

LETTERS TO THE EDITOR

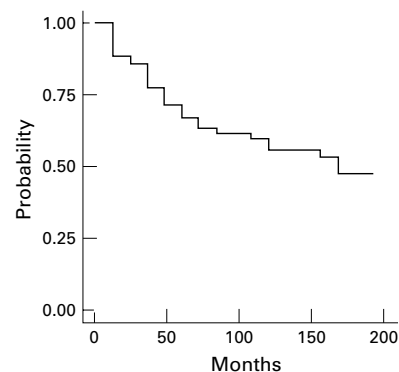
Acute Optic Neuritis in Australia: a 13 year prospective study

The frequency with which multiple sclerosis develops after an attack of acute optic neuritis varies widely in different series and has been reported to range from 11.5% to 85%.¹ The variability in the findings may relate to different methods of patient selection, diagnostic criteria, geographical factors, duration of follow up, and study design.

A cohort of 82 patients (59 females, 23 males) with uncomplicated ON aged 10 to 50 years (mean 29.2) who were examined neurologically and had visual evoked responses (VERs) performed in our department during the period 1973-83 were re-examined in 1983-85. Twenty six of the patients (32%) had progressed to probable or clinically definite multiple sclerosis during the follow up period of 7-114 (mean 57) months. Female sex, young adult age, and the presence of HLA-B7 or DR2 seemed to increase the risk of developing the disease.²

Seventy one of the 82 (87%) (52 females, 19 males) were reviewed in 1991-2; 11 patients could not be traced. Neurological examination was performed on 49; two patients had died with multiple sclerosis and a telephone questionnaire was completed on the remainder. Thirty three (46%, or 40% of the original 82) had developed probable or clinically definite multiple sclerosis after a mean duration of 13.25 years (range 8-29.6 years). Eight cases had developed multiple sclerosis since the previous review. Kaplan-Meier and actuarial methods of assessment,³ predicted that 52% would develop the disease after 15 years (figure). There was a significantly greater risk of developing multiple sclerosis for patients in the 21-30 year age group than those outside this range but there was no significant difference in the rate of progression to the disease for males and females. There was no significant difference in the probability of developing multiple sclerosis in patients with single or recurrent attacks of optic neuritis or bilateral optic neuritis, nor in those who were DR-2 positive (table 1).

The finding in the Australian cohort that 52% of patients with optic neuritis were at risk of developing probable or clinically definite



Probability of patients with a first attack of optic neuritis not developing multiple sclerosis in 15 years.

Clinical features of patients with optic neuritis (ON)

	ON	ON-multiple sclerosis	
Age (y):			
≤20	10	4	
21-30	8	17	
31-40	11	9	
41-50	9	3	$\chi^2 = 8.7, 3df, p=0.07$
Sex:			
Males	13	6	
Females	25	27	$\chi^2 = 1.57, 1df, p>0.10$
ON Type:			
Single	23	17	
Recurrent	11	13	
Bilateral	4	3	$\chi^2 = 0.82, 2df, p>0.5$
HLA Type*:			
DR2+	15	22	
DR2-	19	11	$\chi^2 = 2.63, 1df, p>0.1$

*Four subjects not typed.

multiple sclerosis in 15 years is comparable with that of 57% in 11.6 years in the United Kingdom,⁴ 49% in 20 years in the United States,¹ and 45% in 15 years in Sweden.⁵

JANE A FRITH
JAMES G MCLEOD

Institute of Clinical Neurosciences, University of Sydney and Royal Prince Alfred Hospital, Sydney, Australia

MARIESE HELY

Department of Neurology, Westmead Hospital, Sydney, Australia

Correspondence to: Professor J G McLeod, Department of Medicine, University of Sydney, NSW 2006, Australia email rachelp@med.usyd.edu.au

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Post-traumatic hydrocephalus: influence of craniectomy on the CSF circulation

Post-traumatic ventricular dilatation may have a wide range of aetiological factors: starting from neuronal loss due to head trauma and possible secondary ischaemic insults, to obstruction of CSF circulation resulting in hydrocephalus. It is important to differentiate between post-traumatic hydrocephalus and brain atrophy before considering placement of a shunt. Making this decision can be facilitated by measurement of the resistance to CSF outflow.¹ However, the pattern of the CSF circulation may change dramatically after a cranioplasty resulting from a previous decompressive craniectomy for refractory intracranial hypertension after head injury. The effect of the skull and dura on CSF hydrodynamics has been explored experimentally: the resistance to CSF outflow after craniectomy decreases two-fold and brain compliance (expressed using the pressure-volume index, PVI) increases.² This problem is important clinically as the following case illustrates:

A 44 year old man fell downstairs and was admitted with a Glasgow coma score (GCS) of 4. Brain CT disclosed an intracerebral haematoma, which required a right frontal lobectomy and decompressive craniectomy to control raised intracranial pressure. Five months later he remained severely disabled with deteriorating GCS and increasing spasticity. Brain CT showed a progressive ventricular dilatation with widening of the cortical sulci. Cranioplasty had been delayed because of persistent problems with infections.

The first lumbar computerised infusion test³ was performed 5 months after injury to study the patient's CSF circulation. The opening pressure was low (5 mm Hg) with a very low pulse amplitude. An infusion of normal saline at a rate of 1.5 ml/min increased the intracranial pressure (ICP) to a plateau of 12.2 mm Hg within 22 minutes. The calculated resistance to CSF outflow was normal (5 mm Hg/ml/min) and the pressure-volume index was increased to 28 ml (figure).

It is important to mention here that the normal range for the pressure-volume index, calculated from the constant rate infusion (as an inverse of elastance coefficient⁴) is different from the values obtained by the bolus injection.¹ Values below 13 ml indicate a tight brain, from 13 ml to 23 ml normal compliance, and above 23 ml hypercompliant brain. A slow constant rate infusion tests global compliance of the craniospinal axis whereas a fast bolus volume load probably tests compartmental compliance of the container into which the extra volume is added.

This pattern of CSF circulation with low or normal resistance to CSF outflow, increased brain compliance, and very few vasogenic waves is characteristic of cerebral atrophy.³

Cranioplasty was carried out as his deterioration was attributed to the "syndrome of trephined" where the brain sinks in, particularly with erect posture and dehydration producing deterioration in conscious level and focal signs. However, 1 month later, there had been no progress in the patient's condition and repeat CT again suggested progressive ventriculomegaly. The infusion study was repeated. The opening ICP was not dramatically different (10 mm Hg) to the previous study. However, the pulse amplitude (1.5 mm Hg) was increased, and the calculated resistance to CSF outflow was greatly increased to 20 mm Hg/ml/min, with a normal pressure-volume index of 15 ml. Such a pattern is specific for hydrocephalus. After this test the patient was shunted with a Codman Medos programmable valve (setting 120 mm H₂O) ventriculoperitoneal shunt with remarkable clinical improvement, the GCS rose to 14, he began to talk and his spasticity in his arms decreased dramatically. It is obvious why the pressure-volume compensatory reserve (PVI) decreases after cranioplasty,⁵ but the interpretation of an increase in the resistance to CSF is not immediately apparent. Two explanations are possible:

The patient had developed an acute hydrocephalus, possibly as a result of traumatic subarachnoid haemorrhage. Craniectomy was a factor allowing compensation of CSF circulation in the early stages. It is difficult to explain what is the nature of such compensation. Shapiro *et al*⁶ attempted to offer an interesting but conceptually difficult hypothesis that the time constant (resistance to CSF outflow × compliance of cerebrospinal space) of cerebrospinal system hydrodynamics has a tendency to remain constant. Therefore, a

mechanistic increase in compliance after craniectomy tends to be followed by a decrease in the resistance to CSF outflow. This process may be reversed after cranioplasty—that is, a decrease in PVI may be followed by an increase in the resistance to CSF outflow.

The second possible scenario is more important for clinical management. A large craniectomy may facilitate irreversible ventricular enlargement over weeks or months.⁴ Thus, after cranioplasty, the expanded

