Radiology of stroke

The optimum time frame for imaging embolic infarcts for stigmata of haemorrhagic transformation should have merited discussion under the heading “special clinical circumstances”, not least because of conflicting evidence about the benefits versus risks of early anticoagulation in the context of unpredictable evolution of embolic infarcts with or without anticoagulant treatment. In a study comprising 30 patients with cardioembolic cerebral embolism, three patients with an initially non-haemorrhagic cerebral infarct, visualised by computed tomography within 12 hours of stroke onset, showed symptomatic haemorrhagic transformation in the absence of anticoagulant treatment 2–8 days later. One other patient in this subgroup did, however, develop sudden worsening of hemiparesis despite having initially presented with a small infarct. Among 1457 patients anticoagulated with unfractionated heparin in the presence of embolic cerebral infarct associated with atrial fibrillation, haemorrhagic transformation (within 14 days) was significantly commoner (p < 0.0001) than in their non-heparinised counterparts. Ischaemic stroke recurs with a 4.9% frequency in the latter subgroup (comprising 1612 patients) during that time frame, and this complication was significantly less common (p = 0.001) in their anticoagulated counterparts. Anti-coagulation in the presence of haemorrhagic transformation has been advocated as being without risk on the basis of the outcome in 12 patients so treated, but the caveat is that, in another study also involving patients with embolic stroke, the subsequent development of haemorrhagic transformation in 5 of 231 patients anticoagulated with heparin was associated with significant clinical deterioration. It is this unpredictability in the consequences and tempo of haemorrhagic transformation and in the impact of early anticoagulation on this phenomenon that causes anxiety among clinicians at all levels of experience.

OM P Jolobe
Department of Adult Medicine, Tameside General Hospital, Fountain Street, Ashton-under-Lyne OL6 9RW, UK

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Author’s reply
The strongest risk factor for haemorrhagic transformation of cerebral infarction in patients not treated with any antithrombotic or thrombolytic drug is simply having an extensive large infarct. It so happens that cardioembolic cerebral embolism often results in large cerebral infarcts (because a thrombus arising from the heart are often large and block a largish vessel). There, thus, is an association between cardiogenic cerebral embolism and haemorrhagic transformation. This association may be exaggerated by administering antithrombotic or anticoagulant or thrombolytic therapy to these patients. Unfortunately, it is difficult to draw conclusions on the risks and benefits of anticoagulant treatment from non-randomised studies. The complete data from the international stroke trial (20 000 patients) clearly show that heparin started within the first 48 hours of stroke and continued for the first 14 days may reduce the risk of recurrent ischaemic stroke but at the risk of increasing haemorrhagic stroke and death, and as a result there is no net benefit. When to start or continue anticoagulant treatment after stroke in the presence of atrial fibrillation. One group of patients with a clear cardiac source of embolism is a decision that needs to be made in light of each patient’s risk factors and continues to be a thorny problem. However, the benefits of aspirin (while less effective) are still worthwhile with less risk of haemorrhagic transformation. There is no easy answer to this problem.

J M Wardlaw
Department of Clinical Neurosciences, Western General Hospital, Crewe Road, Edinburgh EH4 2XU, UK

Thunderclap headache, reversible cerebral arterial vasocostriction, and unruptured aneurysms

In his comprehensive review of thunderclap headache, Dr Dodick discusses two patients with the triad of thunderclap headache, cerebral arterial vasocostriction, and unruptured cerebral aneurysms. We recently reported on two very similar patients, in whom the symptoms developed shortly after exposure to commonly used serotonin enhancing drugs. The interrelation between thunderclap headache, cerebral arterial vasocostriction, and unruptured aneurysms is not clear, and in these four patients the aneurysms may well have been incidental findings. However, it is interesting that, in addition to segmental vasocostriction, cerebral angiograms in patients with the Call-Fleming and some other vasocostriction syndromes can have areas of vasodilatation beyond the normal diameter of the artery. Moreover, patients with stroke associated with the use of vasoconstrictive drugs such as cocaine and “ecstasy” are known to have an unusually high number of aneurysms. It is conceivable that patients who develop cerebral vasocostriction or thunderclap headaches (without subarachnoid haemorrhage) are more likely to harbour aneurysms due to primary or drug induced abnormalities of vessel tone.

