

shift from ocular to generalised myasthenia gravis was a more common feature of anti-AChR antibodies-positive myasthenia gravis (14 of 28 patients, 50%) than that of seronegative myasthenia gravis (one of five patients, 20%). Subsequent to a follow-up period of more than one year, the group of anti-AChR antibodies-negative patients consisted of four (3%) ocular cases and 10 (7%) generalised cases.

Consequently, I am unable to confirm Toyka's observation of only 45% anti-AChR antibodies-positive cases in long-standing ocular myasthenia gravis. Toyka also suggests that cases with questionable myasthenia gravis may have been included in the analysis of generalised myasthenia gravis¹ resulting in lower estimates of the sensitivity relating to such cases. This is a very unlikely explanation in view of the scrutiny of all cases including clinical assessment by an experienced examiner, all of which is thoroughly expounded in my article¹ and also in my epidemiological study.²

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Assessing tremor severity with long-term tremor recordings

We have read the paper by Bain *et al*¹ with great interest. This excellent work will be of considerable benefit for future studies. Nevertheless we would like to draw attention to a fact that has been underestimated in this contribution.

Bain *et al* investigate the validity of a clinical rating scale and of short-term, upper-limb accelerometry by comparing the results to various measures of functional impairment, clearly demonstrating the superiority of the rating procedure over the neurophysiological approach. On the basis of our own results it seems most likely that one of the main reasons for the weak validity of accelerometry in their study is the short duration of the recordings, which do not take into account the marked diurnal variations of tremor severity, and the exceptional situation in a clinic laboratory.

In order to overcome these problems which are a general feature of short-term tremor quantification, we have developed a method for measuring tremor for up to 24 hours by recording the EMG of wrist extensors and flexors with a small portable tape recorder.² During the recording period the outpatients are free to move around and maintain their usual activities, allowing us to measure exactly that involuntary muscle activity which produces the daily living impairment. Having gained some experience with this technique, we appreciate such long-term recordings as a reliable tool

for clinical studies.³ Moreover, our measure of tremor severity (which actually is the tremor-occurrence rate) seems to correlate better with a patient's self-rating of functional impairment than the doctor's clinical assessment.

We have investigated this issue in a preliminary manner by evaluating treatment effects in 15 parkinsonian patients with different premedications. The tremor severity was assessed before and after the change in medication, firstly by rating on a six-point scale, and secondly by a 10-hour tremor recording. In addition, the patients were asked to rate the effect on a scale consisting of five grades: marked improvement (2), slight improvement (1), no change (0), slight deterioration (-1), and marked deterioration (-2). When the changes in tremor occurrence rate and clinical rating, and the patient's self-rating are correlated, the coefficients (Spearman's *r*) and *p* values are: doctor's rating—self-rating: $r = 0.25$, $p = 0.37$; doctor's rating—long-term EMG: $r = 0.017$, $p = 0.95$; self rating—long-term EMG: $r = 0.860$, $p < 0.001$.

Although our setup is not directly comparable to the one used by Bain *et al* (we studied parkinsonian patients instead of patients with essential tremor; furthermore EMG and accelerometry might differ in their correlation with functional impairment) our data allow the following conclusion: neurophysiological techniques do have a place in tremor quantification if they are applied for sufficiently long periods of observation. When used in this way, they not only avoid the abovementioned problems, but most importantly, the correlation with functional impairment seems to be higher than in any short-term method, including clinical rating.

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Bain and Findley reply:

We note the findings of Boose *et al* with considerable interest. Their technique of recording parkinsonian tremor for prolonged periods of time (up to 10 hours) and their use of "tremor-occurrence rate" as an index of tremor severity provide a useful insight into the problems involved in assessing tremor severity. We agree entirely about the advantages of assessing patients during their normal activities rather than in an artificial laboratory environment, where patients may (at least initially) be unduly tense and anxious. Their point about diurnal variation of tremor is also well made, and in the case of parkinsonian tremor we have observed that further short-

term fluctuations occur from burst to burst in EMG recordings and can be seen from minute to minute and hour to hour in patients' limbs (phenomena that led us to speculate that parkinsonian tremor may be a fractal process).¹

