

PostScript

CORRESPONDENCE

Benefit of folic acid supplementation in parkinsonian patients treated with levodopa

We read with interest the recent excellent review by Reynolds on the role of folic acid and the risks and benefits of its supplementation in the nervous system.¹ It emphasises the beneficial importance of folate on the numerous methylation processes in combination with S-adenosylmethionine (SAM), which donates its methyl group to prevent hyperhomocysteinaemia.¹ However SAM deficiency, which is associated with, for example, cognitive decline and/or mood disturbances, and increased total homocysteine levels, which support onset of vascular disease, may also be caused by drugs, for example, levodopa.^{2,3} Levodopa is administered with dopa decarboxylase inhibitors (DDI) to prevent its peripheral degradation. This increases conversion of levodopa to 3-O-methyldopa (3-OMD) by the ubiquitous enzyme catechol-O-methyltransferase (COMT) in blood, peripheral tissues and in nigrostriatal neurons.^{2,3} COMT requires Mg²⁺ as cofactor and SAM as methyl donor. Thus O-methylation of levodopa to 3-OMD is associated with conversion of SAM to S-adenosylhomocysteine and subsequently homocysteine.^{2,3} We already demonstrated this association between homocysteine, SAM and 3-OMD in treated Parkinson's disease (PD) patients,^{2,3} who often suffer from depression and bradyphrenia in the course of the disease and show an increased mortality risk of vascular disease.⁴ The objective of our follow up study^{2,3} was to determine total plasma homocysteine in 212 levodopa treated and 29 previously untreated PD patients and 110 controls. Standardised measurement of total homocysteine plasma concentrations with high performance liquid chromatography was only performed in subjects with no metabolic disturbances, like diabetes mellitus, hypertension, reduced levels of vitamin B6, cobalamin and/or folic acid or neurological diseases other than PD. Each PD patient fasted and was withdrawn from drug treatment for at least 12 hours before taking of blood samples in the morning. All participants gave informed consent, the local ethical committee approved this study. Homocysteine levels were significantly (analysis of covariance $F_{(df_2, df_{346})} = 17.5, p = 5.9E-08$; post hoc analysis (Tukey's HSD test): levodopa treated PD patients compared with controls: $p = 2.2E-05$, previously untreated compared with levodopa treated PD patients: $p = 0.005$; previously untreated PD patients compared with controls: $p = 0.92$) increased in levodopa/DDI treated PD patients (17.3 (8.2) $\mu\text{mol/l}$ (mean (SD)) compared with previously untreated PD patients (11.4 (5.8) $\mu\text{mol/l}$) and controls (12.2 (5.5) $\mu\text{mol/l}$). There was no significant impact of covariates age, sex, daily levodopa dose, and Hoehn and Yahr Stage (data not shown). An effective therapeutic approach for reduction of homocysteine levels is additional folic acid supplementation, as folic acid and cobalamin catalyse and increase metabolism of homocysteine to

methionine,^{2,3} or, hypothetically, application of peripherally acting COMT inhibitors as adjunct to levodopa/DDI treatment.³ Methionine acts in combination with pyridoxal phosphate or S-methyl- α -keto-butyric acid as a strong scavenger of strong oxidants, which in turn induce endothelial dysfunction.⁵ Homocysteine induced endothelial dysfunction may further promote atherosclerotic disease in striatal cerebral vessels with subsequent onset of differential susceptibility to impaired energy metabolism, oxidative stress, and basal ganglia dysfunction.⁵ Endothelial response to homocysteine depends on the synthesis of nitric oxide.⁵ Exposure of the endothelium to homocysteine induces release of nitric oxide, a further excitotoxic compound under suspicion for the contribution of the ensuing neuronal degeneration in PD.^{2,3,5} Nitric oxide and reduced methionine levels support increased appearance of free radicals, in particular superoxide. Superoxide and nitric oxide generate peroxynitrite.^{2,3,5} Peroxynitrite mediates tyrosine nitration, which further impairs activity of a variety of enzymes and inactivates tyrosine kinases.^{2,3,5} These kinases are used by a variety of neuroprotective and neurorestorative growth factors, for instance glial cell line derived neurotrophic factor.^{2,3} Accordingly in vitro trials showed neurotoxic effects of homocysteine and its oxidation product homocysteic acid on various types of cultured human neuronal cell lines and their excitotoxic activity partially via N-methyl-D-aspartate agonist and mimicking properties.⁵ In conclusion, additional folic acid supplementation with concomitant lowering of total homocysteine levels in levodopa/DDI treated PD patients will hypothetically reduce progress of PD and increased hazard ratios for both ischaemic heart—and cerebrovascular disease in treated PD patients.⁴