Dr Dodick reviews cases where thunderclap headache was associated with unruptured aneurysms, without cerebral arterial vasocostriction, and where thunderclap headache was associated with vasocostriction, without unruptured aneurysms. It should be noted that unruptured aneurysms are associated with vasocostriction, without thunderclap headache. This point is emphasised by an additional, hitherto unpublished case (courtesy Dr C Miller Fisher) of severe cerebral vasocostriction, stroke, and death associated with two unruptured and asymptomatic intracerebral aneurysms without thunderclap headache. The patient, a 65 year old woman, was admitted in January with probable Guillain-Barré syndrome. The hospital course was notable for episodic hypertension (maximum blood pressure 200/100 mm Hg). On day 4, she developed cortical blindness, abulia, aphasia, and right hemiplegia. Computed tomography showed infarctions in both occipital lobes and a parasagittal meningioma. A selective cerebral arteriogram showed aneurysms in the anterior communicating and left middle cerebral artery, severe attenuation of proximal intracranial arteries, and “sausaging” of distal arteries. After returning from the arteriogram the patient became obtunded, then deteriorated gradually, and died on day 13. A necropsy showed cerebral oedema with bilateral temporal lobe herniations, infarctions in the inferior cerebral and both occipital and frontal lobes, a parasagittal meningioma, and two unruptured aneurysms (a 5 × 5 mm anterior communicating aneurysm and a 10 × 7 mm left middle cerebral artery aneurysm). There was no evidence for arterial inflammation. Lympphyocytic infiltration was present in the sciatic nerves, consistent with infectious polyneuritis. As stated in the review article, it is difficult to account for any mechanism whereby the aneurysms may have precipitated the vasocostriction.

A B Singhal
Stroke Service, VKB-802, Massachusetts General Hospital, Boston, MA 02114, USA; asinghal@partners.org

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Author’s reply
I would like to thank Dr Singhal for his interest and thoughtful insights concerning the review article on thunderclap headache. I will address his comments in order.
Firstly, I had already read with great interest the recent article by Dr Singhal et al regarding three patients with thunderclap headache, reversible vasospasm, and ischaemic stroke possibly secondary to exposure to serotonergic medications. He also correctly points out that the unruptured aneurysms found in some patients with thunderclap headache and reversible vasospasm are possibly incidental—a point that I made in the review article. On the basis of the association with unruptured aneurysms or exposure to sympathomimetic and serotonergic medications in some patients with thunderclap headache and vasospasm, he raises the provocative and interesting possibility that patients who develop thunderclap headache (without subarachnoid haemorrhage) are more likely to harbour aneurysms due to primary or drug-induced abnormalities in vessel wall tone.

There are certainly cases of thunderclap headache with reversible vasospasm that have occurred shortly after exposure to sympathomimetic medications such as cocaine or amphetamines, as well as during hyperadrenergic metabolic states such as eclampsia and hypertensive crisis.1 Most of the patients described in the literature, however, did not have unruptured aneurysms, and prospective longitudinal studies of patients with non-unruptured thunderclap headache have not found an increased risk of subarachnoid haemorrhage. Ideally, a longer prospective study of patients with thunderclap headache with cerebrovascular imaging or careful assessment of a large group of patients with unruptured aneurysms (such as the international unruptured aneurysm study) for a history of thunderclap headache would be required to address the hypothesis raised by Dr Singhal.

Dr Singhal also suggests that unruptured aneurysms present with vasospasm and the absence of a thunderclap headache. The case (courtesy of C Miller Fisher) that he uses to illustrate this point is a very interesting one. While it is certainly possible that the unruptured aneurysms in this case may have given rise to the vasospasm, I believe the vasospasm in this 65 year old woman with Guillain-Barré syndrome was more likely related to the severe labile hypertension of the secondary form of autonomic failure frequently seen in this disease. As alluded to earlier, vasospasm has been well described in patients with acute hypertensive crises such as phaeochromocytoma, eclampsia, and hypertensive encephalopathy. Hypertensive encephalopathy with posterior leucoencephalopathy syndrome (PLES) was recently described in a patient with thunderclap headache, and I have just submitted a similar case for publication in a young woman who also had reversible vasospasm in the setting of the a hypertensive crisis and PLES. In fact, it is possible that in many cases of drug induced cerebral vasospasm, the effect on vascular tone and calcium may reflect the effect of these sympathomimetic drugs on arterial blood pressure in addition to a direct vasocostrictive effect of the drugs. Indeed, it would have been of notable interest to know the arterial blood pressure in the patients he described with reversible vasospasm and stroke in patients exposed to serotonergic medications, since the magnetic resonance imaging abnormalities in his patients are very similar to the changes seen in patients with PLE.

