Intralaminar dural haematoma developing in the contralateral convexity after temporal lobectomy

A so called “subdural haematoma” actually develops in the dural border cell layer, which belongs to the dura; a true intralaminar dural haematoma to our knowledge has not been reported.

A 29 year old right handed man presented with a 14 year history of intractable epilepsy, which did not respond to major antiepileptic drugs. He usually felt an epigastric rising sense as an aura, then stared blankly, and showed oromotoric automatism. Postictal confusion persisted for several hours. The frequency of attacks ranged from several times a month to several times a day, and he had been taking phenytoin, phenobarbitone, and vigabatrin. During childhood, he had had severe febrile seizures.

No neurological deficit was found on detailed physical examination. Brain MRI (1.5 T) disclosed bilateral hippocampal and diffuse cortical atrophy, and sharp waves were seen in the right anterior temporal region on interictal EEG. Prolonged video-EEG monitoring, however, showed sharp waves in the right temporal region and slowing in the left temporal region. Intercitial single photon emission tomography (SPECT) did not show asymmetry between the two temporal lobes. Preoperative routine laboratory examination, including a coagulation study, showed no abnormality. Bilateral depth electrodes were inserted into both temporal lobes on 19 May 1995; postoperative CT showed no haematoma. After confirmation of right temporal onset, right temporal lobectomy and amygdalohippocampectomy were performed 10 days later. Postoperatively, the patient awoke fully and CT showed no unexpected findings. The following day, however, he became drowsy and CT showed an extra-axial haematoma in the contralateral convexity (fig 1). A diagnosis of epidural haematoma was made and he underwent emergency left frontoparietal craniotomy; The bone flap showed no penetration mark from the skeletal fixator used during the previous surgery. There was no haematoma in the epidural space. Incision of the visible dura showed blood clots, which were partially removed by suction; a yellow membrane, which also seemed to be dura, was noted at the bottom of the haematoma cavity. There was no active focus of bleeding. After removal of all the haematoma, it was apparent that this yellow membrane lined the entire cavity, and to expose the pial surface, this inner dura was incised. At the margin of the haematoma cavity, the covering and lining membrane was merged in a single layer, below which was the surface of the brain. Biopsy was performed at the margin, around which the two layered membranes merged to form a single layered dura. Because it adhered tightly, the underlying yellow membrane was difficult to dissect from the pial surface, and so was isolated and left in place. Concern about blood oozing from the underurface of the covering membrane led to the removal of this membrane. Duraplasty was performed, using bovine cadaveric dura.

The patient’s postoperative course was uneventful, and he was discharged on the 7th postoperative day. Histological examination of the biopsy specimen showed separation of the dura and intralaminar dural haematoma (fig 2). There was no vascular malformation in the dura, but hippocampal sclerosis was found in the resected hippocampus. During two years of follow up, the patient remained seizure free without antiepileptic drugs.

Cranial dura mater is a composite structure of cranial peristomeum and dura propria; the second is composed of fibroblasts and a large amount of extracellular collagen, and the innermost part of the dura is formed by the dural border cell layer.1 The dura-arachnoid junction, identified as the subdural compartment (dural border layer), consists of avascular tissue with flake-like, relatively electron lucent cells stacked in several layers with narrow intercellular clefts.2 The dural border layer may be attached to the underlying arachnoid by an occasional cell junction. There is, however, no intervening space between the dural border cell layer and the arachnoid barrier cell layer that would correlate with what has been called the “subdural space.” A survey of reports describing the morphology of the inner and outer capsule of so called subdural haematomas shows that dural border cells are found in both parts of the capsule. "These data support the view that what has been called a subdural haematoma is most often a lesion found within the layer formed by dural border cells."1

The reason for the postoperative delayed development of intralaminar dural haematoma contralaterally is unclear. Postoperative epidural haematomas developing contralaterally after supratentorial craniotomy have been reported.1 The mechanism of this complication was reported to be unclear. In hydrocephalus, these massive epidural haematomas are probably caused by dura-skull detachment when the brain volume is strikingly reduced by a decompressive procedure. On rare occasions, pins from the head rest may detach the dura and cause epidural haematomas.1

In our case, however, there was neither hydrocephalus, nor penetration marks from the pins of the skeletal fixator. We used a negative pressure drainage system epidurally in this case, which might exert negative pressure intracranially. The inner surface of the dura and the pia-arachnoid were difficult to separate during surgery, indicating prior change at the dura-arachnoid junction. There is a possibility that the developing haematoma splits at the dural fibrous layer instead of at the dural border cell layer. To the best of our knowledge, this is the first report of a haematoma occurring between split dura propria.

This work was supported by Seoul National University Hospital Research Fund.
Carbamazepine hypersensitivity syndrome presenting as vasculitis of the CNS

Carbamazepine is a drug widely used in the treatment of partial and generalised tonic-clonic seizures, trigeminal neuralgia and other pain syndromes, affective disorders, and paroxysmal symptoms of multiple sclerosis. Common side effects are diplopia, diziness, headache, nausea, and rash. Less common side effects include blood dyscrasias, toxic hepatitis, hyponatraemia as a consequence of inappropriate antidiuretic hormone secretion, orofacial dyskinesias, and cardiac arrhythmias. Carbamazepine is also known to cause a severe systemic hypersensitivity reaction, known as carbamazepine hypersensitivity syndrome (CHS). It consists of a triad of fever, lymphadenopathy, and rash; so called pseudolymphoma syndrome. Other organs are often involved, most commonly the liver and, more rarely, lungs and kidneys. There are two cases of meningitis described as a complication of the carbamazepine therapy.

