such as Wernicke's encephalopathy, vascular disease involving the brain stem, multiple sclerosis, neuro-Behçet's disease, botulism, myasthenia gravis, brain stem tumour, and pituitary apoplexy, which are listed in table 1 of our article.<sup>1</sup>

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## Parkin gene related neuronal multisystem disorder

We read with much interest the article on Japanese patients with parkin gene related autosomal recessive juvenile parkinsonism (ARJP) complicated by cerebellar and pyramidal tract dysfunction.<sup>1</sup> Recently, we described a Dutch family with parkin gene related ARJP showing typical levodopa responsive parkinsonism. The proband clinically had additional mild gait ataxia and pathologically showed—besides classic parkin gene related ARJP findings—neuronal loss in parts of the spinocerebellar system—namely, Purkinje cell layer, dentate nucleus, and gracile fascicles.<sup>2</sup> Just as our Japanese colleagues, we suspected some kind of hereditary multiple system degeneration with predominant parkinsonism until genetic analysis indicated parkin gene related ARJP. Although the non-extrapyramidal abnormalities in the Japanese and in our patients could have been coincidental, the recent Japanese findings seem to confirm that the spinocerebellar and probably also other systems can be affected in parkin gene related ARJP. The fact that the Japanese patients did not respond to levodopa may have very important clinical consequences because it suggests that neurologists have to request an analysis of the parkin gene in

patients with autosomal recessive levodopa non-responsive parkinsonism accompanied by a multisystem disorder.

The authors found identical parkin gene mutations in two unrelated families—namely, deletions extending from exons 3 to 4. Although it is very striking that two unrelated Japanese families showed identical genetic abnormalities, the degeneration of non-extrapyramidal systems is not exclusively related to these particular genetic abnormalities because our compound heterozygous patients showed clearly different mutations—that is, a heterozygous transversion Lys211Asn in exon 6 and a heterozygous deletion of exon 3. Furthermore, as Kuroda *et al*<sup>1</sup> remarked themselves, other patients with similar parkin gene mutations to Kuroda's patients did not show non-extrapyramidal abnormalities, so the genotype-phenotype relation in parkin gene related ARJP remains to be elucidated. However, taken together the findings of Kuroda *et al*<sup>1</sup> and of our own, it seems very probable that the symptoms of parkin gene related ARJP are not necessarily restricted to parkinsonism but can also include signs and symptoms of a neuronal multisystem disorder.

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## Authors' reply

Since the first report of autosomal recessive juvenile parkinsonism (ARJP),<sup>1</sup> it has been established as a clinical entity on the basis of age at onset (usually before the age of 40), clinical features and neuropathological findings. The clinical symptoms include homogeneous features such as typical signs of parkinsonism (rigidity, tremor, akinesia), foot dystonia, diurnal fluctuations, sleep benefit, hyperreflexia, a striking response to levodopa, and early susceptibility to levodopa induced dyskinesia.<sup>2–3</sup> Levodopa responsive parkinsonism is recognised as one of the most important features of ARJP. However, in 1994 we reported on two Japanese patients from a family with autosomal recessive parkinsonism complicated with multiple system degeneration.<sup>4</sup> The patients exhibited symptoms corresponding to cerebellar and pyramidal tract dysfunctions as well as nigrostriatal dysfunction, and the most prominent feature in the patients was parkinsonism not responsive to levodopa, indicating dysfunction in both nigral dopaminergic neurons and the striatum. The clinical features were sharply contrastive to those in patients with ARJP;

however, an in frame deletion mutation of the parkin gene extending from exons 3 to 4 was unexpectedly detected in our patients. Furthermore, it is notable that the deletion of this region is not specific in the Japanese family and is occasionally found in patients with ARJP in Japan as well as in Europe,<sup>5</sup> although parkin mRNA has been analyzed in only a few studies and it is not well known whether large deletions are in frame or out of frame.

