LETTERS TO THE EDITOR

Familial hydrocephalus

Familial cases of congenital hydrocephalus have often been reported and may result from distinct monogenic disorders or may be multifactorially determined. The commonest cause is X linked hydrocephalus associated with stenosis of the aqueduct of Sylvius and, in most families, the genetic basis of this condition is known. By contrast, familial adult onset cases are unusual and the genetic basis is unknown. We report a family in which the presumed mode of inheritance is autosomal dominant with variable penetrance.

The family pedigree is shown in figure 1. There was no consanguinity. Patient II-1 was a 76 year old man who presented at the age of 62 years with a 3 year history of progressive gait ataxia, an 18 month history of urinary frequency and occasional urge incontinence, and a 12 month history of cognitive impairment. There was no other medical history of note and he was on no medication. Psychometry showed evidence of a severe and selective verbal memory deficit, impaired attention, and a reduced ability to work at speed, with relative preservation of visual memory, perceptual, and spatial skills. His gait was broad based. Examination of the cranial nerves was normal; there was no disc swelling. Tone was normal; there was no disc swelling. There was mild weakness of knee extension bilaterally; reflexes were brisk with flexor plantar responses; there was mild limb ataxia. The remainder of the neurological examination was normal. General examination was normal. Brain CT showed gross communicating hydrocephalus with marked distortion of the fourth ventricle (fig 2). A VP shunt was inserted without perioperative complications; postoperative CT showed some reduction in ventricular size. At review 6 months later his gait and urinary disturbance had largely resolved. Repeat psychometry showed some improvement in his verbal memory and significant improvement in word retrieval skills and ability to work at speed.

Patient III-2 was a 47 year woman with a 20 year history of progressive gait disturbance which had been severe for 2 years and an 18 month history of morning headache associated with nausea and vomiting. She reported a 20 year history of progressive gait disturbance and urinary disturbance and, in one case, urinary symptoms and cognitive decline. Neuroimaging in both cases showed communicating hydrocephalus with marked distortion of the fourth ventricle and each patient gained significant symptomatic benefit from a VP shunt. Although it is possible that this represents a chance association, it seems likely that this family carries a genetic predisposition to the development of communicating hydrocephalus. The presumed mode of inheritance is autosomal dominant with variable penetrance, although X linked inheritance cannot be excluded.

Familial cases of congenital hydrocephalus, both syndromal and non-syndromal, are well described. Most cases of X linked hydrocephalus with associated stenosis of the aqueduct of Sylvius are caused by mutations in the gene for neural cell adhesion molecule L1 (L1CAM), although some families with otherwise typical X linked aqueduct stenosis do not show linkage to this locus. It has been suggested that the aqueduct stenosis seen in this condition may be a secondary phenomenon and that the hydrocephalus begins as a communicating form. Mutations of L1CAM are also seen in families with the MASA syndrome (mental retardation, aphasia, spastic paraplegia, adducted thumbs) and spastic paraplegia type 1 (SPG1). In some other cases of non-syndromal hydrocephalus, autosomal recessive inheritance is suggested by the occurrence of hydrocephalus in siblings of both sexes born to normal but often consanguineous parents. One study of 261 pregnancies suggested that, apart from X linked cases, most cases of congenital hydrocephalus were multifactorially determined with a recurrence risk of about 4%.

We are aware of only one other report of familial adult onset, non-syndromal hydrocephalus. This describes two siblings with late onset gait disturbance, urinary frequency, and cognitive impairment. Neuroimaging demonstrated hydrocephalus; intracranial pressure monitoring was not performed. Both cases improved markedly after shunt procedures. Details of the family history of these cases was not provided but it has been assumed that they represent autosomal recessive inheritance. The phenotype of these cases is strikingly similar to the cases we describe and this may support the suggestion that an autosomal locus contributes to the development of apparent “normal pressure” hydrocephalus.

In conclusion, we report the second case of familial adult onset, non-syndromal hydrocephalus. The presumed mode of inheritance is autosomal dominant but further studies will be required before the genetic basis of such cases can be elucidated.

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Figure 1 Family pedigree.

Figure 2 CT of patient II-1 showing communicating hydrocephalus.

Figure 3 Brain MRI of patient III-2 showing communicating hydrocephalus.

No other family member had any neurological complaints. Patient II-2 (the twin sister of patient II-1 and mother of patient III-2) was reviewed at the age of 75 years. She was asymptomatic and neurological examination was normal. Brain CT showed no evidence of hydrocephalus.