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Dysphagia due to Chiari I malformation mimicking ALS

We read with interest the article by Paulig and Prosiegl¹ concerning a patient initially diag-

nosed with amyotrophic lateral sclerosis (ALS), who had suffered from progressive swallowing difficulties, fibrillations, and tongue atrophy for a year, in the context of a flaccid bulbar palsy. Brain and spinal MRI showed a Chiari I malformation with descent of the cerebellar tonsils. The authors accompany their article with an illustration of the patient, showing extensive bilateral paresis and atrophy of the tongue. The article notes the importance of carrying out an MRI examination on those patients who show bulbar palsy mimicking bulbar onset type ALS in order to rule out Chiari I malformation.

Chiari I malformation has also recently been reported as being associated with bulbar onset ALS.² Nevertheless, the marked improvement in the dysphagia after neurosurgery suggests that Chiari I was the cause of the patient's bulbar palsy.

Dysphagia with predominant signs of lower motor neurone disease as the sole manifestation of adult Chiari I malformation is unusual.³ Pressure exerted by the cerebellar tonsils on the hypoglossal nuclei and other swallowing centres located in the medulla is hypothesised by the authors to be a main cause of the dysphagia.

The importance of the reported case was the appearance of tongue atrophy over a relatively short period of time. In the three patients with dysphagia as the sole manifestation of Chiari I reported to date, the complaint had been present for at least three and a half years and none of the patients had tongue atrophy.⁴⁻⁶

We would like to comment on the importance of asymmetry of the face and mouth. A detailed examination of the picture¹ shows deviation of the mandible to the right, suggesting that there was at least trigeminal nerve motor involvement. Another important clinical detail that was not mentioned is whether the patient had speech abnormalities. The muscles used in speech are basically the same as those used in swallowing (innervated by the hypoglossal, vagal, glossopharyngeal, facial, and trigeminal motor cranial nerves).⁷

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Author's reply

We would like to thank Dr Gamez *et al* for their interest in our case report and their helpful comments on it.

They emphasise the appearance of the tongue atrophy in our patient, which had developed over a short period of time and was not present in three other case reports where dysphagia was the sole manifestation of a Chiari I malformation. Indeed, in those patients signs of lower motor neurone damage were not reported. Obviously, dysphagia as a manifestation of a Chiari malformation can develop from different mechanisms—“central” damage to the medullary pattern generators for swallowing and/or to the (supranuclear) descending corticobulbar pathways in the lower brain stem (that is, dysphagia without tongue atrophy); and “peripheral” damage to the motor neurones of the hypoglossal nerves sited in the dorsal medulla oblongata, possibly accompanied by central damage mentioned above (that is, dysphagia with tongue atrophy).

In our paper our main aim was to emphasise the second mechanism, which clinically mimics a bulbar onset of ALS and may lead to a wrong diagnosis. The period of one year after the first onset of dysphagic symptoms may appear relatively short with regard to the marked tongue atrophy. However, it is very likely that the chronic process of pressure in the Chiari malformation triggers neuronal destruction in the hypoglossal nuclei preceding the clinical manifestation of dysphagia due to compensation of incomplete axonal loss.