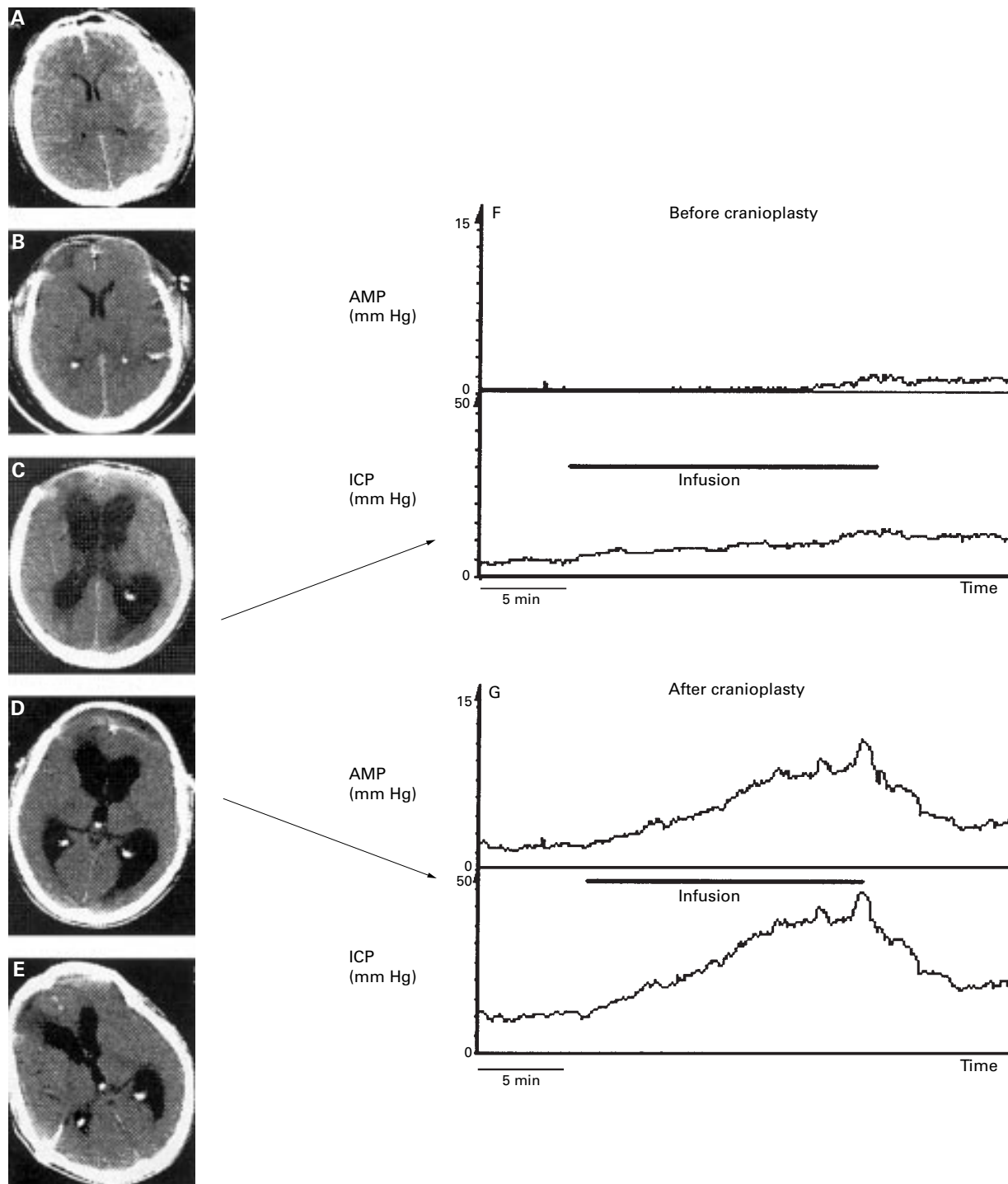
ventricles may, via the cerebral mantle, obstruct the lumen of the cortical subarachnoid space and increase the resistance to CSF outflow.

This case demonstrates that when the CSF circulation is studied in patients with a large craniectomy the CSF outflow resistance cannot be taken reliably as a guide for shunting. Overnight ICP monitoring or CSF infusion study should be performed after cranioplasty, when CSF circulatory reserve decreases dramatically. Moreover, a

prolonged period without a bone flap may encourage ventricular dilatation.

MAREK CZOSNYKA
JO COPEMAN
ZOFIA CZOSNYKA
ROY S MCCONNELL
CATHERINE DICKINSON
JOHN D PICKARD

Academic Neurosurgical Unit, Addenbrooke's
Hospital, Cambridge CB2 2QQ, UK



CT and infusion studies. (A) Scan performed on admission. (B) After right frontal lobectomy and bone flap removal. (C) Four months after injury, before cranioplasty. (F) Infusion test demonstrated low resistance to CSF outflow and increased brain compliance. ICP=mean intracranial pressure; AMP= pulse amplitude of ICP waveform. Constant infusion rate of 1.5 ml/min is indicated by a thick horizontal line. X axis=time. (D) Five months after injury, after cranioplasty. (G) Infusion test demonstrated grossly increased resistance to CSF outflow and normal brain compliance. (E) One month after shunting: normalisation of ventricles. Bicaudate index decreased from 33% to 21% with a decrease in the 3rd ventricle diameter (from 13 mm to 8 mm).

Correspondence to: Dr Marek Czosnyka, Academic Neurosurgical Unit, Box 167, Addenbrooke's Hospital, Cambridge CB2 2QQ, UK email MC141@MEDSCHL.CAM.AC.UK

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Diencephalic amnesia and apraxia after left thalamic infarction

Amnesia and apraxia are unusual manifestations of unilateral thalamic lesions. A patient in whom severe amnesia and apraxia were the presenting features of a left thalamic infarct is presented. The findings support the concept that memory and praxis both utilise circuits which include the dominant thalamus.

A 78 year old right handed Hungarian woman presented with memory loss and disorientation. She had been well and conversed normally with her daughter on the evening before presentation. The next morning, her daughter was alarmed to find her mother's house in a state of disarray. Dishes were unwashed, lights left on, and doors open. The patient seemed baffled by eating utensils, attempting to scoop food with her knife. Later that morning, she failed to recognise longstanding Hungarian friends. She was unable to recall her address, the name of the city in which she lived, or the names of her grandchildren. She subsequently failed to recognise her family doctor of 7 years. History included non-insulin dependent diabetes, hypertension, hyperlipidaemia, and atrial fibrillation. Medications were digoxin,

glibenclamide, and metoprolol. Captopril had been prescribed 4 weeks previously but was ceased 2 days before presentation due to presyncopal symptoms. The patient consumed no alcohol. There was no history of cerebrovascular events.

Cognitive functions were examined at the bedside with the assistance of an interpreter, as the patient spoke no English, although she conversed freely in her native Hungarian. She had no recollection of events since emigrating to Australia 50 years previously, gave her correct maiden name, and could not recognise or name her grandchildren, although she recognised her daughter. She acknowledged she was in a hospital, but maintained it was in Budapest and the year was 1947. Although her recollections regarding her early life and wartime Hungary seemed accurate, she confabulated when asked for details of recent events. Short term recall of verbal material and people was poor. The patient was able to name objects such as a pencil and a watch, and obey two and three stage commands. She wrote her name and copied simple designs correctly, and could imitate gestures such as waving goodbye or blowing a kiss. However, she was unable to use eating utensils or a toothbrush, either in pantomime or when provided with the object itself. Movements of the face and limbs were normal, and there were no sensory abnormalities. Knee and ankle jerks were absent bilaterally and both plantar responses were extensor. General examination revealed atrial fibrillation and mild cardiomegaly.

The patient continued to display severe impairment of anterograde memory. She was reluctant to leave her bed, and quickly became lost unless supervised. She did not recognise familiar staff members and was unable to use ward landmarks to reorientate herself. She required assistance to feed herself, brush her teeth, and shower. When reviewed 3 months later, her memory disturbance and apraxia for simple activities of daily life (such as brushing her teeth) persisted, necessitating care in a supervised environment.

Brain MRI (figure) showed a left anterior thalamic lesion consistent with lacunar infarction and periventricular white matter disease.

Deficits of anterograde and retrograde memory after thalamic lesions are well recognised.¹ The syndrome of diencephalic amnesia after bilateral medial thalamic lesions typically involves striking disorientation for time, loss of autobiographical information (often extending back for many years), confabulation, and severe anterograde amnesia for verbal and visual material, including recognition of familiar faces.¹ These features were well illustrated by our patient, who became "marooned" in an earlier place and time. Amnesia after unilateral thalamic lesions is rare.² There is increasing evidence that thalamic lesions interrupt the multiple brain networks which form the anatomical substrate of memory,¹⁻⁴ encompassing the hippocampus, medial thalamus, frontal and cingulate cortices, and overlapping with the language areas of the left hemisphere.³ The thalamus is activated in retrieval of episodic (autobiographical) and semantic (encyclopaedic) information from long term storage⁴ and execution of learned motor tasks,⁵ which may reflect its widespread connections with other subcortical and cortical structures.

The patient's ability to name or identify objects was not tested systematically. However, on the evidence available, it seems likely that her difficulty in utilising common objects was a manifestation of apraxia for daily tasks rather than, for example, agnosia for the objects involved. Apraxia is a rare manifestation of isolated thalamic lesions.⁵ The ability to access stored motor representations is thought to be crucial for normal execution of learned actions.⁵ These motor representations or "engrams" are analogous to motor memories. Although praxis is generally regarded as a function of distributed cortical regions in the left hemisphere, apraxia in association with thalamic amnesia has not been emphasised in previous reviews of this syndrome.¹⁻³ Involvement of deep hemispheric white matter in association with basal ganglia pathology is thought to be critical for the development of apraxia after lesions of subcortical structures.⁵ The conjunction of diencephalic amnesia and apraxia after thalamic infarction in the present case may be interpreted as further evidence that retrieval of episodic, semantic, and motor memories is mediated by overlapping functional networks in the dominant hemisphere.^{1-3,4}

JD WARREN

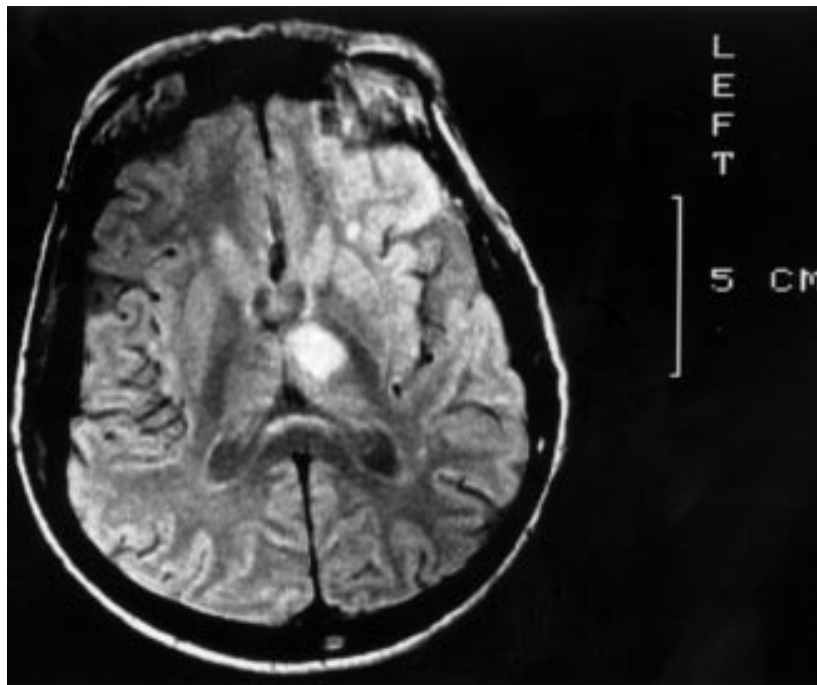
PD THOMPSON

Department of Neurology, Royal Adelaide Hospital, Adelaide, South Australia

PD THOMPSON

University Department of Medicine

Correspondence to: Professor PD Thompson, University Department of Medicine, Royal Adelaide Hospital, Adelaide, South Australia 5000, Australia



T2 weighted axial MRI brain slice showing ischaemic infarction of the left anterior thalamus and periventricular white matter ischaemic changes.

