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 travelled recently. 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 unobserved 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 ruddy, absent ocular reflexes, generalised hypotonia and hyperreflexia, bilateral extensor plantar responses, was afebrile, and had no neck stiffness. Angiography of the vertebral system was normal. Intravenous heparin was started and later intravenous acyclovir. After extubation, he had ongoing cognitive impairment and remained generally hyperreflexic with extensor plantar responses. His admission was characterised by a fluctuating, but slowly improving, delirium. He had short term memory deficits, visual and auditory hallucinations, and paranoid delusions. His upper limb tremor persisted and he had a second generalised seizure. His EEG was diffusely slow without epileptiform activity; this later improved. C-reactive protein was 58 mg/l but other investigations were normal or negative, including routine haematology and biochemistry, erythrocyte sedimentation rate, ANA, ANCA, HIV, and serology, carotid Doppler studies, brain MRI (performed precontrast and postcontrast), and cranio-encephalographic echocardiography, and CSF culture (including herpes simplex virus polymerase chain reaction). By discharge, his mental function had improved and he was taking clonazepam, phenytoin, carbamazepine, and haloperidol. He presented again 3 weeks later with worsening generalised tremulousness. He was orientated but distractable. His CSF pressure was normal (150 mm H2O) and proteins were again high (1.06 g/l). Serum B12, folate, and TSH concentrations were normal and anti-cardiolipin antibodies were negative. His mental state fluctuated dramatically—from coherent, to agitated, to stuporous—over a 24 hour period; his command of English paralleled his mental state. Despite being euthyroid, his antimicrosomal and antithyroglobulin antibody titres were markedly raised (figure, point A). A diagnosis of Hashimoto’s encephalopathy was made and treatment with intravenous methylprednisolone was commenced, followed by oral prednisolone and azathioprine. His level of consciousness improved, as did his memory, and he was able to perform simple arithmetic. He was discharged from hospital, but 4 weeks later he had not returned to his premorbid level of functioning. He continued to have ongoing tremors and difficulties feeding and dressing himself. Additional treatment was considered necessary, and the patient had a course of plasmapheresis (four exchanges, total 26.8 litres), with the rationale being to remove the presumed pathogenic humoral antibody. The volume of plasma exchanged per treatment was 1.5 times twice the total plasma volume, and the number of exchanges was consistent with the treatment of other autoimmune neurological disorders.

His condition improved after the first plasma exchange, and by the end of treatment 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 B). He remained well, with slowly rising antibody titres. A further seizure occurred plasmapheresis (three exchanges, total 21.0 litres) again resulted in a decline in antibody concentrations (figure, point C) and clinical improvement. He continued taking prednisolone and azathioprine throughout.

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Hashimoto’s encephalopathy is a rare autoimmune encephalopathy that has not been previously described. The unique feature of the present case was the patient’s clinical and serological improvement. He continued taking prednisolone and azathioprine throughout.

This patient’s clinical course demonstrates that the response to corticosteroids may be incomplete and that additional clinical and serological improvement can be achieved with the use of plasmapheresis. It is unclear whether the patient’s death was related to his underlying neurological condition. If it was, then it is a further indication of the unpredictability of the course and outcome of Hashimoto’s encephalopathy.

We thank Dr R Lindeman for his assistance with plasmapheresis.

P M BOERS
J G COLERBATCH
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
P.Boers@unsw.edu.au

1 Lord Brain, Jellinek EH, Ball K. Hashimoto’s disease and encephalopathy. 1966;2:512–14.

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 Guillain-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 oral aspirin and intravenous streptokinase was initiated. Fir-
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 mild dysarthria, and an expressive dysphasia.
nerve palsies, an indistinct left optic disc, year, and prime minister), bilateral sixth
out of 10 (he failed to recall the date, current
syndrome occurs some 10–14 days after
c, an abbreviated mental test score of 7
C, an abbreviated mental test score of 7

tions, no serological evidence of syphilis, no


cerebrospinal fluid changes during treatment

<table>
<thead>
<tr>
<th>Week</th>
<th>CSF Protein (g/l)</th>
<th>CSF Leucocytes (&lt;10^{10}/l)</th>
<th>CSF Lymphocytes (%)</th>
<th>CSF Neutrophils (%)</th>
<th>CSF Glucose (mmol/l)</th>
<th>Blood glucose (mmol/l)</th>
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<tr>
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</table>

*Blood glucose measured simultaneously with CSF glucose.