With regard to asymmetry of the face, which was very well identified in our picture by Gamez and his colleagues, there were no clinical signs suggesting involvement of the trigeminal motor nucleus. The latter is situated in the mid portion of the pons, and pressure exerted on pontine structures would have been expected to cause other signs of involvement of this part of the brain stem, but this was not the case. We would prefer an alternative explanation—that is that the patient had difficulty in protruding her tongue, which was asymmetrically impaired (right more than left, as can be seen in the picture) and she tried to overcome this by (unconscious) asymmetrical coactivation of the jaw muscles.

Concerning the question of speech abnormalities raised by Dr Gamez, our patient did indeed have slightly slurred speech, another symptom that may be misinterpreted as a sign of ALS.

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High dose intravenous immune globulin in the treatment of hereditary recurrent brachial plexus neuropathy

We read with interest the article by Klein *et al* providing pathological evidence that the neuropathic attacks in hereditary brachial plexus neuropathy (HBPN) are secondary to

an inflammatory process. As a possible pathogenetic mechanism the authors suggest altered immune modulation. In the absence of controlled clinical trials they treated patients with intravenous methyl prednisolone. This treatment—in their experience—relieved the symptoms, particularly the pain, for a brief time, but as they tapered the corticosteroid dose the signs and symptoms reappeared. The authors concluded that in some cases of HBPN an inflammatory multifocal response arising from an immune dysfunction in the brachial plexus and upper limb nerves causes nerve abnormalities and axonal degeneration. Treatments based on immune modulation may therefore be useful in the management of HBPN.

To further support the immunological pathogenesis we describe a 13 year old girl who since childhood had suffered from recurrent episodes of severe asymmetric pain and weakness of the shoulder and arm involving the same as well as the opposite side. Her father had similar attacks and genetic testing for hereditary neuropathy with liability to pressure palsy was negative. At the age of 4 years the girl experienced severe left shoulder pain that lasted for 20 days and was treated with corticosteroids. Three years later, a left deltoid muscle hypotrophy was still present. At the age of 11 years she had a similar episode associated with marked weakness of left upper limb and was treated with non-steroid anti-inflammatory drugs. The shoulder pain improved in four weeks but muscle strength recovered only after about four months. We observed the girl during a further episode that occurred in July 2002: she complained of severe neck pain that lasted for one day then spontaneously disappeared. One week later she suddenly experienced severe neck and right shoulder pain and mild weakness of the right limb girdle. The neurological examination disclosed bilateral hypotrophy and weakness of the deltoids, secondary to previous episodes, and mild weakness of right subscapular and both spinate muscles. Tendon jerks were absent in the upper limbs. Magnetic resonance imaging (MRI) of the cervical spinal cord yielded normal findings. MRI scans of the brachial plexus and shoulder muscles showed mild abnormalities in the supraspinatus muscle. The cerebrospinal fluid examination disclosed 38 mononuclear cells/mm³ with normal glucose and proteins; oligoclonal bands were absent. Neurophysiological tests showed a mild reduction in the amplitude of the compound motor action potential elicited by both axillary and musculocutaneous nerve; the right median nerve sensory action potential was abnormally small and the F wave was delayed. Needle EMG found no denervation. The standard neuroimmunological screening (anti-GM1, -GM2, -GD1a, -GD1b, -sulfatide, -MAG IgM antibodies) was normal. Because the previous episode failed to respond to corticosteroid treatment, and considering the severity of the episode, the lengthy period needed for a partial recovery in previous episodes, the severity of the patient's pain, her young age, and the muscular atrophy, we started treatment with intravenous immunoglobulin (IG Vena N IV, Sclavo, Siena, Italy, 0.4 g/kg/day for five days). After two days of IVIg treatment the patient reported a dramatic reduction of pain and a progressive improvement in muscle strength. One week after the onset she achieved a complete clinical recovery and no muscle atrophy developed. Two months after the treatment stopped she is still asymptomatic.