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Transverse myelopathy in the antiphospholipid antibody syndrome: pinworm infestation as a trigger?

The antiphospholipid antibody syndrome is a disorder characterised by the production of autoantibodies directed against negatively charged cell membrane phospholipids. Antiphospholipid antibodies have been described in various neurological disorders.

It has been generally accepted that viral, bacterial, and parasitic infections can serve as a trigger factor for autoimmune reactions. Despite the growing knowledge that has accumulated, the relation between parasites and autoimmunity has not been clarified.

Enterobius vermicularis (pinworm) is a nematode rarely found outside the gastrointestinal tract, but allergic reaction due to enterobiasis has been reported.¹ We describe the case of transverse myelopathy preceded by intestinal pinworm infestation in the primary antiphospholipid antibody syndrome. To our knowledge, such an association has not been reported previously. Pinworm therapy was complicated by the Jarisch-Herxheimer reaction manifested by temporary exacerbation of pre-existing neurological symptoms.

In March 1998, a 40 year old woman who complained of perianal itching noticed the presence of worms migrating from the anus. Three days later itching and numbness involved both legs, and the patient had weakness in the legs. These symptoms progressed over the next 3 days to severe paraparesis and urinary urgency. Her medical history was relevant for three unexplained miscarriages which all occurred in midpregnancies. In the local hospital, she underwent brain and lumbar-sacral spine MRI and findings were normal. Cerebrospinal fluid examination disclosed slightly raised proteins of 670 mg/l, 2 lymphocytes/mm³; oligoclonal immunoglobulin (Ig) G bands were absent. She was treated with methylprednisolone (1 g/day) intravenously for 5 days with subsequent gradual tapering off, which was associated with substantial improvement of motor, sensory, and sphincter disturbances. At the end of April 1998, the patient was transferred to our hospital for further investigation.

Neurological examination showed mild spastic paraparesis, bilateral Babinski's sign, and a Th-12 sensory level.

Erythrocyte sedimentation rate was 34. Complete blood count, tests for hepatic and renal function, angiotensin converting enzyme, concentrations of IgG, IgM, IgA, IgE, and immune complexes, screening for antinuclear (HEp-2 cells), anti-ds DNA, antineutrophil cytoplasmic, antimitochondrial, and antiparietal cell antibodies, rheumatoid factor, and the search for antineurotropic virus and antiBorrelia antibodies were normal or negative. A venereal disease research laboratory flocculation test was negative. A medium positive concentration of IgM anticardiolipin antibody was detected, and lupus anticoagulant was negative. Raised titres of serum IgG and IgM anti-GM1 (1:1600 and 1:3200, respectively) and antisuльфatide antibodies (1:6400, for both classes) were also demonstrated. Class II human leucocyte antigen (HLA) typing showed the presence of HLA-DR3, DR4, DR52, DR53, DQ2, and DQ3. Cervical and thoracic spine MRI was normal. Electromyoneurography was normal.

Because the patient complained of reappearance of worms and perianal itching, a cellulose adhesive tape test was performed and diagnosis of enterobiasis was established.

Mebendazole was given in a single dose of 100 mg and the next day the Jarisch-Herxheimer reaction occurred, with deterioration of leg spasticity, inability to walk, and development of urinary retention. At that time, low positive IgG ACA was detected. The dose of prednisone was raised to 60 mg/day and slowly tapered off within the next 2 months. Sphincter disturbances resolved in 1 day and motor dysfunction gradually improved with only mild spasticity left.

Diagnosis of antiphospholipid antibody syndrome in our patient was based on the presence of recurrent fetal loss, transverse myelopathy, and raised ACA. The ACA titre was probably lowered by previously administered corticosteroid therapy. There are several reports of transverse myelopathy as a manifestation of antiphospholipid antibody syndrome in the past decade.^{2,3} A potential pathogenic role of antiphospholipid antibodies in transverse myelopathy might be based either on vasculopathy or on interaction with spinal cord phospholipids.

Infection by helminths is universally associated with activation of T helper 2 (Th2)-type cells. Regardless of the mechanisms and protective value of antihelminthic Th2 responses, such responses may also be detrimental to the host. The presence of ACA, anti-GM1, and antisuльфatide antibodies in our patient suggests a systemic response to *E. vermicularis*, as it has been shown that nematodes contain cardiolipin, ganglioside GM1, and sulfatides within their complex lipid composition.⁴ When parasites share epitopes with host tissue, such molecular mimicry may exploit host immune tolerance against a self determinant. Autoimmunity may occur if immune tolerance is overridden in genetically susceptible hosts. It has been proposed that the presence of pathogenic cross reactive autoantibodies could be the basis for the relation between nematodes and autoimmunity. It may be also postulated that *E. vermicularis* stimulated Th2 response which enhanced polyclonal autoantibody production resulting in the presence of ACA, anti-GM1, and antisuльфatide antibodies. The association of transverse myelopathy, ACA, and enterobiasis might be purely coincidental, which we assume to be highly unlikely. The finding of different autoantibodies, as well as the isotype switch of ACA, strongly suggests that pinworm infestation in our patient was the "triggering event" that increased the production of autoantibodies against cardiolipin and led to the development of transverse myelopathy.

The appearance of the spinal cord damage caused by ACA in our patient might have been facilitated by the simultaneous effect of anti-GM1 and antisuльфatide antibodies. A significant subset of the human anti-GM1 antibodies that reacted with the Gal(b1-3)GalNAc determinant also bound to oligodendrocyte-myelin glycoprotein which is a constituent of the myelin of the CNS. As for antisuльфatide antibodies, their presence has been already shown in some diseases affecting the CNS.

It is clear that parasitic infections can serve as a trigger factor of autoimmune reactivity, but the presence of autoantibodies or self reactive T cells is rarely associated with clinical manifestations. They develop only in patients with adequate immunogenetic and hormonal background for autoimmune diseases. In several studies, increased frequencies of HLA-DR4, DR7, DR53, and DQ7 were found in patients with antiphospholipid antibody syndrome,⁵ and in our patient

HLA-DR4 and DR53 were present. Additional studies are necessary to further elucidate the complex mechanisms of involvement of intestinal helminths in the processes of autoimmune activity.

JELENA DRULOVIĆ
IRENA DUJMOVIĆ
NEBOJSA STOJSAVLJEVIĆ
IVANA TRIPKOVIĆ
SLOBODAN APOSTOLSKI
ZVONIMIR LEVIĆ

*Institute of Neurology, CCS, School of Medicine,
University of Belgrade, Dr Subotića 6, 11000
Belgrade, Yugoslavia*

MARIJA MOSTARICA STOJKOVIĆ
Institute of Microbiology and Immunology

BRANKA BONACI
SLADJANA ANDREJEVIĆ
Institute of Allergy

Correspondence to: Dr J Drulović, Institute of Neurology, CCS, School of Medicine, University of Belgrade, Dr Subotića 6, 11000 Belgrade, Yugoslavia

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Radiologically selective visual pathway involvement in adult onset cerebral adrenoleukodystrophy

A case of adult onset cerebral adrenoleukodystrophy is presented with serial MRI showing selective involvement of the visual system with spread of disease along the fibre tracts of this system.

Adult onset cerebral adrenoleukodystrophy is the rarest presentation of adrenoleukodystrophy.^{1,2} It may present with various symptoms often including visual impairment.³ Brain MRI may show multiple areas of symmetric high signal intensity within cerebral white matter, usually affecting the occipital lobes.⁴⁻⁶ We present a case of adrenoleukodystrophy, in whom serial MRI demonstrated selective progression of demyelination through the visual pathways.

A thirty year old man presented in May 1996 with a 7 month history of deteriorating vision, slurred speech, incoordination, poor balance, generalised weakness, sleep disturbance, and headaches. His symptoms were worse on the right. He had no symptoms of postural hypotension.

His mother had been shown to be a carrier of X linked adrenoleukodystrophy (XL-ALD). His two elder brothers had died of XL-ALD at the ages of 6 and 7 years. In 1993 our patient had been shown to have abnormal serum concentrations of very long chain fatty acids (VLCFAs) and to be a carrier of the XL-ALD gene. At that time he was asymptomatic and had no abnormal neurological signs. Crohn's disease had been diagnosed in 1987 after an ileal resection although this had remained in remission.