We do, however, have some reservations about their approach. Firstly, the equipment is costly and not widely available. Secondly, the time involved in recording and analysing tremor using their technique precludes its routine clinical use except in specialist departments. Thirdly, their measurement of tremor-occurrence rate was compared with a six-point clinical rating scale and a five-point patient self-rating scale, which are both clearly measures of impairment. These scales are not functional measures of disability or handicap in a conventional sense. Boose *et al* do not appear to have assessed disability formally. This is understandable because by choosing to study patients with parkinsonism rather than essential tremor other factors, namely bradykinesia, rigidity, and postural instability, would have influenced any measures obtained by an assessment of handicap or disability.

One factor that we have studied and consider to be critical in determining the impact of tremor upon upper limb function is "tremor suppressability", namely, the extent to which tremor amplitude can be suppressed while performing manual tasks and the period of time that this suppression can be maintained by the patient (the coefficients of amplitude and temporal suppression respectively).^{2,3} This point was nicely illustrated by Jager and King who describe a man with marked hereditary essential tremor who could nonetheless shoot deer with a rifle at a hundred yards.⁴ Any method that solely examines tremor-occurrence rate cannot account for variations in tremor suppressability nor the functional consequences of different types of tremor (for example rest, postural, and intention tremors).

Finally, Boose *et al* appear to have shown that patients are reliable witnesses, a fact that will be of great comfort to the humble and hard-pressed clinician.

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NOTICES

The XIIth International Congress of Neuropathology will be held in Toronto, Ontario, Canada from 18-23 September 1994. This meeting will be conjoint with the American Association of Neuropathologists Annual Meeting and the Canadian Association of Neuropathologists Annual Meeting. For further information please contact Dr JJ Gilbert, Victoria Hospital Research Institute, 375 South

Street, London, Ontario N6A 4G5, Canada. Tel +1 519-667-6649, fax +1 519-432-7367.

The American Neuropsychiatric Association will hold its Sixth Annual Meeting on July 21-23, 1994 in Newport, Rhode Island, USA. The meeting will be a joint session with the British Neuropsychiatry Association and the programme will include invited lectures, platform and poster presentations, and videotaped case demonstrations. The meeting theme is "Subcortical disease in neuropsychiatry". Information regarding this meeting and requests for abstract submission forms can be obtained from: Stephen Salloway, MD, Chairman, Scientific Programme Planning Committee, Department of Neurology, Butler Hospital, 345 Blackstone Blvd. Providence, Rhode Island 02906, USA. Tel. +1 401 455-6403; fax. +1 401 455-6405.

BOOK REVIEWS

Chronic Pain: Reflex Sympathetic Dystrophy: Prevention and Management. By HOOSHANG HOOSHMAND. (Pp 202 Illustrated; Price: £76.00). 1993. Florida, CRC Press Inc. UK Distrib: London, Mosby-Year Book Europe Ltd. ISBN 0-8493-8667-5.

"Chronic pain is being mismanaged universally. Impatient surgeons try unsuccessfully to excise pain, internists load the patient with narcotics and depressing tranquillisers. Chiropractors try to cure everything with their fingers. Acupuncturists shoot darts at the patients". So begins the introduction to this 168 page book. Disciplines from dermatology to psychiatry are attacked for branding patients with inappropriate and unhelpful labels, and prescribing treatment that often worsens their condition. This theme continues throughout.

The initial chapters cover the history and anatomy of RSD and the crucial involvement of the sympathetic nervous system (SNS). The diffuse anatomical nature of the SNS and bilateral representation explains the failure of surgical techniques. Stress, eustress, the limbic system, disuse and ephatic (scar) pain and their role in the development of RSD are described. Aetiology, diagnosis, prevention and management of RSD complete this volume. Thermography is promoted as an essential tool in early diagnosis. Referred pain, trigger points and electrical injuries are well covered.

