

# PostScript

## CORRESPONDENCE

### Measuring carotid stenosis

Comparing a new test with a standard involves measuring disagreement. In the case of measuring carotid artery stenosis, some of the disagreement between different tests is because of inherent differences in how the stenosis is demonstrated (test characteristics). This is what we are most interested in when assessing a new technology. However, some of the disagreement simply reflects variability in how we physically make the measurement with the standard technique. Choosing the point of maximum stenosis, choosing the point in the common carotid artery for use as a denominator, measuring from an eyepiece, or measuring from calipers all introduce variation when measuring carotid stenosis. The resulting observer variability in reporting contributes to disagreement between methods but to some extent is independent of the method used to generate the angiogram in the first place.

In the medical literature, disagreement between methods is often attributed entirely to test characteristics, with little appreciation of the role of observer variability in reporting. When one method is compared with another and disagreements emerge, it is not readily apparent how much of the disagreement is caused by the method used and how much by the process of measurement, unless observer variability data are also presented. In the recent paper from Patel *et al*, interobserver variability data are presented but their significance in relation to overall agreement does not appear to have been appreciated.<sup>1</sup>

Using the data from Patel *et al* (tables 2 and 4) for symptomatic carotid arteries, it is noted that when 34 carotid digital subtraction angiograms (DSA) are measured by one radiologist, there was disagreement in seven cases when the same films were reported by a second radiologist. Therefore if only DSA was used, seven patients would have had "inappropriate" surgery according to which radiologist read the angiogram. This is not surprising, and such disagreement is a consistent finding in observer variability studies.<sup>2,3</sup> Observer variability in reporting DSA therefore accounted for approximately 20% of disagreement in this particular series of angiograms. This sets a limit on the maximum agreement that any alternative method can demonstrate when compared with DSA. It is clearly not reasonable to expect better agreement from another method than can be obtained by re-reporting the DSAs themselves. In Patel's table 2, when the same arteries are assessed by computed tomographic angiography (CTA) there was disagreement with DSA in seven cases, while with magnetic resonance angiography (MRA) and ultrasound there was disagreement in six and seven cases, respectively. The three alternatives thus disagree with DSA to the same extent as can be attributed to observer disagreement in reporting DSA. Put simply, the same number of missed or unnecessary operations would have occurred (roughly 20% in this series) whatever method was used, including DSA alone. Observer variability is

not confined to DSA, and the scatter plots from Patel *et al* (fig 2) would suggest—in keeping with other studies—that observer variability is greater for MRA and CTA than for DSA.<sup>1</sup> It is surprising that this did not translate into more clinically important disagreements when MRA and CTA were compared with DSA. This is probably accounted for by the fact that in this study, for MRA and CTA, consensus views were taken for any disagreements greater than 10% between observers.

This highlights the important point that combining multiple observations made on the same data will reduce observer variability, and ultimately improve agreement with other methods. Partly for this reason, but also because to some extent the strengths and weaknesses of CTA, MRA, and duplex ultrasound are complementary, we would suggest that a combination of tests (we use the combination of ultrasound and MRA) should be used in preference to DSA.

What is clear from this study is that most of the disagreement between the different methods of measuring carotid stenosis can be attributed to observer variability in reporting rather than to the test characteristics of the individual methods themselves. The 10% of patients injured as a result of DSA in this study, and those who continue to be put at risk from catheter angiography in these circumstances, would be quite entitled to ask why they are exposed to a procedure which appears to offer no great advantage over safer alternatives. We suggest that more studies are not required, simply a more thorough understanding of presently available information.