We are very interested in the study by van de Warrenburg *et al* showing that the spinocerebellar system was involved in a patient with parkin mutations who exhibited cerebellar ataxia, because ARJP has been neuropathologically characterised by selective degeneration without Lewy bodies in the substantia nigra compacta and locus ceruleus. Their observation is concordant with our assumption that the parkin protein potentially functions not only in the substantia nigra but also in extranigral regions. It seems unlikely that the non-extrapyramidal involvement in ARJP specifically depends on some mutations or deletions of the parkin gene, as Horstink *et al* suggested. Patients with parkin gene mutations, even those in single families, have generally shown a wide range of clinical signs.<sup>5</sup> These findings suggest that additional factors contribute to the phenotype. Because patients with ARJP have been considered to exhibit homogeneous clinical symptoms, patients with atypical parkinsonism and/or with non-extrapyramidal symptoms have remained to be examined for parkin gene mutations. Further extensive study in these patients will revitalise the insights into pathophysiology of the parkin gene related disorder.

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## Obsessive-compulsive phenomenon and Parkinson's disease

Alegret *et al*<sup>1</sup> have systematically studied patients with Parkinson's disease for presence of "obsessive-compulsive traits". This study is based on the evidence that Parkinson's disease and obsessive-compulsive disorder have neuroanatomical overlap in terms of fronto-basal ganglia circuitry involvement. Anatomical specificity of obsessive-compulsive disorder or obsessive-compulsive phenomenon has been previously studied in Tourette's syndrome, Huntington's chorea, Sydenham's chorea etc, but not in Parkinson's disease.<sup>2</sup> The authors, through a cross sectional design,

found significantly high scores on the Maudsley obsessive-compulsive Inventory (MOCI) and Leyton obsessional inventory (LOI) in severe Parkinson's disease. However, the presentation and interpretation of results merits further elucidation and clarification.

The aim has been mentioned as to "...systematically investigate obsessive-compulsive traits in Parkinson's disease", using MOCI and LOI. Although LOI is used to assess both obsessional symptoms and traits,<sup>3</sup> MOCI is used to investigate the different types and rate severity of obsessive-compulsive complaints in patients with obsessive-compulsive disorder.<sup>3,4</sup> Also, traits are defined as enduring patterns of perceiving, relating to, and thinking about the environment and oneself that are exhibited in a wide range of important social and personal contents<sup>5</sup> and are part and parcel of the personality of any person. On the other hand, obsessive-compulsive disorder is a clinical disorder characterised by recurrent obsessions or compulsions that causes distress or impairment.<sup>5</sup> Hence the MOCI is used to assess the obsessive-compulsive symptoms in patients with obsessive-compulsive disorder and is not applicable for obsessive-compulsive traits or neurotic patients with no obsessional symptoms.<sup>3,4</sup> This issue needs discussion as the authors have interchangeably used the terms "traits", "phenomenon", and "symptoms" leading to considerable semantic confusion. Also, it raises the query as to what is being actually assessed. Are the authors assessing obsessive-compulsive traits or obsessive-compulsive symptoms? To our mind, the attempt has been to assess obsessive-compulsive phenomena (both traits and symptoms); traits using LOI and symptoms using MOCI.

Secondly, it is mentioned that "patients with mild Parkinson's disease had no obsessive-compulsive symptoms". A closer look at the table presented shows that the MOCI total score was 4.83 (SD 3.57) in controls compared with 4.12 (SD 3.15) in patients with mild Parkinson's disease. If such is the case, then the controls demonstrated more (though statistically comparable) obsessive-compulsive symptoms than patients with mild Parkinson's disease. This issue has not been highlighted and discussed. Another related issue is the absence of a cut off score on MOCI that can differentiate between presence or absence of obsessive-compulsive symptoms.<sup>3,4</sup> Hence, the above statement by the authors is itself not tenable.

Thirdly, it has been suggested that obsessive-compulsive symptoms appeared late during progression of Parkinson's disease (based on correlation between years of evolution and MOCI global score). Keeping in mind the previous issue, this suggestion should be modified to: patients with longer duration of Parkinson's disease had greater severity (rather than emergence) of obsessive-compulsive symptoms. Additionally, a correlation between MOCI total score and stage of Parkinson's disease can just simply be interpreted as: the more progressive the Parkinson's disease, the more prominent/severe is the obsessive-compulsive symptomatology. The assertion that obsessive-compulsive symptoms appeared late during disease progression can only be made if there is a correlation between duration of illness and severity of Parkinson's disease.