W D Dodick
Department of Neurology, Mayo Clinic Scottsdale, 13400 East Shea Boulevard, Scottsdale, Arizona 85259, USA, dodick.david@mayo.edu

References

Cochlear implantation in a profoundly deaf patient with MELAS syndrome
In response to the article “Cochlear implantation in a profoundly deaf patient with MELAS syndrome” (mitochondrial myopathy, encephalopathy, lactic acidosis-stroke-like episodes),1 we feel concerned that this patient may have a different diagnosis. This woman who received a cochlear implant is described as having the MELAS syndrome, in both the title and the text. However, when she has less severe maternally inherited diabetes mellitus with deafness (MIDD) syndrome. She has the A3243G point mitochondrial DNA (mtDNA) mutation associated with insulin dependent diabetes mellitus, congenital cataracts, short stature, leg weakness, fatigue, and sensorineural hearing loss (SNHL), with no encephalopathy or strokes. The age of onset of SNHL was 22 years, with a slow deterioration to right profound SNHL at the age of 29 years, and bilateral profound SNHL and tinnitus at the age of 30 years. Caloric testing and computed tomography of her temporal bones were both normal. Her mother suffered from diabetes, glaucoma, and a lesser degree of SNHL, and a sister has profound SNHL and mental retardation.

MELAS is a multisystem disorder with a wide variety of clinical features. Among these multiple features, the diagnostic criteria for MELAS are as follows:1

1. Stroke-like episodes before age 40 years;
2. Encephalopathy (seizures, dementia, or both);
3. Mitochondrial myopathy (lactic acidosis, ragged red muscle fibres, or both);
4. Two of the following three: normal early lactate, Encephalopathy (seizures, dementia, or both);• Diabetes mellitus (ranging in approximately 80% of patients).

Now these clinical findings can be confirmed with a positive molecular genetic test for mtDNA mutations.2 The A3243G mutation in the mitochondrial tRNA<sup>Leu</sup> gene, MTTL1, causes MELAS and is responsible for MELAS in approximately 80% of patients. MIDD has a maternal phenotype of bilateral, progressive, symmetrical SNHL, generally preceding diabetes mellitus (ranging from abnormal glucose tolerance to insulin dependent diabetes mellitus) and occurs in adulthood, with a background of maternal inheritance. Sporadic occurrence has been noted.3 It is associated with short stature and can be expressed as type 1-like or type 2-like diabetes.4 The A3243G transition mutation has been identified as the cause of MIDD in 60% of cases. In patients with mtDNA disease, affected cells and tissues tend to harbour mixtures of mutant and wildtype mtDNA in different proportions. This is called “heteroplasmy”, as opposed to “homoplasy”, where only one type is present. It is hypothesised that phenotypic expression of mtDNA polymorphisms may occur when heteroplasmic within an organ reaches a certain level. This concept is known as the “threshold effect”. The severity of the phenotype is thought to correlate with the degree of heteroplasmic in different tissues. Interestingly, both syndromes, MELAS and MIDD, can be found in a single pedigree with the A3243G mutation. The A3243G mutation is also associated with Kearns-Sayre syndrome. Assuming that all patients with the A3243G mutation have the MELAS syndrome leads to an incorrect diagnosis, with significant implications for patient counselling. A diagnosis of MELAS implies that the patient has developed stroke-like episodes or encephalopathy.

As more people with SNHL become genotyped and the identification of the true prevalence of mitochondrial SNHL becomes more obvious, a database of already successfully treated patients by cochlear implantation will be useful for quantitative analyses of performance of these patients with cochlear implants. Here also, the correct label must be assigned to patients.

More information on mitochondrial SNHL can be obtained on the Hereditary Hearing Loss Homepage on http://www.ual.ac.uk/dnalab/hhh/.