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### References

- 1 Patel SG, Collie DA, Wardlaw JM, *et al*. Outcome, observer reliability, and patient preferences if CTA, MRA, or Doppler ultrasound were used, individually or together, instead of digital subtraction angiography before carotid endarterectomy. *J Neurol Neurosurg Psychiatry* 2002;73:21-8.
- 2 Rothwell PM, Gibson RJ, Slaterry J, *et al*. Prognostic value and reproducibility of measurements of carotid stenosis. A comparison of three methods on 1001 angiograms. *European Carotid Surgery Trialists' Collaborative. Stroke* 1994;25:2440-4.
- 3 Young GR, Sandercock PA, Slaterry J, *et al*. Observer variation in the interpretation of intra-arterial angiograms and the risk of inappropriate decisions about carotid endarterectomy. *J Neurol Neurosurg Psychiatry* 1996;60:152-7.

### Author's reply

Doctors Young and Humphrey highlight that differences between tests arise from several factors, some of which are inherent in the test and some of which arise from aspects attributable to observer variation. Some of the aspects to do with observer variation apply to

interpretation of all tests and some are specific to certain tests. In our study we were endeavouring to quantify the effect on patient management if non-invasive tests were used instead of intra-arterial angiography to assess carotid stenosis. Our study has several limitations, including a relatively small sample size, and the fact that we were not able to get all scans read by all observers but rather had to get pairs of observers to concentrate on reading only CTA, or MRA, or DSA. A better design would have been to keep the same workers together in pairs but randomly assign the CTA, MRA, or DSA films to each pair. As it is, it is possible that some of the apparent difference between imaging modalities is specific to the pair of observers, not to the modality. However, imaging studies are difficult to fund and expensive to do, and the result and design of our study was a compromise involving all these factors.

We identified that the observer reliability of CT angiography or MR angiography was worse than that for digital subtraction angiography, as highlighted by Drs Young and Humphrey. Also in general there was more scatter between the observers for the reading of asymptomatic stenoses than for symptomatic stenoses (emphasising the importance of considering patient characteristics, not just the imaging technique). In the determination of the effect that this disagreement might have on patient management, we used nomograms derived from the European carotid surgery trial which were based on intra-arterial angiographic measurement of stenosis. We therefore had to use the comparison of non-invasive test reading with DSA rather than being able to use the individual observers readings of non-invasive tests. Thus as Drs Young and Humphrey point out, the actual effect of using non-invasive tests maybe worse than we have estimated.

Finally, Drs Young and Humphrey suggest that more studies are not required but we are not entirely sure that that is completely true. Non-invasive imaging tests are continually undergoing modifications, many of which may be improvements in accuracy or practicality, but this cannot be assumed to be the case. Much of this tinkering with technology is driven by the manufacturer's desire to encourage purchase of new machines. Improvements have also occurred in intra-arterial angiography with smaller and more manoeuvrable catheters and greater awareness of the risks, which may have helped to reduce the risk of angiography. Our "snapshot" of CTA, MRA, and ultrasound is already out of date because contrast MRA is now increasingly used. While we would hope that non-invasive tests (probably in combination rather than alone) would eventually replace intra-arterial angiography in the majority of patients being considered for carotid intervention, we feel it likely that there will always be a need for some intra-arterial angiography in specific cases, or depending on local resources. In any case DSA did not appear less popular than MRA among the patients in our study. There is certainly room for much more in depth examination of existing data but we shouldn't close the door on the need for further studies.

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## Cerebral metastasis after primary renal cell carcinoma

The article by Roser *et al.*<sup>1</sup> in which it was shown that the treatment of intracranial metastases originating from renal cell carcinoma can on occasion be successful, was most interesting.

We have followed the clinical course of a patient with a renal cell carcinoma with a low mitotic index since 1989. In this patient the course was distinctly more malignant but the disease has also been successfully treated to date. In the last 13 years, this patient has had four metastases surgically removed and a further nine treated with stereotactically guided percutaneous single dose convergent beam irradiation therapy (stereotactic modified linear accelerator, 6–15 MV photons, 18–20 Gy prescribed to the 80% isodose). Apart from slight mnemonic deficits, the patient is in good health.

