Hashimoto’s encephalopathy responding to plasmapheresis

A 47 year old man presented to the emergency department of our hospital. He was born in Uruguay, but had lived in Australia for many years and had not taken any medication. He had no relevant medical history or record of illicit drug use. He had a 2 week history of a coarse, postural tremor of the upper limbs and an unsteady gait and was brought to hospital after an unwatched fall at home. On arrival he was alert but ‘irritable’; shortly thereafter he had a generalised seizure, which was treated with intravenous diazepam and phenytoin. Several hours later he had failed to regain consciousness; he was breathing spontaneously, with roving eyes, absent oculo-cerebral reflexes, generalised hypotonia and hyporeflexia, bilateral extensor plantar responses, was afibrile, and had no neck stiffness or meningism. Angiography of the vertebral-basilar system was normal. Intravenous heparin was started, and later intravenous acyclovir. After extubation, he had ongoing tremor of the upper limbs and an unsteady gait and was brought to hospital for many years and had not thought he was as well as he had ever been. He presented again 3 weeks later with worsening tremor, exacerbated by exercise. He was able to dress and feed himself and converse in English. He was able to return to part time work as a cleaner. This clinical improvement was accompanied by a further decline in antibody concentrations (figure, point C). He remained well, with slowly rising antibody titres and no further seizures occurred. C-reactive protein was persistently elevated with epilepsyform activity; this in turn suggested a further underlying neurological condition. If it was, then it is a further indication of the unpredictable course and outcome of Hashimoto’s encephalopathy.

We thank Dr R Lindeman for his assistance with plasmapheresis.

P M BOERS

Institute of Neurological Sciences, Level 2, High Street Building Prince of Wales Hospital, Randwick, New South Wales 2031, Australia, and The University of New South Wales, Sydney, Australia

Correspondence to: Dr P Boers
PBoers@unsw.edu.au


Meningoencephalitis after streptokinase treatment

The mechanisms underlying allergic reactions to streptokinase treatment can be divided into three major groups: immediate IgE mediated (type I), immune complex deposition (type III), and antigen antibody mediated (type II). Apart from cerebral haemorrhage the only previously reported neurological complication of streptokinase therapy is the Guillan-Barré syndrome. We present a case of meningencephalitis after streptokinase therapy.

A 52 year old man presented with classic features of an acute anterior myocardial infarction. Treatment with aspirin and intravenous streptokinase was initiated. Fi-
Blood glucose measured simultaneously with CSF glucose. Brain CT, plasma glucose of 15.3 mmol/l, normal. Investigations included a normal muscle power, reflexes, and sensation were out of 10 (he failed to recall the date, current syndrome occurs some 10–14 days after stiffness, or skin rash, but he had a pyrexia of Y, lassie, an occipital headache of gradual onset, the streptokinase, he developed general malaise, an indistinct left opticis, mild dysarthria, and an expressive dysphasia. Muscle power, reflexes, and sensation were normal. Investigations included a normal brain CT, plasma glucose of 15.3 mmol/l, leucocytes 1012 cm3 (20.6 × 109/l) (79% neutrophils), otherwise normal routine biochemistry and haematology, electroencephalographic evidence of a diffuse encephalopathic process, and CSF values in keeping with an infective process (table, week 0). Treatment with broad spectrum intravenous antibiotics, intravenous acyclovir, and insulin was begun. Despite this he developed inappropriate thirst, required intravenous hydration and ventilatory support. Further investigations showed negative cultures of both blood and CSF, no serological evidence of a viral infection, raised C reactive protein to 17.9 mg/l, normal coagulation screen, normum angiotensin converting enzyme concentration, no serological evidence of syphilis, no CSF oligoclonal bands, and CSF values proved normal for a confusional state (table, week 2 and 4). A gradual recovery over 8 weeks was made and he was well enough for discharge, but he was left with disabling symptoms of urinary incontinence, depression, and cognitive dysfunction. Further outpatient investigations included brain MRI, which disclosed only a minor degree of cortical atrophy, a raised titre of GQ1b antibody, and a negative titre of GQ1b antibody. Further CSF findings and clinical features were in keeping with isolated central neurological involvement the cause of the meningoencephalitis was most likely autoimmune in origin and not vasculitic. Our patient is unique in that he had all three of the reported “allergic” reactions after streptokinase treatment; immediate, severe sickness-like, and autonomic. In future, meningoencephalitis occurring as a complication of streptokinase therapy should be borne in mind.

S T Wahid

Department of Diabetes and Endocrinology, South Tees Hospitals NHS Trust, South Cleveland Hospital, Middlesbrough, Cleveland, TS4 3BW, UK

D Lilic

Department of Clinical Immunology

P K Newman

Department of Neurology

Correspondence to: Dr S T Wahid


Atypical course of neuropathic Gaucher’s disease: follow up from early infancy until adulthood

Gaucher’s disease is caused by a deficiency in glucocerebrosidase which gives rise to the accumulation of glucosylceramide (glucocerebroside) in the lysosomes of cells mainly found in the reticuloendothelial system. Type 1, the chronic adult form, is the most frequent, and is characterised by splenomegaly, hepatomegaly, pancytopenia, and skeletal degeneration, but does not involve neurological manifestations. Type 2, also called acute neuropathic, is an early infantile form, usually terminating life in 1 or 2 years. Type 3 is a chronic form which affects the nervous system, usually in late childhood or adolescence. We report here the case of a patient with Gaucher’s disease who was diagnosed in early infancy (6 months) in a paediatric insti-