We report on a family containing two members who presented in adult life with gait disturbance and, in one case, urinary symptoms and cognitive decline. Neuroimaging in both cases showed communicating hydrocephalus with marked distortion of the fourth ventricle and each patient gained significant symptomatic benefit from a VP shunt. Although it is possible that this represents a chance association, it seems likely that this family carries a genetic predisposition to the development of communicating hydrocephalus. The presumed mode of inheritance is autosomal dominant with variable penetrance, although X linked inheritance cannot be excluded.

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Brachial plexopathy related to alcohol intoxication

Brachial plexopathy associated with alcohol intoxication is rarely reported. We describe two patients with injuries to the brachial plexus thought to be the result of either stretch or compression of the plexus while intoxicated. In the first patient, damage was bilateral affecting the entire plexus on the right and the upper plexus on the left. This patient had associated rhabdomyolysis due to direct alcohol myotoxicity or prolonged immobilisation. In the second patient damage was on the right, involving predominantly the upper trunk. Neurophysiological studies and the rapid and complete recovery in our patients suggest that the primary pathology was focal demyelination causing conduction block, although there was also EMG evidence of axonal degeneration, particularly in the right arm of the first patient, in whom recovery was consequentially delayed. Injury to the brachial plexus should be considered in patients with upper limb deficits related to intoxication.

The association between brachial plexopathy and both anaesthesia and intoxication is well recognised but this condition has been rarely described resulting from alcohol. We describe two patients with injuries to the brachial plexus who underwent neurophysiological studies, one with unilateral and the other with bilateral damage arising from prolonged immobilisation associated with alcohol intoxication. The patient had associated rhabdomyolysis due to either direct alcohol myotoxicity or prolonged immobilisation on a hard surface, or a combination of the two.

The patient was an obese 69 year old man who lived on his own and drank at least two litres of vodka (900 g alcohol) a week. He returned from a party where he had drunk a large quantity of alcohol and fell next to his bed but did not lose consciousness. He was unable to get onto his bed and slept the floor. The next morning he woke with profound weakness and sensory loss in both arms but no facial or lower limb weakness and no neck or limb pain. He was admitted to hospital and because of difficulty initiating micturition, a urethral catheter was inserted. He was fully conscious and orientated; examination of his cranial nerves was normal. He had severe right upper limb weakness; shoulder abduction was MRC grade 2 using mainly supraspinatus and there was only a flicker of movement at the wrist and fingers. Left shoulder abduction and elbow flexion power were MRC grade 1, elbow extension grade 4, wrist dorsi and palmar flexion and finger flexion and extension grade 3. Strength in the lower limbs was normal. The deep tendon reflexes were absent in the upper limbs except for the left triceps, normal at the knees, absent at the ankles, and plantar reflexes were flexor. Pain and light touch sensation was diminished in the C5 to T1 dermatomes bilaterally with absent vibration and proprioception in his fingers. He had normal anal tone with mild prostatomegaly, and he was able to pass urine normally when the catheter was removed.

Magnetic resonance imaging of his cervical spine was normal and CT of the brain demonstrated diffuse cerebral and cerebellar atrophy. He had a raised blood urea (10.2 mmol/l) and creatinine (203 µmol/l) due to dehydrogenation of alcohol. His creatine kinase on admission was 15 000 U/l, which was not associated with myoglobinuria. This did not require any further treatment and had returned to normal concentrations (35 U/l) within a week.

Electrophysiological studies in the right arm in the first week showed reduced sensory amplitudes of the right radial (5 µV), median (3 µV), and ulnar (1.5 µV) nerves. Median and ulnar motor conduction velocities were normal apart from reduced F wave persistence. The compound muscle action potential (CMAP) of the deltoid to Erb’s point stimulation was of low amplitude (1.1 mV) and there was a little fibrillation on denervation of the EMG. Left arm conduction studies, including F responses and proximal stimulation and EMG were essentially normal. Repeat testing 2 weeks later showed low amplitude CMAPs from right median and ulnar nerves (both 2.8 mV) with absent F waves. The deltoid CMAP to Erb’s point stimulation was absent on the right and markedly reduced (0.6 mV) on the left. There were moderate but extensive active denervation potentials in the right C5-T1 myotomes but denervation was restricted to the deltoid and biceps muscles on the left. The spinati, rhomboïds, and paraspinal muscles were normal bilaterally, suggesting that the lesions were at the cord rather than trank level in the plexus.

