PostScript

CORRESPONDENCE

Mexiletine on segmental hyperhidrosis

Ishibashi *et al*¹ reported the excellent efficacy of mexiletine for the treatment of segmental hyperhidrosis in two patients (who had syringomyelia and cavernous haemangioma of the spinal cord, respectively). They presented the decrement in the patients' sweat rate by oral administration of mexiletine.¹

Previously we performed a clinical study focusing on sweating and identified 10 patients with segmental hyperhidrosis among 30 patients with syringomyelia. We followed up the patients with hyperhidrosis for 1–10 (mean 5.0) years. The amount of sweating did not change in any of them during the follow up period,² although we did not perform a quantitative analysis. Consequently, we speculated that hyperhidrosis persists for at least a year. It is possible that the course of signs in the cases reported by Ishibashi *et al* were modified by the growth or activity of spinal cord lesions. We consider it imperative that these authors describe any spinal cord lesions and how they may have shifted. However, although they did not mention the duration and time courses of the improvement in their patients, we suppose that the duration of the follow up for each patient would not have exceeded several months, judging from how the authors described their experience. In addition, even though they did not test the effects of mexiletine on control subjects or on other parts of the body in the same patients, we can be assured that the improvement in hyperhidrosis was due to the oral administration of mexiletine, on the assumption that the spinal cord tumour could not have changed in such a short time. We consider that it would be informative for clinicians if Ishibashi *et al* were to disclose the drug dosage and the time course of its effects and to describe the features of the spinal cord lesions.

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Authors' reply

We are grateful Sudo *et al*, as they allow us to clarify a point of our study that was not discussed in the paper recently published in this *Journal*.¹ They asked about the possibility of natural remission and the non-specific effect of mexiletine on sweating.

We administered 200 mg/day mexiletine or 400 mg/day carbamazepine to our patients. Both patients noticed their hyperhidrosis was relieved within two days after administration. Although we did not perform a quantitative analysis several months after treatment, the clinical improvement of hyperhidrosis persisted. In addition, the magnetic resonance images of spinal cord lesions (syringomyelia and cavernous haemangioma) in both patients were followed up for two years. During the follow up period, the spinal cord lesions did not change their size, position, and intensity on magnetic resonance imaging. Therefore, the natural course of the spinal cord lesions could not explain the improvement of hyperhidrosis during the treatment and quantitative analysis in our patients.

The sweat rate of the area of observed hyperhidrosis was decreased without a change of the absolute sweat rate on the healthy side after oral administration of mexiletine. We calculated the ratio of the sweat rate on the affected side to that on the healthy side—the ratio was 2.13 before treatment and decreased to 0.97 on day 7 after the treatment. We therefore consider that the mexiletine had an excellent effect only on the area with hyperhidrosis. Although we did not test the effects of mexiletine on control subjects, we think that the result on a healthy area of each patient was an appropriate internal controls for the evaluation of the drug's effect on hyperhidrosis.

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Patent foramen ovale, cerebrovascular risk, and complement

Nedelchev *et al*¹ report that the presence of a patent foramen ovale (PFO) is a significant risk factor for recurrent cerebrovascular events, the risk being higher in patients with more than one previous embolic event. They highlight the absence of a current proven medical treatment or prevention regimen. Cardiac right to left shunting is present in a quarter of the population. It is thus worth drawing attention to a particular subgroup of patients with PFO that may be at an even more increased risk than the authors report—sport divers, most of whom fall within the age range of the above study.

Neurological sequelae constitute 80% of decompression sickness. Not only has neuroimaging shown an increased frequency of brain ischaemic lesions in divers, but also multiple such ischaemic lesions have been found specifically in sport divers with PFO.² While PFO patency of haemodynamic significance is a risk factor that necessitates habit modification, often the radiological lesions do

not correspond well to the neurological deficits of experienced divers.