We describe a case of severe CHS with a typical pseudolymphoma picture and involvement of other organs, including the CNS. We suggest a possible pathogenetic mechanism for encephalopathy.

A 63 year old woman was started on carbamazepine (2×200 mg), as a seizure prophylaxis after a meningocoea operation. About 3 weeks later she developed a flu-like illness. Two days afterwards, she developed a generalised rash and facial oedema, and fever appeared. She was admitted to hospital where physical examination disclosed a diffuse purpuric rash, oedema of the face and the tongue, pharyngitis, enlargement of lymph nodes, and a raised body temperature (39.5°C). Laboratory data showed leucocytosis (45.1), eosinophilia (42%), and high C-reactive protein (98%).

Liver enzymes were also raised. Additional tests disclosed a polyclonal increase in γ-globulin. Tests for Anti-DNA, anti-ENA, anti-ANA, and anti-ANCA antibodies were negative and complement C3 and C4 were normal. Chest radiography was normal, as well as lung function tests. Abdominal ultrasound investigation showed hepatosplenomegaly. Microbiological investigations failed to show any evidence of bacterial, fungal, viral, or parasitic infections. Skin biopsy showed vasculitis of small vessels with perivascular infiltrates of lymphocytes, monocytes, and macrophages (figure). The findings were compatible with an allergic reaction.

Carbamazepine was withdrawn and she was started on antibiotic treatment. The patient's condition improved after the withdrawal of carbamazepine; the temperature fell, the lymph nodes regressed, the rash started to scale, and laboratory tests began to normalise. Antibiotic treatment was discontinued after a week.

Two weeks after admission and discontinuation of carbamazepine she became confused. Neurological examination disclosed cognitive deficits (mini mental state examination score 18), bilateral facial palsy of peripheral type, pyramidal (brisk reflexes, extensor plantar responses), extrapyramidal signs (rigidity, postural tremor), and ataxia. There was no neck stiffness and her temperature did not rise again. A lumbar puncture disclosed 211 cells/mm³; more than 90% of them were lymphocytes. The concentration of protein in CSF was 1.29 mg/l and the concentration of sugar 2.85 mmol/l (40% of serum concentration). Concentrations of IgG, IgM, and IgA in CSF were raised. Oligoclonal bands were positive in serum and in CSF. Cultures for bacteria, fungi, and acid fast bacilli were negative, as were antibodies to mycoplasma, borrelia, and viruses. Serum and CSF VDRL and TPHA tests were negative. A T2 weighted MR image showed hyperintensive lesions in periventricular and white matter of the frontal and occipital lobes of both cerebral hemispheres. The lesions showed some opacification after injection of gadolinium contrast. There was no meningeal enhancement.

A few days after the deterioration in the patient's condition she started to improve again. The skin lesions remitted completely.
and neurological signs slowly regressed. During her stay in hospital she received topical steroids on her skin lesions without other specific therapy. She did not experience an epileptic seizure.

To confirm the hypersensitivity to carbamazepine we performed a patch test after the regression of the rash. The skin testing undoubtedly showed reactions to carbamazepine in four different concentrations of the drug.

On discharge about 2 months after the beginning of the disease she was left with subtle cognitive deficits (memory impairment). Her facial palsy, pyramidal and extrapyramidal signs, and ataxia resolved.

**Case 1.**

Carbamazepine is a frequently prescribed anticonvulsant. Sometimes other organs are also affected. Liver involvement is very common; less often described are pulmonary disease, various types of renal diseases, and cardiac involvement. Withdrawal of carbamazepine usually leads to rapid improvement of symptoms.

Our patient had a very severe hypersensitivity reaction to carbamazepine with typical pseudolymphoma syndrome, marked leukocytosis, eosinophilia; sedimentation rate may be raised. Sometimes other organs are also affected. Liver involvement is very common; less often described are pulmonary disease, various types of renal diseases, and cardiac involvement. Withdrawal of carbamazepine usually leads to rapid improvement of symptoms.

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days with no symptomatic effect or objective change in his AIMS score.

In April 1997 ventral thalamotomy was performed on the right side in two stages under local anaesthesia. A Berenstein guide had previously been inserted under general anaesthesia using CT guidance and a Leksell frame. Details of the lesions are shown in the table. The first lesion was relatively anterior and it reduced the torticollis, neck pain, hypertonia, and the dyskinesia of the contralateral limbs and allowed him to smile and laugh. One week later a second lesion was placed posterior-medial to the first. This abolished the residual "cogwheeling" of the left upper limb and improved his dexterity. There were no surgical complications.

Postoperative MRI confirming the position of stereotaxic lesions in the right thalamus (black arrows).