The case reported here has two potentially important implications. Firstly, the epineural

mononuclear cell infiltrates observed by Klein *et al* in nerve biopsy specimens, the presence of mononuclear cells in our patient's CSF, and her response to IVIg together strongly support an immune mediated inflammation in the pathogenesis of HBPN. Among others, possible mechanisms underlying the efficacy of IVIg in HBPN include attenuation of complement mediated damage, induction of anti-inflammatory cytokines, inhibition of endothelial cell activation, regulation of helper T cell cytokine production, and neutralisation of T cell superantigens.² Secondly, individual episodes of HBPN are undistinguishable from Parsonage-Turner syndrome and pain can be very severe for weeks. Complete recovery from each episode is frequent although cumulative disability may develop.³ Although Klein *et al* proposed corticosteroid treatment, others report that this treatment produces no definite improvement.⁴ Also our patient in a previous episode had no benefit from corticosteroid treatment. The rapid benefit and the long term efficacy of IVIg in our patient suggest that episodes may be safely and effectively treated with this drug. To our knowledge this is the first report of a patient treated with IVIg. The encouraging results prompt controlled therapeutic trials at least for patients with severe forms of HBPN and, possibly even for those with Parsonage-Turner syndrome.

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Authors' reply

The patient described by Ardolino and colleagues provides an example of a hereditary episodic illness of the upper extremities, which may have responded favourably to IVIg. The patient's young age of onset, tendency to recurrent events, and a reported family history would all support the diagnosis of hereditary brachial plexus neuropathy (HBPN). We note, however, the unusual feature of an increase in the CSF mononuclear cells (38/mm³), and therefore request further information; that is, concordant exacerbating infection or immunisation and precise timing of CSF examination given that IVIg may increase CSF white cell blood count. It would also be helpful to know more details of the EMG needle examination in support of the multifocal neurogenic axonal process characteristic of this disorder. Her father was reported to have the disorder, but details of his history are not provided. Lastly, because they are commenting on the absence of response to corticosteroids the dose and route used in the previous episode should be specified. We

noted in our patients that low dose oral corticosteroids were not as effective as high dose 1.0 g/treatment IV methylprednisolone.¹ Because our pathological studies of nerve during episodes showed features characteristic of microvasculitis we elected to use methylprednisolone.

As with all anecdotal reports their patient's improvements must be interpreted cautiously. This is especially true in disorders such as HBPN where individual episodes have a considerably varied course.² The morbidity of this disorder, the pathological observations, and the results of open trials with IV methylprednisolone and possibly IVIg warrant clinical trials. It will be necessary to carefully distinguish inherited from cryptogenic variants to ensure that a potentially non-responsive group does not interfere with recognition of a responding group. We believe this condition is more common than appreciated and therefore clinical trials are feasible. Knowing if such treatments are beneficial is important as correction of the underlying gene(s) defect is currently not possible.

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BOOK REVIEWS

Autonomic failure. A textbook of clinical disorders of the autonomic nervous system, 4th edition

Edited by Christopher J Mathias and Sir Roger Bannister (Pp 562, £70.00). Published by Oxford University Press, Oxford, 2002. ISBN 0 19 262850 X

The concept of autonomic disorders or dysfunction is an uncomfortable one for neurologists and as such remains poorly understood and managed within neurology. Part of this problem is because autonomic dysfunction spans several specialties of medicine, is largely based on good understanding of basic human physiology and anatomy, and interpretation of autonomic function testing is difficult. The 4th edition of the well known textbook of autonomic dysfunction, "Autonomic failure. A textbook of clinical disorders of the autonomic nervous system" aims to do this and much more. A huge collection of internationally renowned authorities contribute to this book.