This point, coupled with the increased risk of arterialisation of venous bubbles and the paradoxical nature of bubble genesis, suggest that a PFO is a risk factor in this subgroup for the development of neurovascular disease.³ Unknown is the added risk with age that remains to former divers. A poorly understood mechanism of bubble induced complement involvement in the pathogenesis of the neurological sequelae in decompression sickness has been suggested.⁴ Similarity of such symptoms to the postcoronary bypass syndrome lends support (and hope?) to complement based neuroprotective strategy options for the future.⁵

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Authors' reply

We thank Dr Demetriades for his comments on our study. While the average person with a patent foramen ovale (PFO) may not be at increased risk for neurological events, there seem to be subgroups of patients at increased risk. PFOs with large diameters, right to left shunting at rest, or high membrane mobility and PFOs associated with atrial septal aneurysms have been identified as “dangerous PFOs” by several investigators.^{1–3} In addition, coagulation abnormalities may promote paradoxical emboli in patients with PFO.⁴ To this list, Dr Demetriades adds special occupations or sports that may be dangerous in people with PFOs, specifically divers. Playing wind instruments has also been mentioned previously.⁵

However, many problems related to PFO remain unresolved. Even in groups that are believed to be at high risk for neurological events, deciding whether and how to treat a PFO cannot be derived from evidence based medicine. Deciding how to proceed depends on the opinion of the attending physician and is not based on data from randomised studies.

The PICSS (PFO in cryptogenic stroke study) showed that secondary prevention of cryptogenic stroke in patients with PFO by using warfarin or aspirin does not result in any difference.⁶ The PC-trial is an ongoing randomised trial we initiated to compare

endovascular PFO closure versus medical treatment alone. We hope that it will provide useful information on secondary stroke prevention in patients with presumed paradoxical embolism. It is also conceivable that divers who have ever had "the bends" would benefit from PFO closure.

Recently reported data suggest links between decompression illness, migraine with aura, and right to left shunts.⁸ These observations not only extend the clinical manifestations of PFO but also bring into discussion new pathophysiological aspects of migraine. If the association between complicated migraine and PFO can be corroborated, a randomised trial on PFO in such patients may be worth while.

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Demyelination in the brain as a paraneoplastic disorder: candidates include some cases of seminoma and central nervous system lymphoma

We read with interest the report of Ayuso-Peralta *et al*,¹ which describes a 58 year old woman who presented with several neurological symptoms. Brain imaging was consistent with leukoencephalopathy, and analysis of blood and cerebral spinal fluid was unrevealing. A few months later the patient experienced further neurological deterioration and an open brain biopsy showed central nervous system (CNS) lymphoma, together with diffuse demyelination.

The authors observed that the presentation of cerebral lymphoma as a diffuse leukoencephalopathy is not frequent and they discuss

possible aetiologies of the predominant demyelination in their case. They do not mention the possibility of a paraneoplastic aetiology.

The authors reference a similar case² previously reported in the *Journal*. That report also does not acknowledge a possible paraneoplastic aetiology for prominent diffuse brain demyelination preceding the discovery of CNS lymphoma. Two other recent reports in the *Journal*^{3–4} described focal tumour-like lesions of brain demyelination that preceded the discovery of CNS lymphoma. Only one of these reports⁴ mentioned laboratory data that suggested consideration of a paraneoplastic aetiology, the presence of serum antibodies directed against myelin oligodendrocyte glycoprotein.

One report elsewhere⁵ has described a patient who had a non-neurological malignancy and seminoma and who subsequently developed a paraneoplastic syndrome simulating encephalitis associated at autopsy with multiple foci of demyelination confined to cerebral white matter. Two other reports elsewhere^{6–7} have described biopsy confirmation of large focal demyelinating lesions in the brain associated with seminoma. The authors of these three reports all strongly considered the possibility of a paraneoplastic aetiology for the brain demyelination associated with seminoma, probably because the temporal association was close and the spatial association was distant.

The associations between brain demyelination and CNS lymphoma have been close, both temporally and spatially, making considerations of aetiology more complex. Taken together, the seminoma reports and the CNS lymphoma reports have many similarities in their patterns of associated brain demyelination, raising the possibility of similar mechanisms of demyelination. Many questions concerning aetiology remain unanswered. Given the information available, we suspect a paraneoplastic aetiology in all of these cases. We feel that future reports of brain demyelination associated with CNS lymphoma should consider this possibility in their data collection and in their discussion of results.