Greenhouse-Geisser corrected P < 0.05. The differences of CSF protein, CSF leucocytes, and CSF glucose were significant (P < 0.05).


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 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-
tution. He was followed up again between the ages of 26 and 34, a period during which he benefited from enzyme substitution therapy.

This male patient had no familial history of Gaucher’s disease. Pregnancy and birth were normal. At 6 months, he presented with dys-
function of oculomotor cranial nerves, the red spot, and was found to carry Gaucher’s cells in his bone marrow. Abnormal gait and pyramidal signs followed around 4 years of age. There was a macular cherry red spot. Acid phosphatases were increased at that age. Nevertheless, there were no abnormalities of statorumperdinal milestones and no cognitive dysfunction. He went to school until the age of 16.

The patient was seen at the age of 26. He had difficulties in walking which progressively worsened and falls became frequent. He could, however, walk without aid and work as a clerk. He also complained of paroxysmic dyspnoea. Neurological examination dis-
played a static and kinetic cerebellar s
drome associated with a tetrapyr-amidal syndrome. Falls were mainly due to paroxys-
tic dystonic movements of the trunk and a hesitant gait. Dyspnoea were also concomitant with par-
oxysmic and abnormal contractions of the abdominal musculature which were consid-
ered of dystonic origin. The paroxysmic mani-
festations were not as brisk as myoclonus and were actually reinforcements of abnormal dystonic postures which could be seen in both the arms and legs. Both dystonia and cerebellar syndrome were responsible for a dystonic tremor of the head and a shaking of the arms was seen. There was an oculomotor paralysis. Voluntary movements were abol-
ished in both vertical and horizontal gaze. The oculocephalic movements were, how-
ever preserved, although at a very low speed and low amplitude, in the horizontal move-
ments. The abdominal echography showed the absence of hepatomegaly, but the size of the spleen was increased (18.5 cm along its major axis). There were no radiographic bone abnormalities. Bone scintigraphy was also normal. Neuropsychological testing showed the following: Binois-Pichot test for cognitive capacities 91/100; Wechsler test for memory 80/100. There was a slowing of the conscious process, there was no significant defect. Behavioural abnormali-
ties were noted with impulsivity and aggres-
vitivity. Clastic attacks were reported by his family. Brain MRI and EEG were normal. ECG and cardiac echography were also nor-
mal. β Glucosidase was diminished in leuco-
cytes (0.45 Units; normal 6.5–10.5 Units) and in cutaneous fibroblasts (23 Units; nor-
mal 80–370 Units). The haemogram was normal except for a thrombocytopenia with 71 000 cells/mm³. Acid phosphatases were increased (10.0 Units; normal 2.2–8.14 Units). Chitotriosidase when tested after 4 years of treatment, was still clearly increased (1012 Units; normal mean 20 Units).

The healthy parents, of Italian origin, were not consanguinous. They were tested for β glucosidase in leucocytes; the concentrations were 1 Units for the father and 3.0 Units for the mother. The brother and sister refused testing.