A R Sinnathuray, V Rout, J G Toner
Department of Otologyangology, Belfast City Hospital, Belfast, UK

A Magee
Department of Medical Genetics, Queen’s University, Belfast at the Belfast City Hospital

Correspondence to: Mr J G Toner, Director, Regional Cochlear Implant Centre, Belfast City Hospital, Lisburn Road, Belfast BT9 7AB, Northern Ireland, UK, jgtone@ntheWorld.com

References

Author’s reply
We are grateful to Dr Sinnathuray and colleagues for their very useful comments on the precise diagnosis of our patient’s condition. We agree entirely with the comment that the A3243G mutation also occurs in maternally inherited diabetes mellitus with deafness (MIDD). In our patient the original diagnosis was made by a clinical geneticist in 1994 and therefore, in a rapidly changing field,
greater precision in diagnosis might have been possible with a further genetics consultation at a later date. We should point out that this article was originally submitted in November 2000 and this, also, may have contributed to the diagnosis of MELAS syndrome rather than MIDD syndrome. We are most grateful to Dr Sinnathuray and colleagues for their useful comments.

J Graham
UCL Cochlear Implant Unit, Royal National Throat, Nose & Ear Hospital, 330–332 Gray’s Inn Road, London WC1X 8DA, UK

Bilateral lesions restricted to the posteroventral pallidum are unlikely to provoke corticobulbar syndrome and psychic akinnesia

Merello et al reported a randomised study comparing bilateral simultaneous posteroventral pallidotomy (PVP) with a combination of unilateral PVP and contralateral pallidal stimulation.1 After having included three patients in each group, the study had to be aborted because of the severe complications encountered in the patients who had had bilateral pallidotomy. This interesting paper raises some serious concerns.

First, the three patients who had bilateral PVP had a mean age of 67 years and those who had PVP and contralateral pallidal stimulation had a mean age of 55 years. This difference in age is said to be non-significant. As there are only three patients in each group it would perhaps have been more appropriate to have given the ages of the individual patients rather than the means.

Second, at three months after surgery, the patients who had bilateral PVP showed deterioration in parts I (mood) and II (activity of daily living) of the unified Parkinson’s disease rating scale (UPDRS). The subscopes of gait and postural instability worsened significantly. The patients showed deterioration in depression and apathy scores, and it was not possible to perform neuropsychological evaluation after surgery. The patients required feeding tube, their gait freezing deteriorated, and they had no benefit from increased levodopa dosage. They suffered from severe loss of initiative and motivation. In my opinion, even though bilateral pallidotomy may increase the risks of complications,2 the disastrous outcome of the three patients described in Merelo’s paper poses serious questions as to the exact location of the lesions. I believe that in order to provoke the severe corticobulbar syndrome and “psychic akinnesia” described, the pallidal lesions must have encroached on the internal capsule bilaterally, and also have included antero-dorso-medial parts of the GPi.

The authors wrote that “brain MRI three months after surgery showed that all nine lesions and the three electrodes were located entirely within the GPi. Coordinates of the lesion/lead as well as lesion volumes were not significantly different between the groups.” The authors concluded: “Our present findings argue against the possibility that lesion inaccuracy is responsible for the unacceptable rate of side effects of bilateral procedures as targets were confirmed by microrecording, lesions checked by MRI and the same criteria were followed either for lesioned or stimulated patients.” It is indeed very fortunate that the authors did perform the postoperative MRI at three months after surgery—that is, when the surgical oedema that would disturb the interpretation of the lesion location had completely resolved. From a didactic point of view, and to allow the reader to learn more about the anatomical substrate of this rather catastrophic outcome in patients with bilateral PVP the MRI scans should have been shown in this important paper. I invite Merello et al to publish relevant axial and coronal postoperative brain MRI scans of these three patients in their answer to this letter, showing the locations of the bilateral posteroventral GPi lesions that were responsible for the reported “corticobulbar syndrome and psychic akinnesia.”

M I Hariz
Department of Neurosurgery, University Hospital, 901 85 Umeå, Sweden; marwan.hariz@neuro.umu.se

References

Author’s reply
We greatly appreciate the publication of the letter from Professor Hariz, which gives us occasion to provide more information about our paper and confirm the dangerous effect of simultaneous bilateral lesions within the GPi. We all know how limited the literature is on negative results of surgical procedures and how important they are. Surgery for Parkinson’s disease is an extremely useful tool in a certain subgroup of patients, but it is not entirely risk-free and unfortunately many of the side effects seen at the bedside are poorly represented in published reports.