A diagnosis of bilateral brachial plexopathy due to prolonged immobilisation with associated rhabdomyolysis was made. The patient underwent active rehabilitation and at discharge from hospital 2 months later, his left arm was almost fully functional. His recovery continued and at follow up, about 4 months after the episode, strength was normal in his upper limbs and he was able to perform coarse movements of the right hand, whereas the left C5/6 dermatome but he had developed severe truncal and gait ataxia due to the continued consumption of alcohol.

Patient 2, a 67 year old woman, known to be alcoholic, had gone to bed at midday. She denied having been drunk but this was considered very likely. On waking at 4.00 pm she was unable to move her head or limbs. There was no pain and the only sensory symptom was occasional tingling in the inside of her forearm. Her condition had improved marginally when she first presented after 2 weeks. Examination of her cranial nerves and left upper limb was normal and she had mild gait ataxia. There was no power (MRC grade 0) in the right deltoid, biceps, and brachioradialis and severe weakness (MRC grade 2) in the supraspinatus and infraspinatus muscles. She was brisk and symmetric apart from an absent right biceps reflex. Sensation was normal.

Magnetic resonance imaging of her cervical spine showed minor disc osteophyte bars at the C5/6 and C6/7 levels, the canal dimensions were generous, and there was no evidence of either cord compression or signal change in the cord. She had a raised y-glutamyl transferase (66 IU/l) and alanine aminotransferase (82 IU/l) and a macrocytosis (mean corpuscular volume 98.1 fl), compatible with chronic alcohol misuse.

Nerve conduction studies showed normal right upper limb sensory and motor nerve amplitudes comparable with the left side. The only abnormal motor conduction study was prolongation of the distal latency (9.9 ms) and reduction of the CMAP (0.8 mV) in the right median and ulnar nerves. EMG showed no voluntary activity and frequent fibrillations and positive sharp waves in the right supraspinatus, infraspinatus, biceps, brachioradialis, and pronator teres, and occasional fibrillations in the deltoid, all mainly C5/6 innervated muscles via the upper trunk. An EMG of the right triceps, flexor carpi radialis, and first dorsal interosseus were normal as was sampling of the cervical paraspinal muscles.

These findings were thought to be most compatible with a partial brachial plexopathy involving the upper trunk due to compression or traction. Three weeks later the patient had markedly improved, with a minor gait ataxia (MRC grade 4) in the previously severely affected muscles. The right biceps reflex was still absent. Three months later, she was asymptomatic with a normal neuro- logical examination.

These patients represent a range of alcohol related brachial plexus injury. In our first patient, the right side showed extensive damage involving the entire brachial plexus (C5-T1 myotomes) whereas the left involved mainly the upper part (C5-6 myotomes). This pattern of involvement, with sparing of the spinati and rhomboïds suggests that the site of injury was distal in the trunk at the level of the cords. The findings in the second patient are most compatible with a partial brachial plexopathy involving the upper trunk. The findings in both patients are most likely due to compression or stretching of the brachial plexus. Both patients had normal paraspinal EMG and cervical MRI studies, making more proximal lesions unlikely.

Clinical studies have shown that shoulder abduction to 90°, particularly if bilateral, combined with contralateral rotation of the head and arm extension increases tension on the plexus. We postulate that our patients slept with the affected arm extended and the head rotated to the left, giving maximum
traction to the right plexus. Seventy five per cent of postoperative plexopathies show involvement of the whole plexus whereas 18% are restricted to the upper trunk, usually in its entirety. Our cases were consistent with these findings.

The neurophysiological features and pattern of recovery suggest that compressive brachial plexopathy is primarily due to focal demyelination with some degree of axonotmesis depending on severity. Rapid recovery in our patients suggests that the primary pathology was focal demyelination, causing conduction block, although there was also clear EMG evidence for axonal degeneration, particularly in the right arm of the first patient, in whom recovery was consequently delayed. Ultimately, both patients made a good recovery as is typical in postoperative plexopathy, recovery time depending on the balance between demyelination and axonal degeneration. The occurrence of bilateral plexopathy, as in our first patient, is unusual after closed trauma but has been reported after bilateral shoulder dislocations and postoperatively.