Gabapentin in the treatment of painful diabetic neuropathy: a placebo controlled, double blind, crossover trial

Painful neuropathy is a common and disabling problem in patients with longstanding diabetes mellitus. Tricyclic antidepressant drugs and other chronic analgesics have been beneficial in some, but not all patients. Gabapentin, a new antiepileptic drug, selectively blocks the sodium channel of neuronal axon membranes and stabilizes the neuronal membrane. It reduces neuronal excitability and reduces pain associated with neurological or other neurological conditions with few side effects. We conducted a randomised, double blind, placebo controlled trial to study the effect of low dose gabapentin in patients with painful diabetic neuropathy.

We recruited 40 patients with painful diabetic neuropathy who had (1) diabetes for at least 6 months on a stable dosage of insulin or oral hypoglycaemic agent, (2) distal symmetric sensorimotor neuropathy as shown by impaired pin prick, temperature, or vibration sensation in both feet and absent or reduced ankle reflexes, and (3) daily neurogenic pain in the acral extremities, of at least moderate severity, for over 3 months that interfered with daily activity or sleep. Excluded were those with diabetes and chronic renal insufficiency, painful diabetic plexopathy, or lumbosacral polyradiculopathy, peripheral vascular disease, another painful neurological condition, or other cause for neuropathy. Patients were randomly assigned to gabapentin (300 mg capsules) or placebo for 6 weeks (phase I) followed by a 3 week washout period and then crossover (phase II). The dose of gabapentin or placebo was increased by one capsule every 3 days to a stable dosage of one capsule three times daily (900 mg/day) that was maintained throughout the remainder of the treatment period. The low dosage of gabapentin was chosen to minimise adverse effects and to compromise blinding. Treatment with stable dosages of non-steroidal anti-inflammatory agents or narcotic analgesics was permitted during the trial but patients discontinued all other chronic analgesic medications 3 weeks before study entry.

At the beginning and end of each treatment period, patients rated their level of pain over the preceding 24 hours on a 10 cm visual analogue pain scale (VAS), ranging from 0 ("no pain") to 10 ("worst pain ever"). Present pain intensity (PPI), "rate how much you have at this moment," using a similar 0–10 scale) and the McGill pain questionnaire (MPQ) were recorded at the initial and final visits of each treatment period. At the end of each treatment period patients provided a global assessment of pain relief: none, mild, moderate, or excellent, as compared with the level of pain prior to each treatment period. The global assessment of pain relief was dichotomised (none/mild v moderate/excellent) for purposes of analysis. The protocol was approved by the Institutional Review Board at St Elizabeth's Medical Center and all patients gave written informed consent.

There were 31 men and nine women, with an average age of 62 years (SD 10.9 years, range 43–82 years). All but one had onset diabetes mellitus, with a mean duration of 14 years (SD 9.9 years, range 6 months–40 years). Ten had neuropathic pain limited to the feet, 19 had pain in the feet and legs, and 11 had pain in the feet, legs, and hands. The mean duration of neuropathic pain was 4 years (SD 3.5 years, range 4 months–15 years). Twenty five had previously used narcotics or other chronic analgesics to manage their pain.

Nineteen patients were randomised to the active drug and 21 to placebo during the first treatment period. The mean reduction in the MPQ score was 8.9 points with gabapentin compared with 2.2 points with placebo (p=0.03, two sample t test). There were no differences in the mean change of the VAS or PPI scores between gabapentin and placebo (table). Fourteen patients reported moderate or excellent pain relief with gabapentin only, six with placebo only, and three with both; 17 reported none or mild relief after both treatments (p=0.11, McNemar's test). There were no serious adverse events. Adverse effects were significantly more common with gabapentin (12 patients) compared with placebo (four patients, p<0.001, McNemar's test). The most common side effects of gabapentin were sedation (six patients), dizziness, and rash and imbalance (three). All adverse effects resolved promptly after discontinuation of the drug.

Anecdotal reports suggest that gabapentin has beneficial effects in patients with various painful neurological conditions, including HIV neuropathy, postherpetic neuralgia, and reflex sympathetic dystrophy. The mechanism of action of gabapentin in ameliorating pain is unknown, but it has been suggested that its pain modulating properties may be linked to the release of the neuroendocrine system. We conducted a randomised, double blind, placebo controlled trial to study the effect of low dose gabapentin in patients with painful diabetic neuropathy.

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transmitter GABA in spinal cord pathways that modulate pain perception. There was statistical improvement in only one of four end points, the MPQ score, with gabapentin compared with placebo. The MPQ is a valid, consistent, and reliable measure of subjective pain experience, and usually correlates with other measures of pain intensity, including the VAS and PPI scales. We designed the study to have an 80% power to detect a 50% reduction in pain scores, reflecting a modest but clinically important improvement. The mean change of the VAS and PPI scales and the patient's global assessment of pain relief were not significantly different from placebo. We used a crossover design because of its statistical efficiency, but the MPQ and VAS scores did not return to baseline after crossover in patients who received gabapentin in phase I (the washout period was inadequate); therefore, we may have underestimated improvement with gabapentin in the VAS scale that may have been detected using a parallel group design. Furthermore, a limitation of our study was that quantitative measures (for example, nerve conduction studies, quantitative sensory thresholds) were not used to further characterise the type of neuropathy. Because of the heterogeneous nature of neuropathic pain in our study patients, we may not have identified a subset of patients who improved with gabapentin. Alternatively, the dosage of gabapentin may have been too low to induce analgesia in patients with painful diabetic neuropathy, although similar regimens have been reported to be effective in patients with other painful conditions.