On the basis of unpublished descriptions by many neurosurgeons, bilateral procedures are performed by placing a normal lesion on one side, involving as much as possible of the motor portion of the GPi, followed by a smaller contralateral lesion. An excellent point arises from the concern expressed by Hariz: should both lesions be the same size? Perhaps staged asymmetric lesions could provide an alternative, but this was not the case in our report; we made simultaneous lesions which both involved as much as possible of the motor portion of the GPi, and our conclusions should not be extended to other surgical contexts.

As requested, we provide MRIs of our cases (fig 1) and fully agree that lesion placement is crucial, as Hariz is well aware, given his reported outcome of five of 13 patients (that is, almost 40%) who subsequently required seven further procedures, presumably because of initial lesion misplacement.1 Whatever the importance of descriptive photography, we believe it was more important that non-significant statistical differences were found in lesion/stimulation placement between the groups, and clinical psychic akinnesia was only present in simultaneous bilaterally lesioned cases.

We are sure that Hariz must have already read a recent review by Laplante and Dubois,2 which clearly describes the psychic akinnesia syndrome as a result of bilateral basal ganglia lesions, providing deep insight into the non-motor roles of the basal ganglia, such as behavioural activation, cognitive processing, affectivity, and conscious awareness, with which we fully agree.

M Merello
Movement Disorders Section, Raul Carrea Institute for Neurological Research, FLENI, Buenos Aires, Argentina; mmmerello@fleni.org.ar

References
Ischemic cerebrovascular disease


The most recent book in the very successful “black book” Contemporary neurology series from Oxford University Press is a monograph on brain ischaemia. The book is written by three experienced and well respected North American authors—Adams from the United States and Hachinski and Norris from Canada. The present monograph is a successor to a previous book entitled The acute stroke by Hachinski and Norris published 16 years ago.

There are now many books on stroke and on brain ischaemia. While reading this present endeavour I continued to ponder the role of this monograph among the already burgeoning library of books. Whom is it aimed at? Who will profit most by its content? When, why, and how will readers use this book?

The text may be conveniently divided into four parts. The initial portion consists of four chapters: an introductory general chapter followed by single survey chapters on epidemiology, clinical presentation of ischaemic and transient ischaemic strokes, and imaging and laboratory evaluation of these patients. The second portion of the book consists of five descriptive chapters: four concern different stroke subtypes—atherosclerotic diseases, non-atherosclerotic vasculopathies, cardiac sources of embolism, and prothrombotic states; the fifth chapter considers ischaemic strokes in the young. The final five chapters discuss medical therapy, surgical therapy, acute management of patients with ischaemic stroke, and hospital management and rehabilitation. The management section, although consisting of only five chapters, makes up 245 pages, nearly half of the 575 pages of the book.

The book has some attractive features that make it very user friendly. It is well organised. There is a detailed outline at the beginning of the book and at the beginning of each chapter. Furthermore, there are clear bold subheadings and a detailed index. These features make it quite easy to locate desired information. Tables are sprinkled amply throughout and the tables succinctly summarise key points. The book is very heavily referenced and the references are up to date. There are ample figures that illustrate well the main disorders and the main diagnostic tools. A unique feature is the inclusion of clear diagrams and figures of echocardiograms. Cardiac investigations are not usually covered nearly as well in monographs about stroke.

The most useful portion of the book is the section on management of patients with ischaemic stroke. This was the core of the predecessor of this book. Treatment discussion is practical, detailed, evidence based, and up to date. The chapter on management of patients with acute ischaemic stroke is especially well done and will be quite useful for non-neurologists and non-stroke neurologists who lead stroke treatment in hospitals and stroke units. The chapters on clinical presentation and stroke aetiologies are less successful. Except for coverage of cardiac investigations and prothrombotic states, these chapters are rather brief and general, and serve only as introductions to the subjects discussed. In the non-management chapters, the authors seek to cover the waterfront and at least mention most things neophytes and non-stroke experts would want to look up. These non-management chapters are covered much better in other texts in other chapters. The treatment to cover all topics means that some are very scantily considered. The sections on vertebral artery disease, cerebellar infarction, and lacunar infarction are extremely brief. Many of the non-atherosclerotic conditions and cardioembolic sources are mentioned only in brief pithy paragraphs. Non-stroke experts would derive mostly from the last two sections of the book and at the beginning of each chapter.