However, the thread of continuity is sometimes lost or repeated in this book. For example, it would be difficult to find a "user friendly" table/diagram of how to interpret blood pressure and heart rate changes following head up tilting. There is considerable repetition of information. Chapters on autonomic and neurohumoral control of cerebral circulation is followed in part II of the book by a

chapter on autoregulation and autonomic control of cerebral circulation. Similarly, most neurologists would find chapters on cardiovascular autonomic regulation and control of blood pressure and circulation in man rather difficult to understand. It is also questionable how much of the information contained within "Clinical autonomic testing" (Part III) is clinically applicable. Most investigation related chapters such as chapters 21 and 24 appear to be largely research based and information in these and other chapters shifts between research studies and clinically established observations. However, chapters on postprandial hypotension, sleep dysfunction, and sudomotor function are outstanding, although the lack of mention of postprandial hypotension and its clinical significance in Parkinson's disease is surprising.

Part IV of the book concentrates on the relatively common autonomic syndrome of multiple system atrophy (MSA) and the exceedingly rare pure autonomic failure (Part IV). Bannister and Mathias contribute to a most useful and clinically relevant chapter on clinical features and evaluation of the primary chronic autonomic failure syndromes. A more detailed discussion on the rather controversial notion of Parkinson's disease and autonomic failure and its differentiation from MSA with manifest dysautonomia is lacking and would have been useful. There is also confusion in terminology. According to the recent consensus committee definition, MSA is now subdivided in MSA-P and MSA-C subtypes, older terms such as striatonigral degeneration and olivopontocerebellar atrophy being obsolete. However, such terms keep on appearing both in the chapter by Bannister and Mathias and also in the chapter by S Daniel on neuropathology, which is nevertheless very informative. The following chapter by Matthews revisits much of the information already contained in previous sections of the book, such as a repetitive and confusing classification of autonomic dysfunction followed by a detailed neuropathological description of changes in ganglia and preganglionic neurones in dysautonomia. It seems this chapter is possibly better suited in the basic pathology introductory section of the book. The continuity and flow of this section is thus hampered by the order of chapters. Chapters detailing complex neuropathology, largely of research interest, follow chapters on clinically relevant tests of autonomic dysfunction. There is an excellent and clinically relevant chapter on management of postural hypotension, a clinical issue that perplexes a large number of neurologists and physicians for the care of the elderly. The latter chapter could have been enhanced by the inclusion of a flow chart outlining a step by step guide to treatment of postural hypotension, progressing from "first line treatment" to adjunctive treatment strategies. Furthermore, in the current climate of clinical governance and evidence based medicine, inclusion of evidence base for the use of the various treatment strategies mentioned in this chapter would have been useful. There are other omissions, such as the lack of mention of cardiac SPECT studies using MIBG in MSA and Parkinson's disease, a technique that is increasingly being recognised as an important tool to help differentiate between early Parkinson's disease and MSA.

Part V of the book concentrates on peripheral autonomic neuropathies and there is an excellent chapter on diabetic autonomic failure. However, then a chapter is devoted to dopamine beta hydroxylase deficiency, which resembles a series of case reports of a

condition few will encounter. A shorter, clinically relevant account of this condition could easily be accommodated under genetic causes of dysautonomia. In part VI, other important aspects of dysautonomia are discussed, notably syncope and ageing related changes. A simple diagram/table of interpretation of various haemodynamic changes following head-up tilting test would have been very useful for most neurologists who use this test clinically. In clinical practice, syncope is often confused with epileptic seizures, however, surprisingly little is mentioned about clinical differentiation and aspects of syncope and seizure. Once again, chapters on hypertension and cardiac failure overlap with previous ones and are of questionable clinical significance.

The book is clearly written, although sometimes the chapters vary in preparation, practical value, and clarity. The quality of illustrations is high and there are few, if any, frank errors. In summary, this is an essential book for its target audience and would be useful in most medical libraries and to researchers working in the area of autonomic dysfunction.

Ray Chaudhuri

Functional rehabilitation in neurosurgery and neurotraumatology

Edited by K R H von Wild (Pp 147, €76). Published by Springer-Verlag Wien, New York, 2002. ISBN 3 211 83739 6

This volume is *Acta Neurochirurgica* (Suppl 79), archiving the proceedings of the First International Conference of Neurosurgical Rehabilitation, held in Münster in 2000, together with some abstracts presented at a Conference on Early Rehabilitation held in Maribor in 2001. It is of some interest.

