Anti-GQ1b IgG antibody syndrome: clinical and immunological range

We read with interest the article by Odaka et al. 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 ophthalmoplegias 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. Since the 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 ophthalmoplegias 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 ophthalmoplegias, 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 entities. 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 ophthalmoplegias, ataxia, areflexia, or altered sensorium. 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 ophthalmoplegias 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,4 but whether patients with Miller Fisher syndrome, Guillain-Barré syndrome with ophthalmoplegia, acute ophthalmoplegias 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 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 receive treatment equivalent 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 ophthalmoplegias without ataxia, it cannot lead us to make a syndromic diagnosis clinically and infer about therapy.

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References


Authors’ reply

These patients showing either consciousness disturbance (coma, senoica, or stupor) or pyramidal signs (hyperreflexia or pathological reﬂexes) were diagnosed as “Bickerstaff’s brain stem encephalitis” in our article. Of the authors, however, has proposed that “brain stem encephalopathy of Bickerstaff type” or “Bickerstaff’s encephalopathy” is an appropriate diagnosis for such patients. The lack of inflammatory changes in the clinical range will be supported.

Grouping these patients into an antibody syndrome also does not help in deciding therapy as patients without this antibody may receive treatment equivalent 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 ophthalmoplegias without ataxia, it cannot lead us to make a syndromic diagnosis clinically and infer about therapy.

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Authors’ reply

These patients showing either consciousness disturbance (coma, senoica, or stupor) or pyramidal signs (hyperreflexia or pathological reﬂexes) were diagnosed as “Bickerstaff’s brain stem encephalitis” in our article. Of the authors, however, has proposed that “brain stem encephalopathy of Bickerstaff type” or “Bickerstaff’s encephalopathy” is an appropriate diagnosis for such patients. The lack of 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. We mentioned that recognition of this syndrome is useful for understanding the aetiological relation among Miller Fisher syndrome, Guillain-Barré syndrome, Bickerstaff’s encephalopathy, and acute ophthalmoplegias without ataxia.

Our excellent studies provide us with the following key points: (1) the presence of antecedent infections and autoimmunity in 15 (60%) of the 25 patients with Bickerstaff’s encephalopathy with (n=37) and without (n=25) limb weakness. 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 re-examine the clinical and immunological continuity among patients with Miller Fisher syndrome, Bickerstaff’s encephalopathy, and Guillain-Barré syndrome. For example, we investigated clinical and immunological profiles of 62 patients with Bickerstaff’s encephalopathy with (n=37) and without (n=25) limb weakness. There was not a 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 re-examine the clinical and immunological continuity among patients with Miller Fisher syndrome, Bickerstaff’s encephalopathy, and Guillain-Barré syndrome. For example, we investigated clinical and immunological profiles of 62 patients with Bickerstaff’s encephalopathy with (n=37) and without (n=25) limb weakness. There was not a 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 re-examine the clinical and immunological continuity among patients with Miller Fisher syndrome, Bickerstaff’s encephalopathy, and Guillain-Barré syndrome. For example, we investigated clinical and immunological profiles of 62 patients with Bickerstaff’s encephalopathy with (n=37) and without (n=25) limb weakness. There was not a 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 re-examine the clinical and immunological continuity among patients with Miller Fisher syndrome, Bickerstaff’s encephalopathy, and Guillain-Barré syndrome. For example, we investigated clinical and immunological profiles of 62 patients with Bickerstaff’s encephalopathy with (n=37) and without (n=25) limb weakness. There was not a 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 re-examine the clinical and immunological continuity among patients with Miller Fisher syndrome, Bickerstaff’s encephalopathy, and Guillain-Barré syndrome. For example, we investigated clinical and immunological profiles of 62 patients with Bickerstaff’s encephalopathy with (n=37) and without (n=25) limb weakness. There was not a 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 treatment for anti-GQ1b IgG antibody syndrome. 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, neuro-Behçet’s disease, botulism, myasthenia gravis, brain stem vascular disease involving the brain stem, multiple sclerosis, neuro-Behçet’s disease, botulism, myasthenia gravis, brain stem tumour, and pituitary apoplexy, which are sometimes seen in patients with parkinsonism not responsive to levodopa. 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. 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. 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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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. 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. Just as our Japanese colleagues, we suspected some kind of hereditary multiple system degeneration with predominant parkinsonism on the basis of eye movements showing a bilateral hypometric saccade deficit. The most prominent feature in the patients was parkinsonism not responsive to levodopa. The clinical symptoms include homonymous 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.1-4 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.5 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.

References

Authors’ reply
Since the first report of autosomal recessive juvenile parkinsonism (ARJP),5 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 homonymous 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.1-4 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.5 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.