Fourthly, the statement "slowness might be expected ...did not increase" is conceptually not tenable as the slowness characteristic of Parkinson's disease can in no way be equated (or compared) with the slowness in obsessive-compulsive disorder (or obsessive-compulsive

slowness); as evidenced from items of slowness and repetition of MOCI.<sup>4</sup> Also, the obsessive-compulsive slowness is related to obsessions<sup>5</sup> whereas the slowness in Parkinson's disease has no such cognitive basis.

Lastly, a very interesting and important finding in this study has been that no patient with Parkinson's disease had obsessive-compulsive disorder. Hence, the link between these two may be lacking. But, at the neuroanatomical level, the basic psychopathology seems to be somewhat similar. It may be that a pathoplastic effect is exerted by the frontal and temporal lobes on some basic dysfunction of basal ganglia leading to differing clinical manifestations. This study, indeed, opens up new vistas of research for understanding the neurobiological basis of obsessive-compulsive disorder.

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## Authors' reply

We are grateful to Sharma and Gupta for their comments.

(1) We concur with them that the term "phenomena" may be the most appropriate to describe our results because they included measures of traits and symptoms. Patients with Parkinson's disease may show both symptoms and traits. There are several studies suggesting the presence of a characteristic premorbid personality profile in Parkinson's disease. Similarly to obsessive-compulsive disorder, patients with Parkinson's disease demonstrated a previous tendency to inflexibility and mental rigidity.<sup>1</sup> In addition, it has been shown that basal ganglia lesions and induced parkinsonism produce obsessive-compulsive disorder symptomatology.<sup>2</sup> We think, accordingly, that the use of both MOCI and LOI was pertinent. On the other hand, despite the fact that traits and symptoms can be well differentiated in clinical diagnoses, there is also some evidence supporting a continuum hypothesis.<sup>3,4</sup>

(2) It is true that the mean of the MOCI scores of patients with mild Parkinson's disease was slightly lower than that of the controls, but without statistical relevance. Thus, we considered it inappropriate to include that issue in the discussion.

(3) Regarding the issue of co-occurrence of severity of Parkinson's disease and obsessive-compulsive disorder phenomena, in addition to the correlation reported in the paper we

found that the duration of illness was highly correlated with Parkinson's disease severity ( $r=0.66$ ;  $p<0.0001$ ), supporting the view that obsessive-compulsive disorder phenomena appeared late during disease progression. Moreover, patients with more than 10 years of evolution ( $n=37$ ) significantly differed from patients with less than 10 years of evolution ( $n=35$ ) in MOCI scores ( $7.37$  (SD 4.28)  $v$  4.91 (SD 3.62) ( $t=-2.6$ ,  $p=0.007$ ).

(4) We agree with Sharma and Gupta regarding the absence of a clear explanation about the link between Parkinson's disease and obsessive-compulsive disorder. We think that although both pathologies share frontostriatal dysfunction, there is not a direct relation because obsessive-compulsive disorder phenomena are not present in the early stages of the disease. Within basal ganglia dysfunctions we suspect that obsessive-compulsive disorder is more closely related to dyskinesic motor symptoms such as Huntington's disease. Dyskinesia also appears with progression of Parkinson's disease. Moreover, MOCI scores in obsessive-compulsive disorder improve after pallidotomy similarly to dyskinesic manifestations.<sup>3</sup>

(5) Finally, the Sharma and Gupta hypothesis claiming a pathoplastic effect exerted by frontal and temporal lobes on some basal ganglia dysfunction is suggestive although perhaps somewhat speculative in the light of the available evidence.

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## BOOK REVIEWS

### Multiple sclerosis: the guide to treatment and management, 5th edition

Edited by C H Polman, A J Thompson, T J Murray, *et al* (Pp 148, £24.95). Demos Medical Publishing, New York, 2001. ISBN 1 888799 54 4

This book is a welcome addition to the multiple sclerosis literature. It is regularly updated and is reasonably comprehensive with regard

to its small size. Most treatment areas are covered and in particular the disease modifying drugs are detailed. A particular advantage of the book is the regular review section expressing the opinion of the medical committee of the Multiple Sclerosis International Federation. Although the committee's views are relatively conservative as might be expected from a committee decision, the conclusions are sensible and tend to encourage further research in certain treatment areas. There is a very welcome review of symptomatic treatments and rehabilitation. There is also a section on alternative and complementary therapies. The reviewer had some difficulty with the difference between conventional and alternative. For example, it seemed unusual to include thalamotomy and thalamic stimulation for tremor in multiple sclerosis in the alternative therapy section. However as an overview of possible therapies it was considered an important section of the book. Overall this publication will allow a rapid update and assimilation of present wisdom in treating multiple sclerosis from editors of international standing and an international committee of high repute. It should be useful for clinicians as well as paraclinical specialists and also to a certain extent patients with the disease.