As is usually the case in collations of this sort, the contributions cover a wide range of aspects of acute and post-acute rehabilitation of neurosurgical and neurotrauma patients. Some broader topics covered include service organisation, outcome predictors, uniform dataset development, long term psychosocial outcomes, and problems in healthcare management. These chapters are necessarily short and sketchy, and largely serve to highlight the gaps in the evidence base, as well as the gaps in the service coverage! Nevertheless, there is an undercurrent theme here, to the effect that brain injury rehabilitation services are a hot potato in many countries. The reason for this is that their cost is potentially vast. Adequate brain injury rehabilitation is a heavy, prolonged consumer of skilled professional time. Patient numbers are much larger than those for spinal injury, which forms the closest analogy in the health service. To set up a comprehensive regional brain injury rehabilitation service, comparable to that for spinal injury, would be an enormous commitment, which public and private health providers the world over have been shamefully unwilling to fulfill.

Perhaps the more readable contributions, however, are that briefly outline the current status of specific interventions, such as the neurosurgical management of pain, botulinum toxin treatment for upper and lower limb spasticity, or sensory stimulation programmes in PVS.

There are several chapters on various specialist emergent forms of therapeutic and functional electrical stimulation, such as

motor cortex stimulation for pain and movement disorder; deep-brain stimulation for pain; functional implanted stimulators for standing and walking in paraplegia; peroneal nerve stimulator implantation for central drop-foot; vagus nerve stimulation for epilepsy; and cochlear nucleus stimulation for deafness in NF2. Other contributions, such as that on BTXA for tension headache, are rather far removed from what we would recognise as the field of rehabilitation.

David Rushton

Radiosurgery, volume 4

Edited by D Kondziolka, M McDermott, J Rgis, R Smee, and K Takakura (Pp 294, EUR196.50). Published by Karger, Basel, 2002. ISBN 3-8055-7365-0

Radiosurgery is a periodical for papers from the biannual meetings of the International Stereotactic Radiosurgical Society. Volume 4 of the periodical includes selected reports presented at the 5th biannual meeting. The publication is divided into sections on clinical subjects and contributions to physics and radiobiology. There are seven papers on intracranial vascular malformations, five on benign and seven on malignant intracranial tumours, two papers deal with radiosurgery for functional disorders, and eight are devoted to physics and radiobiology. The physics papers deal mainly with quality assurance issues of radiosurgery and are of interest to physicists working in the field.

One paper describes how 3D ultrasound images can be used to realise stereotactic radiation of extracranial targets where movements create a problem. A brief report on the histology of thalamic lesions in the baboon after stereotactic radiosurgery is the only contribution to radiobiology. Two thirds of the book are clinical papers of varying quality. Encouraging results of radiosurgical treatment for arteriovenous malformations are again presented, including a paper specifically devoted to treatment of larger malformations, which until now have eluded this technique. Another paper supports the value of gamma knife surgery for brainstem cavernous angiomas. Three chapters present positive results of gamma knife surgery for hormone secreting pituitary adenomas and the role of radiosurgery and stereotactic radiotherapy in the management of pituitary adenomas are reviewed in another chapter. The section on malignant tumours includes a paper describing the integration of metabolic data from stereotactic PET scanning in dosimetry planning. In the section on radiosurgery for functional disorders an update on the results of gamma knife surgery for mesial temporal lobe epilepsy is given. It is suggested that a therapeutic effect can be achieved even with subnecrotic radiation doses.

The book is of interest to persons working in the field of radiosurgery and is of limited interest also to neurosurgeons, neurologists, and neuro-oncologists who want to keep up with developments in the field.