The concurrent plexopathy and raised creatine kinase in our first patient is noteworthy. This may have been due to either prolonged immobilisation on a hard surface, diabetic neuropathy, or a combination of the two. Rhabdomyolysis was common in a series of elderly patients who remained on the floor for at least an hour after collapse, as evidenced by a raised serum myoglobin in 16 of 18 and creatine kinase in 14 of 18. Concurrent rhabdomyolysis and brachial plexus lesions have been described in the neurologic malignant syndrome and alcohol intoxication.

Alcohol related brachial plexopathy is part of the multitude of alcohol related neurological disorders. It is surprising that this entity is rarely reported, by comparison with plexopathy associated with other nervous system depressants; perhaps this is due to differences in the depth and duration of intoxication. It should be considered and looked for in patients with upper limb deficits related to intoxication.

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Positive response to therapy in a patient with seropositive paraneoplastic cerebellar degeneration and an endometrioid carcinoma of the vesicovaginal septum

Paraneoplastic cerebellar degeneration is a rare complication of human cancer. This disorder is characterised by subacute onset of pan cerebellar symptoms, often associated with dysfunction of other areas of the CNS. The onset of the degeneration may occur months before or after the detection of the primary cancer, and may recur on recurrence. It is usually associated with antineuronal antibodies directed against antigens coexpressed by the cells that undergo degeneration and by the associated tumour. Anti-Yo antibodies can be found in serum and CSF of patients with paraneoplastic cerebellar degeneration with breast or gynaecological tumours. These antibodies show a coarse granular staining pattern of the cytoplasm of Purkinje cells, while the nucleus remains unstained. Patients with paraneoplastic cerebellar degeneration without anti-Yo antibodies may have other tumours, most commonly bronchial carcinoma or Hodgkin’s lymphoma, and may be positive for anti-Hu, anti-voltage gated calcium channels, or anti-Tr antibodies. Although the antibodies provide a diagnostic test for the associated tumours, it is generally thought that destruction of the Purkinje cells by autoreactive T cells is the major pathogenic mechanism, and previous reports suggest a lack of response to conventional immuno-suppressive treatment.

A 47 year old woman had no history of neurological disease until March 1996. There was a history of surgical correction of a urethral diverticulum at the age of 34, and at 44 years she had been treated for a “vaginal cyst” (likely a Naboth cyst) by aspiration. In March 1996 she complained of blurred vision, diplopia, dysphagia, and gait ataxia with balance disturbance. Brain MRI and an ultrasound of the pelvis were reported as negative, but serum anti-Yo antibody was positive by immunohistochemistry, confirmed by immunoblotting with purified antigen (DPC Bierrmann). By 29 October 1996 there was marked gait ataxia, nystagmus, diplopia, dysphagia, cerebellar dysarthria, pyramidal signs, and arm and leg dysmetria with tremor. At this time MRI demonstrated cerebellar atrophy (figure A) and CT and MRI of the pelvis (figure C, D) both revealed a 3.5 cm diameter lesion located in the vesicovaginal septum, infiltrating the bladder and vaginal wall. A transvaginal biopsy was performed and the histological examination showed the presence of malignant cells. The staging markers excluded further distant tumour localisation and the patient underwent an anterior pelvic exenteration with ileal conduit. Pathological examination disclosed a very rare endometrioid carcinoma, and confirmed extensive bladder and vaginal involvement. The tumour seemed to arise from islands of endometriosis. Four cycles of adjuvant chemotherapy with carboplatinum and cyclophosphamide (respectively 300 mg/m³ and 500 mg/m², day 1, every 3 weeks) were administered between April and September 1997. From then until the present time she has been treated monthly with cyclophosphamide at a dose of 1 g, day 1, every 4 weeks.

Before months after commencement on chemotherapy, the patient began to show neurological improvement. Over subsequent months, diplopia and pyramidal signs disappeared and ataxia, tremor, and dysmetria progressively improved. However, 1 year after surgery a small vaginal tumour recurrence was diagnosed during a follow up gynaecological examination. Brain MRI demonstrated a slight progression of the cerebellar atrophy (figure B). The patient was subsequently submitted to external radiation therapy followed by intracavitary boosts. At the last follow up examination (September 1998, 21 months from primary surgery) the patient was in complete remission and able to read, to eat precut meals, to sit independently, and to walk short distances by using a wheeled walking support.