Diagnosing RSD in the early stages is often difficult. Investigated appropriately with thermography, followed by vigorous treatment with physiotherapy, sympathetic nerve blockade and antidepressants, rather than narcotic analgesics, will produce good results. Late stages of RSD are easy to diagnose and very difficult to treat. Dietary counselling (avoidance of stimulants and alcohol) is stressed and patients urged to

adopt a different lifestyle. Much of this is reasonable advice, although the emphasis on, and illustrations for, thermography were not always convincing. Frequent repetition of favourite themes irritated rather than enlightened. There are many typographical errors, and the writing style hinders clarity. A thorough revision would considerably improve this work without detracting from the content and provide a useful addition to this fascinating field.

R D E BATTERSBY

Multiple Sclerosis: Its Impact from Childhood to Old Age. (Major Problems in Neurology Series 126). By HELMUT J BAUER and FOLKER A HANEFELD. (Pp 177; Price: £30.00). 1993. London, WB Saunders Co. Ltd. ISBN 0-7020-1606-3.

It is not surprising that something of a research industry has developed on the back of epidemiology in multiple sclerosis. Surveys are easy to carry out, if somewhat laborious, and they generate concepts through the use of large numbers, thus satisfying both the intellectually curious and the statistically cognate. Over the last decade, population based surveys of patients with multiple sclerosis, involving many thousands of cases, have defined the natural history of the disease and show surprising consistency of results despite marked variations in methodology. *Multiple Sclerosis: Its Impact from Childhood to Old Age* summarises the clinical experience of 660 patients with multiple sclerosis from Gottingen studied over the last 15 years. The clinical features in this cohort are considered on the basis of age with a further emphasis on practical aspects of the disease, its treatment and management.

Others have described more cases, but Professors Bauer and Hanefeld establish beyond doubt, that multiple sclerosis can manifest in childhood and the diagnostic pitfalls and presentations in this age group are well described. The clinical features in young adults from Gottingen provide a comprehensive survey of symptoms and signs, each analysed in sub-groups defined by age, duration of the disease and disability, and with many useful tables; but the authors do not make clear that these frequency data are not point prevalence morbidity statistics or lifetime risks for individual manifestations of multiple sclerosis observed in their population based cohort. In older age, the practical issues are disability and the causes of death in individuals with multiple sclerosis; here, Professors Bauer and Hanefeld discuss in detail the often neglected issue of suicide in multiple sclerosis.

The book concludes with a critique of management which contains useful guidance on what is offered by state and charitable institutions in different countries. Throughout, the approach is practical and—despite the epidemiological substrate for this monograph—retains an emphasis on the individual with multiple sclerosis as person and not as statistic.

As the latest issue in the Saunders *Major Problems in Neurology* series, individuals will do well to buy this volume and keep their collection intact.

ALASTAIR COMPSTON

Gamma Knife Surgery: A Guide for Referring Physicians. By JEREMY C GANZ. (Pp 163 Illustrated; Price: DM69, US\$45, Softcover). 1993. Wien, Springer-Verlag. ISBN 3-211-82476-6.

Jeremy Ganz has written an excellent introduction to the field of Stereotactic Radiosurgery. It comes in the guise, as its title suggests, of a guide to physicians thinking of referring patients to a unit with a Gamma Knife, the method of radiosurgery which was launched by Professor Lars Leksell in Stockholm in 1968. The layout is logical, clearly set out and the style lucid, if at times somewhat pedantic. What emerges is a useful description of the method, the radiological principles behind it and an outline of the conditions for which it has been used, the doses used, the results obtained and some of the difficulties and side effects encountered. It provides a good summary of the basic information which would be useful to a newcomer to any form of radiosurgery whatever the system of stereotactically directed beams of ionising radiation to be used.

DAVID FORSTER

Epileptogenic and Excitotoxic Mechanisms (Current Problems in Epilepsy Series No. 8). By G AVANZINI, R FARIELLO, U HEINEMANN and R MUTANI. (Pp 158; Price: £32.00, US\$64.00 H/bk). 1993. London, John Libbey & Co. Ltd. ISBN 0-86196-386-5.