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Genotype predisposition to leukoaraiosis

Leukoaraiosis, which can cause symptoms ranging from a mild cognitive impairment to severe subcortical dementia,¹ is a significant public health problem. One quarter of subjects aged 65 years or over are affected by some degree of white matter changes.² Ischaemic demyelination and small vessel disease seem to be important features of the underlying pathological process of this entity.^{1,2} Age, hypertension, and a previous stroke event have been proved to be the main clinical risk factors.^{1,2} A number of genetic susceptibility factors for leukoaraiosis have been put forward, with the assumption of polygenic aetiological factors. We were pleased to read the article by Hassan *et al* in this journal.³ The authors stated that the angiotensin converting enzyme insertion/deletion (ACE I/D) polymorphism D/D genotype was a significant independent predictor for leukoaraiosis in patients presenting with classic lacunar syndromes.³ We earlier conducted large prospective studies in which we also examined the importance of the ACE D allele and other common mutations in the development of small vessel infarction and leukoaraiosis.^{4,5} Our results were consistent with the findings of Hassan *et al* and support their results from several other aspects. (1) Our stroke study confirmed the genetic heterogeneity of ischaemic stroke in that the ACE D/D genotype proved a significant susceptibility genotype for small vessel brain infarction, as did the Leiden V mutation for large brain infarction.⁴ (2) In our leukoaraiosis study, the ACE D/D genotype was found to be a significant risk factor for leukoaraiosis in combination with brain infarction.⁵ (3) We also reported that clustering of the homozygous MTHFR 677TT and ACE D/D mutations in one person can mean a moderate (about fivefold risk), but highly significant ($p < 0.0005$) risk of leukoaraiosis without infarction.⁵ These data from different approaches reconfirm the possible aetiological role of the ACE D/D genotype in leukoaraiosis relating to small vessel brain disease. The genotype differences may explain why some patients who are exposed to clinical risk factors such as hypertension, exhibit a much higher susceptibility to leukoaraiosis than other subjects with the same clinical risk factors. Besides the classic clinical risk factors, the consistently growing knowledge of the genetic background of leukoaraiosis may permit the recognition of a large population at high risk of a new type of white matter damage, and hence this may lead to a more effective prevention.

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BOOK REVIEWS

Neurochemistry of consciousness: neurotransmitters in mind

Edited by Elaine Perry, Heather Ashton, and Allan Young (Pp 346, EUR65.00). Published by John Benjamins Publishing Company, Amsterdam, 2002. ISBN 90-272-5156-8

Consciousness is a portmanteau word, full of rich and different meanings: contrast Marxian, Freudian, and anaesthesiologists' use of the term. In recent years it has also become a fashionable hunting ground for neuroscientists, who are rarely troubled by such complexities. For them, consciousness is being awake rather than asleep, being reducible to awareness. Sweeping aside centuries of philosophical debate, they ponder over whether "it" "resides" in specific anatomical brain structures, in microtubules, in patterns of neurotransmitter release, or whatever. The present book is typical of this type of cheerfully unsophisticated empiricism: its hunt for what the editors call "NCCs"—neural correlates of consciousness—focuses on neurotransmitters, hence the subtitle. However, the concern with "mind" ceases at that point; this elusive phenomenon finds no place in the book's index. The central question for the editors seems to be whether the acetylcholine or the dopaminergic system is the more likely substrate for conscious awareness. This reductionism characterises most of the chapters. That on memory, for instance, abandons even animal memory for a discussion of a physiological phenomenon called long term potentiation, and even the psychoanalyst Mark Solms, on dreams, who surely ought to have a broader perspective, confines himself to contrasting cholinergic and dopaminergic hypotheses. However, the authors are clearly writing to an editorial brief: each chapter, in a book ranging from discussions of attention and motivation through psychotropic drug mechanisms to mental retardation and autism, following a brief nod to marginally wider concerns, offers a neurotransmitter list of potential associations or correlations with "states of awareness." Within these limitations many of the chapters provide competent student friendly overviews of their themes. If the book's pretensions weren't so much larger this would be fine; as it is, those hoping for a more multilevel or theoretically informed discussion will be disappointed.

