the patient is receiving local botulinum toxin, with an excellent response. This treatment was chosen because its secondary effects are scarce and limited in time, and it is beneficial for a great proportion of patients. Also, systemic complications have not been described.² Undoubtedly, it is a symptomatic treatment based on the blockade of neuromuscular transmission. With respect to surgery, microvascular decompression is an excellent treatment when it is performed by an experienced team,³ although it poses potential complications and sequelae. Many patients, as in our case, are not willing to undergo such risks. For these reasons, we think that the treatment of choice in our patient is local injection of botulinum toxin.

R PEGO REIGOSA

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Measuring the rate of progression and estimating the preclinical period of Parkinson's disease with [¹⁸F] dopa PET

Morrish *et al*¹ report in great detail the PET data on 32 patients with Parkinson's disease, from which they conclude that the mean preclinical period "is unlikely to be longer than 7 years". This conclusion is based on calculations using the [¹⁸F] dopa influx constant (Ki) of the putamen, although they acknowledge that other methods of analysis and extrapolation yielded estimates of anything between 2.8 and 37.2 years. The authors justify using putamen Ki because it was "more sensitive to increasing disability" than either total striatal assessment or using the alternative ratio approach, but fail to justify a much more fundamental and unwise assumption on which their arguments rest—that is, the intercorrelation between the PET index, clinical progression, and the UPDRS.

The paper gives little detail about how the UPDRS was administered, presumably only once, before each of the two PET scans an average of 18 months apart. A linear regression was then applied to the mean of each patient's two UPDRS and PET assessments, the gradient of which was expressed as a percentage change in the PET index for a change of 10 points "in the total UPDRS".

Some questions can be raised:

- (1) Did the same observer administer the UPDRS blinded to the clinical diagnosis, on their 16 normal controls as well as to each patient on both occasions and, if not, was interobserver reliability studied?
- (2) Presumably the "total UPDRS", judging by the scale shown on their figure A, was actually the total score from the 14 items in the motor subset of the UPDRS, which measures impairment rather than disability.
- (3) The UPDRS is neither a perfect nor a linear scale. Indeed two coauthors of this paper have pointed out elsewhere the low interrater reliability in some items and redundancy in others.² It is a composite multi-item index of severity of disease, each item being an ordinal rather than an interval 0-4 scale of one clinical feature. The key distinction is that an ordinal scale permits the recording of data in rank order (for example, mild, moderate, severe) but without uniform intervals. Thus tremor score 4 is not twice as

bad as 2, still less a total motor UPDRS score of 40/70 *v* 20/70. For these reasons, the use of simple arithmetic means as well as other parametric statistical methods is inappropriate, however tempting.

One illustration of the non-linearity of the UPDRS manifest to anyone who has used it regularly in clinical trials is the bias towards intermediate scores. Those with advanced disease and high scores are seldom if ever recruited, and some of the items scored as 1, indicating slight or mild impairment, "could be normal for some" according to the definition. In one study of Alzheimer's disease, 56% of 78 cases and 12 of the 20 age matched controls were found to have isolated extrapyramidal signs with motor UPDRS scores of 4.5 ($\pm$ 4.8) and 2.8 ($\pm$ 1.8) respectively using observers not blinded to the diagnosis.³ It would be interesting to know whether a UPDRS score >0 is sensitive to or predictive of preclinical parkinsonism and/or abnormal PET.

Furthermore, as it is acknowledged that Parkinson's disease may progress at varying rates between patients and possibly within the same patient at different ages and stages, it is perhaps not surprising that the authors found no significant correlation between change in UPDRS and change in any PET index over 18 months. Thus it seems unwise to draw such firm conclusions based on the assumption that both measures are linear and directly correlated.

RICHARD J HARDIE

St George's Healthcare, Wolfson Neuro-rehabilitation Centre, Regional Neurosciences Unit, Atkinson Morley's Hospital, Copse Hill, Wimbledon, London SW20 0NE, UK.

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Morrish replies:

We thank Hardie for his comments but are surprised that he finds difficulty in our assumption of a relation between PET index, clinical progression, and the UPDRS. Whether clinical severity is measured by UPDRS, bradykinesia scores, rigidity scores or Purdue pegboard scores^{1,2} such a relation has been a consistent finding in [¹⁸F]dopa PET imaging studies of Parkinson's disease. The UPDRS was administered on 57 of 64 occasions by one observer (PKM) and on seven occasions by a second observer (JSR). UPDRS scoring was not carried out on the normal volunteers. Gonera *et al* have identified some non-specific symptoms that may predate the development of Parkinson's disease³ but we know of no population study of the predictive value of UPDRS score in normal subjects. By total UPDRS score we mean the combined scores of sections I, II, III, and IV. Similar results were found when motor scores alone were examined.⁴ The UPDRS scale is the most widely used index of global disease severity in Parkinson's disease. We accept that a linear correlation between UPDRS and PET index may have been inappropriate. The PET index represents a figure of mean [¹⁸F] dopa metabo-