Cerebrospinal fluid changes during treatment

<table>
<thead>
<tr>
<th>Week 0</th>
<th>Week 2</th>
<th>Week 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF Protein (g/l)</td>
<td>0.98</td>
<td>0.87</td>
</tr>
<tr>
<td>CSF Leucocytes (×106/l)</td>
<td>170</td>
<td>94</td>
</tr>
<tr>
<td>CSF Lymphocytes (%)</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td>CSF Neutrophils (%)</td>
<td>60</td>
<td>0</td>
</tr>
<tr>
<td>CSF Glucose (mmol/l)</td>
<td>4.6</td>
<td>5.1</td>
</tr>
<tr>
<td>Blood glucose (mmol/l)*</td>
<td>11.8</td>
<td>9.8</td>
</tr>
</tbody>
</table>

*Blood glucose measured simultaneously with CSF glucose.
The treatment was started at the age of 27 by the cerebroside β glucosidase of placental origin alfaglucerase (Ceredase, Genzyme, Cambridge, MA, USA), with 60 Units/kg body weight, by intravenous perfusion every 2 weeks until the age of 31. After this period, alglucerase was replaced by the recombinant enzyme imiglucerase (Cerezyme, Genzyme, Cambridge, MA, USA) and the patient has been treated up to the present (age 34) with the same posology and an identical time interval. Thus the patient has been treated for 8 years so far.

The propositus was heterozygous for the L444P and the D409H mutations. Sequencing showed that the patient did not have other point mutations. His father carried the L444P mutation and his mother the D409H mutation (figure). Informed consent was obtained for genetic studies.

The treatment was well tolerated. No anti-bodies against either form of the enzyme were found. The asthenia rapidly disappeared. His spleen, still hypertrophied at the age of 28, was found to be normal (7.5 cm for the great axis) at the age of 31. The aggravation of the gait stopped. The ophthalmoplegia remained unchanged. The paroxystic dystonic manifestations disappeared. The tremor of the head and of the arms had also decreased in intensity. During this period, the only new medications were the substitutive enzymatic therapy and carbamazepine (600 mg/day). We are aware of the fact that the prescription of carbamazepine may in itself ameliorate paroxystic dystonic manifestations. No clonic attacks occurred. FA Hommes, ed. Tissue specific glycosphingolipids. Berlin: Springer Verlag, 1983 p. 225: 2/6. Conceptualisation was correct for precise tasks. Brain MRI was still normal except for a slight cortical atrophy. There was a normal concentration of thrombocytes: 110 000/mm3 thereafter. Acid phosphatases tested at the age of 28 were normal (2.7 Units). The patient and his family noted a great improvement in his behaviour and dependency.

In infancy, this patient presented with the apparent type 2 acute neuropsychic form. Although death usually occurs by 2 years of age in the infantile form, this patient is still alive, and able to lead a nearly normal life with a professional activity. In type 3 Gaucher’s disease, neurological signs develop between 6 and 15 years of age although there are some cases with earlier manifestations.

The number of mutations involved in Gaucher’s disease is great.11 The L444P mutation is often associated with a more severe neurological manifestation. Patients carrying the L444P mutation and the D409H mutation have been reported to develop a form of type 3 Gaucher’s disease in which the oculomotor signs are predominant and the visceral symptoms are discrete. This case differed significantly from these other cases.

In conclusion, there was a neurological form of Gaucher’s disease and could be evaluated over 3 decades. Before enzyme substitutive therapy, the patient and his family reported a progressive deterioration of his neurological state. When he was treated, visceral and haematological symptomatology became normal; and there was a stabilisation or even a slight improvement of his neurological symptoms as well as modification of mood and behaviour, allowing a better integration in social life. Thus some patients with Gaucher’s disease with early neuronopathic manifestation may have a benign course and profit considerably from enzyme supplementation.

We acknowledge Mrs Marri Verhoek for her skilful contribution. The follow up was performed in collaboration with the French Evaluation Committee for Treatment of Gaucher disease (CETG), who we also gratefully acknowledge. This work was possible through grant PHRC AOA 94033 from Assistance-Publique-Hôpitaux de Paris, and grants from the lysosomal disease association VML and the Caisse Nationale de Prévocance CNP.


Creutzfeldt-Jakob disease in a young person with valine homozygosity at codon 129: sporadic or variant?

To date there have been 52 reported cases of variant Creutzfeldt-Jakob disease (vCJD) in the United Kingdom. All cases that have undergone genetic investigation have been methionine homozygotes at codon 129 in the prion protein (PrP) gene. There has been speculation as to whether valine homozygosity or heterozygosity at codon 129 confers resistance to vCJD, delays clinical onset of disease,1 or may lead to a clinical syndrome distinct from cases of CJD described so far.2 Here we report on a young patient with CJD who was a valine homozygote at codon 129.

A previously well 27 year old electrical engineer complained that he had difficulty concentrating at work. His wife noticed that he had become more forgetful and increasingly agitated which she attributed to work. He was seen in December 1997 and at this stage appeared anxious and with communication difficulties in that he could understand what his wife was saying to him but could not understand anyone else. Neurological examination was otherwise unremarkable. Haematology and biochemistry, a cranial CT, and an EEG were normal. He was diagnosed as having an anxiety state and referred to a psychiatrist who thought that an
organic brain syndrome was more likely. By February 1998 it was clear that he had a receptive and expressive dysphasia and right extensor plantar response. Thyroid function, B12 and folate, an autoimmune screen, protein electrophoresis, serum copper, serum ceruloplasmin, heavy metal screen, pyrhythmia screen, IgA antibodies to gladin, serological tests for Treponema and human immunodeficiency virus tests were all normal. Protein investigation of such cases by strain typing importance of detailed clinical, neuropathological, and radiological findings since 1970.