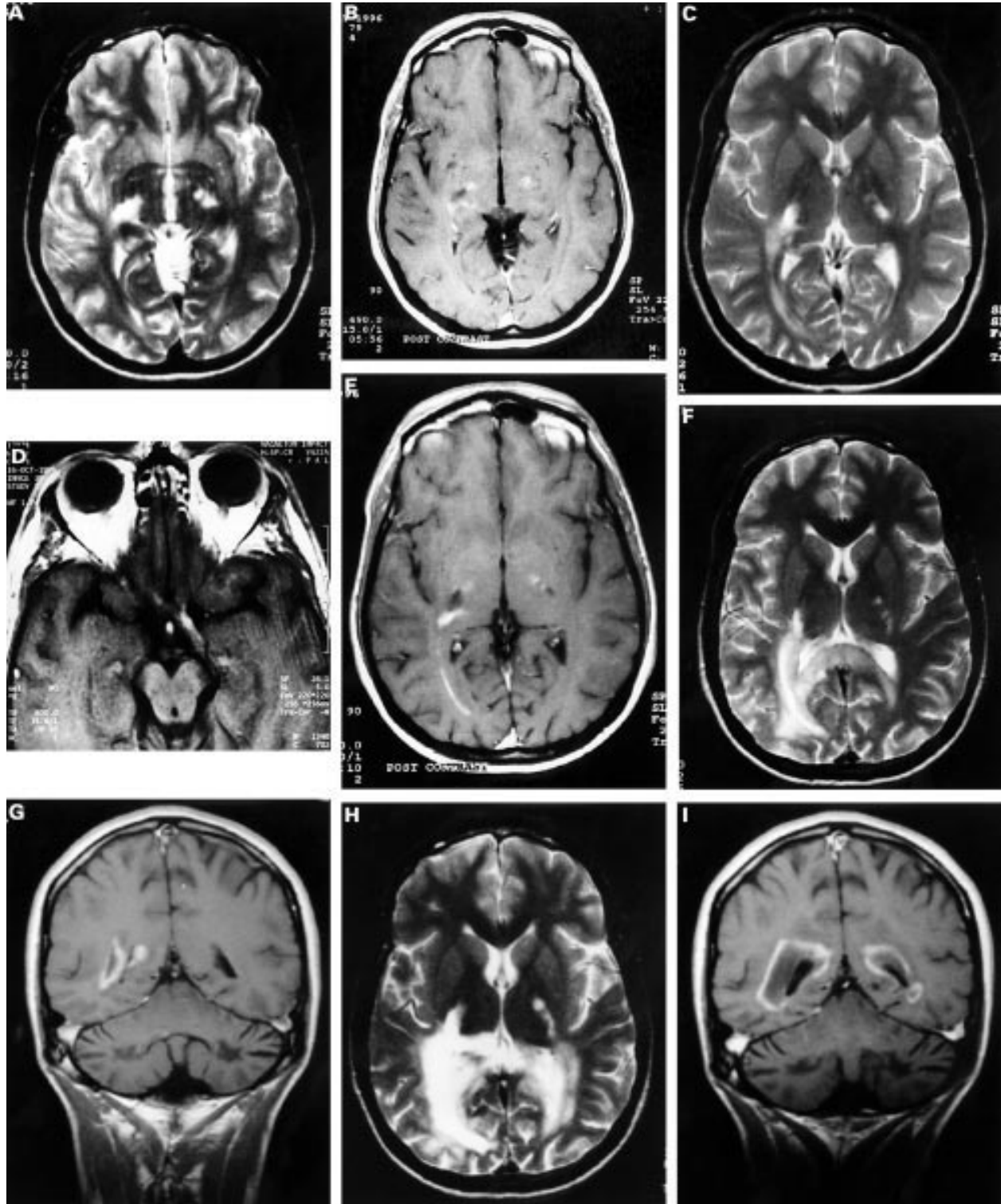
On examination, visual acuities were 6/12 (right), 6/9 (left). Fields were full to confront-

tation using a finger but there was a left homonymous field defect to a red pin and he had a left afferent pupillary defect. Fundoscopy showed bilateral optic atrophy. The remainder of the cranial nerve examination was normal. In the arms tone and power were normal, but coordination was mildly impaired on the right. The reflexes were exaggerated and Hoffman's sign was present

bilaterally. A palmomental reflex was present on the right. In the legs power was normal, but tone was increased and there were several beats of ankle clonus; reflexes were exaggerated and plantar responses were upgoing. Coordination was impaired in both legs, his gait was ataxic, and Romberg's test was positive. He had a minor reduction in vibration sensation at the right ankle; otherwise sensa-

tion was normal. He appeared moderately tanned, but there was no other hyperpigmentation. Supine blood pressure was 114/78, falling to 108/80 on standing. The remainder of the examination was normal.

Routine biochemistry was normal. A morning cortisol was 469 nmol/l (normal >160 nmol/l), but a short synacthen test showed an abnormally flat response (serum



Brain MRI at four different times spanning 2 years. (A) May 1996: T2 weighted axial. (B) May 1996: contrast enhanced T1 weighted axial. (C) October 1996: T2 weighted axial. (D) October 1996: T1 weighted contrast enhanced axial. (E) October 1996: T1 weighted contrast-enhanced axial. (F) August 1997: T2 weighted axial. (G) August 1997: T1 weighted contrast enhanced coronal. (H) May 1998: T2 weighted axial. (I) May 1998: T1 weighted contrast enhanced coronal.

cortisol rise from 338 to 449 nmol/l over 1 hour). His plasma VLCFA profile was abnormal consistent with XL-ALD. Humphrey visual field testing demonstrated a left homonymous field defect. Brain MRI was abnormal (figure A and B). He was placed on a very low fat diet with supplements of glycerol trioleate oil.

By October 1996 his headaches had settled but his eyesight, memory, coordination, and walking were worse. Visual acuity was below 6/60 in both eyes. Brain MRI was repeated (figure C-E). By August 1997 there had been no new clinical developments (MRI figure F-G). In May 1998 he complained of navigational difficulties in familiar surroundings, further memory loss, and cognitive decline (MRI figure H-I).

In May 1996 (figure A) T2 weighted axial imaging showed high signal intensity areas in the region of the right lateral geniculate nucleus and left optic tract. The occipital white matter was normal. T1 weighted images with gadolinium contrast enhancement (figure B) showed bilateral enhancement of the intracerebral optic tracts.

By October 1996 (figure C) T2 weighted axial imaging showed spread of the areas of high signal intensity continuously from the lateral geniculate nuclei posteriorly along the optic radiations into the white matter of both occipital lobes, more prominent on the right. T1 weighted images showed contrast enhancement in the optic chiasm and optic tracts (figure D), lateral geniculate nuclei, origins of the optic radiations, and right occipital white matter (figure E).

By August 1997 (figure F) there had been further progression in the white matter changes in both occipital lobes, with spread to the splenium of the corpus callosum. Contrast enhancement (figure G) was seen in the optic radiations and right occipital white matter. The cerebellar white matter was of low signal intensity, with a small area of contrast enhancement above the fourth ventricle to the right of the midline.

In May 1998 (figure H and I) the changes in white matter were yet more extensive with the appearance of ring enhancement.

Our case illustrates MRI appearances typical of adrenoleukodystrophy and demonstrates in particular the evolution of these changes with time. The tendency of this condition to affect the visual pathways selectively is well illustrated as is the spread of disease along the fibre tracts of that system. This allowed visualisation of parts of the visual system, the anatomy of which is usually hidden—for example, the intracerebral portion of the optic tracts. The characteristic MRI appearances are thought to result from an advancing front of active demyelination, followed by an area of inflammatory cellular response demonstrating contrast enhancement, surrounded by areas of established damage, gliosis, and neuronal loss.⁷

D S FARRELL
M C LAWDEN

Department of Neurology, Leicester Royal Infirmary,
Leicester, UK

N MESSIOS
Department of Radiology

Correspondence to: Dr M C Lawden, Leicester Royal Infirmary, Leicester, LE1 5WW, UK

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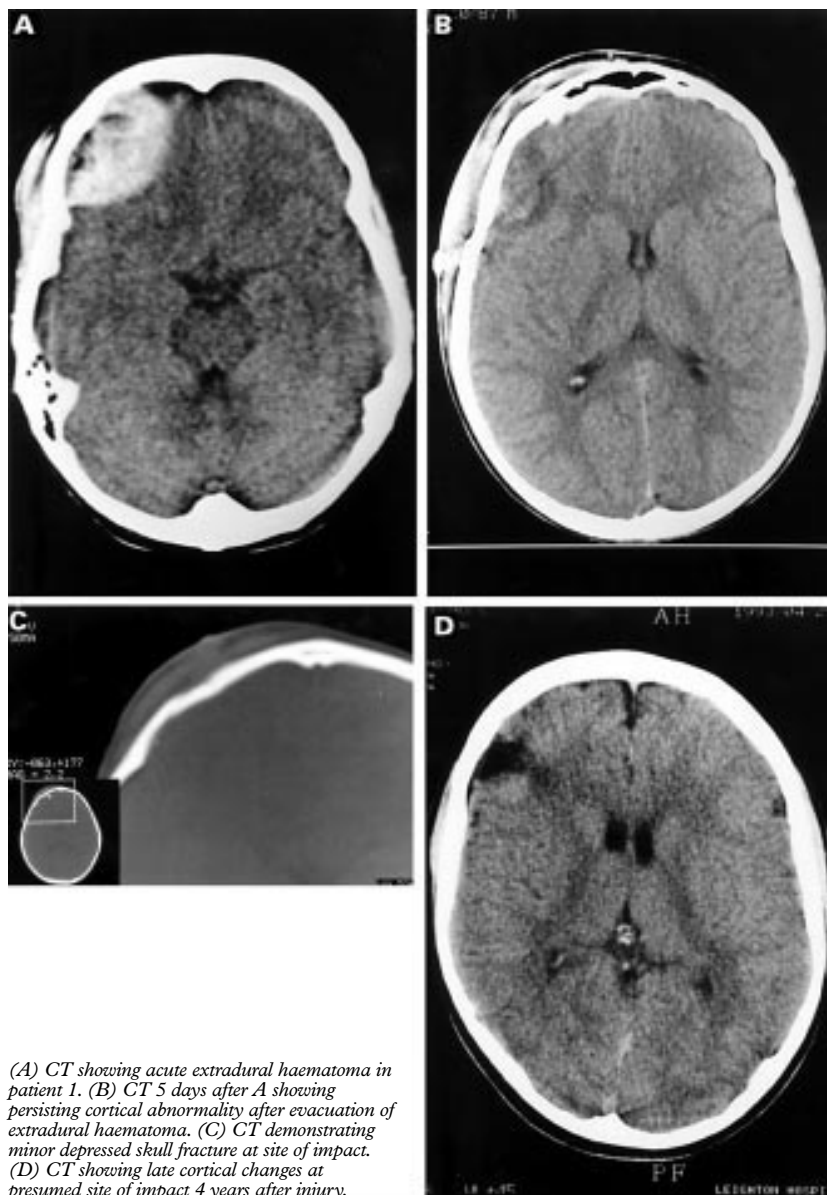
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Golf ball epilepsy