The results of this study suggest that gabapentin is probably ineffective or only minimally effective for the treatment of painful diabetic neuropathy at a dosage of 900 mg/day.

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Single motor unit activity pattern in patients with Schwartz-Jampel syndrome

Two sisters, 9 and 11 years old, with typical clinical symptoms of Schwartz-Jampel syndrome were investigated. Conventional electrophysiological investigation with concentric needle electrodes in the biceps brachii and tibialis anterior showed continuous muscle activity (myotonic burst, high frequency discharges of single motor units with “bi- zare” rhythmic activity). The single motor unit action potential (MUAP) was studied in detail by monopolar surface selective electrode with a small leading off area. The pattern suggests that the muscle membrane alone is the not the only reason for abnormality.

Continuous muscle activity is a prominent symptom in patients with Schwartz-Jampel syndrome. Some authors maintain that this may originate in the nerve or end plate. Lehmann-Horn et al showed two muscle membrane abnormalities by voltage clamp and patch clamp techniques and concluded that spontaneous activity in the Schwartz-Jampel syndrome originated in the muscle membrane itself. Arimura et al found a normal end plate function and assumed that the motor unit pattern influenced interdischarge interval changes. It is difficult to make a precise analysis of the MUAPs with concentric needle electrodes because of other interfering spontaneous activities. Thus a monopolar surface selective electrode with a small leading off area was employed to obtain a more precise assessment of a single MUAP pattern.

The patients were two sisters, 9 and 11 years old, from consanguineous parents. They displayed short stature, bone deformities (kyphoscoliosis, pigeon breast, short neck, pes equinovarus), facial dysmorphism, muscle stiffness, and missing tendon reflexes in the lower limbs. Concentric needle EMG was performed when the patients were 7 and 9 years old and disclosed abnormality. The needle insertion, mechanical stimulation, and mild muscular contraction induced spontaneous activity. Myotonic discharges (fig 1 A and B) were found in all examined muscles (abductor digiti minimi, quadriceps femoris, tibialis anterior, biceps brachii). There were also spontaneous high frequency biphasic potentials. Some of the high frequency discharges appeared as doublets or complex repetitive discharges. Routine nerve conduction studies (motor conduction velocity, distal latency, compound muscle action potentials, and sensory action potentials in upper and lower limbs) were normal. Electromyographic investigations of single MUAPs were performed in biceps brachii and tibialis anterior muscles. Involuntary motor unit activity was recorded by monopolar surface selective electrode with a small leading off area for 30 minutes. A Misto 5+ electromyograph and a Teac type recorder were employed to register the action potentials. Distances between the negative peaks of MUAP was measured with a resolution of 0.1 ms. After applying these electrodes we found single MUAP trains between myotonic discharges. They showed without provoking a burst of activity, as usually happens during needle electromyography.

Motor unit firing began with doublet discharges (fig 2 trace 1). After a few seconds MUAP alternated between doublets and triplets (fig 2 trace 2), and then the motor unit fired with stable triplets (trace 3). Similarly, triple discharges turned into quadruplets, and then multiplets (traces 4 to 11) and the number of firing impulses increased at the end of motor unit discharge. All multiplet impulses were similar in shape.

Figure 1 Myotonic discharge recorded by monopolar surface electrode with a small leading off area (A) and needle electrode (B) from biceps brachii muscle.
Amplitude of the second impulse in the doublet was lower or higher than the amplitude of the first impulse (fig 2 trace 1). Amplitude of the second impulse in the triplet was predominantly lower than that of the first impulse but could also be higher (traces 2 and 3), whereas amplitude of the second impulse in the doublet was lower or higher than the amplitude of the first impulse (fig 2 trace 1).

Electrophysiological studies of patients with the Schwartz-Jampel syndrome (normal nerve conduction, spontaneous activity myotonic discharge) have implied that spontaneous activity originates in the muscle membrane. The single MUAP pattern of repetitive neuronal discharges, however, suggests that a defect in the muscle membrane is not the only reason of abnormality. The MUAP pattern found supposes an influence at a higher level than the muscle. Multiplet discharge with an interpulse interval of 2 to 10 ms probably originated in the muscle membrane but the increasing number of impulses in multiplets and the long intermultiplet intervals cannot be explained simply by the known abnormalities of the muscle membrane. Moreover, doublet, triplet, and multiplet electromyographic phenomena are neuromyotonic. In our opinion the reasons for the abnormality are complex and not yet understood.