Two possible explanations arise for the case history. Biochemical and radiological studies showed a spongiform encephalopathy which was most marked in the basal ganglia, with widespread neuronal loss and gliosis. No amyloid plaques were identified. Immunocytochemistry for PrP on lymphoid tissue in the spleen and appendix was negative. Western blot analysis of frozen cerebral tissue showed a PrP\textsuperscript{res} type 1 pattern.\textsuperscript{2}

Early age of onset, protracted psychiatric prodrome, and duration of illness distinguish variant CJD clinically from sporadic CJD. The post-mortem findings which provide the strongest evidence are pathologically reflected in the Gegenhalten tone in the limbs, and bilateral extensor plantar responses. In March 1999 he was in a state of akinetic mutism and died in August 1999. Necropsy disclosed cerebral atrophy, and radiological and pathological studies showed a spongiform encephalopathy which was most marked in the basal ganglia, with widespread neuronal loss and gliosis. No amyloid plaques were identified. Immunocytochemistry for PrP on lymphoid tissue in the spleen and appendix was negative. Western blot analysis of frozen cerebral tissue showed a PrP\textsuperscript{res} type 1 pattern.\textsuperscript{3}

Multiple sclerosis treatment trial precipitates divorce

We have noted an unusually high rate of divorce among participants in a recent small treatment trial of multiple sclerosis.\textsuperscript{4} Of the 29 patients in the study, only one was married at entry. During the 18 months of follow up, six patients (31%) became involved in divorce proceedings. In four of these, the unaffected spouse left the marriage for another partner. There was a transient breakdown in one other marriage, which did not lead to divorce, after an extramarital affair by the unaffected partner. Since the study ended, there has been one further divorce after an affair by the unaffected spouse. Those patients who became divorced were not distinguishable by their disability, the efficacy of their treatment, or the duration of their disease or marriage. The divorce rate in this study is considerably lower than the annual divorce rate in the United Kingdom for age and sex matched married couples of 2.4%-3.1%.\textsuperscript{5} Physical disability due to any cause is a risk factor for divorce\textsuperscript{1} and multiple sclerosis is no exception.\textsuperscript{2} However, this effect is not sufficient explanation to account for the exceptionally high divorce rate seen during this study. In one Australian study, the most severely disabled patients with multiple sclerosis were four times more likely to have been divorced than the less disabled; but even among the most disabled the prevalence of divorce was only 13%-19% of all prevalent patients.\textsuperscript{3} We suggest that participation in a treatment trial indirectly precipitates divorce, by exposing marital dissatisfaction in the unaffected spouse. The possible explanation may be that trial participation focuses attention on the affected spouse's disability. Alternatively, perhaps the frequent attentions of an interested medical team during a trial relieve the unaffected partner of a sense of responsibility towards his or her spouse. Another interpretation might be that recruitment to therapeutic trials is biased towards those patients who perceive a greater degree of dissatisfaction with their personal situation. To the best of our knowledge, in no previous treatment trial in multiple sclerosis, nor indeed of any other disease, has such a high rate of divorce been noted.

In the light of these findings it may be prudent to make patients and their spouses (or partners) aware, during the recruitment interviews for clinical trials of the strains which participation may expose in their relationship.
In humans, areas in the left inferior frontal and right superior parietal cortex become active both when producing and when seeing finger movements in others.1 Could similar mirror activity arise in a purely sensory context, such that a person, due to inhibition failure, may experience pain in a finger or limb when seeing sudden trauma (for example, a blow) to a corresponding area in another person? We report the anecdotal account, from a widow, of her late husband’s apparent experience of such “mirror pain” or, as we would suggest, “alldynia”.

The deceased, a long time smoker, died in late February 1993 with the diagnosis of “extensive metastatic carcinomatosis”, ante-mortem diagnosis of “cancer of the right lung”. (The widow, however, questions the lung cancer diagnosis, and claims that symptoms of serious rheumatoid disease involving cervical spine and dysphagia were misinterpreted.) As a consequence of increasing pain and stiffness beginning in the neck and upper body, and chest symptoms, he underwent radiography of the cerebral spine and chest in August 1990, disclosing opacity in the right lung and slight radiological deviation he had been increasing difficulty swallowing with food inhalation. Unwillingly, he underwent radiotherapy in early November 1990 to alleviate dysphagia, although according to the widow subsequent gastroscopy indicated that this may have been unnecessary.

He was reported to be very sensitive to touch; even the slightest hand contact gave the impression of sharp fingernails. Of particular interest was his widow’s recent observation that “If I slightly knocked my finger, spontaneously showing him, he would immediately grasp his own finger and say “don’t do that” (meaning not to show him); He actually felt it. If I merely commented (that I had knocked my finger), there was no such reaction”. In interview, she recounted other similar events. The experience was suddenly immediate and intense, and, apparently, qualitatively similar to the hypersensitivity that I had knocked my finger, spontaneously showing him, he would lead to a chronic progressive encephalopathy, not necessarily related to hyperammonaemia, known as acquired hepatoparenchymal degeneration (AHD).1 The pathogenesis of AHD is unclear, but the relation with the acute form of hepatic encephalopathy seems a crucial point. Cerebral deposition of manganese may have a pathogenic role. The disease may appear after one or more episodes of hepatic coma or, rarely, become manifest in the absence of them. Neuropathology typically discloses degenerative changes in the basal ganglia. The modern techniques of neuroimaging disclose these lesions in vivo.1 The clinical picture varies for neuropsychiatric changes and movement disorders usually being prominent. The syndrome is poorly responsive to medical therapy, thus being considered largely irreversible.

We report on a patient with AHD who was cured by liver transplantation.