**C P Hawkins**

### Cognitive rehabilitation, an integrative neuropsychological approach

Edited by M M Sohlberg and C A Mateer (Pp 492, £41.95). Guilford Press, New York, 2001. ISBN 1 57230 613 0

People working in rehabilitation will appreciate this book, which is a follow up to the influential *Introduction to cognitive rehabilitation* by the same authors that appeared in 1989. Sohlberg and Mateer say they began with the intention of updating the earlier version but because of so many advances in the field, they realised a new text was called for. The new book is indeed very different from the earlier one.

The book contains 15 chapters divided into four sections. (1) fundamentals for practising cognitive rehabilitation, (2) management approaches for cognitive impairments, (3) interventions for behavioural, emotional, and psychosocial concerns and (4) working with special populations.

The authors' considerable experience in rehabilitation is apparent throughout, and it is particularly noticeable in sections 2 and 3. They are obviously "hands on" rehabilitation experts who recognise the need to address behavioural, emotional, and psychosocial concerns together with cognitive difficulties. The text reflects the major changes that have occurred since their previous book in 1989. Influences from other notable rehabilitation practitioners such as Prigatano can also be detected. I particularly liked chapter 13 on "working collaboratively with families", one of several topics not addressed in the first book. The following chapter on "rehabilitation of children with acquired cognitive impairments" is also new. Those who work with children with brain injury will, no doubt, find that one chapter is insufficient for them but for those who work with adults it is helpful to have this account. The table in this chapter providing an example of a daily lesson design for children with cognitive difficulties could also be used as a guide for both individual and group work with adults.

Even experienced practitioners will benefit from the many tips and guidelines that occur with such regularity throughout the text. Relative newcomers to the area will find the book even more useful.

**B A Wilson**

### Clinical cases in neurology

Edited by A H V Schapira and L P Rowland (pp 261, £32.50). Butterworth Heinmann, Oxford 2001. ISBN 0 7506 4304 8

Any review of a compendium of case histories must resemble that of a crime novel. How much do you say so as to whet the appetite without inducing such a degree of satiation as to make the meal not worth eating? Different people learn their neurology in different ways, and only some will wish to tease themselves by solving illustrative clinical case histories. This volume contains 29 cases covering the breadth of neurology, to which a total of 27 neurologists have contributed variously. The editors' choice of the range of clinical problems cannot be faulted. The test of such a volume is to expect to solve those cases which consider one's own subspecialty area, and to judge whether the cases are presented fairly, while being difficult enough to induce a frisson of uncertainty, and then to decide whether you agree with the range and balance of the ensuing discussion. Of course one's better registrars should be able to get them all, whatever the subspecialty.

Compendiums of case histories should focus on the clinical method rather than merely acting as a vehicle for science, which can be reached more systemically in textbooks. A few of the cases in this volume slightly miss this clinical target. For instance an obvious case of hemiplegic migraine described in one and a half pages is followed by eight pages of discussion which do not illuminate the clinical discussion of differential diagnosis, but are largely concerned with molecular genetics and functional imaging. By way of contrast, another case of ataxia manages to discuss the different spinocerebellar ataxia mutations in terms of their clinical phenotype; indeed one can estimate how up to date is the text by the number of SCA mutations describable at that point in time (this book coincides with SCA-11). A few of the cases are not really diagnostic challenges. For instance the text of a case of spontaneous low pressure headache contains the answer that radiological contrast was noted to seep from nerve root sleeves; wouldn't it have been better simply to show the relevant CT myelogram and leave the reader to inspect this in forming their own diagnostic opinion? And the first sentence of the discussion of the case of brain tumour tells us that it was an oligodendroglioma. I am always nonplussed to the point of irritation by those tacticians who withhold crucial information when they present case histories. That of a young man with a movement disorder and accompanying speech disturbance contains no mention of any search for Keiser-Fleischer rings, and we are only told on the second page of the discussion that "the diagnosis of Wilson's was made by careful examination at the bedside of the eyes". Yet the photograph of this difficult physical sign is not really very illuminating, and surely should have been presented during the case history. The book is mercifully short of repetitive themes, although two separate cases present demyelination masquerading as a mass lesion.