Blunt head injuries may cause epilepsy. We present the cases of four young people whose heads were all subject to contact with golf balls travelling at speed. Each had post-traumatic seizures, three early and one late, despite the apparent absence of post-traumatic amnesia. Although many patients who develop epilepsy recall some type of head injury preceding their first seizure, post-traumatic epilepsy probably accounts for less than 5% of all the epilepsies.¹ There is good

evidence that the risk of post-traumatic epilepsy increases with the severity of the injury. Thus, Jennett² identified the presence of intracranial haemorrhage, dural laceration, and early post-traumatic seizures as the chief risk factors for late post-traumatic epilepsy. Annegers et al also emphasised that in the absence of a post-traumatic amnesia of 30 minutes or greater, there was no significant increased risk for the development of post-traumatic epilepsy.³

From a practical point of view and for medicolegal purposes, it is necessary to decide if a seizure is post-traumatic. As a general rule it may be stated that if the person concerned does not give a history of a post-traumatic amnesia lasting for a significant period of time (an hour or more), and there is no history of a compound or depressed fracture with dural tear, it is reasonable to exclude the possibility that the epilepsy is post-traumatic. However, it is worth noting that this view is based on Jennett's work and precedes CT. There is no good evidence from a large series to indicate whether findings on acute imaging add anything to the prediction of post-traumatic epilepsy.



(A) CT showing acute extradural haematoma in patient 1. (B) CT 5 days after A showing persisting cortical abnormality after evacuation of extradural haematoma. (C) CT demonstrating minor depressed skull fracture at site of impact. (D) CT showing late cortical changes at presumed site of impact 4 years after injury.

Four examples of acute symptomatic seizures and epilepsy developing after head injuries with golf balls are described, which seem to be an exception to these clinical rules.

An 11 year old boy was struck on the right temple by a golf ball resulting in right frontal scalp contusion. His consciousness was not impaired until about 3 hours later when he became drowsy and had two focal motor seizures affecting the left arm. He was intubated and ventilated. A head CT showed a right frontal extradural haematoma with no skull fracture (figure A). The haematoma was evacuated (figure B). He was woken and extubated the next day and was discharged without neurological impairment two days later on phenytoin. No further follow up is yet available.

A 16 year old boy, who was a keen golfer with a single figure handicap, was struck on the head by a golf ball which rebounded several yards after striking him on the forehead. He experienced local pain, bruising, and swelling. Although he was never unconscious, some 4-5 hours later he developed repetitive jerking of the right face and arm. He was taken to his local casualty department where a diagnosis of serial focal motor seizures was made. His consciousness was then somewhat obtunded. A brain CT was performed which showed a small, discrete, spherical intracerebral haematoma in the left frontal lobe immediately beneath the skull at the point where he had been struck (similar in shape, but more hyperintense than the appearance in the figure B). The haematoma gave the distinct impression of a golf ball embedded in the surface of the cerebral hemisphere!

He was treated with parenteral anti-epileptic drugs and subsequently with thiopentone requiring ventilation for 48 hours while he was loaded with phenytoin.

He was maintained on phenytoin for 12 months but subsequently this was withdrawn and he has remained seizure free.

A 5 year old girl was struck on the forehead above the right eye by a golf ball struck 10 metres away. On arrival in the accident and emergency department she was fully alert, orientated, and neurologically intact. A laceration was present but there had been no apparent impairment of consciousness or vomiting. However, 90 minutes after the injury she had a generalised tonic clonic seizure lasting 25 minutes. She was intubated and ventilated. A CT scan showed a very small depressed fracture with minimal haemorrhagic contusion in the cortex of the right frontal lobe (figure C). She was woken and extubated later that day. She has had no further seizures.

A 12 year old boy was practising golf with a friend. He was struck on the front of the head by a golf ball which rebounded a considerable distance after striking him. He did not lose consciousness and had no more than localised pain, tenderness, and bruising at the site of impact. He did not seek any medical advice about the injury. Over the next 4 years he had three well documented tonic-clonic seizures that started during sleep.

A CT scan 3 years after the original injury showed a small, wedge shaped area of low density affecting the cortex close to the point at which he recalls being struck (figure D).

The heads of these four young people were all subject to contact with golf balls which at club level travel at speeds of up to 130 miles/hour. Each had post-traumatic seizures, three early and one late, despite the apparent absence of post-traumatic amnesia.

Patients 1 and 2 would indicate that this kind of injury is capable of transferring energy across the skull, independent of a skull fracture, to cause an acute extradural or cortical haematoma.⁴ In patient 4 the lesion identified at a later date by CT is consistent with the late consequences of a localised intracranial haematoma. It therefore seems reasonable to assume that the late epilepsy in patient 4 was also related to the initial golf ball injury.

In the third patient, a minor depressed fracture and contusion were again associated with an early seizure without evidence of intervening impairment of consciousness.

It does therefore seem that golf ball injuries are capable of giving rise to both acute symptomatic seizures and late epilepsy without causing post-traumatic amnesia, skull fracture or dural tear. CT evidence, however, would predict the possibility of seizures in these examples in whom the development of post-traumatic epilepsy probably results from the physical properties of golf balls and their ability to transmit considerable mechanical energy at a small site of impact. The problem is one of which spectators on golf courses (and their doctors) should be aware.

DAVID CHADWICK
DANIELA B CLEAR
PAUL ELDRIDGE
CONNOR MALUCCI

The Walton Centre for Neurology and Neurosurgery,
Lower Lane, Liverpool L9 7LJ, UK

Correspondence to: Professor D Chadwick, University Department of Neurological Science, The Walton Centre for Neurology and Neurosurgery, Lower Lane, Liverpool L9 7LJ, UK

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Sensory predominant neuropathy with GM₁ antibodies, conduction blocks, and orbital pseudotumour

Two male patients developed multifocal sensory neuropathy with high titre IgM anti-GM₁ antibodies (up to 1: 64 000) and infiltrative orbitopathy. Nerve conduction studies showed multiple motor conduction blocks and evidence of a similar phenomenon in sensory nerves. Both patients deteriorated after corticosteroid administration but benefited substantially from intravenous immunoglobulin therapy. Our findings suggest the existence of a predominantly sensory subtype of multifocal motor neuropathy (MMN) and challenge the postulated motor specificity of anti-GM₁ antibodies.

Anti-GM₁ antibodies have been implicated in the aetiology of multifocal motor neuropathy (MMN) and are assumed to be specific for this disease when occurring at high titres.^{1,2} We report on two patients with high titre IgM anti-GM₁ antibodies and electrophysiological features typical of MMN presenting with severe sensory neuropathy.

Patient 1 was a man who developed asymmetric numbness of limbs and difficulty in performing fine motor movements around the age of 55. Sensory deficits showed a multifocal pattern (multiple mononeuropathy) and involved proximal limb regions, trunk, and

face. The course of illness was steadily deteriorating with some episodes of prominent disease progression usually preceded by minor infections. After 10 years he was unable to write, needed assistance for dressing and walking, and complained of diplopia. Neurological examination showed profound loss of all sensory modalities in the arms and legs and pseudoathetosis of the fingers and wrist. Deep tendon reflexes were preserved and muscle strength was normal. The patient showed marked protrusion and downwards and outwards deviation of the left eye with a complex impairment of all eye movements.

Patient 2, a 68 year old man, reported an insidious onset and gradual worsening of asymmetric sensory loss and painful patchy dysaesthesia. At a neurological examination 15 years after disease onset, pinprick sensation, vibration, and proprioception were prominently affected in his arms and legs. There was severe ataxia of gait. Postural maintenance and voluntary movements strongly depended on visual guidance. Muscle strength was normal except for slight bilateral paresis of the tibialis anterior and intrinsic hand muscles (4+/5 MRC scale). There was no evidence of autonomic nerve or pyramidal tract dysfunction. Tendon reflexes were absent. The patient had an incomplete left side third nerve paresis and ipsilateral visual loss.

General physical examination was normal in both patients, as were repeated screenings for neoplastic and connective tissue diseases. Enzyme linked immunosorbent assays (ELISAs)³ showed IgM antibody activity against GM₁, asialo-GM₁, and GD_{1b}, presumably recognising the Gal(β1-3)GalNAc group (table). Clonality of ganglioside antibodies was not investigated. Serum immunoelectrophoresis did not show monoclonal gammopathy. All the following laboratory indices were normal or negative: creatine phosphokinase, erythrocyte sedimentation rate, renal and liver function, antinuclear antibodies, thyroxine, vitamins B₁₂, B₆, B₁₂, folic acid, urine porphobilinogen, and serum cryoglobulins. Cerebrospinal fluid was acellular with 52 mg/dl and 90 mg/dl protein, respectively (normal <50 mg/dl).