A 59 year old man came to us in November 1997 for a neurological consultation before inclusion in the waiting list for liver transplantation. He had a history of chronic hepatic disease—alcohol and HCV related liver cirrhosis—which had begun some years before. No familial hepatic or neurological diseases were reported. In 1995 he had an episode of hepatic encephalopathy, consisting in somnolence and confusion lasting 36 hours. At the time of examination, the patient had stopped alcohol consumption 1 year before; liver failure was grade C-10 of the Child-Pugh classification. Copper balance was normal. Neurological examinations and EEG gave normal results. The patient was put on the waiting list for liver transplantation. In February and March 1998, he had two episodes of mild ascites with signs of encephalopathy (confusion and asterixis), both reversed by medical therapy. In April 1998 the patient began to complain of sleep disorders, tremor, dysarthria, motor slowness, and subtle cognitive dysfunction, not reversed by medical therapy or hepatic dysfunction. On 6 June 1998, his neurological suitability for liver transplantation was reconsidered. He seemed alert, oriented, and cooperative, with a slight slowness of psychomotor activity. The neurological examination showed hypomimia, dysarthria, bradykinesia, oral dyskinesia, and mild bilateral hand tremor. Neuropsychological examination showed a remarkable impairment of information processing control (attention, vigilance, memory, learning) as well as a significant decrease in psychomotor speed. The patient began to complain of sleep disorders, tremor, dysarthria, motor slowness, and subtle cognitive dysfunction, not reversed by medical therapy or hepatic dysfunction. On 6 June 1998, his neurological suitability for liver transplantation was reconsidered. He seemed alert, oriented, and cooperative, with a slight slowness of psychomotor activity. The neurological examination showed hypomimia, dysarthria, bradykinesia, oral dyskinesia, and mild bilateral hand tremor. Neuropsychological examination showed a remarkable impairment of information processing control (attention, vigilance, memory, learning) as well as a significant decrease in psychomotor speed.
lance, psychomotor speed, intelligence) with sparing of memory (table). An EEG disclosed diffuse slow activity. Cerebral MRI showed circumscribed bilateral lacunae on the lentiform nuclei on T1 weighted images. On 10 July liver transplantation was performed, with a successful course and a rapid improvement of the neurological disturbances. Immunosuppressive treatment with cyclosporine did not induce neurological complications. One month after liver transplantation only a mild dysarthria persisted. An EEG was normal. A neuropsychological assessment 3 months after surgery showed a remarkable improvement in the cognitive performances, especially in information processing speed tasks (table), whereas cerebral MRI was unchanged. Twelve months later, neurological examination was normal and cerebral MRI disclosed a reduction of basal ganglia lacunae. Neuropsychological testing documented a slight further improvement in control functions of information processing, with a slight decline in some memory performances (table). No other neurological problems emerged during subsequent follow-up.

This patient had an AHD presenting with movement and cognitive disorders. The first consisted in disabling movement disorders, with severe bradykinesia and dystarkia. The cognitive impairment included both a decreased functioning of the frontal executive functions and single function deficits (especially visuospatial abilities and language), conveying a picture of “hepatic dementia”. Cerebral MRI documented the basal ganglia lesions usually seen in AHD.1 Both the clinical and the neuroradiological abnormalities were reversed by liver transplantation. After surgery, the recovery from neurological impairment was prompt and complete, whereas neuroimaging improvement occurred later. This outcome resembles that previously seen in a patient with Wilson’s disease.1 Despite the different pathogenesis, the similarities between AHD and Wilson’s disease are remarkable for pathological lesions and clinical and neuroradiological presentation.1,2 Liver transplantation has been reported to reverse neuroradiological manifestations in most patients with Wilson’s disease.2 Liver transplantation in AHD is confined to two cases. A cirrhotic patient with improved chronic cognitive and motor disorders after liver transplantation was described in 2001.3 Twenty years later, Powell et al4 reported a case of successful liver transplantation in AHD. Their patient had a significant improvement in intellectual functions and chronic neurological signs early after surgery. Our present finding confirms these positive results and also documents that neuroradiological abnormalities are reversible. It is conceivable that both Wilson’s disease and AHD are characterized by an early stage neuro-iatrogenic process mainly affecting the basal ganglia, where MRI detectable hepato- cerebral degeneration is slowly reversible and liver transplantation can rapidly improve neuropsychological outcomes. The duration of the disease does not seem to be a crucial factor, as patients with long standing encephalopa- thy may also recover after liver transplanta- tion both in AHD5 and in Wilson’s disease.6 This conclusion has pathogenetic and thera- peutic implications: the presence of signs and symptoms of chronic hepato-cerebral degeneration, both in Wilson’s disease and in the acquired non-Wilsonian form, should not be considered a contraindication for liver trans- plantation and surgery may be the elective treatment for the neurological syndrome.

We are indebted to Dr Katia Mattarozzi who administered the neuropsychological tests.

A STRACCIARI
M GUARINO
PAZZAGLIA
Neurological Service, S Orsola-Malpighi University Hospital, via Alberturn 15, 40136 Bologna, Italy

G MARCHESINI
Department of Internal Medicine, Unit of Metabolic Diseases

P PISI
Clinical Department of Radiological and Histopathological Sciences

Correspondence to: Dr A Stracciari
neuro@orsola-malpighi.med.unibo.it


CORRESPONDENCE

Unexpected sudden death after lateral medullary infarction

I read with interest the study of Fitzek et al1 which included 15 patients with lower brain stem infarction. One patient with a “complete Wallenberg’s syndrome” (No. 15) died during the period of observation. Details on that patient’s death are not included in the paper.

Through personal communication with the authors I have learned that their patient No. 15, a 69 year old man, died unexpectedly 14 days after an acute brain stem infarction. Because the family refused a necropsy, we do not know with certainty whether some other acute process was involved in the patient’s death. However, an ECG and chest radiograph after presentation had been normal.