Furthermore, there are clear bold subheadings and at the beginning of each chapter. The layout of the text the styles vary. The book is divided into eight main parts: basic science, assessment of channel function (in vitro and in vivo), genetic and acquired neuromuscular channel disorders, central nervous system disorders, toxin induced channel disorders, and potential channel disorders. Recent genetic discoveries indicate that proximal myotonnic myopathy and Schwartz-Jampel have in fact both bitten the dust as potential channelopathies! I found the chapters on the central nervous system disorders especially readable although already out of date in what is such a rapidly expanding area.

This is one of the first texts on this subject and I can recommend it to interested neurologists and neuroscientists.

Michael Hanna

Disorders of voluntary muscle, 7th edn


It is estimated that at least one in 500 people will be affected by specific genetic or other lifelong neuromuscular disorders. Inevitably
Several of the dystrophies, congenital myopathies, and, of course, the inflammatory myopathies are covered in some detail, each in separate sections. These are, generally speaking, up to date and provide, in particular, a good account of the recent advances in the molecular genetics, particularly of the dystrophies. The section on mitochondrial disorders is also comprehensive and provides a useful algorithm for assessment of patients with possible mitochondrial disease. It is the section on the inflammatory myopathies that will probably be most used by generalists, including both neurologists and rheumatologists. The section written by Dalakkas and Karpi is excellent for its comprehensive overview of the clinical, morphological, aetiological, and therapeutic aspects of these disorders. In particular, the discussion of the involvement of muscle in other inflammatory disorders is helpful. My only suggestion might have been an algorithm to help guide clinicians in the treatment of these disorders.

Genetic counselling in muscle diseases has now become a critically important area. Therefore, the section on this topic is very welcome. This sets out clearly the approach that clinicians should take to achieving a diagnosis and to counselling patients and relatives with the various types of inherited muscle disease. I imagine that this section in particular will find its way in some easily accessible form into the clinic drawer.

Finally, the last chapter deals with practical management issues in patients with muscle disease. This is clearly a very important area for patients who sadly often progress inexorably and require an increasing degree of help from carers and the medical profession as each year passes. In addition, the involvement of muscle in other inflammatory disorders. In particular, the discussion of the involvement of muscle in other inflammatory disorders is helpful. My only suggestion might have been an algorithm to help guide clinicians in the treatment of these disorders.

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Neurological eponyms


I enjoyed this book. It is one to delve into rather formally. It appears to have had a rather long gestation since the introduction is dated September 1999. The book is separated into five sections though at times the inclusion of a particular chapter in a particular section seems somewhat arbitrary. The editors have aimed for a uniformity of approach in which a brief historical survey is followed by a resume of the original description and then a setting of that description in a modern context. Inevitably the quality and interest of the contributions vary considerably. The chapters are well illustrated with both portraits of the person and, where relevant, illustrations from original descriptions. In general the editing has been thorough though curiously the chapter on Creutzfeldt-Jakob disease ends with a paragraph covering data that had been previously discussed in the middle of the text. Some authors chose not to question the appropriateness of the attribution of a particular syndrome or sign to a particular person; others do so sometimes amusingly as, for example, in the essay on Horner and William Goodyear on Horner's syndrome. There is little to quibble with in terms of the attributions, though why on earth cluster headache is entitled Horton's syndrome is not entirely clear to this reviewer. Although Horton himself had the temerity to suggest that the specific type of headache he described in 1899 had not been described adequately in the literature, he clearly had not read Wilfred Harris's contributions published in Neuritis and neuralgia in 1926 and later in The facial neuralgias in 1937. Harris described virtually all the characteristic features of cluster headache including distribution, periodicity, duration, frequency, presence of conjunctival injection and lacrimation, the sometimes associated Horner's syndrome, and the response to subcutaneous ergotamine. So much for a headache that had not been described adequately in the literature.

My only concern about this book is that the publishers, who seem now to be publishing as frequently from New York as from Oxford, seem to have acquired a taste for American spelling. Perhaps they need a visit down the road at Oxford to the OED.

