ing in her hair, were seen. Her intellectual function was within the normal range, and her social activity was normal. Multiple angiomyolipomas in both kidneys, plaques in the retina, and a small calcified tuber by the left lateral ventricle were found. Her habitual seizures consisted of loss of awareness, incoherent speech, staring, and right hand dystonic posture. Routine EEG showed normal background activity. Prolonged EEG monitoring recorded ictal rhythmic discharges mainly at the right posterior quadrant. The patient had been on VPA (200 mg/day) and phenobarbitone (80 mg/day) for more than six months, with steady state trough blood concentrations of 66.6 mg/l and 20.2 mg/l respectively. VPA was switched to CBZ to achieve better seizure control, that was increased up to 600 mg/day in one month. Two months afterwards, when the blood concentration of CBZ was 6.5 mg/l, the patient had appreciable hair loss, and especially over the front of her head her hair became very sparse. When the dose of CBZ was reduced to 200 mg/l in two weeks, moulting stopped, and new hair began to grow. No other skin lesions developed simultaneously, and no white tuft hair was seen. Throughout the clinical course, the patient had no pregnancy, endocrine disorders, or autoimmune disturbance. CBZ had been given in a different hospital one year before the present episode, but at that time the patient took the drug only for a week, because it caused dizziness and ataxia.

CBZ often causes allergic reactions such as skin rash, and also systemic lupus erythematosus, both of which can potentially cause hair loss.⁴ Pregnancy, fever, thyroid dysfunction, and malnutrition are also potential causes of hair loss.⁵ In the present two patients, there were no such accompanied causes to explain their hair loss. In the previous case report of hair loss associated with CBZ, it occurred a week after CBZ was initiated.³ Human hair follicles have two phases: an anagen (growth) phase of four years, and then a telogen (resting) phase of three months, followed by normal hair loss.⁵ Therefore, the onset of the hair loss within a week of CBZ administration was interpreted as a disturbance of growing of hair follicles (anagen phase).² However, in the present report, it took two and three months in patients 1 and 2 respectively, until hair loss started. This can be explained by the premature ending of the anagen phase, as usually seen in treatment with antithyroid drugs, anticoagulants, and VPA.⁵ This type of hair loss occurs about three months after the insults—namely, at the end of the telogen phase,⁵ as seen in the present cases. This may explain why in patient 2 hair loss was not recognised when she had taken CBZ for a week previously. Both of the present patients had been on VPA previously, and patient 1 had hair loss most likely caused by VPA. This did not happen in patient 2. Thus it suggests that hair loss caused by CBZ and VPA does not necessarily occur by a common mechanism. The common characteristics in these two patients are that both were young women with partial seizures, which were treated by polytherapy with anticonvulsant drugs. A recent double blind, multi-institution trial to compare CBZ and VPA showed that changes in hair texture or hair loss were seen in 6% of the patients treated by CBZ.⁷ As the authors did not specifically differentiate between changes in hair texture and hair loss, it is uncertain how often hair loss occurred in

association with CBZ, and what the patient population with this side effect was. Although alopecia resulting from treatment with CBZ is not often seen, attention must be given to epileptic patients, especially when precipitating factors of hair loss are present, and also especially in young women.

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Neurological manifestations of coeliac disease

The association between progressive myoclonic encephalopathy (Ramsay Hunt syndrome; progressive myoclonic ataxia) was recently the subject of a clinicopathological report in this *Journal*¹ and of a review by Bhatia *et al.*² A notable feature of these cases was the rapidly progressive nature of the encephalopathy. Most patients were unable to walk or died within two years of the onset of their neurological symptoms. The patient that we report is therefore remarkable in that her neurological illness began 13 years ago. Progressive myoclonic encephalopathy associated with coeliac disease may take a more benign course and we suggest that the condition should be considered in all patients with cerebellar ataxia, particularly if there is myoclonus.

The patient, now aged 64, presented at the age of 55 with a four year history of difficulty with fine finger movements in both hands, worse on the right such that she had difficulty picking up coins and doing up buttons. Her walking had also become slower. Examination at the age of 55 disclosed a jerky upper limb tremor with myoclonus but no gait ataxia. The tremor and myoclonus have slowly worsened and she has developed an ataxic gait. She now walks with a frame indoors, but has frequent falls. She uses a wheelchair outdoors. She has never had a seizure.

She has never had any specific bowel symptoms, but investigation of a macrocytic anaemia and folate deficiency associated with weight loss eventually led to the diagnosis of coeliac disease five years ago, confirmed by small bowel biopsy. However, coeliac disease was almost certainly present 10 years before

this when she was investigated for anaemia at another hospital and an abdominal ultrasound disclosed hyposplenism. Reticulin antibodies were present. She was started on a gluten free diet and the haematological indices returned to normal. Vitamin E concentrations were normal. Her other medical history included pulmonary tuberculosis at the age of 22.

On examination she had spontaneous, and reflex and action myoclonus in the upper limbs and, to a lesser extent, in the leg. In addition, there was a postural upper limb tremor and finger-nose ataxia bilaterally. Her gait was ataxic and she walked with a frame. Tendon reflexes were normal and plantar responses flexor. Vibration sensation was absent below the knees, but proprioception in the big toes was normal. Neurophysiological studies confirmed multifocal spontaneous, reflex and action myoclonus particularly of the hands. Back averaging from the action jerks disclosed time locked cortical activity over the contralateral hemisphere, preceding each jerk by 27 ms. Somatosensory evoked potentials after finger stretch were pathologically enlarged.