Nerve conduction studies showed multifocal slowing of motor nerve conduction velocities and F wave latencies (table). Despite near normal muscle strength we found motor conduction blocks at sites not prone to compression. Sensory nerve potentials could not be elicited in the median, ulnar, radial, or sural nerves. Electromyography showed fibrillation activity, generalised fasciculations, and features of chronic neurogenic damage. Magnetic resonance imaging of the brain, spinal cord, and dorsal nerve roots did not show relevant abnormalities. Both patients had non-progressive orbital infiltration with slight gadolinium enhancement suggestive of ectopic lymphoproliferative tissue. Lesion extension was most pronounced at the apex orbitae and fissura orbitalis superior and caused compression of the left optic and oculomotor nerves in one patient and mechanical interference with eye movement in the other. Analogous orbital infiltration has been described in patients with paraproteinemic neuropathies and antibody mediated autoimmune diseases such as myasthenia.

Administration of methylprednisolone at dosages of 40 to 60 mg/day was followed by marked deterioration of sensory ataxia in both patients. By contrast, substantial and rapid benefit was achieved by means of intravenous immunoglobulin (IVIg) therapy (0.4

Ganglioside antibody patterns and electrophysiological characteristics

Variable	Patient 1	Patient 2
Antibody titres:		
IgM GM ₁	1:64000	1:4000
IgG GM ₁	—	—
IgM asialo-GM ₁	1:32000	1:8000
IgG asialo-GM ₁	—	—
IgM GD _{1a}	—	—
IgG GD _{1a}	—	—
IgM GD _{1b}	1:500	1:32000
IgG GD _{1b}	—	—
IgM GT _{1b}	—	1:2000
IgG GT _{1b}	—	—
IgM GQ _{1b}	—	—
IgG GQ _{1b}	—	—
IgM sulfatide	—	—
IgG sulfatide	—	—
Nerve conduction studies:		
Right median nerve:		
DL (ms)/NCV ₁ /NCV ₂ (m/s)	4.5/48/56	4.6/32/65
F wave latency (ms)	33.0	43.6
Motor conduction block	+	+
SNAP	Absent	Absent
Right ulnar nerve:		
DL (ms)/NCV ₁ /NCV ₂ (m/s)	2.6/56/50	3.0/35/45
F wave latency (ms)	32.5	43.9
Motor conduction block	+	—
SNAP	Absent	Absent
Right peroneal nerve:		
DL (ms)/NCV ₁ /NCV ₂ (m/s)	6.6/42/39	5.2/33/31
F wave latency (ms)	86.9	62.5
Motor conduction block	+	+
SNAP	Absent	Absent

Antibody titres presented are those before treatment (baseline). SNAP=sensory nerve action potential; DL=distal latency; NCV=motor nerve conduction velocity in the following segments: median nerve: wrist-elbow (NCV₁, normal >50m/s), elbow-axilla (NCV₂, normal >56m/s); ulnar nerve: wrist-elbow (NCV₁, normal >50m/s), elbow-axilla (NCV₂, normal >55m/s); peroneal nerve: ankle-fibula neck (NCV₁, normal >42m/s), fibula neck-popliteal fossa (NCV₂, normal >41m/s).

g/kg body weight/day for five consecutive days). Gait normalised, fine motor movements and ophthalmoplegia markedly improved, and motor conduction blocks partially resolved. In addition, low amplitude sensory nerve action potentials reoccurred.

In the literature, there is circumstantial evidence of a pathogenic role of high titre IgM anti-GM₁ antibodies in the mediation of motor conduction blocks in MMN.^{1,2} Often, the antibody attack is directed at the Gal(β1–3)GalNAc epitope of GM₁. This carbohydrate group, however, is also an obligatory constituent of GD_{1b} (cross reactivity), which was implicated in the aetiology of sensory neuropathies. GD_{1b} distributes on human dorsal root ganglion cells and paranodal myelin and shows comparable immunostaining with anti-GM₁ antibodies with Gal(β1–3)GalNAc specificity and antibodies to disialosyl residues of GD_{1b}.⁴ This and various other findings challenge a motor specificity of anti-GM₁ antibodies and, instead, suggest a vulnerability of part of the sensory system. Actually, nerve conduction studies in previous series of patients with MMN showed numerous sensory abnormalities, as did pathological evaluations of sensory nerve biopsy specimens.^{5,6,7} We report on a predominantly sensory variant of MMN found in two male patients. Both had IgM anti-GM₁ and anti-asialo-GM₁ antibodies at titres high enough to be assumed specific for MMN.^{1,2} Despite near normal muscle strength both of our patients had multiple motor conduction blocks. Rapid clinical improvement after IVIg therapy despite a more than 10 year history of illness tempts us to speculate on a similar phenomenon in sensory nerves (sensory conduction block).

Good response to therapy argues against a pathogenetic significance of high titre GD_{1b} antibodies in patient 2, because the rare GD_{1b} associated sensory axonal neuropathy (sensory ganglionopathy) is mostly irreversible. In addition, this patient showed multiple con-

duction blocks and slowing of nerve conduction velocities rather than predominantly axonal damage and had no monoclonal gammopathy, which is usually present in cases with the GD_{1b} associated neuropathy.

We propose that multifocal neuropathies with conduction blocks and high titre anti-GM₁ antibodies have a clinical range from predominantly sensory to predominantly motor variants and suggest that all these variants be subsumed under the term “multifocal motor-sensory neuropathy (MMSN)”. This concept is of clinical relevance in that all phenotypes share the same therapeutic peculiarities including good response to IVIg and ineffectiveness (most cases) or even unfavourable effects of corticosteroids, which are first line drugs in the treatment of other immune neuropathies. Our report aims to increase awareness for sometimes prominent sensory involvement in MM(S)N and to facilitate early and accurate diagnosis in such patients.

STEFAN KIECHL
JOHANN WILLEIT
FLORIAN DEISENHAMMER
WERNER POEWE

Department of Neurology, Innsbruck University Clinic, Austria

Correspondence to: Dr S Kiechl, Department of Neurology, Innsbruck University Clinic, Anichstr 35, A-6020 Innsbruck, Austria. email: STEFAN.KIECHL@UIBK.AC.AT

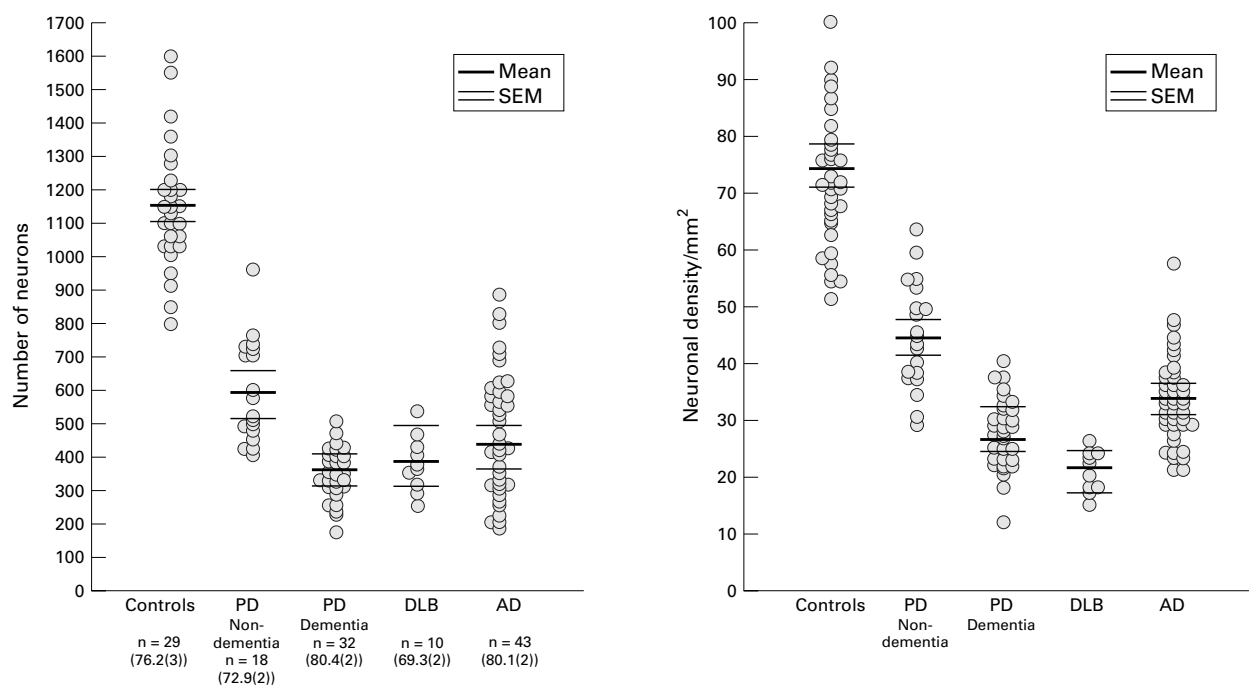
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CORRESPONDENCE

Alterations of muscarinic acetylcholine receptor subtypes in diffuse Lewy body disease: relation to Alzheimer's disease