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

<table>
<thead>
<tr>
<th>Anti-GQ1b IgG</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>10/5</td>
<td>7/3</td>
</tr>
<tr>
<td>Median age (range)</td>
<td>52 (17–63)</td>
<td>48 (3–91)</td>
</tr>
<tr>
<td>Antecedent illness:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper respiratory infection</td>
<td>8</td>
<td>53</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>Initial symptoms:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diplopia</td>
<td>8</td>
<td>53</td>
</tr>
<tr>
<td>Consciousness disturbance</td>
<td>4</td>
<td>27</td>
</tr>
<tr>
<td>Gait disturbance</td>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td>Blepharoptosis</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>Photophobia</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Dysphasia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Neurological signs during the course of the illness:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consciousness disturbance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drowsiness</td>
<td>4</td>
<td>27</td>
</tr>
<tr>
<td>Stupor, semicoma, or coma</td>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td>Blepharoptosis</td>
<td>4</td>
<td>27</td>
</tr>
<tr>
<td>External ophthalmoplegia</td>
<td>15</td>
<td>100</td>
</tr>
<tr>
<td>Internal ophthalmoplegia</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td>Nystagmus</td>
<td>8</td>
<td>53</td>
</tr>
<tr>
<td>Facial weakness</td>
<td>5</td>
<td>33</td>
</tr>
<tr>
<td>Bulbar palsy</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>Tendon reflexes:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brisk</td>
<td>7</td>
<td>46</td>
</tr>
<tr>
<td>Normal</td>
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<td>7</td>
</tr>
<tr>
<td>Decreased</td>
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</tr>
<tr>
<td>Absent</td>
<td>4</td>
<td>27</td>
</tr>
<tr>
<td>Babinski’s sign</td>
<td>4</td>
<td>27</td>
</tr>
<tr>
<td>Ataxia</td>
<td>15</td>
<td>100</td>
</tr>
<tr>
<td>Deep sensory impairment</td>
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<td>0</td>
</tr>
<tr>
<td>Superficial sensory impairment</td>
<td>1</td>
<td>7</td>
</tr>
</tbody>
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References
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 in this region is not specific in the Japanese family and is occasionally found in patients with ARJP as well as in Europe, 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.

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 characterized 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 in the substantia nigra but also in extranigral regions. It seems unlikely that the non-extra-pyramidal 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. These findings suggest that additional factors contribute to the phenotype. Because parkin protein expression in ARJP have been considered to exhibit homogeneous clinical symptoms, patients with atypical parkinsonism and/or with non-extra-pyramidal symptoms have remained to be examined for parkin gene mutations. Further extensive study in these patients will revitalize the insights into pathophysiology of the parkin gene related disorder.

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References

Obsessive-compulsive phenomenon and Parkinson’s disease

Alegret et al. 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.Autosomal recessive juvenile parkinsonism and obsessive-compulsive phenome
non has been previously studied in Tourette’s syndrome, Huntington’s chorea, Sydenham’s chorea etc. but not in Parkinson’s disease. The authors, through a cross sectional design, found significantly high scores on the Maudsley obsessive-compulsive Inventory (MOCI) and Leyton obsessionnal inventory (LOI) in severe Parkinson’s disease. However, the presentation and interpretation of results merits further elucidation and clarification.

The aim has been modified to “...systematically investigate obsessive-compulsive traits in Parkinson’s disease”, using MOCI and LOI. Although LOI is used to assess both obsessive-compulsive traits and traits, MOCI is used to investigate the different types and rate severity of obsessive-compulsive complaints in patients with obsessive-compulsive disorder. Also, traits are defined as enduring patterns of neurotic concerns accompanied by perceptions about the person’s environment and oneself that are exhibited in a wide range of important social and personal contents and are part and parcel of the person’s identity. On the other hand, obsessive-compulsive disorder is a clinical disorder characterised by recurrent obsessions or compulsions that causes distress or impairment. Hence the MOCI is used to assess obsessive-compulsive symptoms in patients with obsessive-compulsive disorder and is not applicable for obsessive-compulsive traits or neurotic patients with no obsession or compulsion. These findings suggest that 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 investigating 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 4.93 (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. 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 the 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. Also, the obsessive-compulsive slowness is related to obsessions 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 basic neurostructural level the basic pathology 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 manifestation. This could, hence, opens up new vistas of research for understanding the neurobiological basis of obsessive-compulsive disorder.

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References

Authors’ reply

We are grateful to Sharma and Gupta for their comments.

(1) We concord with the authors that the term “phenomenon” 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. In addition, it has been shown that basal ganglia lesions and induced parkinsonism produce obsessive-compulsive disorder symptomatology. We think, accordingly, 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.

(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
Closely related to dyskinetic motor symptoms that obsessive-compulsive disorder is more within basal ganglia dysfunctions we suspect obsessive-compulsive disorder phenomena are both pathologies share frontostriatal dysfunc-
ing the absence of a clear explanation about the 

et al T J Murray, et al. Edited by C H Polman, A J Thompson, edited by C H Polman, A J Thompson, 

mation of children with acquired cognitive 

tual treatment and management, 5th edition 

Clinical cases in neurology 

Cognitive rehabilitation, an integrative neuropsychological approach 

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

BOOK REVIEWS 

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Cognitive rehabilitation, an integrative neuropsychological approach 

Clinical cases in neurology 

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

BOOK REVIEWS
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 variety 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 consult 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 spondylotic 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 protein 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 "counseling" 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