The clinical and neurophysiological characteristics of her condition conform closely to those previously reported in patients with coeliac disease and the Ramsay Hunt syndrome, except that the rate of progression of her disease has been much slower. Of 11 cases reported in the literature,¹⁻³ seven have been unable to walk or stand or have died within two years of the onset of their neurological illness. The longest reported survival after the onset of neurological symptoms has been six years (case 1 of Lu *et al.*) at which time the patient was unable to walk. Our patient has now had neurological symptoms for more than 13 years and remains ambulant, albeit with a frame.

The present case shows that myoclonic encephalopathy associated with coeliac disease does not invariably have a rapidly progressive course. This case and the recent report of anti-glutadin antibodies in 17 out of 25 patients with ataxia of unknown cause (of whom four subsequently had abnormal small bowel biopsies consistent with coeliac disease⁴) suggests that coeliac disease should be considered in all patients with ataxia, particularly if there is myoclonus.

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Successful outcome with aggressive treatment of acute haemorrhagic leukoencephalitis

Acute haemorrhagic leukoencephalitis was first described as a pathological entity by Hurst in 1941.¹ It is a rare acute inflammatory myelinopathy of the CNS characterised by progressive loss of consciousness leading to coma accompanied by focal neurological dysfunction. It is now generally accepted that acute haemorrhagic leukoencephalitis is the severe end of the range of acute disseminated encephalomyelitis.²

A 34 year old man presented with rapidly progressive dysphasia, right hemiparesis, and deteriorating level of consciousness over 24 hours after a flu-like illness in the preceding week. He had no history of any other relevant previous illnesses, travel, or immunisation and was not taking any medication.

On initial examination he was febrile at 38°C. He had an expressive dysphasia, was drowsy, and had mild neck stiffness. A right central facial weakness was present and a gag reflex was absent. He moved his left arm and leg to command but only flexed his right arm and leg to painful stimuli. Computerised tomography of the brain showed left frontoparietal oedema with mass effect causing effacement of the sulci and the frontal horn of the lateral ventricle and 5 mm midline shift (fig 1).

There was further deterioration in his consciousness over the next several hours leading to intubation and transfer to the intensive care unit with a presumptive differential diagnosis of viral encephalitis, bacterial cerebritis, or acute disseminated encephalomyelitis. Treatment with acyclovir, ceftriaxone, flucloxacillin, phenytoin, and dexamethasone was commenced. Cerebrospinal fluid from ventricular puncture showed 25 000 red blood cells/mm³, 53 white blood cells/mm³ (72% polymorphonuclear cells, 24% lymphocytes, 4% monocytes), 1257 mg/l protein, and 6 mmol/l glucose. Gram stain, bacterial cultures, and cryptococcal antigen were negative.

On day two of the hospital admission he developed signs of increasing cerebral oedema and his intracranial pressure was 90 mm Hg (normal 15 mm Hg). Medical therapy to lower intracranial pressure was started with hyperventilation, mannitol, and

lignocaine. Despite these measures the pressure remained high with haemodynamic instability. Consequently, a partial left frontal lobectomy was performed without replacement of the bone flap on day 3.

Because of his deterioration on broad spectrum antibiotics and acyclovir along with the antecedent flu-like illness, a presumptive diagnosis of acute haemorrhagic leukoencephalitis was made and 1000 mg methylprednisolone daily for three days was given. Subsequently, histology of the brain biopsy confirmed the clinical diagnosis (fig 2). Immunoperoxidase for herpes simplex virus was negative. Polymerase chain reaction amplification of herpes simplex type 1 DNA on brain tissue and in CSF was negative.

Intravenous immunoglobulin was given at a dose of 30 g daily for five days initially but the patient remained in coma. Plasmapheresis (five 2 l exchanges on alternate days) and 100 mg/day cyclophosphamide were commenced on day 9. Methylprednisolone was given at a dose of 1000 mg daily for a further five days followed by a reducing course of steroid.

First signs of recovery were noted on day 14 when he opened his eyes and moved his left hand to command. He was extubated on day 17. Steady neurological recovery continued and he was walking with assistance and speaking by day 30. Cyclophosphamide and steroids were ceased on day 40 and 50 respectively. At four months a cranioplasty was performed. At nine months he is back at work as an accountant and sailing competitively with minimal neurological deficit.

Aggressive treatment of patients with acute haemorrhagic leukoencephalitis may lead to a favourable outcome despite the presence of severe neurological disability at the beginning of the illness.³⁻⁵ Recognition of acute haemorrhagic leukoencephalitis may be difficult but there are several useful clinical signals: (a) the antecedent flu-like illness, (b) early changes on brain CT,⁶ (c) the presence of red cells and a neutrophil pleocytosis in the CSF, and (d) deterioration despite broad spectrum antibiotics and antiviral therapy. Brain biopsy, however, is essential for diagnosis.

Management consists of early diagnosis, aggressive control of raised intracranial pressure in intensive care, and immunosuppres-

sive therapy with a combination of corticosteroids, plasmapheresis, and cyclophosphamide. Immunosuppressive treatment for acute haemorrhagic leukoencephalitis is based on the assumption that it is an autoimmune disorder. The strongest evidence for this comes from its similarity to experimental allergic encephalomyelitis and in humans with acute disseminated encephalomyelitis there is evidence of activation of autoreactive T cells against myelin basic protein.^{7,8} Of the immunological therapies that have been reported to be effective it is not clear which is superior or which combination is best. Nonetheless, in a severely disabled patient it would seem prudent to maximise treatment.

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Figure 1 Brain CT showing left hemispheric oedema with mass effect and midline shift. There is no contrast enhancement to suggest an abscess.

Figure 2 Luxol fast blue stain for myelin showing perivenous demyelination and punctate haemorrhages (original magnification $\times 10$).