The article by Shiozaki *et al*¹ demonstrating significantly less muscarinic acetylcholine receptor binding sites in the temporal cortex in dementia with Lewy bodies than in Alzheimer's disease and different upregulation of the m1 and m2 receptor subtypes suggests differences in the manner of degeneration of the cholinergic system between both dementing disorders that may be of basic and practical therapeutic relevance. The more severe reduction of ChAT activity in the neocortex in dementia with Lewy bodies than in Alzheimer's disease, the higher upregulation of the postsynaptic m1 receptor in dementia with Lewy bodies, and the higher level of the presynaptic m2 receptor subtype in Alzheimer's disease suggest a severe depletion of presynaptic projection neurons in dementia with Lewy bodies but their relative preservation or upregulation in Alzheimer's disease.¹ These data are in line with previous—including personal—findings on cell loss and shrinkage in the cholinergic magnocellular posterior part of the nucleus basalis of Meynert in dementing neurodegenerative disorders:² In Parkinson's disease (brain stem type of dementia with Lewy bodies), cell depletion in the nucleus basalis of Meynert averages 30% to 40% without correlation with age or duration of the illness. It is much higher in demented patients with Parkinson's disease (similar to Alzheimer's disease range 50% to 70%) than in non-demented patients (0% to 40%), who show neuronal loss similar to or only slightly higher than age matched controls. Cell loss in the nucleus basalis of Meynert in non-demented patients with Parkinson's disease is usually associated with little or no cortical Alzheimer's disease pathology, whereas in severely demented patients with Parkinson's disease, heavy cell depletion in the nucleus basalis of Meynert is often, but inconsistently, accompanied by severe cortical neuritic Alzheimer's disease pathology suggesting threshold levels of cholinergic forebrain impairment and deficit for the development of dementia.² Even more severe depletion of the nucleus basalis of Meynert with 75% to 80% loss of large cholinergic neurons is found in dementia with Lewy bodies (figure). There were no major differences in cell loss in the nucleus basalis of Meynert between dementia with Lewy bodies with “plaque only” Alzheimer's disease (two cases) and with “true” Alzheimer's disease (eight cases with Braak stages V or VI). Lewy bodies and neurofibrillary tangles in the nucleus basalis of Meynert neurons were seen in eight brains of patients with Lewy body disease.³



(A) Total number and (B) mean density of neurons in the magnocellular part (Ch4) of the nucleus basalis of Meynert in Parkinson's disease (PD) with and without dementia, Alzheimer's disease (AD), Lewy body variant of Alzheimer's disease (DLB), and age matched controls. Numbers in parentheses are mean age (SD).

These changes are associated with a decrease in cholinergic innervation of the cortex and hippocampus that may or may not correlate with the severity of cell loss in the nucleus basalis of Meynert and mental status. Neocortical cholinergic activity (choline acetyl transferase) is far more severely depleted in dementia with Lewy bodies than in Alzheimer's disease and Parkinson's disease, and correlates well with dementia and nucleus basalis of Meynert pathology (neuron loss, tangles, and Lewy bodies), but not with local cortical pathology.⁴ The heterogeneity of degeneration of cholinergic neurons in the basal forebrain and its relative independence from cortical pathology suggests primary involvement of the basal forebrain in Parkinson's disease, by contrast with probable retrograde damage in Alzheimer's disease and dementia with Lewy bodies confirmed by defective retrograde transport of nerve growth factor to the nucleus basalis of Meynert in Alzheimer's disease.⁵

These morphological differences in the degeneration of the cholinergic forebrain system between various dementing neurodegenerating disorders are, at least in part, supported by the data presented by Shiozaki *et al*¹ indicating differences between Alzheimer's disease and dementia with Lewy bodies as are also to be suggested between Alzheimer's disease and Parkinson's disease. These and other genetic, morphological, and biochemical differences between the three disorders may strengthen the hypothesis that they represent different nosological entities. This, however, needs further confirmation.

KURT A JELLINGER

Ludwig Boltzmann Institute of Clinical Neurobiology,
Vienna, Austria

Correspondence to:

Dr Kurt A Jellinger, Ludwig Boltzmann Institute
of Clinical Neurobiology, PKH/B-Building,
Baumgartner Hoehe 1, A-1140 Vienna, Austria

Correspondence to: Kurt A Jellinger
email kurt.jellinger@univie.ac.at

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Mortality from Parkinson's disease

The publication of the 10 year mortality data from the Sydney multicentre study of Parkinson's disease serves as a timely reminder that patients with this condition still die at a rate in excess of their peers despite advances in therapeutics and surgery.¹

This fact has been lost on many of our colleagues working in this area, both on the clinical and the research fronts. On many occasions at local and national meetings, I have been forced to remind people that levodopa has not normalised mortality rates in this condition.

Figure A indicates, as Hely *et al*¹ point out, the fall in standardised mortality rates (SMRs) in the early years of levodopa use but a return to mean SMRs of between 1.5 and 2.0 over the past decade. All of the studies over the past 10 years show a statistically significant difference as the 95% confidence intervals (95% CIs) do not embrace 1. In some, the upper 95% CI overlaps the original Hoehn and Yahr study in the prelevodopa era. These results mirror national mortality statistics for England and Wales (figure B). The fall in death rates in the

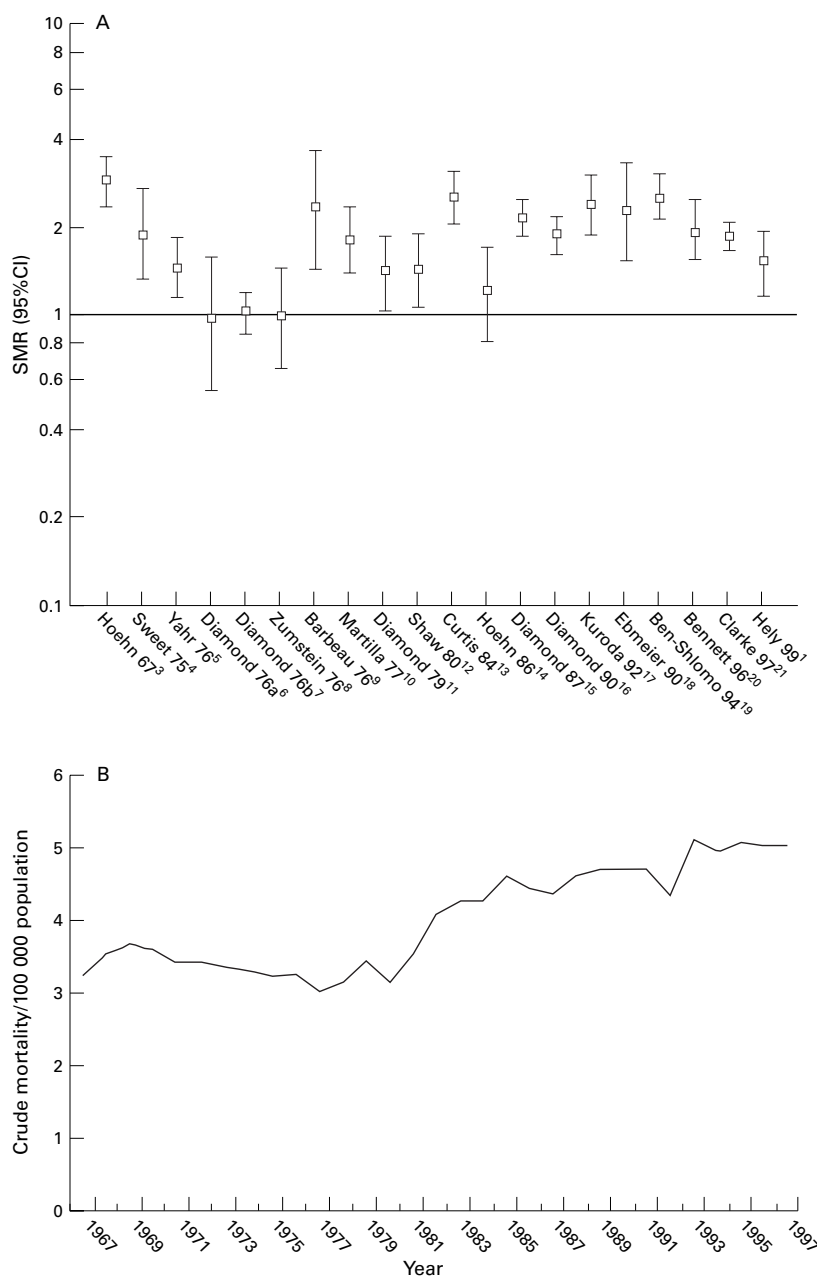
late 1970s and early 1980s has now returned to a steady rise, thought to be due to the aging of the population.²

These data must act as a spur to attempts to develop neuroprotective or restorative therapies which substantially reduce mortality from Parkinson's disease. Large pragmatic studies in the future which examine novel treatments or approaches in early Parkinson's disease must consider not only quality of life and health economics issues, but also mortality in the hope of establishing reduced death rates.

C E CLARKE

Department of Neurology, City Hospital NHS Trust,
Dudley Road, Birmingham B18 7QH, UK

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(A) Standardised mortality ratios (SMR) for previous cohort and case-control series (first author only given) examining mortality in Parkinson's disease plotted in chronological order of year of publication. Ratios greater than 1 with 95% confidence intervals (95% CIs) that do not embrace 1 indicate increased mortality in parkinsonian patients. (B) Crude mortality rate for Parkinson's disease in England and Wales over the same period as in (A). Corrected 1984-93 for changes in method of coding death certificates. (Source: Office of Populations, Censuses and Surveys mortality statistics.)

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Anaphylactoid reaction to methylprednisolone. Is it surprising when pharmacological and immune effects of a drug differ?