David Perkin

Arachnoiditis: the silent epidemic


This book provides a comprehensive analysis, and comments on a condition we hope will be significantly reduced in incidence with new immunosuppressors. It provides an extensive bibliography providing reference on the views expressed, the likely multifactorial aetiological factors responsible for the development of a very disabling combination of signs and symptoms, and management strategies. The earlier chapters provide a historical perspective together with relevant anatomical, pathological, and physiological information, which will be useful to the reader while reading the later chapters. Although the book discusses predominantly the spinal arachnoiditis, it also covers important cranial subdivisions of the condition, in addition to associated conditions such as syringomyelia. There is an interesting section on questionable causes of arachnoiditis, which are very relevant because the previously predominant mode of entry, injection of foreign materials into the intrathecal compartment of the spine for diagnostic and therapeutic purposes—are no longer used or are regarded with circumspection. The final sections relate to the thorny question of diagnosis, which is extremely difficult, and to the limited treatment options available. Arachnoiditis is a condition that would be better prevented than treated. Unfortunately, the prognosis remains bleak for these patients but the management strategies in dealing with multiple concerns faced by such patients are well described. The senior author is to be congratulated on producing a single volume, based on some eight thousand references, and his undoubted unique experience of dealing with hundreds of such cases, which is a unique contribution to our body of knowledge.

It is salutary reading for some of the more senior members of our profession and will provide guidance to the younger members. It is a useful book for anyone treating patients with this awful affliction and it can provide guidance to those involved in dealing with patient complaints or litigation. The book provides both philosophical and scientific viewpoints.

J Van Dellen

Texture of the nervous system of man and the vertebrates, volume II


This is the second of three projected volumes that present for the first time in English one of the great classics of microscopical anatomy: Santiago Ramón y Cajal's Texture of the nervous system, which first appeared in Spanish in 1904. The Texture and Sherrington's integrative action of the nervous system, which appeared in 1906, are the fundamental works from which modern neurological science grew. The editor, Pedro Pasik, was one of the few who could have translated only the original Spanish and in the somewhat enlarged French edition of 1911, reprinted in 1952.

This new edition is important, not only because it makes Ramón y Cajal's contribution widely accessible, but also because the translators have gone back to the original illustrations, which are preserved in the Museum of the Instituto Cajal in Madrid. The high quality of the paper compared with that of earlier editions means that much detail is now visible that was formerly obscure. This is well shown by comparing the section of the medulla and cerebellum in figure 238 in the present volume with figure 78 in volume II of the French edition: the beautiful cellular detail is simply not visible in the latter.

Modern investigators are further in the debt of the translators for the many illustrations provided and (almost always) checked. The full references cited by Cajal, correcting errors that had escaped his attention, and annotating the text sparingly but helpfully when modern research had clarified issues that remained unclear to him. The book is beautifully produced and pleasant to hold in the hand.

Ramón y Cajal's work is central to neurological research today as it was century ago. The translators and publishers deserve our gratitude for bringing this essential work to a new generation of readers.

W I McDonald

Clinical evaluation and management of spasticity


This is a useful and interesting book. It is increasingly recognised that several treatment strategies can be beneficial in the management of spasticity, particularly using more recent drugs such as tizanidine and botulinum toxin. The book is a comprehensive review of the subject. No important topics are missed although the length and complexity of the chapters vary to a significant degree.

The book opens with a brief chapter on the physiology and pharmacology of spasticity. Although the book is targeted towards a clinical audience, and as such is a practical textbook, it is a pity that this opening chapter is so brief with regard to the neurophysiology of spasticity. An understanding of the underlying principles is important for logical treatment. Alex Dromerick produces a good chapter covering the clinical features of spasticity and a brief resume of complications. This is followed by an excellent chapter on the measurement of spasticity by David Good, which I found to be one of the most useful summaries of this field that I have read for some time. My major disappointment in the book is the brevity of the following chapter on physical and occupational approaches. The involvement of a neurological physiotherapist in the management of spasticity is vital and while this chapter is thorough it is too brief and fails to do justice to the key involvement of a physiotherapist in the spasticity team. This defect is partially overcome with an excellent subsequent chapter on orthotic management, which is a very clear and useful overview of an increasingly complex subject. The standard pharmacological interventions (baclofen, tizanidine, dantrolene, and the benzodiazepines) are thoroughly covered in the ensuing chapters with an additional brief chapter on alternative pharmacological therapies. Nerve blocks, botulinum toxin, and intrathecal medications are adequately covered. The chapter by Mary Keenan and Patrick Nicholas on orthopaedic interventions for the management of limb deformities in spasticity is the best chapter on this subject I have ever read and certainly should be compulsory reading for the physician who must need to refer to surgical colleagues for the management of complex and drug resistant spasticity.