The following factors which affect the prognosis<sup>2–4</sup> were all met by our patient:

- The interval between the diagnosis of renal cell carcinoma and the first detected brain metastasis exceeds 17 months (our patient, 18 months; the patient described by Roser *et al.*<sup>1</sup> 36 months);
- Age below 60 years at the time of initial diagnosis;
- Primary tumour of the left kidney, initial nephrectomy;
- Diameter of primary metastasis < 2 cm;
- Not more than one brain metastasis at the time of initial treatment;
- Solely intracranial metastases;
- Karnofsky > 70%;
- No systemic symptoms such as fever or weight loss at the time of diagnosis;
- Blood sedimentation rate under 50 mm/h at diagnosis of renal cell carcinoma.

Patients in whom prognostic factors predict a good outcome should be treated with intent to cure.

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**References**

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- 3 Wronski MD, Maor MH, Davis BJ, *et al.* External radiation of brain metastases from renal carcinoma: a retrospective study of 119 patients from the M D Anderson Cancer Center. *Int J Radiat Oncol Biol Phys* 1997;**37**:753–9.
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## BOOK REVIEWS

### Seizures, medical causes and management

Edited by Norman Delanty (Pp 352, US\$125.00). Published by the Humana Press, New Jersey, 2002. ISBN 0-89603-827-0

This book is unusual among books about seizures because it focuses on acute symptomatic (“situation-related”) seizures, rather than “epilepsy” (although there is inevitably some overlap between the two). It provides definitions and describes the epidemiology and pathophysiology of acute symptomatic seizures in the initial section, which is followed by chapters detailing the specific circumstances in which such seizures are likely to occur, often (although not invariably) including points of management specific to the situation. Subjects covered include seizures occurring in the context of multisystem disease, infection, hypoxic-ischaemic cardiopulmonary conditions, endocrine disorders, cancer, and other conditions. Situation-related seizures occurring as a result of drugs or alcohol misuse are also addressed, as are those occurring in the intensive care situation, and the difficult, but important, differentiation of seizures from syncope. The book ends with a very practical chapter entitled “Anticonvulsants in acute medical illness”, in which the considerations affecting the choice of antiepileptic drug in the acute situation are reviewed.

Although situation-related seizures are usually discussed in books about epilepsy, they do appear to constitute a distinct group in a number of respects including prognosis. To a certain extent the topics discussed in the book form a rather disparate group linked only by their tendency to cause such seizures as a reflection of central nervous system disturbance. Nevertheless, they are all conditions likely to be encountered at various times by general physicians, neurologists, and those working in the accident and emergency department, and this book, which is both readable and comprehensively referenced, will be of interest to all these groups.

Yvonne Hart

### Subcortical stroke, 2nd edition

Edited by Geoffrey Donnan, Bo Norrving, John Bamford, and Julien Bogousslavsky (Pp 450, £79.50). Published by Oxford University Press, New York, 2002. ISBN 0-19-263-157-8

This book is a must read for clinicians and researchers with an interest in stroke. The four editors are all specialist stroke clinicians who have been thinking about and leading research in subcortical stroke for many years, and they have put together a well constructed and comprehensive multi-author work. This second edition is longer and more extensive than the first, reflecting the considerable and

rapid advances in our understanding of subcortical strokes in recent years, and in particular the increasingly sophisticated neuro-imaging techniques. Given the large number of contributors, consistency of style and approach is limited, but this is more than made up for by the breadth of expertise and opinion.

There are some particular strengths. These include the editors’ short chapter providing a summary classification of subcortical infarcts, which is best appreciated if read both before and after tackling most of the other chapters. The excellent chapter on pathology of lacunar infarction is a welcome addition to this edition, while the chapters discussing risk factors and prognosis provide very useful commentaries and summary tables of all the relevant studies. The discussion around the usefulness (or not) of clinical diagnosis of lacunar syndromes, carefully updated with the information from recent clinicoradiological studies, is both thoughtful and logical, with plenty of clinical and epidemiological common sense.