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carried out four times. On day 6, the patient regained consciousness but remained immobile and confused. Neurological examination on day 7 disclosed a positive Babinski's sign and bilateral hyperreflexia. On day 8, rigidity was needed again for 24 hours. Even after vigorous pyramidal and cardiovascular stabilization the patient remained completely immobile, unable to turn around in bed or to speak. Because rigidity, tremor, akinesia, and bradyphrenia persisted on day 24 the diagnosis of parkinsonism was suspected and treatment with amantadine intravenously (300 mg/day) was started. Within 1 day there was marked improvement of consciousness, orientation, mobility, and speech. Furthermore, the disturbance of swallowing improved and, therefore, feeding by tube was no longer necessary. Only 6 days later, on day 30, the patient left the intensive care unit and moved to the neurological department. During this improvement treatment with amantadine was stopped on day 40. After discontinuation no relapse occurred. When the patient was discharged on day 61 he had completely recovered from parkinsonian symptoms.

Between day 33 and day 53 various additional diagnostic examinations such as MRL, [[18F]-fluorodesoxyglucose-positron emission tomography ("[18F]-FDG-PET"), "[18F]-FDOPA-PET"], and "[18I]-iodobenzamide-single photon emission computed tomography ("[18I]-IBZM-SPECT") were performed but showed no pathological findings. In addition, on clinical examination and electrophysiological studies there were no signs of an intermediate syndrome or delayed polyneuropathy. Furthermore, the patient had no history of parkinsonism and antiparkinsonergic therapy, and family history was unremarkable.

This is a description of a patient who developed the complete picture of severe parkinsonism after acute OP poisoning with demeton sulfide, an S-substituted phosphorothionate. Parkinsonian symptoms were noticed 8 days after intoxication, more, salivation, and disturbance of swallowing disappeared on day 10 pyramidal signs disappeared. On day 30, the patient left the intensive care unit was no longer necessary. Only 6 days later, on day 35, the patient was able to walk again. Only 6 days later, on day 40, the patient was able to walk again. On day 40, the patient further improved the diagnosis should not be overlooked or will be masked by other complications. So far it is unclear whether the occurrence of extrapyramidal symptoms depends on the type of the organophosphate agent or on the severity of poisoning. In conclusion, transient parkinsonism has to be added to the possible acute organophosphate poisoning persisting even after cholinergic symptoms have resolved. Although parkinsonian symptoms spontaneously improved the diagnosis should not be missed because complications such as aspiration pneumonia, thrombosis, and prolonged mechanical ventilation could be prevented by appropriate treatment.

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Letters, Correspondence, Erratum, Book reviews

Oropharyngeal palsy in Guillain-Barré and Fisher's syndromes is associated with muscle weakness in the neck and arm

Guillain-Barré syndrome is an immune mediated peripheral neuropathy characterised by acute onset of symmetric limb weakness and areflexia. Patients with typical Guillain-Barré syndrome have muscle weakness than arm weakness, with an ascending progression. Some patients with Guillain-Barré syndrome, however, present muscle weakness only on the face, neck, and proximal upper limb muscles, and a descending pattern of weakness appears as illness progresses. Ropper proposed that the second group of patients had a variant of Guillain-Barré syndrome who had oropharyngeal palsy. Ophthal moplegia and cerebellar ataxia, however, are often noted in patients with PCB. Therefore, it is unclear whether PCB is an “atypical” Fisher's syndrome or a variant of Guillain-Barré syndrome. To clarify this, we investigated the relation of neck and limb weakness with cranial nerve involvements. We report here that oropharyngeal palsy in Guillain-Barré syndrome is associated with neck and arm dominance whereas ophthal moplegia does not. We made prospective examinations of 113 patients with Guillain-Barré syndrome and 39 patients with Fisher's syndrome who had been referred to our neuroimmunological laboratory between December 1996 and February 1998 with cranial nerve dysfunction and weakness in the neck and limbs on the day of admission. All the patients fulfilled the accepted clinical criteria for these syndromes. Diagnosis of Fisher's syndrome was also made in patients who initially presented with ophthal moplegia, ataxia, and dysarthria and later developed generalised muscle weakness. On admission, 53 patients with Guillain-Barré syndrome or Fisher's syndrome (Guillain-Barré syndrome, 14 (12%); Fisher's syndrome, 39 (100%); organophosphate poisoning, 48 (Guillain-Barré syndrome, 41 (36%); Fisher's syndrome, seven (18%)) had oropharyngeal palsy. Generalised muscle weakness was present in six (11%) patients with Fisher's syndrome. Of the 48 patients with Guillain-Barré syndrome or Fisher's syndrome who had oropharyngeal palsy, 36 (75%) and 20 (42%) respectively had neck and arm dominant weakness, compared with 33 (32%) and 13 (13%) of the 104 patients without oropharyngeal palsy (table). Patients with oropharyngeal palsy showed a significant increase in the frequency of neck weakness (p<0.001) and arm dominant weakness (p<0.001). By contrast, leg dominant weakness was less common in patients with oropharyngeal palsy (11 (23%)) than in patients without (50 (48%) (p=0.003). This was no significant association of ophthal moplegia with neck or arm dominant weakness (p=0.5 and p=0.9 respectively).