It is well recognised that microscopic ovarian cancer, only detected at laparotomy, can be associated with paraneoplastic cerebellar degeneration. Malignant transformation of benign endometriosis is a well documented phenomenon, but it occurs most commonly in the ovaries, and carcinomas arising at extraovarian sites is a rare event. In our patient we found an endometrioid adenocarcinoma located in the vesicovaginal septum, probably arising from islands of asymptomatic endometriosis and the delay in diagnosis was due not only to the small size but also to the unusual position of the tumour. We are not aware of any previous reports of paraneoplastic cerebellar degeneration associated with malignant transformation of non-ovarian endometriosis arising neither from the adnexa nor from the uterus.

A striking feature of this case was the improvement in neurological status due to chemotherapy of the tumour and subsequent immuno suppressive treatment. In most previous cases of paraneoplastic cerebellar degeneration, the early detection and removal of the tumour has not affected the neurological symptoms, nor has there been improvement or slowed progression of the disease after immuno suppressive treatment. There are only rare reports of successful immunosuppressive treatment of intravenous immunoglobulin therapy or courses of cyclophosphamide. In the second case, a very good response to cyclophosphamide was described but the sudden interruption of drug treatment led to the reappearance of symptoms, indicating that the clinical response was related to immunosuppression rather than a long term effect of tumour therapy.

In agreement with other authors we think that the presence of anti-Yo antibody in patients with cerebellar symptoms warrants an aggressive diagnostic approach that must begin with careful clinical examination, then proceed with mammography, pelvic CT, and
MRI. If no malignancy is found, surgical exploration should be considered, particularly in postmenopausal women. In addition, although many cases may not respond to plasma exchange, intravenous immunoglobulin or immunosuppressive drugs, perhaps because the neuronal damage is irreversible, the successful results in the present case indicate that continuous immunosuppressive therapy should be carefully considered.

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Isolated infarction in the territory of lateral posterior choroidal arteries

Lateral posterior choroid arteries (LPCAs) originate from the distal PCA trunk in the proximity of the origin of thalamogeniculate arteries or the cortical branches. Infarction of LPCAs, therefore, often accompany lesions of other PCA cortical branches or perforating branches. Their clinical features have often been masked by the associated and combined cortical and subcortical lesions. Accordingly the clinical features of a discrete infarction of the LPCA have been reported.
This paper reports on two such patients and pertinent articles are reviewed.

The first patient, a 62 year old woman with a history of untreated supraventricular arrhythmia for 10 years had sudden onset of non-pulsatile headache on the vertex. At the same time she noted blurred vision in the left visual field for a few days. The headache continued for 5 days and she visited a nearby hospital. No visual field defect was noted on confrontation. Brain CT showed a low density lesion in the posterior thalamus. As the location of the lesion was unusual, the patient was referred to our institution 3 weeks later. On admission she was free of neurological deficits including higher cortical function. The visual acuity was 12/20 on the right and 10/20 on the left. Goldman's perimetry did not disclose any visual field defect, either. The repeated CT showed a localised low density lesion at the posterolateral thalamus extending to the area of the lateral geniculate body inferolaterally and the posterior part of the caudate nucleus superiorly (figure A, B, and C). No other remarkable lesions were noted. Laboratory study was normal but the ECG showed atrial fibrillation. Vertebral angiography showed no obstructive or stenotic change in the posterior cerebral arteries. LPCAs were demonstrated on both sides. Brain MRI demonstrated a lesion of abnormal intensity at the posterolateral thalamus, the posterior part of the caudate nucleus, and the lateral geniculate body (figure D). She was medicated with 200 mg/day ticlopidine and remained free of stroke for the next 4 years.

The second patient, a 72 year old woman with an 8 year history of hypertension noted right sided homonymous type hemianopia for a few minutes on waking up in the morning. At the same time she felt transient bilateral hand dysaesthesia. She had no headache or dizzy sensation. When she arrived at the hospital 2 hours later, she was free of neurological deficits including visual field on confrontation. Three hours later CT showed no abnormality. Results from Goldman's perimetry were normal. Three days later repeated CT showed a newly appearing low density lesion at the left posterior thalamus, the lateral geniculate body, and the tail of the caudate nucleus (figure E, F). The superconductive MRI with T1 and T2 weighted images a month later and the CT scan 2 months later showed no abnormality. Cerebral angiography was not carried out. She was medicated with 200 mg/day ticlopidine and 300 mg/day pentixyline and has been well for the past 2 years.

We reported two cases of infarction at the posterolateral thalamus, the lateral geniculate body, and the posterior part of the caudate nucleus.