The problem with these early chapters is that they lack an overall strategic approach to the patient with spasticity. The editors have tried to correct this problem with the last four chapters in the book, which give individual views of the management of spasticity in children with cerebral palsy and in adults with multiple sclerosis, traumatic brain injury, and spinal cord injury. These are useful chapters that bring the rest of the book together, although there is some rather unavoidable repetition. A few illustrative case histories might have been useful in this section.

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Overall this is a thorough, reasonably comprehensive, well referenced, and up to date textbook, which can be recommended to the multidisciplinary spasticity team and is a useful reference for any neurologist.

Michael Barnes

Autoantibodies in neurological diseases


Antineuronal antibodies were initially described 40 years ago and since then many autoantibodies have been discovered and characterised. Despite this, there is a limited number of texts devoted to the subject of autoantibodies in neurological diseases. Even less common are books that describe autoantibodies and clinical-immunological associations in a manner useful to both clinicians and investigators. This book fills the void. Although the title evokes a laundry list of antibodies this edition offers an even balance between clinical descriptions, immunological mechanisms, and therapeutic implications. The inevitable overlap of topics in a multi-authored book is kept to minimum. An introductory chapter on techniques used for measuring and evaluating the pathogenic role of autoantibodies will be useful for clinicians not directly involved in laboratory research. Subsequent chapters comprehensively cover disorders of the neuromuscular junction and peripheral nerve and less extensively disorders of the central nervous system associated either with autoantibodies or with other evidence of autoimmunity. Among the latter are chapters on autoantibodies and epilepsy and vasculitis of the central nervous system, topics rarely encountered in other texts. Two chapters on autoimmunity and pregnancy, particularly in association with myasthenia gravis, nicely discuss the effects of immunity on the embryo and newborn. With the exception of disorders associated with antibodies to gangliosides that are not discussed, descriptions of most of the recently described paraneoplastic and non-cancer related autoantibodies, as well as possible pathogenic mechanisms, are up to date and clear. A chapter on the ontogeny of skeletal muscle cells, although well written, is out of place in this text. The book is well edited and illustrated and the references are thorough. The focus of the text is weighted towards disorders of the peripheral nervous system, likely reflecting the more extensive literature on these disorders. Clinicians and basic investigators in neurology and immunology will find this book an excellent resource.

Joseph Dalmau

CORRECTIONS


Single exponential function was erroneously used for the calculation of figure 2. The correct figure 2 is reproduced below, which shows the predicted probability of recurrent TIA and stroke as calculated from the cumulative underlying hazard and the prognostic index (mean values of co-variables, and number of embolic signals) by double exponential function.


Table 2 Adverse events (%) according to FDA and EMEA standards.

<table>
<thead>
<tr>
<th>Adverse reaction* (FDA)</th>
<th>Undesirable effects† (EMEA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levetiracetam (n=769)</td>
<td>Placebo (n=439)</td>
</tr>
<tr>
<td>Levetiracetam (n=672)</td>
<td>Placebo (n=351)</td>
</tr>
<tr>
<td>Somnolence 15</td>
<td>8</td>
</tr>
<tr>
<td>14</td>
<td>8</td>
</tr>
<tr>
<td>Aesthesia 15</td>
<td>9</td>
</tr>
<tr>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>Dizziness 9</td>
<td>4</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Infection 13</td>
<td>8</td>
</tr>
<tr>
<td>13</td>
<td>8</td>
</tr>
</tbody>
</table>

*Adverse reaction: any event reported during clinical trial; FDA, Food and Drug Administration;
†undesirable effect: all adverse events at least possibly related to the study drug; EMEA, European Medicinal Evaluation Agency.

Note: Adverse reactions and undesirable effects are derived from three efficacy and one safety, double blind placebo controlled trials. Patient numbers differ because the FDA included the crossover part of the study in the analysis, and some of these patients were counted twice.

W I McDonald

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