Recent reports2-6 have described patients who experienced unexpected sudden cardiorespiratory arrest several days after lateral medullary infarction, at a time when they were convalescing well and were stable medically and neurologically after a stroke which caused minimal motor disability. The reports have speculated about mechanisms by which cardiorespiratory arrest occurred; cardiac arrhythmia is among these.7

Although I do not know many pertinent details surrounding the death of the 69 year old man described by Fitzek et al, I speculate that his death may have resulted from cardiovascular arrest caused by an intermediate event in which the lateral medullary infarction and surrounding brain tissue disturbance (possibly ischaemic penumbra) influenced brain stem cardiac and respiratory centres together with autonomic pathways in a manner which at this time is not understood.

A recent neuropathological study8 of five patients described similar characteristic ischaemic lesions in the solitary tract nuclei of the medulla after subacute hypoperfusion of the brain during acute heart failure. It was speculated that these medullary lesions had in turn caused autonomic instability which precipitated death in each case. It is plausible that ischaemic lesions of the solitary tract nuclei result initially with some lateral medullary infarctions, and that such lesions may in turn precipitate some occurrences of cardiorespiratory arrest.

J H JASTER
Delta Medical Center, 1905 Harbert Avenue, Memphis, TN 38104, USA


Postictal psychosis related regional cerebral hyperfusion

I wish to comment on the postictal psychosis related regional cerebral hyperperfusion reported by Fong et al.1 Based on the their findings of hyperperfusion on SPECT within the time frame of postictal psychosis, the authors argue against the hypothesis that postictal psychosis is a psychic manifestation of an ictal Todd’s phenomenon. Two previous studies have shown a focal increase in cerebral blood flow on brain imaging during traditional motor Todd’s paresis.2-4 An angiogram during a Todd’s paresis may demonstrate a vascular “blush” perhaps representing loss of cerebrovascular autoregulation at the site of the epileptic focus.5 Hence, hyperperfusion may signal hypofunction, and the findings of Fong et al are indeed consistent with postictal psychosis as a Todd’s equivalent.

The strongest argument that postictal psychosis is not a Todd’s equivalent is the delayed onset of psychosis compared with the decerebrocorticospinal course of Todd’s motor, cogni- tive, and visual phenomena.1,3

L S BOYLAN
Department of Neurology, New York University, New York, NY, USA

Significant improvement in ADC symptoms, signs, and function (to the point where some patients can return to full-time work) is now possible with highly active antiretroviral therapy.1

Fong replies: We thank Boylan very much for the interesting letter providing a second thought on the pathogenesis of postictal psychosis. Our data showed a definite increase in regional cerebral blood flow (rCBF) in both patients with postictal psychosis. As pointed out by Boylan, postictal psychosis may or may not be secondary to Todd’s paralysis. In fact, the clinical features of postictal psychosis point against the hypothesis of Todd’s phenomenon being the underlying pathophysiology. We also agree that the underlying mechanism of postictal psychosis is due to activation of a subcortical circuit. In our patients, the antiepileptic agents were restarted after a bout of secondary generalised tonic-clonic seizures. The re-institution of anticonvulsant drugs may cause a preferential suppression of abnormal cerebral cortical activities and hence normalise the surface EEG recording. In turn, it may result in a gradual build up of abnormal electrical activities propagating via subcortical neuronal networks which is shown by cerebral SPECT studies as areas of enhanced rCBF. This can explain the characteristic lucid interval of postictal psychosis and the activation of subcortical circuits may cause clinical psychosis.3

To understand the pathophysiology of postictal psychosis, we wish to study the electrical activities of patients with postictal psychosis by intracranial electrodes and regional cerebral metabolism by cerebral PET.

G C Y FONG
Division of Neurology, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong cyfongmedicine@graduated.hku.hk

HTLV-I and HIV infections of the CNS in tropical areas

I read with interest the recent article by Cabrè et al.1 I make three comments on the section of the review pertaining to HIV disease. I disagree with the statement made on page 551 that chorea is pathognomonic of toxoplasmosis encephalitis in patients with AIDS. Chorea may also occur in patients with AIDS dementia complex (ADC).2 Second, there are several errors in table 2. Fluconazole is not given as 400 mg four times a day for acute cryptococcal meningitis therapy but rather as 200 mg/day; pyrimethamine is not given at 50–100 mg four times a day or sulfadiazine 4–8 g four times a day but rather pyrimethamine 50–100 mg/day, sulfonilic acid 10 mg/day, and sulfadiazine 4–8 g/day; pyrimethamine for suppressive therapy is not given at 25–75 mg four times a day but rather 25–75 mg/day and sulfonilic acid should be given at a dose of 10 mg/day; the toxoplasmosis prophylactic dose of trimethoprim 160 mg with sulfamethoxazole is one tablet per day. Finally, the statement on page 552 “antiretroviral therapy can only improve ADC symptoms” is no longer correct.

Statistics and analysis of the Camino ICP monitor

We have concerns about the mathematics, account for 71% of implementatons and three positive cultures from 16 subdural devices do not account for 10.7%. Furthermore, the precision suggested by the use of decimal places in reporting percentage data is totally unwarranted.

There is also concern about the failure rate of probes from the authors’ analysis of infection rates and zero drift, which was performed on only 65 of 108 indications for monitoring and zero drift of a series of probes. The protocol should have included procedures to minimise this. It may be that there was a high failure rate of the catheters but this is not reported. More details should be given to ascertain whether any bias is likely to have been introduced by excluding so many probes.

Figure 3 suggests huge drifts (24 mm Hg ± 35 mm Hg) and is clearly significant and unacceptable, with 39% of probes tested failing to comply with the manufacturer’s specifications. The authors demonstrated that there was no correlation between duration of monitoring and zero drift which is in agreement with previous work.1 However, the authors fail to highlight the fact that regardless of the duration of monitoring, 23% of probes tested had a zero drift of ≥10 mm Hg, which is clearly unacceptable.