Reports on patients with discrete LPCA infarction are few.\textsuperscript{2–5} The main symptom has been related to visual field defect. It is commonly quadrantanopia or hemianopia. Characteristic visual field defects of LPCA occlusion have been described as homonymous horizontal sectoranopia or wedge shaped homonymous hemianopia.\textsuperscript{4–5} These authors stated that, with and without evidence of CT, these unusual visual field defects were due to ischaemia at the lateral geniculate body, and dual blood supply from the LPCA of PCA and anterior choroid artery of the ICA may explain this unusual visual field defect. Neau and Bougossavisky have also stated that, although it occurs infrequently, its is specific to the lesion at the lateral geniculate body.\textsuperscript{5} The other signs were hemisensory disturbance, to a lesser extent neuropsychological.
dysfunctions such as aphasia, hemineglect, and memory disturbance, and more rarely hemiparesis. 

In our patients the symptoms were mild and transient. The first patient had blurred vision on the left side for 5 days and in the second patient, the visual field defect lasted for a few days. When two or more branches are present, anterior branches penetrate the choroid fissure to supply the choroid plexus of the inferior horn of the lateral ventricle. Posterior branches supply the choroid plexus in the trigone of the lateral ventricle and anteriorly in the third ventricle. They also supply the pulvinar, medial, and lateral geniculate bodies, fornix, and midbrain tegmentum. Many anastomoses between the branches of the LPCA and anterior choroidal arteries are present at the anterior third of the temporal horn as are many connections between the LPCA and medial posterior choroidal arteries at the level of the fornem of Monro. 

In frequent occurrence of occlusion of the LPCA is speculated to be due to such multi-
ple branches and rich anastomosis. The number of arteries and development of anastomosis vary. Such ample anatomical variation in the supplying territory of these arteries may explain the wide range of severity and duration of symptoms of both our patients and others reported. Our patients represents the milder form of the clinical features of infarction of the LPCA, which has not been highlighted. The LPCA occlusion may present only with such minor complaints. Because LPCA occlusion may be prodromal signs of much more serious brain ischaemia, we need to know a wide range of the clinical symptoms related to occlusion of the LPCA.

Neurostimulation of the ventral intermediate thalamic nucleus alleviates hereditary essential myoclonus

Therapy in hereditary essential myoclonus (HEM), a disabling movement disorder, is difficult in most cases, especially in regard to the myoclonic syndrome. This is the first report on the amelioration (around 65%) of HEM by high frequency deep brain stimulation of the ventral intermediate thalamic nucleus (VIM) in a 16-year-old male patient with medically intractable HEM. The jerk movement disorder began in his neck and shoulders around the age of 6 and gradually progressed, especially in the proximal right arm, leading to a severe reduction of dexterity and inability to write. He was unable to continue working as a janitor when he was 55.

On examination he presented mainly oscillating, “lightning”, irregular, jerk, asynchroneous movements of his forehead, neck, proximal right arm, less severe of the left arm, and discreetly of the upper trunk, which was exaggerated by walking, writing or drinking and could be elicited by loud acoustic stimuli. The disorder improved at rest and disappeared in sleep. Additionally, he had a slight torticolis to the left, superimposed by inconstant no-no myoclonus and a discrete action tremor of both hands, all of which complies with the HEM criteria as outlined by Quinn. The remaining neurological status was unremarkable. Four of the six children of the patient had possible myoclonus in a 61-year-old male patient. Additionally, two of four siblings of our index patient were definitely affected by the movement disorder, whereas the parents seemed to be unaffected (a full account of the family history will be provided elsewhere, manuscript in preparation). Alcohol consumption markedly attenuated the movement disorder with a clear rebound phenomena after alcohol withdrawal, leading to chronic alcohol misuse. A latent suicidal wish with regard to the exhausted medi-
cal and social perspectives complicated the situation.

Extensive drug treatment trials (including monotherapy or combination therapy with the following agents: apomorphine, both oral and intrathecal baclofen, cerebral application of butylum toxin, carbazapsein, carbipoda, clonazepam, clonidine, clozapine, fluphenaza-
mine, haloperidol, hydrotropine, levetryptophan, levo-
dopa, lithium, paroxetine, piracetam, primidone, propranolol, tiapride, trihexyphenidyl, and valporate) had no effect on the myoclonic syndrome except for a mild improvement under diazepam.

Electroencephalography, including back averaging of the EEG activity preceding spontaneous jerks, polymyography, and somatosensory evoked potentials of the median nerve, cranial Cz, and anterior tibial muscle did not show any abnormalities.