Overall this is a successful armchair vehicle for discussing common problems in neurological diagnosis. It contains succinct and contemporary discussion of relevant pathogenic mechanisms, often genetic, even if arguably this is not the point of a compendium of case histories. One or two cases illuminate areas not really covered well in textbooks—the chapter on headache caused by sinusitis being an example. I suspect that it is those in training who will make most use of this book; some of the cases could be used by regional training advisers as vehicles for group discussion. But it is quite expensive for what I would see as a single usage book—would you read a compendium of case histories more than once?

M Donaghy

### Contemporary treatments in neurology

Edited by Neil Scolding (Pp 446, £45.00). Published by Butterworth Heinemann, Oxford, 2001. ISBN 0 7506 3918 0

The very fact that this book has been published and runs to 400 pages tells us how far we have come in the past 30 years. That it has to be multiauthored reflects the wide varieties of treatments now available to patients with neurological disorders, despite interventions by the National Institute for Clinical Effectiveness. Perhaps most impressive is that the use of so many neurological therapies are evidence based and here Peter Rothwell's chapter on clinical trial methodology sets the tone for the book. Each chapter is suitably bite sized and well referenced with a clinical introduction so that the reader can coast through the subspecialties of neurology that he or she might not see in regular practice. Most areas of neurology are covered

and it would be invidious to single out individual chapters but it was reassuring to read Rod Lang's view that, even amongst neurosurgeons, there was uncertainty about the treatment of cervical spondylosis that would only be resolved by a long term trial. Therapeutic nihilists should read this book to see where we are with treatments, enthusiasts should look critically again at the evidence for effectiveness, and the people who should really read this book are those who commission our services; they would be surprised if they saw what we could now offer.

G S Venables

### Myotonic dystrophy, 3rd edition: major problems in neurology series, No 37

By Peter S Harper (Pp 436, £55.00). Published by W B Saunders, London, 2001. ISBN 0 7020 2152 0

This is the third edition of Peter Harper's exemplary monograph, and it has been much awaited. Myotonic dystrophy transcends virtually all medical disciplines and few clinicians will not find something of value to their own practice. Every neurologist and geneticist with frequent involvement with such patients should have a personal copy, and for the rest there should be copies in departmental and postgraduate libraries. It has been written in a style that also makes it accessible to some patients and their families and I recently met an American with the condition who takes her copy of the second edition to every clinical consultation, often to the benefit of her physician!

It is extraordinary to recollect the enormous advances that have been made in our understanding of the condition since the second edition, published in 1989. This is partly

reflected in an increase in size of some 50 pages, despite omission of significant sections from the previous edition. The isolation of the gene in 1992 has revolutionised our diagnostic approach, and gone are the days of slit lamp examination and neurophysiological studies to identify gene carriers. The genetic basis, an unstable trinucleotide repeat expansion, is now known to be common to several neurological disorders and whole meetings are now devoted to "unstable DNA". The past few years have seen the evolution of theories to explain how such a mutation, in an untranslated region of a gene, can lead to the protean manifestations of the disease. For this third edition, Harper has sought the collaboration of David Brook and Emma Newman who have contributed a chapter on the molecular and cell biology of myotonic dystrophy. One proposed mechanism to explain the widespread consequences of the condition is that there is disruption of RNA metabolism. The clinical similarities with proximal myotonic myopathy (PROMM), a condition which had not been recognised at the time of the last edition, suggested a common mechanism and indeed, very shortly after Harper's book went to press the genetic abnormality causing PROMM was identified, and found to be a quadruplet repeat expansion in the zinc finger protein gene.

The book is uniformly good, but I must select three chapters for special mention. The complexities of genetic counselling for this particular disorder are immense, and anybody offering such a service must read the relevant chapter. Some who currently offer "counselling" might well decide that they shouldn't! There is an excellent chapter on the disease in infancy and childhood, which is a must for paediatricians. The final chapter, on management and therapy, summarises the experience of a very experienced clinician.

D Hilton-Jones