Genomic DNA was analysed and partially sequenced. The patient gave informed con-
sent according to bioethics in French Law and the Declaration of Helsinki. The pres-
ence of the L444P and D409H mutations was detected exactly as described in Boot et al. The Ncil restriction enzyme was used for the mutagenic L444P and the StyI restriction
The treatment was started at the age of 27 by the cerebroside β-glucosidase of placental origin alglucerase (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 antibodies 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 paroxysmal 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 paroxysmal dystonic manifestations. No clonic attacks occurred in the 2 years of the treatment. At the age of 34, neuropsychological evaluation was as follows: mini mental state examination score 25/30; Mattis scale for memory 23/25; Wisconsin test for verbal fluency: 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 after 6 months and between 130–150 000/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 neuropathic 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. 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, the patient had 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 neuropsychiatric 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 (CEFG), 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 Prévoyance CNP.
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, purinergic screen, IgA antibodies to gladin, serological tests for Tropenella and human immunodefiency virus tests were all normal. Protein in CSF was mildly raised at 0.62 g/l and conalbumin at 2.8 white cells/mm³. Oligoclonal bands and CSF 14–3–3 protein were negative. Repeat EEG demonstrated a left hemispheric slow wave focus, cranial MRI showed atrophy of the whole of the left hemisphere, and a SPECT perfusion scan demonstrated marked underperfusion of the posterior temporal parietal cortex on the left. A tonsil biopsy for protease resistant PrP was negative. The open reading frame of the prion protein gene demonstrated no mutations. The codon 129 genotype was valine homozygous. By October 1998 he was dependent on his wife for dressing, toileting, and feeding. He was mute with eyelid apraxia, generalised motor and speech primitive reflexes reflected in 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 neuropathological 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^RES type 1 pattern.

Early age of onset, protracted psychiatric prodrome, and duration of illness distinguish variant CJD clinically from sporadic CJD. The post-mortem findings for this case described. Firstly, the case represents sporadic CJD, of which there have only been two cases younger than 30 in the United Kingdom since 1970. Neuropathological review of these two earlier cases has found changes in the brain consistent with sporadic CJD; full molecular and phenotypic analysis of 300 subjects. Ann Neurol 1999; 46:224–33.

The National Creutzfeldt-Jakob Disease Surveillance Unit and Population Sciences School of Hygiene and Tropical Medicine. CJD Surveillance in the UK; eighth annual report 1999, 2000; 81–53.


We have noted an unusually high rate of divorce among participants in a recent small treatment trial of multiple sclerosis. Of the 29 patients in the study, only 10 were 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. After 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 divorced patients were four times more likely to have been divorced than the less disabled; but even 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 3%–15% of all prevalent patients. We suggest that participation in a treatment trial indirectly precipitates divorce, by exposing marital dissatisfaction in the unaffected spouse. No 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 relieves the unaffected partner of a sense of responsibility towards his or her spouse. Another interpretation might be that recruitment to therapeutic trials is biased toward 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. Could similar mirror activity arise in a purely sensory context, such that a person, due to inhibitory 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, “allodynia”.

The deceased, a long time smoker, died in late February 1993 with the diagnosis of “extensive metastatic carcinomatosis”, ante-mortem considered the “carcinoma 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 cervical spine and chest in August 1990, disclosing opacity in the right lung and slight mediastinal 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, apparendy, qualitatively similar to the hypersensitivity occasioned by actual contact. She had initially contacted one of us (JLB) after hearing a radio broadcast by him of phantom limb phenomena, and, wondered whether an analogous mechanism of some kind may have been operating with her late husband.

Although mirror motor neurons may be fundamentally important in learning to act, an adaptive role is far less obvious for perceiving another’s pain. Perhaps during infancy avoidance of noxious stimuli is facilitated by early recognition of pain in others. Alternatively the phenomenon may merely be adventitious consequence of disruption of convergent sensory systems. Thus hyperalgesia, where a light touch induces an unpleasant sensation in the same person, is typically attributed to dysfunction of convergent sensory neurons in the neuraxis, though any of several CNS levels may be involved. However where, as here, a separate person is implicated, there may be additional limbic involvement, given the rather intensely emotional aversive aspects of the sensory experience.

Unfortunately no CT or MRI seem to have been performed of the brain, but it is probable that there was fairly widespread CNS involvement. He had also, apparently, experienced head trauma in his childhood. In the war, it would be of interest to know whether similar “allodynia” has been seen after known damage that includes left inferior cortex (cortical region), or the rostralmost region of the right superior parietal lobule. It would also be interesting to get persons, normal or hyperalgesic, to note reactions to noxious stimuli in others while judging the intensity of mildly aversive tactile stimuli they receive themselves.