lism throughout the putamen, caudate, or total striatum whereas the clinical presentation and severity of parkinsonism is likely to depend on the distribution and severity of loss of dopaminergic function (and that of other neurotransmitters) within and outside the basal ganglia. It is unlikely that the relation is so simple yet this approach has allowed the demonstration of an aspect of the measurement of progression by PET that has not previously been considered, that of sensitivity to clinical severity. It should be noted that this discussion is not relevant to the major findings of the study (that measurement of progression is dependent on the PET method and that the average preclinical period is likely to be short), only to our explanation of these findings. However, it does suggest an important debate; should clinical indices or functional imaging indices be used independently in studies of progression in Parkinson's disease? When the reproducibility of both measurements is taken into account it is, as Hardie comments, not surprising that we found no significant correlation between change in UPDRS and change in PET index.

PAUL MORRISH

Department of Neurology, University Hospital of Wales, Heath Park, Cardiff CF4 4XN, UK

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Utilisation and costs of profession care and assistance according to disability of patients with multiple sclerosis in Flanders (Belgium)

In their detailed cost of illness study, Carton *et al* estimate the total annual costs in their population of 5500 people with multiple sclerosis to be ECU 13 106 000 (£8.7m) for ambulatory care and ECU 26 581 000 (£17.7m) for hospital and institutional care.¹

They have adopted a "bottom up" approach which allows costs to be identified for different levels of disability, a distinct advantage from previous "top down" costs of illness studies.^{2,3}

They conclude, as have others,⁴ that the costs of multiple sclerosis rise with increasing disability and that the information is useful for cost effectiveness studies.

However, to be useful for such studies, the costs would need further description, in particular we would need to know which costs were fixed, and which were semifixed or non-fixed. In our own institution we know that 40% of the cost of a bed-day is fixed and at most 5% of costs are non-fixed. The remaining costs are semifixed—for example, staff salaries (Robert Hudson, Scottish Health Purchasing Information Centre, personal communication January 1998). The important point is that most of the costs in their paper are probably fixed or semifixed, and interventions to reduce disability are unlikely to have a significant impact on these costs as

described. Nevertheless, their data do allow the cost implications of interferon- β for secondary progressive multiple sclerosis to be assessed, albeit given some gross assumptions. If we assume that the effect of treatment with interferon- β lb for secondary progressive multiple sclerosis⁵ is to delay time to a wheelchair by 1 year, we could argue that the cost of disability grade III patients would be postponed for 1 year. Given that the trial data for secondary progressive multiple sclerosis suggest that 12 people require treatment for 30 months to save 1 year of wheelchair use, treating 96 people should produce 8 wheelchair-years avoided. From table 7 the cost for a year in grade II is ECU 122 570 for 24 people (therefore ECU 40 917 for eight people), and the cost for a year in grade III is ECU 298 769 for 22.75 people (ECU 105 061 for eight people). The difference (the marginal cost per grade III year avoided) is ECU 64 144 for eight people (ECU 105 061–ECU 40 917). It costs ECU 3.45m (£2.3m) to treat 96 people with interferon β lb for 30 months, assuming ECU 1200 (£800)/month/patient. The net cost of producing 8 wheelchair free years is ECU 3.38m (£2.25m) (ECU 34 500 000–ECU 64 144). The cost per wheelchair free year is thus ECU 42 250 (£28 1000).

It is interesting that to offset the costs of disability entirely a drug of similar effect to interferon β lb in secondary progressive multiple sclerosis would need to cost ECU 64 144 for 30 months of treatment for 96 people—that is, ECU 22.27 (£14.83)/patient/month—assuming that all costs as described are in fact avoided.

The study by Carton *et al* has limited value as a stand alone exercise. However, further exploration of the data, as above, leads to the conclusion that disability is expensive to treat, although it is clear that if neurologists are going to prevent disability it will have a price, and it would be naive to suggest that a drug with such an effect will pay for itself.

RAEBURN B FORBES
ROBERT J SWINGLER

Dundee Royal Infirmary, Dundee DD1 9ND, UK

Correspondence to: Dr Raeburn B Forbes, Dundee Royal Infirmary, Dundee DD1 9ND, UK.

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BOOK REVIEWS

Erratum

The author of the book review on **Handbook of Neurologic Rating Scales** published in *J Neurol Neurosurg Psychiatry* 1998;65:615 should have read Derick Wade, not Derick White.