The representation of the data as mean, median, and SD in table 3 is misleading as it is clear from fig 3 that there is a wide distribution of both positive and negative offset sets. Consequently, a near zero mean drift is likely to occur even though the magnitude of the zero drift in individual cases is large. Clinically, it is the zero drift from a single patient that is important and not the zero drift of a series of probes.

The recommendation to change the catheter if a long monitoring period is expected is to allow for rezeroing is not held up by the data shown in fig 3, which would suggest that there is more likely to be a larger zero drift than the manufacturer’s specification in the early days.


BOOK REVIEWS


One of the most interesting fields of research in epilepsy in the past 5 years or so has concerned cortical dysgeneses. In some series of chronic epilepsy, overt dysgenesis underlies 15% of all epilepsies, and more subtle forms might account for some apparently cryptogenic cases. This book is therefore timely. It is a record of the proceedings of a conference held in Venice in October 1997, within the framework of the Mariani Foundation Colloquia in Childhood Epilepsy. The book is organised into sections on cortical development, animal models, electroclinical imaging and neuropathological studies, genetics, and surgical treatment. The faculty and chapter authors are distinguished figures in this research field largely from the United States, Canada, and Italy.

The recognition of the importance of these conditions in epilepsy has been due to the introduction of structural MRI and also the advances in understanding of the processes of cortical development. The second field particularly is one in which advances are being made rapidly, both clinically and in the laboratory, and the authors and editors do a superb job in marshalling this information into a readable and well organised form. I found many of the chapters exceptionally interesting. The heavy emphasis on molecular genetics and pathology is appropriate to this area and is a model for how the modern topics of epilepsy should be approached.

My only reservation about the book is that in this fast moving field some of the basic science and genetic data are already out of date,
but otherwise the information is of high standard. The clinical chapters are exemplary, however, and I particularly enjoyed the two fascinating chapters on surgery for epilepsy in cases with dysgenesis. A minor grumble about the book is not about the content, but the poor standard of book production (a common trend in medical books), with for instance horrible margins and without a list of contributors. In all other ways though, this is a superb book, and one which I thoroughly and wholeheartedly recommend to both clinical and basic scientists. It is a definitive contribution to this important area.

SIMON SHORVON


There is something about the autonomic nervous system that causes undergraduate students and doctors alike to lose interest, switch off and for their eyes to glaze over. Professor Alison Brady suggests in her preface that this is due to “uninspired teaching and inadequate coverage in many textbooks”. Although one can only imagine that Professor Brady’s is an exception to the first generalisation, this book, an obvious labour of love, is a brave attempt to correct the second.

The text is best suited to the physiology undergraduate student, medical or otherwise. Certain chapters will also appeal to the specialist registrar starting out in areas such as cardiology, respiration, gastroenterology and, of course, neurology. It is concisely written in a style that is willing the student to stay with her, to follow her logic and read on and beautifully illustrated with clear diagrams and cartoons as well as many good quality electron micrographs. Although Brading herself is based in Oxford, much of Gaskell and Langley’s pioneering study of the autonomic nervous system was in Cambridge around 100 years ago. This book begins with a historical overview to set what follows in historical perspective. Then follow chapters on anatomy, neuromuscular, and synaptic transmission, the molecules involved and their function, and finally, the relevant body systems. This is not a clinical textbook but mention is made of possible pharmacological manipulation of the autonomic nervous system where appropriate.

If you have always wanted to get to grips with the autonomic nervous system but have found the available literature too dry or anti-quant, now’s your chance!

GILLIAN HALL


This book, by its own admission, is neither a comprehensive textbook nor teaching manual. The author’s stated intention is for “To be a bedside reference to which to quickly look up how to perform a technique … or to look up reference values…”. It is just that—a reference book or paper data base of up to date normal values. In the case of commonly collected data, this is tabulated with respect to age, sex, height (F waves), and body mass index. In all cases, the number of subjects, machine settings, and skin temperature are documented.

Ideally all EMG departments would collect and compile their own normal values but in reality this seldom happens. Given this failing, this is the book for the purist who, for example, wishes to check that his lateral antebrachial cutaneous sensory peak latency falls within two standard deviations of the mean. Or whether that slight apparent prolongation of median F waves is acceptable in the young, six foot something basketball ball player. As such, it is a useful reference book to be found on the shelf of your EMG department, if not actually always with you by the bedside.

Its wider appeal for the novice or junior practising electrophysiologist is its descriptions and diagrams detailing electrode positioning and examples of typical, expected waveforms. It is for this reason that I might find myself with this book at the bedside, especially for some of those more obscure cutaneous sensory nerves.

Buschbacher intends his book to be a practical manual with lists of acceptable differences, helpful hints, references, and pointers to additional reading and alternative techniques as well as space for the operator to make his or her own observations.

GILLIAN HALL


This is a clear, basic textbook outlining the main neuropsychiatric syndromes prevalent in patients with multiple sclerosis. It can be divided into three main sections: (1) an introductory chapter summarising briefly the pathogenesis, pathology, and clinical features of multiple sclerosis and concentrating on some useful definitions and guidelines for diagnosis, (2) four chapters on the psychiatry of multiple sclerosis—namely, depression, bipolar affective disorder, pathological laughing, and crying and psychosis, and (3) five chapters on the neuropsychology of multiple sclerosis, specifically examining their nature, detection, course, and neuroimaging correlates. The emphasis of the book is thus predominantly on the cognitive dysfunction associated with multiple sclerosis. This is a well presented section with a clear and comprehensive overview of research in this area. By contrast, it is somewhat disappointing that the section on psychiatry of multiple sclerosis is so small, particularly as depression in multiple sclerosis is so prevalent, and the contribution of cognitive dysfunction to overall quality of life is so small, particularly as depression in multiple sclerosis is so prevalent, and the contribution of cognitive dysfunction to overall quality of life is so small, particularly as depression in multiple sclerosis is so prevalent, and the contribution of cognitive dysfunction to overall quality of life is so small.
The choice of topic is sometimes surprising: flashbulb and flashback memories may be of interest in their own right, but they are far from prominent in most memory clinics and sit rather awkwardly there. There is little on the effect of normal aging on memory or on alcohol-related memory disorders. The writing is at times uneven and in too many chapters detailed accounts of historical development take precedence over contemporary analysis. There are nevertheless useful contributions on the neuropsychological investigation of malingered and a refreshingly pragmatic chapter on recovered and forced memories.