Clear reports a case of anaphylactoid reaction to methylprednisolone which developed after starting treatment with interferon β -1b. She states that "allergic reaction to steroids is rare and anaphylactoid reaction to methylprednisolone rarer still with only three reports in the literature."¹ Her report surprised us as on the week of publication of her case we had a patient with multiple sclerosis who developed an urticarial rash within 15 minutes of commencing treatment with intravenous methylprednisolone. Although we thought this to be an unusual response to methylprednisolone, we were not overly perplexed by the drug's capacity to induce a presumably IgE mediated immune response. Surely for almost all drugs the pharmacological and immune properties are quite distinct.

I undertook a brief literature search. The database was interrogated using Medline Pubmed and the words "anaphylaxis" and "methylprednisolone". At least 29 cases of anaphylactoid reaction to methylprednisolone are documented in this simple search. Kamm and Hagemeyer systematically review allergic reactions to corticosteroids in the April 1999 publication of *Annals of Pharmacotherapy*.² Their primary data source is a Medline search from January 1966 to December 1997. They report 56 allergic-type reactions to intravenous corticosteroids, including death in 12 patients suspected to be related to corticosteroid anaphylaxis. Methylprednisolone and hydrocortisone were the most commonly implicated corticosteroids. Is it surprising that the frequency of reporting of anaphylactoid responses to corticosteroids is low? I can see no inherent paradox between the ability of methylprednisolone to bind IgE and its pharmacological anti-inflammatory action. Clear's speculation about mechanisms by which interferon β may predispose to anaphylaxis may be interesting. However, it is unreasonable to ascribe the anaphylactoid response to methylprednisolone to therapy with interferon β .

M F YOUNG
J P MCCONVILLE
Department of Neurology, Royal Victoria Hospital,
Grosvenor Road, Belfast, Northern Ireland, UK
Correspondence to: Dr J P McConville,
10 Shorte Close, Oxford OX3 7FG

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Clear replies:

Mea culpa! The disparity in yield of our literature searches reflects different search strategies. These are often problems in electronic search systems.

It is still reasonable to state, though, as Van den Berg and Van Eikema Hommes do in their report,¹ that anaphylactoid reaction to methylprednisolone is rare. Few clinicians have come across it.

I agree that it is unreasonable to ascribe the anaphylactoid response to methylprednisolone therapy with interferon β . Nevertheless, it remains the case that a man who had had numerous courses of methylprednisolone without adverse effect had

anaphylactoid reactions to the drug soon after the introduction of interferon β , and that such an unusual event should alert us to the possibility that interferon β may have paradoxical effects. If we see only what we expect to see we run the risk of missing the truth.

DANIELA CLEAR
University Department of Neurological Science,
Liverpool, UK

1 Van den Berg, Van Eikema Hommes. Anaphylactoid reaction to intravenous methylprednisolone in a patient with multiple sclerosis. *J Neurol Neurosurg Psychiatry* 1997;63:813-14.

Overall, although the book presents a series of short unrelated articles that often contain biases and no overall context for interpretation, it is of use to people familiar with the field of restorative neuroscience, but even then it is often only helpful in summarising small islands of work. However, to those not familiar to the field, this book will be misleading and hard to follow, and as result it is unlikely to appeal to many neurologists or neuroscientists.

ROGER BARKER

Atlas of psychiatric pharmacotherapy. By RONI SHILOH, DAVID NUTT, and ABRAHAM WEIZMAN. (Pp 235, £49.95). Published by Martin Dunitz, London, 1999. ISBN 1-85317-630-3.

What I liked most reading through the Shiloh, Nutt, and Weizman's *Atlas of Psychiatric Pharmacotherapy* is its completeness. It is indeed a minicyclopedia of basic and clinical psychopharmacology, divided into four main sections: *basic principles of psychiatric pharmacotherapy, abused substances, drug interactions, and treatment strategies.*

As a basic science researcher, I like the fact that these authors succeed, in the first section, in the very difficult task of translating complex biochemical mechanisms into concise pictures and legends. I particularly like those on second messengers/signal transduction pathways, as these are rare to find and difficult to understand in other books. Switching to more specific psychopharmacology topics, the tables explaining the mechanisms of action of the various drugs are also very well made and updated. For example, the tables illustrating the mechanisms of action of antidepressant drugs go beyond the "catecholamine hypothesis" into explaining the effects, at the genomic level, on the synthesis of growth factors. There is also a great deal of information on the side effects of psychotropic medications, including the pharmacological mechanisms involved. In this regard, the tables describing sexual dysfunctions are particularly useful, as they describe the physiology and the pharmacology of sexual functions in both males and females.

The second section deals with well established as well as novel findings in the field of substance abuse. For each substance, the book explains the receptor mediated effects, the acute psychiatric and non-psychiatric effects, and the biological mechanisms responsible for dependence, adverse effects, and treatments. The book also gives up to date information on drugs for which biological pathways are less well known, such as phencyclidine and LSD.

The third section is on drug interactions. For each class of medication—and, if relevant, for each single drug—the book lists different drugs, the serum concentrations of which are decreased or increased by the index one, interact with the index one at the receptor site, or potentiate its side-effects. This section is very useful in a clinical setting, and also gives an interesting theoretical framework with which to understand drug interactions at a pharmacodynamic as well as at a pharmacokinetic level.

The final section contains algorithms for treatment of 35 (!) different psychiatric conditions. These include well described entities such as treatment resistant depression, acute manic episode, and acute exacerbation of schizophrenia. However, what I find most useful are the treatment strategies for

conditions that are frequent in clinical practice but have received less attention as far as treatment protocols are concerned—for example, seasonal and atypical depression, delusional disorder, generalised anxiety disorder, post-traumatic stress disorder, anorexia nervosa, and bulimia nervosa. There are also strategies for treatment of rarer disorders and/or disorders with few evidence based recommendations, such as borderline personality disorder, obsessive-compulsive personality disorder, schizoid personality disorder, and attention deficit hyperactivity disorder adult type. Of notice is that the authors do not restrict the guidelines to biological treatments, but recommend, where appropriate, specific psychotherapies. Also, the authors indicate whether the advised treatment have clear cut, partial, or only anecdotal support from scientific literature.

So far, so good. So, what is the problem? The authors say in the Introduction that "this book is written, first and foremost, for the clinician who is required to... decide efficiently about options for biological treatments". A second target is "students in other fields—for example, pharmacology, psychology, and neuroscience". Unfortunately, one possible problem of this book is that the tables, schemes, figures, and algorithms may be too complex for it to be used as a "quick" reference by the busy clinician or by somebody without prior knowledge of the topic. It is possible, therefore, that the book could not reach these two stated target audiences. However, it is well suited to be used in "various academic spheres" (the third stated target). In an academic setting, this book will be used as a teaching tool or as a consultation book to find important details that are not readily available from other sources. The book also has two other minor shortcomings: the absence of an index and some misspellings.

In summary, the *Atlas of Psychiatric Pharmacotherapy* is clearly the result of a detailed and updated revision of the literature in all fields of psychopharmacology, from basic science to treatment of rare psychiatric conditions. It may be too complex to be used as the main or only source of knowledge by a student or by a clinician involved with everyday clinical practice, but is definitively a must for those academics involved in psychopharmacology teaching or research. Also, departmental or medical school libraries should buy this book, because it will be used by those doctors and students who are looking for an answer to specific or difficult psychopharmacology questions.

CARMINE M PARIANTE

BOOK REVIEWS

Advances in Research on Neurodegeneration. Volume 6. Edited by W POEWE and G RANSMAYR. (Pp147, DM168). Published by Springer, Wien, 1999. ISBN 3 211 83262 9.

This slim volume is the result of a small meeting held towards the end of 1997 by a largely European group of scientists designed to explore recent advances in the treatment of some neurodegenerative conditions. The result is a highly eclectic collection of short chapters ranging from the general to highly specific, which overall makes the book hard to follow and thus recommend. For example the second chapter discusses a whole variety of different types of myelin mutant mice, whereas three chapters later we are treated to a discussion on the inhibitory effects of apomorphine on the proliferative potential of a Chinese hamster ovary cell line.

In addition the book tends to leap from clinical to scientific topics with no obvious linking sections; thus we move from a discussion on the newer dopamine agonists to others on animal models of multiple system atrophy and their treatment by neural transplantation. Indeed, the book, by presenting short, often unrelated topics, suffers from being misleading to the uninitiated reader. For example it begins with a chapter on neural precursor cells isolated from the rat spinal cord and their differentiation potential. This is an area of great current interest given the potential of these cells for repairing the damaged and diseased CNS. However this chapter, while, giving an insight to the field is bereft of companion chapters, and so it is not obvious to the newcomer how this chapter relates to embryonic stem (ES) cells, neural precursor cells from other mammalian species as well as those isolated from the adult CNS. Furthermore, it is not clear how the conclusions of the studies presented in this chapter relate to other strategies being adopted with neural precursor cells in animal models of Parkinson's disease, for example. Indeed many chapters can mislead the reader as a result of their failure to be put their topic fully into context—for example, the use of riluzole and gabapentin in amyotrophic lateral sclerosis as discussed by Ludolph *et al* in their chapter. However, other chapters are more successful by virtue of being more balanced and as a result are more appealing. For example, the chapters by Karl Kiebitz on emerging drug therapies in Huntington's disease and Steve Dunnett on striatal grafts are particularly good examples of this.

CORRECTION

Sheppard DM, Bradshaw JL, Mattingley JB, Lee P. Effects of stimulant medication on the lateralisation of line bisection judgements of children with attention deficit hyperactivity disorder. *J Neurol Neurosurg Psychiatry* 1999;66:57-63. In this paper figs 2 and 3 were wrongly ascribed the legends for figs 4 and 5 and figs 4 and 5 were given the legends for figs 2 and 3.