Statistical analysis showed that muscle weakness in the neck and upper limbs was frequent in patients with Guillain-Barré syndromes or Fisher's syndrome who had oropharyngeal palsy. This may account for the distribution of muscle weakness that occurs in PCB. According to the clinical criteria of Ropper et al for PCB, it should be diagnosed
only in patients who have a restricted distribution of muscle weakness in the pharynx, neck, and proximal upper limbs but no weakness or areflexia in the legs. In his original report, however, one of the three patients with PCB had generalised areflexia. Moreover, the patient with Guillain-Barré syndrome described by Mizoguchi et al, whose initial symptoms were lower cranial nerve dysfunction and upper limb weakness, later developed generalised muscle weakness. These patients with PCB with generalised areflexia or weakness indicate that the preservation of the tendon reflex and muscle power in the legs depends on the severity of the involvement of the limbs. None of the patients in our study met the clinical criteria proposed by Ropper. However, the close association of weakness of the pharynx, neck, and upper limbs in Guillain-Barré syndrome and Fisher’s syndrome indicates that PCB is a distinct variant of Guillain-Barré syndrome, because ophthalmoplegia, a cardinal sign in Fisher’s syndrome, is not associated with oropharyngeal palsy, neck weakness, or arm dominant weakness.

Our finding is also supported by detection of serum antibodies against GT1a ganglioside in patients with PCB which show different reactivity from those in patients with Fisher’s syndrome. IgG anti-GT1a antibodies in patients with PCB are not absorbed by GQ1b ganglioside whereas those in patients with Fisher’s syndrome are. Because only GT1a is recognised by serum IgG from the patient who had a restricted distribution of muscle weakness in the pharynx, neck, and proximal upper limbs, we speculate that anti-GT1a and anti-GD1a antibodies respectively contributed to the development of PCB and generalised weakness in the patient described by Mizoguchi et al.

**Cumulative meta-analysis of aspirin efficacy after cerebral ischaemia of arterial origin**

In 1996 we reported in this *Journal* that there was virtually no difference in relative risk reduction for low (<100 mg/day), medium (300 to 325 mg/day), and high (>900 mg/day) doses of aspirin in the prevention of vascular events in patients with cerebral ischaemia of arterial origin.3 A meta-analysis of the cumulative data showed a modest 13% (95% confidence interval (95% CI) 4% to 21%) relative risk reduction. Recently the final data of the second European Stroke Prevention Study (ESP2) were reported.4 One of its comparisons was between 50 mg aspirin daily and placebo in patients after cerebral ischaemia; the relative risk reduction of 13% (95% CI 0% to 24%) was exactly the same as that resulting from our previous meta-analysis. This similarity allows the calculation of an update of the meta-analysis. The overall relative risk reduction of course remains 13%, but the 95% CI has narrowed from 6% to 19%. The figure shows the results of the updated cumulative meta-analysis, in chronological order. These data once more underscore the need for more efficacious treatment strategies. For this reason we started the European and Australian Stroke Prevention in Reversible Ischaemia Trial (ESPSTR).5

**Hemifacial spasm**

We have looked with interest at the scan of a patient with hemifacial spasm by Reigosa and Rios.1 Indeed, this is a very nice MRI which shows an arterial loop and the internal auditory meatus. However, this loop is not the cause of the hemifacial spasm.

Typical hemifacial spasm, which begins in the orbicularis oculi and gradually progresses down the face, is caused by a blood vessel on the non-fascicular portion of the facial nerve on the caudal or anterior aspect, including the intrapontine nerve. Atypical hemifacial spasm, which starts in the buccal muscles and progresses up the face, is caused by a blood vessel on the posterior or rostral side of the nerve. This is much less common. The compression is also at the brainstem. A distal artery, as shown in the scan, does not cause hemifacial spasm. The sylvogism that Reigosa and Rios bring out—namely, that botulinum toxin helped and that this picture showed the pathology, is inadequate. They do not have a completed explanation.

This patient’s spasm will recur because the cause has not been treated. The spasm has an excellent chance of responding to a microvascular decompression of the facial nerve performed by a neurosurgeon who has experience in the nuances of the operative procedure.

Nevertheless, Reigosa and Rios have shown a beautiful scan.

**CORRESPONDENCE**

Pete Reigosa replies:

We thank Jannetta and Kassam for their interest in our article.3 We think that the vascular loop that appears in the MR image is indeed the cause of the hemifacial spasm of our patient, as it is the only abnormal finding encountered, as is the caudal aspect of the VII cranial nerve next to the pons. Moreover, it is evident that the hemifacial spasm will reappear or recur. For this reason,
the patient is receiving local botulinum toxin, with an excellent response. This treatment was chosen because its secondary effects are scarce and limited in time, and it is beneficial for a great proportion of patients. Also, systemic complications have not been described. Undoubtedly, it is a symptomatic treatment based on the blockade of neuro-muscular transmission. With respect to surgery, microvascular decompression is an excellent treatment when it is performed by an experienced team, although it poses potential complications and sequelae. Many patients, as in our case, are not willing to undergo such risks. For these reasons, we think that the treatment of choice in our patient is local injection of botulinum toxin.