In common with all recently published medical textbooks, this one is already a little out of date. This is most noticeable for the chapter on therapy, where recent advances (for example, new evidence on blood pressure lowering from the PROGRESS trial and on cholesterol reduction with a statin from the Heart Protection Study) are likely to have most impact on clinical practice. If the editors have the energy to produce a third edition, there is (as always) some room for improvement. The series of chapters on infarcts in specific subcortical territories would be enhanced by some figures illustrating the vascular anatomy that is discussed in the text. In addition, the quality of the discussion of study methodology varies considerably between chapters, and some would benefit from a more systematic and accurate approach to statistical and epidemiological concepts.

Cathie Sudlow

### Medical risks in epilepsy

Edited by Svein I Johannessen, Torbjörn Tomson, Matti Sillanpää, and Birthe Pedersen (Pp 140, £29). Published by Wrightson Biomedical Publishing Ltd, Hampshire, 2002. ISBN 1-871816-46-7

This is a very useful, reasonably comprehensive yet succinct multi-author small book on medical risks associated with epilepsy. Areas covered include methodological aspects; accidents and risks in everyday life; traffic accidents; driving regulations; mortality, including SUDEP; psychiatric comorbidity and suicide; fatal adverse drug reactions reporting data (which are rather difficult to interpret); seizure-warning systems and risk prevention; as well as insurance related issues. It also highlights many areas where further research is required. The book generally provides an overview of the more recent research and publications in this area and includes some regulatory issues. Inevitably it has a Nordic emphasis; it includes very useful advice on precautionary measures to minimise risk of injury for people with uncontrolled epilepsy, including safer sauna. Some chapters, by necessity, serve purely as a compilation of available incomplete data. Others are written by key researchers directly involved in the area addressed and provide a very balanced review of current knowledge. On psychiatric comorbidity, while agreeing that “the positive

effects of drug therapy on cognitive and affective functioning because of the reduction in seizure activity are usually far greater than the negative effects", more information would have been welcome in an otherwise very well balanced chapter. The book would well serve those for whom it is intended, namely epileptologists, neurologists, paediatric neurologists, psychiatrists, and other professionals who deal with patients with epilepsy. The editors rightly stress the "official line" that the majority of patients with epilepsy can achieve good control, with low associated risks.

Lina Nashef

### Greenfield's neuropathology, 7th edition

Edited by David I Graham and Peter L Lantos. (2 Vol set (HB), Vol 1 pp1190, Vol 2 pp1140, £395). Published by Arnold, London, 2002. ISBN 0-340-74231-3. CD rom (£145) ISBN 0-340-76-221-7.

What can one say. The latest (7th) edition of *Greenfield's Neuropathology* has hit the book-shops, and indeed what a resounding thud it makes! The present edition is bigger than ever, again running into two volumes, but now totalling a staggering 2330 pages and costing an equally staggering £395. It comes equipped with a handy CD version of the illustrations, a mere snip at £145.

The 7th edition has undergone considerable changes in content, since the last edition five years ago, reflecting the ever expanding increase in knowledge of diseases of the nervous system and muscle that has come from the exponential growth in neuroscience research over the past decade. Areas of cellular and molecular neurobiology, and the contributions that genetics and neuroimaging have made towards improving our understanding of the causes of disease and our clinical investigative and diagnostic skills, are more strongly featured. Hence, while greater emphasis has been placed on the basic science of disease, the classic descriptive morphology for which Greenfield's is renowned is well maintained. There are new chapters on "Metabolic and neurodegenerative diseases of childhood" and "Peroxisomal and mitochondrial diseases". The chapter on "Pathology of schizophrenia" has been shrewdly expanded to cover "The pathology of psychiatric disorders". Other chapters have been retained as such, but many have been rewritten with new authors reflecting the pre-eminence of each