Steven Rose

Risk control and quality management in neurosurgery

Edited by H-J Steiger and E Uhl (Pp 227, EUR108.000). Published by Springer Verlag Wien, Wien, 2001. ISBN 3-211-83678-0

This is an interesting and timely publication. The book contains a compilation of material presented at an international meeting held in October 2002. It has been divided into various sections that take the reader through grouped papers and topics and finally a projection into the future. As would be expected, the material covers experience and lessons gained in other areas such as aviation and nuclear research. The authors, generally senior in status, originate from Europe, the United States, and the United Kingdom and therefore offer a diverse collection of views, opinions, and experience relevant to a very wide readership. The increasing requirements for quality assessment and competency make this a very valuable reference book for both departmental and institutional libraries. However, it certainly will be of value to individual readers. It should be recommended reading for trainees to understand the principles and the ongoing thought behind many of the practices and control measures that they will encounter and will need to participate in as their experience and seniority advance. The quality of contributions and the outline of the information do vary, as would be expected in such a compilation, but overall very few pages or chapters do not prove insightful nor provide useful information and guidelines. It will be of value to all medical disciplines, since the principles are universal and the terms of reference or yardsticks used are convertible or transferable. It is highly recommended.

J Van Dellen

Primary progressive multiple sclerosis

Edited by M Filippi and G Comi (Pp 128, EUR47.95). Published by Springer, Milan, 2002. ISBN 88-470-0167-6

The field of multiple sclerosis (MS) is awash with literature on every aspect of the disease ranging from epidemiology and genetics to pathology and treatments. It is unusual, therefore, to find a lacuna in this niche but this book seems to have found one.

Primary progressive multiple sclerosis is written to encapsulate the latest evidence on aspects of this condition, which until recently was not regarded as important in understanding demyelinating disease. Filippi and Comi have brought together all the important players in the study of primary progressive MS. Their contributions summarise the latest information on the epidemiology, genetics, immunology, pathology, imaging, and clinical trials and therapies in primary progressive MS. This book is meant to be a useful guide to the subject and does not profess to be an authoritative account. However, it occasionally is a little too brief in its explanations and definitely lacks pictures, tables, and diagrams in the early part of the book. This makes it a rather bland and dry account initially. When the diagrams and scanned images do appear in the latter parts of the book, many of them lack definition and it is not always easy to see the details that are being referred to.

All in all this is a good up to date summary of the latest news in primary progressive MS and in particular the imaging aspects of the disease, as would be expected from the interests of the editors. It would be a useful adjunct to other literature for those working in the field of demyelinating disease.

Omar Malik

Multiple sclerosis: a guide for the newly diagnosed, 2nd edn

By N J Holland, T J Murray, and S C Reingold (Pp 160, US\$21.95). Published by Demos Medical Publishing Inc, New York, 2002. ISBN 1-888799-60-9

This book is an invaluable guide for patients with multiple sclerosis (MS), as well as their friends and families. The fact that a second edition has become necessary is extremely encouraging for those involved with MS and highlights the recent therapeutic advances for this still devastating diagnosis. Most people who develop MS are desperate for information about their new disease and many turn to the internet to find this. Unfortunately, they are then faced with misleading or simply incorrect information, which can leave patients confused or disillusioned.

The authors present detailed information in the first two chapters covering the pathological processes causing the symptoms of MS and the diagnostic tests in use. Uncertainties in both these fields are explained. The next two chapters deal with treatments, including conventional and alternative or complementary therapies; the text is clear about the lack of a cure for MS but discusses all the options including steroids for acute attacks, disease modifying drugs, and symptomatic treatments. There is a whole chapter on the important issues of lifestyle—diet, rest, sexual function, pregnancy, etc.—that help patients to control their condition. A further chapter concentrates on the psychological impact of a diagnosis of MS and its effect on relationships. Employment issues are deservedly dealt with on their own, with practical advice on when and how to disclose the diagnosis and the legal implications of disclosure both at work and on application forms such as those for health and life insurance.