R PEGO REIGOSA

Measuring the rate of progression and estimating the preclinical period of Parkinson's disease with $^{[18]F}$ dopa PET

Morrish et al report in great detail the PET data on 32 patients with Parkinson's disease, from which they conclude that the mean pre-clinical period “is unlikely to be longer than 7 years”. This conclusion is based on calculations using the $^{[18]F}$ dopa influx constant (Ki) of the putamen, although they acknowledge that other methods of analysis and extrapolation yielded estimates of anything between 2.8 and 37.2 years. The authors justify using putamen Ki because it was “more sensitive to increasing disability” than either total striatal assessment or using the alternative ratio approach, but fail to justify a much more fundamental and unwise assumption on which their arguments rest—that is, the intercorrelation between the PET index, clinical progression, and the UPDRS.

The paper gives little detail about how the UPDRS was administered, presumably only once, before the two PET scans, taken an average of 18 months apart. A linear regression was then applied to the mean of each patient’s two UPDRS and PET assessments, the gradient of which was expressed as a percentage change in the PET index for a change of 10 points “in the total UPDRS”.

Some questions can be raised:

(1) Did the same observer administer the UPDRS blinded to the clinical diagnosis, on their 16 normal controls as well as to each patient on both occasions and, if not, was interobserver reliability studied?

(2) Presumably the “total UPDRS”, judging by the scale shown on their figure A, was actually the total score from the 14 items in the motor subset of the UPDRS, which measures impairment rather than disability.

(3) The UPDRS is neither a perfect nor a linear index of severity of disease, each item being an ordinal rather than an interval 0–4 scale of one clinical feature. The key distinction is that an ordinal scale permits the recording of data in rank order (for example, mild, moderate, severe) but without uniform intervals. Thus tremor score 4 is not twice as bad as 2, still less a total motor UPDRS score of 4070 ± 2070. For these reasons, the use of simple arithmetic means as well as other parametric statistical methods is inappropriate, however tempting.

One illustration of the non-linearity of the UPDRS approach is the fact that it has used it regularly in clinical trials is the bias towards intermediate scores. Those with advanced disease and high scores are seldom if ever recruited for clinical trials and are scored as 1, indicating slight or mild impairment, “could be normal for some” according to the definition. In one study of Alzheimer’s disease, 56% of 78 cases and 12 of the 20 age matched controls scored 0 for one particular extrapyramidal sign with motor UPDRS scores of 4.5 (± 4.8) and 2.8 (± 1.8) respectively using observers not blinded to the diagnosis. It would be interesting to know whether a UPDRS score 0 is sensitive to or predictive of preclinical parkinsonism and/or abnormal PET.

Furthermore, as it is acknowledged that Parkinson’s disease may progress at varying rates between patients and even within the same patient at different ages and stages, it is perhaps not surprising that the authors found no significant correlation between change in UPDRS and change in any PET index over 18 months. Their previous paper to draw such firm conclusions based on the assumption that both measures are linear and directly correlated.

Richard J Hardie

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Morrish replies:

We thank Hardie for his comments but are surprised that he finds difficulty in our assumption that severity of disease is correlated with PET index, clinical progression, and the UPDRS. Whether clinical severity is measured by UPDRS, bradykinesia scores, rigidity scores or Purdue pegboard scores such a relation has been a consistent finding in $^{[18]F]$dopa PET imaging studies of Parkinson’s disease. The UPDRS was administered on 57 of 64 occasions by one observer (PKM) and on seven occasions by a second observer (JSR). UPDRS scores were carried out on the normal volunteers. Gonera et al have identified some non-specific symptoms that may predate the development of Parkinson’s disease but we know of no population study of the predictive value of the UPDRS score in normal subjects. By total UPDRS score we mean the combined scores of sections I, II, III, and IV. Similar results were found when motor scores alone were examined. The UPDRS score is the most widely used index of global disease severity in Parkinson’s disease. We accept that a linear correlation between UPDRS and PET index may have been inappropriate. The PET index represents a figure of mean $^{[18]F}$dopa metabo-

ism throughout the putamen, caudate, or total striatum whereas the clinical presentation and severity of parkinsonism is likely to depend on the distribution and severity of loss of dopaminergic function (and that of other neurotransmitters) within and outside the basal ganglia. It is unlikely that the relation is so simple yet this approach has allowed the demonstration of an aspect of the measurement of progression by PET that has not previously been considered, that of sensitivity to clinical severity. It should be noted that this discussion is not relevant to the major findings of the study (that measurement of progression is dependent on the PET method and that the applied period is likely to be short), only to our explanation of these findings. However, it does suggest an important debate; should clinical indices or functional imaging indices be used independently in studies of progression in Parkinson’s disease? When the reproducibility of both measurements is taken into account it is, as Hardie comments, not surprising that we found no significant correlation between change in UPDRS and change in PET index.