In this therapeutically hopeless situation, which was complicated by a latent suicidal syndrome secondary to the lacking therapeutic options, unilateral deep brain stimula-
tion of the left VIM (essentially as outlined in Benabid et al.) was performed after informed consent of the patient, for three reasons: Firstly, VIM stimulation is considered to be a “low risk” and effective therapy in patients with drug refractory essential tremor, which is also characterized by alcohol attenuation. Secondly, there are anecdotal reports on the improvement of myoclonic disorders by thalamotomy. Thirdly, in the absence of a therapeutic effect the electrode could have been removed or switched off.

Intraoperatively and in the subsequent 12 months deep brain stimulation (2.8 V, 130 Hz, 90 µs) produced a pronounced and persis-
tent reduction of the jerks and the action tremor of the right arm and neck and a mere reduction of the jerks of the neck and the trunk. The improvement could be postoperatively quan-
tified by a roughly 65% decrease in myoclonus score (table). In practical terms, this was reflected by the use of the right hand for handwriting for the first time after 15 years of incapacity. Interestingly, the optimal stimula-
tion parameters corresponded to those used in deep brain stimulation for essential tremor. The mild dystonic symptoms (slight cervical dystonia) were not affected by DBS with different stimulation parameters. Preop-
erative medication comprised 60 mg di-
azepam a day and could be reduced to 10 mg diazepam a day at 12 months postoperatively.

Stimulation of the VIM is an established neurosurgical method for the treatment of pharmacologically intractable essential tremor, although its mechanisms of action remain to be elucidated. It is interesting to note that both diseases (HEM and essential tremor) may be improved by alcohol intake, which could hint at overlapping pathophysi-
ological mechanisms. Importantly, it has been reported that low frequency stimulation (2 Hz-5 Hz) of the VIM in patients with Par-
kinson’s disease may even trigger myoclonus. However, we have been unable to aggravate the myoclonic syndrome in our patient by low frequency stimulation (2 Hz-5 Hz), which may point to different mechanisms of actions of stimulus induced myocloni in Parkinson’s disease versus HEM. In conclusion, our case report suggests that neurostimulation of the VIM may be a effective therapeutic alternative for medically intractable HEM and suggests that the thala-
mus may be a myoclonic sensitive site.
Invasive intracranial aspergillosis secondary to intranasal corticosteroids

Intranasal corticosteroids are widely available; we describe a serious and previously unreported complication of their use. A 41 year old Asian woman was admitted acutely, 6 weeks after two generalised seizures. She described a 2 year history of anosmia, nasal stuffiness, and rhinorrhea which was diagnosed 12 months previously, by both her general practitioner and an ear, nose, and throat surgeon, as allergic rhinitis, with patch testing confirming allergy to house dust mite II, although no imaging was performed at this time.

This was treated with the topical nasal steroid spray Fluticasone (fluticasone propionate 50 mcg/spray). The remainder of the history was unremarkable and she had not been back to Asia for 6 years.

General examination was normal and there were no focal neurological signs, although she was rather confused and disinhibited.

Full blood count; urea and electrolytes; liver function tests, serum calcium; random blood glucose; thyroid function tests; serum angiotensin converting enzyme; blood cultures; cyttoplasmic pattern (c-) antineutrophilic antibodies (ANCA) and perinuclear (p-) ANCA; an ECG; and chest radiography were all normal.

An EEG showed only diffuse slowing, consistent with a postictal state. Brain CT showed an ill defined area of reduced attenuation in the right frontal lobe, with no contrast enhancement, and a soft tissue mass in the paranasal and sphenoid sinuses, which was eroding through the base of the skull.

Brain MRI (fig 1) showed swelling of the right frontal pole with oedema and a small, intensely enhancing, soft tissue mass in the floor of the anterior fossa, which was probably in communication with the soft tissue mass in the paranasal sinuses.

A biopsy of the posterior ethmoid region showed granulomatous change with fungal hyphae seen and Aspergillus fumigatus was grown on culture. Cultures for tuberculosi were negative and HIV type 1 and 2 serology was negative.

Anti-convulsant therapy with modified release carbamazepine (carbamazepine MR) was started and the nasal spray was stopped. She was commenced on intravenous amphotericin B (250 mcg/kg/24 hours), which within 2 days led to renal impairment and had to be discontinued.

Itraconazole syrup (200 mg twice daily) was substituted and adjusted according to serum concentrations, and the therapeutic range (4 hours postdose 5–15 mcg/l) was achieved with a dose of 300 mg twice daily.