within their particular subspecialty. There is increased reliance on colour illustrations, line diagrams and tables to illuminate the text, and these are of excellent quality throughout. As to be expected, all chapters are written authoritatively with clarity and style, comprehensively illustrated, and lavishly referenced. Judging by the content of the chapters on ageing and dementia, prion disease, and movement disorders, it is my guess that if anything is not included in each chapter, it's probably not worth including anyway. The accompanying CD rom is user friendly, and the images are downloadable—a boon to those wishing to produce a ready made lecture or presentation of distinction. The book is a must for practicing and trainee pathologists, but is equally compelling for workers in other clinical neuroscience disciplines and basic researchers interested in the roots of the dysfunctional nervous system. Possession of the 7th edition is guaranteed lasting quality and full value, but before lashing out make sure both your arms and shelving are strong enough to accommodate its presence.

David MA Mann

### Smell and taste complaints

Edited by Christopher H Hawkes (Pp 176, £16.99). Published by Butterworth-Heinemann, Woburn, 2002. ISBN 0-7506-7287-0.

Despite the fact that problems with tasting and smelling are common in the general population, few physicians have the knowledge and training to authoritatively deal with them. Christopher Hawke's *Smell and Taste Complaints* provides a straightforward guide to the understanding and management of chemosensory disturbances, reflecting the first clinically oriented book of its kind since Ellis Douek's *The Sense of Smell and its Abnormalities* (Edinburgh: Churchill Livingstone, 1974). This 180 page pocket sized book provides a cogent overview of the anatomy and physiology of the olfactory and gustatory systems, practical approaches towards their assessment, and suggestions for therapy and management. Importantly, it provides the practitioner with the names and addresses of specialised taste and smell clinics throughout the world, aiding the referral process. Although there is little new in this guide, and much of the material seems to have been derived from second hand sources, it presents the available information in a well organised

and easy to read manner. Moreover, it addresses basic clinical issues rarely addressed in a single publication. Its major drawback is the lack of reference backing for many of its statements, some of which are questionable. I found, for example, some of the "facts" unfamiliar, and would have welcomed knowledge of their source. Bits of the material are dated (for example, the role of IP<sub>3</sub> receptors in olfactory function, the nature of olfactory receptor cell regeneration) and several sections of the book seem lengthy, uncritical, and of little practical value. Thus, nearly seven pages are devoted to the topic of odour memory, a topic with inherent theoretical issues and problems that are not addressed by the author. However, the book is not intended to be a research book and, despite such shortcomings, it accomplishes its goal of educating the practitioner and providing him or her with a practical roadmap for clinical assessment and treatment. Indeed, the clinical information provided is comprehensive and well illustrated. This inexpensive book is a must for any physician who has the occasion to see patients with chemosensory disturbances or has even a casual interest in chemosensation, and should serve to elevate the level of appreciation of these senses within the medical community at large.

Richard L Doty

## CORRECTIONS

The following errors occurred in the short report by Merlini L, Carbone I, Capanni C, *et al.* Familial isolated hyperCKaemia associated with a new mutation in the caveolin-3 (CAV-3) gene. *J Neurol Neurosurg Psychiatry* 2002;**73**:65–7. On page 66, left column, line 9, proline should replace leucine, line 12, protein should replace enzyme, and in table 1, line 8 Del-TFT (63–65) should replace ?TFT (63–65).

We regret that an editing error occurred in the correspondence from Jaster JH, Dohan FC, and O'Brien TF. Demyelination in the brain as a paraneoplastic disorder: candidates include some cases of seminoma and central nervous system lymphoma. *J Neurol Neurosurg Psychiatry* 2002;**73**:352. The description of a patient was altered, in the first line of the fourth paragraph the text should read "...patient who had a non-neurological malignancy, seminoma, and subsequently developed a paraneoplastic syndrome...".