Paul Morrish

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Utilisation and costs of profession care and assistance according to disability of patients with multiple sclerosis in Flanders (Belgium)

In their detailed cost of illness study, Carton et al estimate the total annual costs in their population of 5000 people with multiple sclerosis to be ECU 13 106 000 (€ 8.7m) for ambulatory care and ECU 26 591 000 (€ 17.7m) for hospital and institutional care. They have adopted a “bottom up” approach which allows costs to be identified for different levels of disability, a distinct advantage from previous “top down” costs of illness studies. The conclude, as have others, that the costs of multiple sclerosis rise with increasing disability and that the information is useful for cost effectiveness studies. However, to be useful for such studies, the costs would need further description, in particular we would need to know which costs were fixed, and which were semifixed or non-fixed. In our own institution we know that 40% of the cost of a bed-day is fixed and at most 5% of costs are non-fixed. The remaining costs are semifixed—for example, staff salaries (Robert Hudson, Scottish Health Purchasing Information Communication January 1998). The important point is that most of the costs in their paper are probably fixed or semifixed, and interventions to reduce disability are unlikely to have a significant impact on these costs as...
BOOK REVIEWS

Erratum

The author of the book review on *Handbook of Neurologic Rating Scales* published in *J Neurol Neurosurg Psychiatry* 1998;65:615 should have read Derick Wade, not Derick White.


This atlas has three parts, the first a 16 page summary of Parkinson’s disease and related disorders, the second a selection of bibliography, and the third 77 colour and black and white plates. The text section comprises a brief pathological description of each disorder followed by a clinical description and then treatment and imaging findings if appropriate. The bibliography contains 37 papers mainly published between 1987 and 1996—a golden age of movement disorders? The illustrations are about a third pathological, a third imaging (including CT, MRI, and functional imaging), and a third clinical. The book is aimed at neurologists in training and medical students.

The excellent illustrations, particularly the pathological ones, are the outstanding feature of the atlas. The plates are large and the quality of reproduction good. However, I would have expected rather more pictures in an atlas—many ordinary textbooks have more than 77 figures and quantity as well as quality is desirable. The quality of the captions is variable, the pathological plates are well described but the functional imaging captions are not adequate to interpret the pictures. Similarly most abnormalities in the pathological and structural imaging plates are indicated on the plates but the abnormalities on the functional imaging plates are not.

The text provides a brief overview of the specialty and is a useful introduction. The text is lucid and informative. I thought that the section on striatongral degeneration, olivopontocerebellar and multiple system atrophy would have benefited from further editing to make their interrelation clearer and to ensure consistency between text and tables.

I would recommend this atlas for medical school and hospital libraries. The neurologist in training and neurologist would certainly benefit from perusing the atlas in the library but might choose to start saving for a CD-ROM version.

JERRY BROWN


I bought the first edition of this popular book in 1989, shortly after it was published. I dipped into it enthusiastically for a few months, even scribbling some notes in the margins. However, since 1990 it has been unopen. The reason for this neglect is not its content, but rather its presentation. The dense text is relieved by few illustrations and the paragraph headings are too uniform in style to easily understand the chapter structure. These may be superficial criticisms, but they are sufficient to blunt success in the highly competitive market place of neurology text books for students and junior doctors.

JERRY BROWN

This second edition could not be more different. It is beautifully organised. From the original text, clinical bon mots have been highlighted and long paragraphs have been broken up in to plain and boxed text. The introductory chapter on examination of the nervous system is particularly helpful; for instance, Marsden distinguishes between hard and soft neurological signs and describes how to deal with conflicts between them. The scope is wide, including chapters on paediatric neurology and the neurology of general medical disorders, psychiatry, and neurorehabilitation. There is plenty for the Gower’s Round hack too: the differential diagnosis of progressive myoclonic ataxia, the subtypes of neuronal ceroid lipofuscinoses, and such favourites. All these were there in the first edition but, at least to my taste, hard to access. For the first time ever, I find myself preferring a sequel.

ALASDAIR COLES


The editors have sought to create a user friendly handbook for the trainee in the specialties that treat these disorders and have succeeded admirably. They give the view of the joint pituitary clinic at the National Hospital, Queen Square, which mirrors the consensus guidelines published recently by the Royal College of Physicians. It is essential that pituitary tumours are managed by a multidisciplinary team—the days of competition between the disciplines should be past. The authors are not afraid to tackle the difficult issue of subspecialisation. There is only sufficient workload for one neurosurgeon in any region of 2-3 million to look after the microadenomas, invasive macroadenomas, giant adenomas, craniopharyngiomas, and third ventricular tumours. Only endocrinologists and neurologists with a specialised interest in neuroendocrinology should be managing the endocrine problems of pituitary patients beyond the initial diagnosis. Have you heard the story of the eminent neurologist who could not understand why a young lady’s prolactin level continued to rise despite escalating doses of bromocriptine until all was revealed during the third trimester?

The transatlantic authorship covers the subject in 11 readable chapters devoted to pathophysiology, clinical and visual assessment, imaging, medical and surgical management, radiotherapy, miscellaneous lesions, and controversial issues. The imaging section is particularly useful for explaining the findings of MRI. The sections on results and third ventricular tumours are a little too brief.

This handbook is complimentary to the much larger, definitive textbook published also by Churchill Livingstone—*Pituitary Adenomas*— by Landolt, Vance, and Reilly (1996). I recommend both unreservedly to their respective audiences.

JOHN PICKARD
Intralaminar dural haematoma developing in the contralateral convexity after temporal lobectomy

CHUN-KEE CHUNG, YEON M KIM and JE G CHI

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