An Atlas of Parkinson's Disease and Related Disorders. Edited by G DAVID PERKIN. (Pp 95, £48.00, US\$85.00). Published by Parthenon Publishing, Lancashire, 1998. ISBN 1-85070-943-2.

This atlas has three parts, the first a 16 page summary of Parkinson's disease and related disorders, the second a selected bibliography, and the third 77 colour and black and white plates. The text section comprises a brief pathological description of each disorder followed by a clinical description and then treatment and imaging findings if appropriate. The bibliography contains 37 papers mainly published between 1987 and 1996—a golden age of movement disorders? The illustrations are about a third pathological, a third imaging (including CT, MRI, and functional imaging), and a third clinical. The book is aimed at neurologists in training and medical students.

The excellent illustrations, particularly the pathological ones, are the outstanding feature of the atlas. The plates are large and the quality of reproduction good. However, I would have expected rather more pictures in an atlas—many ordinary textbooks have more than 77 figures and quantity as well as quality is desirable. The quality of the captions is variable, the pathological plates are well described but the functional imaging captions are not adequate to interpret the pictures. Similarly most abnormalities in the pathological and structural imaging plates are indicated on the plates but the abnormalities on the functional imaging plates are not.

The text provides a brief overview of the specialty and is a useful introduction. The text is lucid and informative. I thought that the section on striatonigral degeneration, olivopontocerebellar atrophy, and multiple system atrophy would have benefited from further editing to make their interrelation clearer and to ensure consistency between text and tables.

I would recommend this atlas for medical school and hospital libraries. The neurologist in training and neurologist would certainly benefit from perusing the atlas in the library but might choose to start saving for a CD-ROM version.

JERRY BROWN

Clinical Neurology. Second Edition. Edited by C DAVID MARSDEN and TIMOTHY J FOWLER. (Pp 448, £27.50). Published by Edward Arnold, London, 1998. ISBN 0-340-69611-X.

I bought the first edition of this popular book in 1989, shortly after it was published. I dipped into it enthusiastically for a few months, even scribbling some notes in the margins. However, since 1990 it has been unopened. The reason for this neglect is not its content, but rather its presentation. The dense text is relieved by few illustrations and the paragraph headings are too uniform in style to easily understand the chapter structure. These may be superficial criticisms, but they are sufficient to blunt success in the highly competitive market place of neurology text books for students and junior doctors.

This second edition could not be more different. It is beautifully organised. From the original text, clinical bon mots have been highlighted and long paragraphs have been broken up in to plain and boxed text. The introductory chapter on examination of the nervous system is particularly helpful; for instance, Marsden distinguishes between hard and soft neurological signs and describes how to deal with conflicts between them. The scope is wide, including chapters on paediatric neurology and the neurology of general medical disorders, psychiatry, and neurorehabilitation. There is plenty for the Gower's Round hack too: the differential diagnosis of progressive myoclonic ataxia, the subtypes of neuronal ceroid lipofuscinoses, and such favourites. All these were there in the first edition but, at least to my taste, hard to access. For the first time ever, I find myself preferring a sequel.

ALASDAIR COLES

The Management of Pituitary Tumours.

Edited by M POWELL and S L LIGHTMAN. (Pp 238, £29.50). Published by Churchill Livingstone, Edinburgh 1997. ISBN 0443060231.

The editors have sought to create a user friendly handbook for the trainee in the specialties that treat these disorders and have succeeded admirably. They give the view of the joint pituitary clinic at the National Hospital, Queen Square, which mirrors the consensus guidelines published recently by the Royal College of Physicians. It is essential that pituitary tumours are managed by a multidisciplinary team—the days of competition between the disciplines should be past. The authors are not afraid to tackle the difficult issue of subspecialisation. There is only sufficient workload for one neurosurgeon in any region of 2–3 million to look after the microadenomas, invasive macroadenomas, giant adenomas, craniopharyngiomas, and third ventricular tumours. Only endocrinologists and neurologists with a specialised interest in neuroendocrinology should be managing the endocrine problems of pituitary patients beyond the initial diagnosis. Have you heard the story of the eminent neurologist who could not understand why a young lady's prolactin level continued to rise despite escalating doses of bromocriptine until all was revealed during the third trimester!

The transatlantic authorship covers the subject in 11 readable chapters devoted to pathophysiology, clinical and visual assessment, imaging, medical and surgical management, radiotherapy, miscellaneous lesions, and controversial issues. The imaging section is particularly useful for explaining the findings of MRI. The sections on results and third ventricular tumours are a little too brief.

This handbook is complimentary to the much larger, definitive textbook published also by Churchill Livingstone—*Pituitary Adenomas*—by Landolt, Vance, and Reilly (1996). I recommend both unreservedly to their respective audiences.

JOHN PICKARD