J L BRADSHAW
Neuropsychology Research Unit, Department of Psychology, GPO Box 17, Monash University, Victoria 3800, Australia

J B MATTINGLEY
Department of Psychology, School of Behavioural Science, University of Melbourne, Parkville, Victoria 3010, Australia

Correspondence to: Professor J Bradshaw j.l.bradshaw@sci.monash.edu.au


Acquired hepatocerebral degeneration: full recovery after liver transplantation

Lever diseases may give rise to variable degrees of neurological impairment, which mostly consist of the syndrome of hepatic encephalopathy, due to the toxic effect of ammonia on the brain during episodes of liver decompensation. In a minority of patients, repeated episodes of liver failure can lead to a chronic progressive encephalopathy, not necessarily related to hyperammonaemia, known as acquired hepatocerebral degeneration (AHD). 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 pathogenetic 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. The clinical picture varies neurologically, with different 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 the 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. On 6 June 1998, his 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, short term and long term memory).

Neuropsychological testing before and after liver transplantation (LT)

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<th>Test</th>
<th>Cut off</th>
<th>Score* before LT</th>
<th>Score* after LT (3 months)</th>
<th>Score* after LT (12 months)</th>
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<td>Supraspan spatial learning</td>
<td>5.7</td>
<td>4</td>
<td>14.6</td>
<td>8.7</td>
</tr>
</tbody>
</table>

*Corrected for age and schooling when needed.
lance, psychomotor speed, intelligence) with sparing of memory (table). An EEG disclosed diffuse slow activity. Cerebral MRI showed circumscribed bilateral lacunae on the lentiform nucleus 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 and some fine tasks (table), where cerebral MRI was unchanged. Twelve months later, neurological examination was normal and cerebral MRI disclosed a reduction of basal ganglia hyperintensities. 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 evaluation.

This patient had an AHD presenting with movement and cognitive disorders. The first consisted in disabling movement disorders, with severe bradykinesia and dysarthria. The clinical examination 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.2 Despite the different pathogenesis, the similarities between AHD and Wilson’s disease are remarkable for pathological lesions and clinical and neuroradiological presentation.1,3 Liver transplantation has been reported to reverse neurological manifestations in most patients with Wilson’s disease.4 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 1990.5 Twenty years later, Powell et al. 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 neuropathological process mainly affecting the basal ganglia, where MRI detectable hepato-cerebral degeneration is slowly reversible and liver transplantation can rapidly improve neurological outcomes. The duration of the disease does not seem to be a crucial factor, as patients with long standing encéphalopatia may also recover after liver transplantation both in AHD6 and in Wilson’s disease.2 This conclusion has pathogenetic and therapeutic 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 transplantation 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
P PAZZAGLIA
Neurological Service, S Orsola-Malpighi University Hospital, via Albertoni 15, 40138 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


Unexpected sudden death after lateral medullary infarction

I read with interest the study of Fitzek et al.,1 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 were unable to ascertain whether this patient’s death are not included in the paper.

Recent reports2–5 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.6

Although I do not know many pertinent details surrounding the death of the 69 year old man described by Fitzek et al.,1 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 study7 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 part 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 Harbor Avenue, Memphis, TN 38140, USA

Postictal psychosis related regional cerebral hyperperfusion

I wish to comment on the postictal psychosis related regional cerebral hyperperfusion reported by Fong et al.8 Based on the their finding 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 Todd’s phenomenon. Two previous studies have shown a focal increase in cerebral blood flow on brain imaging during traditional motor Todd’s paresis.9 An angiogram during Todd’s paresis may demonstrate a vascular “blush” perhaps representing loss of cerebrovascular autoregulation at the site of the epileptic focus.10 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 decerebroencephalic course of Todd’s motor, cognitive, and visual phenomena.1,4

L S BOYLAN
Department of Neurology, New York, New York, 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.

Statistics and analysis of the Camino ICP monitor

We have concerns about the mathematics, account for 71% of implantations and three positive cultures from 16 subdural devices do not account for 10.7%. Furthermore, the positive cultures from 16 subdural devices need to be “zeroed” before insertion to “calibrate” and “to zero” interchangeably not “calibrated.”