This volume represents the proceedings of an advanced course on epileptology held in Sicily in January, 1992. It is mainly intended for people with a special research or clinical interest in epilepsy, and it focuses on the underlying mechanism of epileptogenesis, especially in the developing brain. It is a slim volume with 14 brief chapters, approximately half of which are from Italian laboratories, and the other half from leading laboratories in North America and Europe. The format and scope of the chapters vary: some give a general overview of their assigned topic (with useful up-to-date citations on the whole), while others present more detailed recent findings in an article format.

The topic of epileptogenesis is approached mainly from two angles: 1. a conventional cellular, electrophysical approach, and 2. a developmental approach. Attempts are made to correlate the developmental profile of different types of seizure manifestations in the neonate with the maturation of inhibitory and excitatory transmitter systems and neuronal connectivity, thereby providing insights into the mechanism of initiation and propagation of seizure activity.

In addition, the process of amygdala kindling in adult and neonatal rats is the topic of two chapters. Other chapters that discuss general animal models of epilepsy or mechanism of action of antiepileptic drugs, appear to be more tangential to the central theme of epileptogenesis.

David Prince provides an excellent, succinct summary on the membrane properties that account for the progression of epileptogenic events. Uwe Heinemann and co-workers successfully combine an electrophysiological and a developmental approach

Neural Prostheses: Replacing Motor Function After Disease or Disability. Edited by R B STEN, P H PECKHAM and D P POPOVIC. (Pp 345; Price: £55.00 H/bk). 1992. Oxford University Press. ISBN 0-19-507216-2.

Technological developments take about 20 years to reach the marketplace. The first functional neuromuscular stimulator was used in 1961 so why haven't we got useable products to restore motor function after spinal cord injury or stroke? This book will inform you, not that it sets out to answer the above question, but it is a comprehensive state-of-the-art review with 15 chapters and 20 contributors.

There is a comprehensive review of models of muscle activity but muscle models do not feature much in the work of designers and engineers of functional electrical stimulation (FES) systems. Possibly this is because models are designed to predict muscle activity in limited laboratory situations and over strictly limited ranges and speeds of movement. Controlled lengthening features very little in models but is an important function of muscle in movement.

As soon as engineers realised that a contracting muscle normally feeds back information about itself and its joints, they began to implement various feedbacks into FES systems, with improved results. Feedback however means sensors. A review of mechanical sensors concludes that developments in flexible microelectronic devices made from polymers with arrays of silicon chips will perhaps provide a sensory glove to operate with hand control FES. There is, however, an alternative strategy. Quadruplegics and hemiplegics have intact skin sensors so why not try to tap into their signals in the peripheral nerves? This is technically feasible and a consideration of the practicality of it in man appears in Chapter 5.

This leads to another fundamental debate that runs through several chapters—should stimulating electrodes be implanted and what should be their design? There is no doubt that implantation is safe and reasonably reliable but will it always work? It works well enough for cardiac pacing and as root stimulation for micturition but hand function requires such a variety of different loci and degrees of stimulation that getting every aspect to function well becomes a superhuman effort.

Walking should be easier to control than the many different hand functions. Multichannel stimulation to produce stepping movements has been unkindly called "electronic puppetry". The devices that seem to work are cruder and simpler than the designs to which engineers aspire. There are hybrid devices of mixed mechanical and electrical function and the simple peroneal nerve stimulator for footdrop. Both these operate close to the limit of patient "gadget tolerance". Most other devices are well above this threshold and only used by the patient when the doctor or engineer insists.

The final chapter on the transfer of technology from laboratory to the real world gives a useful insight into how corporations develop, manufacture and market devices. Some fascinating "case histories" are given

and the legal framework within which one must operate is set out. The authors are from the North American Continent. What will strike the British reader is how few of the right conditions exist in Britain. This type of research requires very close working relationships between engineers, physiologists and clinicians. Which of our Universities or Trust Hospitals has the facility for this?

This is a very nicely produced book. The editors have done well to cover the field in breadth and depth. It seems that the really juicy prize of FES making significant advances in motor rehabilitation is almost within our grasp but, like Tantalus, we realise it is still just out of reach.