This is a book which, although something of a curate’s egg, approaches memory as a first published his Pathology of Peripheral Nerve in 1977. Now, with an increase in knowledge of peripheral nerve disease, and advances in electron microscopy and the genetics of inherited neuropathies, the publication of this Atlas of Peripheral Nerve Pathology is timely.

Broadly the book is divided into two sections. In the first the author takes us through the normal light and ultrastructural appearance of peripheral nerve. There then follow chapters on biopsy techniques and importantly a section devoted to artefact. After chapters on morphometry and abnormal structure of peripheral nerve the reader is led into the second section which is devoted to pathological changes. In summary, there are sections on the pathology of the axon, myelin sheath, Schwann cell, interstitium, and vasa nervorum.

This is a handsome well illustrated book with good quality and well annotated photomicrographs, many in colour. The electron micrographs are clear and crisp. The text is well written and indexed. This book is primarily an atlas so it would be unfair to criticise deficiencies in the text. However a discussion on the indications for nerve biopsy with some suggested guidelines would have been useful. I think some mention should have been made of the procedure’s potential complications.

This book has obvious appeal to clinicians with an interest in disease of the peripheral nerves and to neuropathologists, but the generalist in both specialties will find it useful. For such a heavily illustrated book it is reasonably priced at £125.


Schmidley’s book on CNS angitis is an absolute gem. He concisely summarises the salient information on various rare and often puzzling conditions that affect the blood vessels of the brain. The writing is clear and lively and easy to read and digest. After summarising the data, Schmidley always lets the reader know where he stands on issue. He reviews the major common features of each condition and yet also mentions unusual and rare features and often illustrates with exerpts from individual patients.

The book begins with an in-depth but concise review of the clinical and pathological features and the diagnosis and treatment of isolated CNS angitis. Included is an excellent chapter on pathogenesis which reviews complex immunological theories in a very readable summary form. Later chapters deal with postpartum angitis, cases of supposed angitis diagnosed by angiography, and various infectious and systemic and vascular disorders that have been postulated or proved to include angitis of the brain’s vasculature. Coverage of individual disorders such as neurosarcoïdosis, Behcet’s disease, scleroderma, Eales’ disease, lupus, and to a lesser degree but data rich summaries. The entire book covers 165 pages of text. The illustrations are excellent and there are many useful tables that contain summaries of the data. The reference list is extensive.

Schmidley emphasises several very important points that are not widely known to neurologists. I mention only a few here. (1) Isolated CNS angitis represents as a stroke. (2) The angiographic findings that radiologists dub as vasculitis are quite non-specific and are found in various non-angiitic conditions. (3) Angiograms are often normal in patients with isolated CNS angitis because the vessels (arteries and veins) involved are usually quite small and the brain imaging findings in this condition are very non-specific. Isolated CNS angitis can only be confirmed diagnostically by biopsy. (4) Stroke is almost never the first presentation of polyarteritis nodosa or temporal arteritis. (5) Most strokes in patients with lupus erythematosus are not attributable to a CNS vasculitis. (6) The brain’s vasculitis’ predilection for the PNS is probably related to a meningoencephalomyelitis rather than a true angitis.

I recommend this little book highly to all neurologists. It will prove very handy when confronted with difficult patients of undiagnosed brain diseases and will be useful when looking up the key findings and literature references in patients suspected of having any form of systemic or CNS vasculitis.

LOUIS R CAPLAN


In the past decade, many new treatments for migrainous headache have been developed and marketed. The flow has slowed up in the past year or two, not least because several good theoretical ideas have not proved valuable in clinical practice, and the comprehensive review of current drugs is therefore timely. Professor Christopher Diener, who has published distinguished research on the pathophysiology of headache as well as its treatment, has assembled a panel of authorities to review all current treatments for migraine, both analgesic and prophylactic. At the end of the book there are individual chapters on cluster headache, tension headache, paroxysmal hemihemian, drug induced headache, and post-traumatic headache.

In the main section of the book on migraine, all the triptans are covered, including almotriptan and frovotriptan, which have yet to reach the market, as well as opioids and the different drugs used in prophylaxis, including fluoxetine, valproate, gabapentin. The industry based pharmacologist who developed each drug gives an account of its theoretical properties, and then one of the principal clinicians responsible for the trials reviews its role in clinical practice. Each chapter is thoroughly referenced, and the book will prove to be an excellent source of references to classic trials. There is some duplication within the pairs of chapters, and occasionally commercial pride seems to inhibit a truly independent discussion of the merits of the drugs. Much of the clinical material, inevitably, amounts to a catalogue of trials that does not lend itself to easy consecutive reading. Some of peripheral neurologists make valuable comments—notably Goadsby emphasising the 2 and not the 4 hour response data for naratriptan, Ferrari on the analysis of recurrence rates for different drugs, and Tfelt-Hansen and Saxena on the limited likely role of 5HT1 receptor inhibition on the mechanism of successful prophylaxis. Jim Lance distils a lifetime’s experience of migraine prophylaxis into six pages. The reviews of simple analgesics in tension headache by Schoenen, and of post-traumatic headache by Keidel are excellent, providing material difficult to find elsewhere. In many respects this is an outstanding book. It provides an invaluable source of published evidence for the treatment of patients with headache—It needs some dedication to read it through, but it would be a useful addition to every departmental library.