The paper reports on 108 probes in 101 patients. Details of patients should relate to patients with postictal psychoses by cerebral PET. In our patients, the nonen being the underlying pathophysiology.

We think that the underlying mechanisms 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-emergence 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. To understand the pathophysiology of postictal psychosis, we wish to study the electrical activities of patients with postictal psychoses by intracranial electrodes and regional cerebral metabolism by cerebral PET.

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

I read with interest the recent article by Cabre et al. 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). 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, sulfadiazine 4–8 g/day; pyrimethamine for suppressive therapy is not given at 25–75 mg four times a day but rather as 25–75 mg/day and folinic 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.
Manual of Nerve Conduction Studies


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 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. The book begins with a historical overview to set what follows in historical perspective. Then follow chapters on anatomy, neuromuscular, and synaptic transmission, the morphology 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-quated, now’s your chance!

Gillian Hall

Manual of Nerve Conduction Studies


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 basket 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.

Buschacher 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.

Simon Shorvon

The Autonomic Nervous System and its Effectors.


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 cognitive changes in 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 review 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 author, more prevalent than cognitive dysfunction. Again, this psychiatry section is clear and structured (with summary points at the end of each chapter) detailing DSM-IV definitions of the above disorders, providing some treatment guidelines, and incorporating illustrative case vignettes. However, the focus on DSM-IV is not in line with the perspective that is taken mainly from the multiple sclerosis rather than from the psychiatry aspect, results in some limitations to the given account.

There is also a regrettable disregard for the non-English literature, particularly on the association between depression and multiple sclerosis (for example, the great book by Ombredane). The range of psychiatric symptoms and syndromes seen in patients with multiple sclerosis (for example, anxiety symptoms, fatigue, irritability syndromes, adjustment reactions, personality effects, etc.) is not covered and there is little on the description of such psychopathology. Similarly, discussions on the nature of the association between psychiatry and multiple sclerosis is restricted and superficial (despite excellent papers in English where this is treated in depth). Explanations for a lack of clear association between multiple sclerosis and psychiatric problems, are focused on the variability inherent in multiple sclerosis and the diversity of its course. Other possible explanations—for example, relating to the nature of the psychopathology of the way in which it is elicited—are not explored.

Overall, the main contribution of this book is in the chapters on cognitive changes in multiple sclerosis which are clearly and concisely presented. It will be useful for anyone involved in the management of patients with multiple sclerosis.

Simon Shorvon

The Clinical Neuropsychiatry of Multiple Sclerosis


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 cognitive changes in 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 review 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 author, more prevalent than cognitive dysfunction. Again, this psychiatry section is clear and structured (with summary points at the end of each chapter) detailing DSM-IV definitions of the above disorders, providing some treatment guidelines, and incorporating illustrative case vignettes. However, the focus on DSM-IV is not in line with the perspective that is taken mainly from the multiple sclerosis rather than from the psychiatry aspect, results in some limitations to the given account.

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Overall, the main contribution of this book is in the chapters on cognitive changes in multiple sclerosis which are clearly and concisely presented. It will be useful for anyone involved in the management of patients with multiple sclerosis.

Simon Shorvon

Memory Disorders in Psychiatric Practice


Until the end of the 19th century little distinction was made between complaints of poor memory due to disorders that have since been shown to be organic in nature and memory disturbances of a less certain provenance—for example, Ganserian states. Since then, and increasingly over the past decade, memory disorder as a clinical concept has narrowed to embrace only those disorders in which memory impairment can be objectively demonstrated and measured. The authors deprecate this development and the main purpose and thrust of this volume is to rectify it. They, a psychiatrist and a neurologist, together run a memory “complaints” clinic and this is fitting as it is the diverging pattern taken by these two clinical disciplines as much as the emergence of cognitive neuropsychology that is responsible for the fragmentation of the clinical concept of memory disorder.

The contributions are from psychologists, psychiatrists, and neurologists; some are clinicians, some researchers, some both. The book is divided into thirds. The first sector comprises general overviews—topics such as the dementias, the psychopathology of the dementias, and for their eyes to glaze over.