Over subsequent weeks she improved and became less confused and disinhibited, although the anosmia remained. On review 8 months later she remained well and a repeat MRI (fig 2), although still showing residual disease, showed a marked reduction in its extent and in particular a dramatic decrease in the size of the subfrontal lesion.

The fungal genus Aspergillus causes a range of diseases including allergic; non-invasive; invasive and fulminant aspergillosis. The two commonest strains are A fumigatus and A flavus. Invasive aspergillosis is characterised by tissue invasion with Aspergillus hyphae and is most commonly seen in immunocompromised people, but there are a few case reports in apparently immunocompetent people. It differs from allergic aspergillus sinus and allergic bronchopulmonary aspergillosis, which are immune mediated reactions to Aspergillus infection.

There are three possible routes of invasion into the CNS: haematogenous, usually from the lung; direct spread from an area adjacent to the CNS, and iatrogenic introduction, usually after neurosurgical procedures.

The commonest route of spread is haematogenous and the most frequent CNS manifestation is an intracerebral abscess, but it can also cause meningitis or meningoencephalitis; granulomas; cerebrovascular disease; vasculitis, or cranial nerve palsies.

Intracranial extension from an adjacent area is only seen in advanced cases, and extension through the skull base is rare.

The prognosis in this disease is very poor and invasive CNS aspergillosis is often a fatal disease regardless of the mode of therapy, with mortality upwards of 80%, and very few long term survivors of cranial and intracranial aspergillosis have been reported in the literature. Amphotericin B is effective against Aspergillus but its toxicity and mode of administration limit its usefulness. Itraconazole is well absorbed orally, is comparatively non-toxic, and is effective against Aspergillus; however, serum concentrations need monitoring.

Figure 1  Gdolinium enhanced, T1 weighted, sagittal MRI, showing diffuse disease throughout the sinuses (thin arrow) and an enhancing lesion in the subfrontal area (thick arrow).
Local antifungal chemotherapy delivered recently, stereotactic surgery, tried, from formal craniotomy to, more zole and amphoterecin B. Evidence suggests antagonism between itraconazol... treatment, and some evidence suggests antagonism between itracona-

There is little advantage of combined therapy over monotherapy, and some evidence suggests antagonism between itraconazole and amphoteracin B.

Various surgical approaches have also been tried, from formal craniotomy to, more recently, stereotactic surgery, all with varying, although usually poor, rates of success. Local antifungal chemotherapy delivered to the lesion via a closed reservoir system has been tried and may prove a useful adjunct to treatment.

The correct method for treating this condition is unknown and its rarity makes large randomised trials of surgical or combined approaches untenable. Most studies to date advocate early aggressive surgical intervention, but the evidence to support this approach is not strong. It is probable that the most effective treatment will be a combination of different modalities, which is likely to vary depending on the extent of the disease.

In our patient there was no evidence of immunodeficiency and the biopsy confirmed invasive aspergillosis with the imaging showing continuity between the sinuses and frontal lobe lesions. We think that there can be little doubt about the important part played by the intranasal steroids in our patient. Even if intranasal steroids did not lead to the introduction of Aspergillus, they certainly allowed the Aspergillus to flourish, possibly by impairing local cell mediated immunity. A similar situation to that which occurs when topical steroids are applied to fungal skin infections that are mistaken for eczema.

In view of the lack of consensus on management we decided to continue with antifungal chemotherapy alone, particularly given the likely importance of the intranasal steroids in our patient.

Antifungal chemotherapy alone was previously thought to be largely ineffective due to its inability to cross the blood-brain barrier and reach fungal hyphae buried deep in fibrous tissue, and previous case reports have not shown any reduction in the disease bulk with chemotherapy alone. This was clearly not the case with our patient; however, how long we will need to continue treatment and whether she will ultimately still need surgery, remain unanswered questions.

Although a rare condition, in view of the high mortality, we think that this report emphasises that the continuing need for intranasal steroids should be assessed on a regular basis. Clinicians should also be alert to the possibility of an underlying condition, other than allergic rhinitis, in these patients.

Some reports suggest that the syrup form is more reliably absorbed and hence the choice of this preparation for our patient. Other antifungal agents do not have sufficient activity against Aspergillus to be of any value, with the possible exception of the newer agent voriconazole.

There is little advantage of combined approaches over monotherapy, and some evidence suggests antagonism between itraconazole and amphoteracin B.