The latter part of the book deals with clinical and research trials in MS that will help patients to understand how trials are designed and why treatments are offered to patients with specific disease types. The many fields in which MS research is ongoing are described and the questions being asked by investigators are well presented.

The book ends with more practical advice on how to get further information about specific topics; however, this is predominantly aimed at the North American readership with emphasis on the MS societies of the United States and Canada.

In summary, this is an excellent book, which presents all the facts in a straightforward but sympathetic way. As well as the medical facts about the disease, it is full of practical advice covering all life topics, areas that are often neglected by busy physicians. It is highly recommended to all those whose lives have been affected by this disease.

Valerie Stevenson

Disordered mind and brain: the neural basis of mental symptoms

By Peter F Liddle (Pp 320, £40.00). Published by Gaskell, London, 2001. ISBN 1-901242-65-X

The premise of this book is that the key to understanding the neural basis of the major mental disorders is an understanding of the origin of five symptom clusters or dimensions common to these disorders. These are reality distortion (hallucinations and delusions); disorganisation (of thought and behaviour); psychomotor poverty and excitation; depression and elation; and anxiety. Thus, there are five chapters each devoted to a description of a specific dimension and an exposition of how it is correlated with cognitive abnormalities derived from the dysfunction of specific neural processes.

These central chapters are preceded by five chapters describing the neuroscience of brain systems thought to be involved in generating the various symptom clusters. These are brief and the literature reviews are in no way comprehensive. Nevertheless, they serve the purpose of informing the reader of the basic neuroanatomical and neurophysiological concepts that underpin Professor Liddle's approach to understanding mental illness.

The final four chapters summarise the current evidence regarding the neurobiology of schizophrenia, bipolar affective disorder, obsessive compulsive disorder, and psychopathy.

Each ends with a synthesis that integrates this with the previous account of how the symptom clusters arise.

The explanatory power of Professor Liddle's thesis concerning the neural basis of mental symptoms is stronger for some symptom dimensions, such as reality distortion, than others, such as distortion. But it is the general unifying approach that is the major strength of this book—the detail will certainly be honed over the next decade. Another strength is that this is a self contained book! It assumes no neuroscientific or medical knowledge other than the most basic. There are many excellent colour illustrations. Therefore, this book can be highly recommended to anybody interested in the disordered mind and brain.

Eileen Joyce

CORRECTIONS

Rosso SM, van Swieten JC, Roks G, *et al.* Apolipoprotein E4 in the temporal variant of frontotemporal dementia. *J Neurol Neurosurg Psychiatry* 2002;**72**:820.

Due to the style used in house for listing authors affiliations in the Letters section of the journal, the author's names have been incorrectly listed. The correct order should read as follows:

Rosso SM, Roks G, Cruts M, van Broeckhoven C, Heutink P, van Duijn CM, van Swieten JC

This also applies to:

Lünemann JD, Kassim N, Zschenderlein R, *et al.* Rhabdomyolysis during interferon- β 1a treatment. *J Neurol Neurosurg Psychiatry* 2002;**72**:274.

The correct order of the authors is: Lünemann JD, Schwarzenberger B, Kassim N, Zschenderlein R, Zipp F.

Aarsland D *et al.* Donepezil for cognitive impairment in Parkinson's disease: a randomised controlled study. *J Neurol Neurosurg Psychiatry* 2002;**72**:708–12. An error occurred in the production process in which the codes of the two lines were erroneously interchanged. The correct figure appears below:

Figure 2 Change in mini mental state examination (MMSE) score from baseline over the two treatment sequences. Values are mean (SE).

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.¹

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.^{2,3} 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.¹ 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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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.*¹ 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^{2–4} 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.*¹ 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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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 IP₃ 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...".