The rationale for the second section is less clear. Chapters on organic disorders—for example, transient global amnesia—rub shoulders with chapters on normal aging, and on disconnection syndromes. The Cambridge Clinic is described with the authority that comes from assessing 100 patients a year over 8 years (although the number of self report scales used in the psychiatric assessment must be a computational nightmare).

The final section is given over to the “clinically disenchanted” areas of memory disorder. Paradoxically, given the authors stance, this is the least successful part of the book.
The choice of topic is sometimes surprising: flashbulb and flashback memories may be of interest in their own right, but they are unlikely to figure prominently in most memory clinics and sit rather awkwardly there. There is little on the effect of normal aging 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 malinger- ing 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 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 the commercial demics 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 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 is a book that one would be happy to read through, but it would be a useful addition to every departmental library.

R.C. PEATFIELD


This multimedia 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 with three 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.

David J Dick


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

BRIAN TOONE


Whether it is because peripheral nerve has a limited repertoire of responses to pathologi- cal insults or whether it is because advances in other areas of neuropathology have side- lined interest, for many years peripheral nerve disease has been the Cinderella of that specialty. Indeed there have been very few monographs on this subject since Boy Weller first published his Peripheral 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 anatomy of peripheral nerve. There then follow chapters on biopsy techniques and importantly a section devoted to artefact. After chapters on morphometry and abnor- mal 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 referenced and well annotated and clearly the book is a useful addition. It is not however a book that one 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.

CENTRAL NERVOUS SYSTEM ANGIITIS. By JAMES W SCHMIDLEY (Pp 240, £70.00). Published by Butterworth Heinemann, Oxford, 2000. ISBN 0 7506 7153 X.

Schmidley's book on CNS angiitis is an absolute gem. He concisely summarises the salient information in a concise 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 sumamrising 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 excerpts from individual patients. The book begins with a breadth in depth but concisely reviews the clinical and pathological features and the diagnosis and treatment of isolated CNS angiits. Included is an excellent chapter on pathogenesis which reviews complex immunological theories in a very readable summary form. Later chapters deal with postpartum angiitis, cases of supposed angiitis diagnosed by angiography, and various infectious and systemic and vascular disorders that have been postulated or proved to include angiitis of the brain's vasculature. Coverage of individual disorders such as neurosarcoidosis, Behcet's disease, sclerodema, Eales' disease, inclusion body myositis, lupus, vasculitis 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 impor- tant points that are not widely known to neuro- logists. I mention only a few here. (1) Isolated CNS angiitis presents 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 angiitis 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 angiitis can only be confidently diagnosed on biopsy. (4) Stroke is almost never the first presentation of polyarteritis nodosa or temporal arteritis. (5) Most strokes in patients with lupus erythema- tosus are not attributable to a CNS vasculitis. (6) The brain lesions in Behcet's Syndrome are probably related to a meningoencephalo- myelitis rather than a true angiitis. (7) The brain lesions in Behcet's syndrome are not attributable to a CNS vasculitis. (8) Most strokes in patients with lupus erythema- tosus are not attributable to a CNS vasculitis. (9) The brain lesions in Behcet's Syndrome are probably related to a meningoencephalo- myelitis rather than a true angiitis.

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 refer- ences in patients suspected of having any form of systemic or CNS angiitis.

LOUIS R CAPLAN


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.

David J Dick

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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 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

Table 2 Treatment and prophylaxis of cryptoccocosis and toxoplasmosis in HIV infection

<table>
<thead>
<tr>
<th></th>
<th>First choice</th>
<th>Alternative</th>
</tr>
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<tbody>
<tr>
<td><strong>Cryptoccocosis:</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><strong>Prophylaxis (patients with positive IgG serology and CD4 count &lt;100/mm³)</strong></td>
<td>Trimethoprim 160 mg plus sulfamethoxazole 800 mg orally/day</td>
<td>Trimethoprim, 160 mg plus sulfamethoxazole, 800 mg orally/day</td>
</tr>
<tr>
<td></td>
<td>Dapsone 50 mg/day plus pyrimethamine 50 mg/week plus folic acid 25 mg/week</td>
<td></td>
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</tbody>
</table>
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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