Christer Lindquist

Textbook of neuropsychiatry and clinical neurosciences, 4th edition

Edited by Stuart Yudofsky and Robert Hales (Pp 1375 \$219.00) Published by the American Psychiatric Publishing, Washington DC, 2002. ISBN 1 58562 004 1

“Clinical neurosciences” has been added to the title of this well known textbook of neuropsychiatry to acknowledge that, if they are to be effective, clinicians need to be conversant with advances in neurosciences. With over 1300 pages, it is a real heavyweight. Physically it’s the same size as Lishman’s most recent edition of *Organic Psychiatry*. The editors realise that their book is likely to be compared with this classic, and suggest that their book is a dependable American Jeep in contrast to the elegant Rolls Royce of previous “grand European texts”.

They have been able to attract some very authoritative authors and have endeavoured to ensure that each chapter is complete in itself. This works well by and large, but does result in quite a lot of duplication and I could find no attempt to signpost the reader to other relevant parts of the text. The book aims to please quite a wide target audience, from medical students through to specialists. This makes for a book that is easy to read and well presented; plenty of figures, boxes and tables break up the text. But there are some lacunae: if you are looking for a reference book offering a comprehensive review of all aspects of neuropsychiatry then you may be left wanting. For example, I did not find it of much use when investigating the neuropsychiatric sequelae of viral encephalitis. The chapter on cerebrovascular disease was almost entirely limited to a discussion of stroke. As a result there is very little coverage of subarachnoid haemorrhage. I was also disappointed by the rather limited attempts to define the evidence base for some assertions.

There are some excellent review chapters. I particularly recommend “Bedside neuropsychiatry”, “Clinical imaging in neuropsychiatry”, and “The neuropsychological evaluation”; in fact almost all of the early chapters on principles of neuroscience and neuropsychiatric assessment. The last chapter will be invaluable for those of us interested in neuropsychiatric training. The book covers a very large ground to a very high standard. I have a great deal of confidence in the content.

Neurologists and psychiatrists will find it extremely useful; it is dependable, easy to access, and right up to date.

Simon Flemingier

Acquired damage to the developing brain—timing and causation

Edited by Wanley Squier (Pp 227, £95.00 hb). Published by Arnold, London, 2002. ISBN 0 340 75930 5

Brain damage is a major burden to the affected individuals, their families, and to society. When it occurs around the time of birth parents will often question the adequacy of clinical care and seek redress in the courts. This book discusses the causes and timing of neonatal brain injury and is therefore likely to be of great interest to clinicians caring for infants and children, and to parents, and members of the legal profession.

The first few chapters deal with the clinical features and management of cerebral palsy, the epidemiology, aetiology, and genetic causes. The definition of what constitutes cerebral palsy can be confusing, which is probably why the definition is repeated in several of the chapters. Neuroimaging, genetic, and metabolic studies have identified disorders that were previously considered under the umbrella term ‘cerebral palsy’. A recent consensus statement from European cerebral palsy registers is helpful. Even more problematic has been the study of the timing of cerebral injury and the causes of cerebral palsy. Current publications emphasise the importance of prenatal factors in the aetiology of cerebral palsy, and this view is repeated in the book. However, when recognisable developmental and metabolic conditions are excluded, most full term infants who develop encephalopathy after birth have suffered hypoxic ischaemic injury, and the chapters on pathophysiology and pathology deal mainly with this type of injury. The patterns of damage that occur at different developmental ages are clearly described and the illustrative plates are superb. In infants who survive brain injury, the aetiology and timing of the injury must be assessed by clinical examination and investigations. MRI is currently the key technique and this is well described in two chapters with the aid of several images. The final chapter discusses the legal considerations that determine the outcome of litigation and will be of interest to many clinicians.

In summary, this is a useful overview of brain damage in newborn infants. However, brain injury in the preterm is not discussed in sufficient detail and is mainly limited to the classical problems of haemorrhage and severe white matter injury, which are now less common. There is much repetition throughout the book and this gives the impression that the book is a collection of review articles rather than a cohesive account.

Denis Azzopardi