EM SEDGWICK

Alzheimer's Disease: Advances in Clinical and Basic Research. Edited by B CORAIN, K IQBAL, M NICOLINI, B WINBLAD, H WISNIEWSKI and P ZATTA. 1993. (Pp 633 Illustrated; Price: £110.00). Chichester, John Wiley & Sons Ltd. ISBN 0-471-93840-8.

This book contains brief chapters based on presentations at the Third International Conference on Alzheimer's Disease and related disorders held in Padua in July 1992. The 73 brief chapters are arranged in sections ranging from basic biochemical defects in Alzheimer's disease to care giving for the patient and family. As a report of an international meeting this book inevitably seeks to cover a large number of topics, none of them very deeply. Nevertheless, all the major researchers in the Alzheimer field have contributed in one form or another and certain sections including those on mechanisms of cell death and genetic factors are interesting and stimulating. One of these is a section by Cotman *et al* on neuronal death in Alzheimer's disease which discusses the possible contribution of apoptosis to neurodegenerative disorders. There is some evidence that β amyloid may not only enhance the susceptibility to apoptosis as well as necrosis but also enhance the cells' vulnerability to glutamate induced toxicity. This concept of multifactorial causation of cell death in Alzheimer's disease is likely to be paralleled in other neurodegenerative disorders, such as Parkinson's disease. Another valuable contribution is the review by Stanley Prusiner on prion disease.

Are published transactions of meetings useful? At best they are a fairly rapidly published series of brief chapter reviews providing relatively up-to-date information, focused usually on a high number of related topics. At worst, they are a vehicle for publication of some rather questionable data in a number of short and superficial articles. Overall, this book tends more towards the former model. It will provide a useful summary of a variety of topics, many of which will be of use to the researcher. This is not a book for those looking for a succinct and comprehensive review.

AHV SCHAPIRA

Management of the Acutely Ill Neurological Patient. Edited by JAMES C GROTTA. (Pp 192; Price: £11.95). 1993. Edinburgh, Churchill Livingstone. ISBN 0-443-08870-5.

This multi-author book is written for "emergency room physicians, non-neurologists and intensivists" who look after acutely ill neurological patients. The editor, who has written an excellent chapter on acute stroke, points out the direction the management of neurological problems is taking. More elective investigations are being undertaken on an out-patient basis so that now there is an increasing need for the provision of care often in an intensive care unit, for the acutely ill neurological patient. Perhaps in the future such patients will be managed by a multi-disciplinary team.

The book covers a number of common clinical problems: epilepsy and status, neuromuscular emergencies, brain death, head injuries, infections, intracranial pressure and cerebral resuscitation—to name some. Like many multi-author works some topics appear better covered. I found the chapters on head injuries and neuromuscular emergencies very helpful, but spinal cord problems are only discussed following acute injury. Surely an acute myelitis or vascular cord lesion deserves mention. There is no discussion of encephalitis or of acute demyelination. The last may affect the brain stem acutely with life-threatening bulbar problems. I found the section on metabolic disturbances patchy but enjoyed the chapter on difficult behaviour. Some useful charts are used but surprisingly only two diagrams and four pictures (two of apparatus and two scans showing spinal injuries). The text is written for an American reader: this is clear in the discussion on the withdrawal of life support. There are useful comments about the role of the EEG and evoked potentials to monitor patients with brain damage.

Overall this book succeeds. It is easy to read, it contains a wealth of helpful information and the price is modest so that its intended readers should benefit from its purchase. I recommend it.

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SHORT NOTICES

Physical Aspects of Stereotactic Radiosurgery. Edited by MARK H PHILLIPS. (Pp 286 Illustrated; Price: \$59.50). 1993. New York, Plenum Publishing Corp. ISBN 0-306-44535-2

Alzheimer's Disease and Related Disorders Series: Advances in the Biosciences Vol 87. Edited by M NICOLINI, P F ZATTA and B CORAIN. (Pp 474 Illustrated; Price: £90.00, \$144.00). 1993. Oxford, Pergamon Press Ltd. ISBN 0-08-042330-2