R C PEATFIELD


This multiauthor book aims to provide physicians with an approach to the management of patients with chronic neurologic disease.

The first part of the book describes a general approach to the management of neurologically disabling conditions. There are chapters entitled Nature of the problem, Character of the solution and Measurement of effectiveness. The first describes the prevalence of disability with particular reference to the United States and then goes on to describe the nature of the disease, impairment, disability, and handicap, with an interesting discussion of the meaning of illness. The second chapter provides a good overview of a particular approach to rehabilitation. It describes a specific framework that encompasses many of the ideas and concepts that are common to rehabilitation throughout the world. The final chapter considers issues surrounding measurement of outcome.
The second part of the book applies this approach to specific diagnostic groups. The book has been well edited with each of the chapters following the same standard format with the nature of the problems being covered with sections reviewing the epidemiology of the disorder, the nature of the disease, and the associated impairments, disabilities and handicaps followed by sections on the character of the solution discussing management techniques and outcome measurement. A particularly good chapter is on spinal cord injury by Pamela Ballard with very specific descriptions of the impairments, disabilities, handicaps, and quality of life issues associated with spinal cord injury and their management. Other chapters are less coherent which may reflect the fact that for some disorders (spinal injury, multiple sclerosis) rehabilitation approaches are better established than for others. Each of the chapters illustrates the approach using clinical anecdotes. These emphasise the importance of the physician taking a patient centred approach.

Overall this book is worth reading for its description of a rehabilitation approach. The second section is less likely to appeal to neurologists but may have wider appeal to non-neurologically trained physicians working with patients with chronic neurological disease.

DIANE PLAYFORD


The field of autism research has been growing very fast in the past decade. The book reflects the increasing need to understand the complexity of medical findings on the biological basis of the autistic syndromes. The authors provide the readers with a useful framework in which much emphasis is placed on autism as a disease with many causes and a wide range of clinical presentation. A great deal more is known than at the time of writing of the second edition (1992), and this new edition reflects the update at all levels. It is a comprehensive reference book as well as stimulating reading for various disciplines as such as electrophysiology, neuropathology, and brain imaging: currently available studies are summarised and discussed pinpointing limitations and suggesting new relevant questions. The chapter on genetics has been extensively rewritten, and even the lay reader will find useful information about the development of understanding genetic components of autism.

Practising clinicians working with patients affected by the syndrome will find of particular interest the chapters outlining the clinical picture of autism developing from infancy to adulthood, in addition to those discussing the relation of autism with medical diseases and the phenomenon of comorbidity. Different diagnostic criteria for Asperger syndrome are discussed, and clear guidelines are given for early screening of infants.

I cannot imagine anyone being disappointed by reading this book and, in particular, cognitive psychologists will be flattered by the claim that “the most interesting constructs of the whole field of autism have been generated by cognitive psychologists”.

FULVIA CASTELLI

CORRECTION

Cabrè P, Smadja D, Cabié A, et al. HTLV-1 and HIV infections of the central nervous system in tropical areas. J Neurol Neurosurg Psychiatry 2000;68:550–7. During the editorial process the doses given in table 2 were misquoted. The correct table is as follows:

<table>
<thead>
<tr>
<th></th>
<th>First choice</th>
<th>Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cryptococcosis:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute infection</td>
<td>Amphotericine B, 0.7 mg/kg/day iv and flucytosine, 100 mg/kg/day orally or iv in 4 divided doses for 2 weeks, then fluconazole, 400 mg orally/day for 8 weeks</td>
<td>Fluconazole, 400 mg orally/day for 10 weeks, or Fluconazole 200–400 mg orally/day for 10 weeks and flucytosine 150 mg/kg/day orally or iv in 4 divided doses for 2 weeks</td>
</tr>
<tr>
<td>Suppressive therapy</td>
<td>Fluconazole 200 mg orally/day</td>
<td>Amphotericine B, 0.6–1.0 mg/kg iv/week, or Itraconazole, 200 mg orally/day</td>
</tr>
<tr>
<td><strong>Toxoplasmosis:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute infection</td>
<td>Pyrimethamine 100–200 mg loading dose (2 days), then 50–100 mg orally/day plus folic acid 10 mg orally/day+ sulfadiazine 4–8 g orally/day for at least 6 weeks</td>
<td>Pyrimethamine plus folic acid plus clindamycin 900–1200 mg iv/6h or 300–450 mg orally/6h for at least 6 weeks, or Trimethoprim 160 mg plus sulfamethoxazole 800 mg/8h orally or iv for at least 6 weeks</td>
</tr>
<tr>
<td>Suppressive therapy</td>
<td>Pyrimethamine 25–75 mg orally/day plus folic acid 10 mg orally/day+ sulfadiazine 500–1000 mg orally/6 h</td>
<td>Pyrimethamine plus folic acid plus clindamycin 300–450 mg orally/6h, or Trimethoprim, 160 mg plus sulfamethoxazole, 800 mg orally/day</td>
</tr>
<tr>
<td>Prophylaxis (patients with positive IgG serology and CD4 count &lt;100/mm³)</td>
<td>Trimeprorphim 160 mg plus sulfamethoxazole 800 mg orally/day</td>
<td>Dapsone 50 mg/day plus pyrimethamine 50 mg/week plus folic acid 25 mg/week</td>
</tr>
</tbody>
</table>

Table 2  Treatment and prophylaxis of cryptococcus and toxoplasmosis in HIV infection
Hashimoto's encephalopathy responding to plasmapheresis

P M BOERS and J G COLEBATCH

*J Neurol Neurosurg Psychiatry* 2001 70: 132
doi: 10.1136/jnnp.70.1.132

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