degeneration of the spinal cord two weeks after nitrous oxide anaesthesia given during surgery for stabilisation of a femoral fracture.

At the present time there is growing acceptance that the clinical picture of neurological dysfunction due to contact with nitrous oxide takes the form of vitamin B12 deficiency. This finding is supported by a sizeable body of laboratory investigations indicating that nitrous oxide exerts its biological effects exclusively through interference with vitamin B12, necessary for DNA synthesis and for the maintenance of myelin sheaths.[4]

The neurological effects of long term nitrous oxide exposure were first reported in 1978 in several people who used nitrous oxide for recreational purpose.[4 5] A neurological syndrome identical to that of vitamin B12 deficiency was noted.[6]

Whereas short term nitrous oxide exposure in healthy people seems to have no appreciable sequelae, the administration of nitrous oxide anaesthesia in patients with unsuspected vitamin B12 deficiency can induce neurological changes, highlighting a previous subclinical condition.

Preoperative vitamin B12 concentrations should be obtained in patients with increased mean corpuscular volume indexes, or affected with gastric mucosa atrophy or previous gastric or intestinal resections. In this way vitamin B12 deficiency would be easily corrected before and after anaesthesia and surgery to avoid possible neurological complications.

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Acute polyneuropathy with chronic lymphocytic leukaemia and paraproteinaemia: response to chlorambucil and prednisolone

Paraproteinaemic polyneuropathies are usually chronic and respond poorly to treatment.[1] An exception to this is seen in the POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes),[2] in which polyneuropathy may improve after treatment for the osteosclerotic myeloma with which it is often associated. Progressive paraproteinaemic neuropathies may also be associated with multiple myeloma, Waldenstrom's macroglobulinaemia, monoclonal gammopathy of undetermined significance, amyloidosis, and Castleman's disease.[3] Monoclonal gammopathy is often detected in patients with chronic lymphocytic leukaemia,[4] but the association between paraproteinaemic polyneuropathy and chronic lymphocytic leukaemia has not previously been reported.

A 73 year old woman with diet controlled diabetes developed, over three days, progressive, bilateral leg weakness without sensory disturbance or sphincter symptoms. Examination disclosed a profound flaccid leg weakness with areflexia and flexor plantar responses. There was a partial right third cranial nerve palsy and poor adduction of the left eye, which improved spontaneously within two weeks of admission. The spleen tip was palpable, but there was no hepatomegaly or lymphadenopathy. Investigations included a white blood cell count of 160×10^9/l, platelets 90×10^9/l with normal haemoglobin, electrolytes, and liver function. An IgG κ-paraprotein band (33 g/l) was detected on protein electrophoresis. Morphology and immunophenotyping of the white cells in peripheral blood and bone marrow were diagnostic of chronic lymphocytic leukaemia. MRI of the brain and thoracolumbar spine was normal. Total protein in CSF was 1.3 g/l (normal 0.3–0.6 g/l) and glucose was 3.4 mmol/l (plasma 4.7 mmol/l). No atypical lymphocytes were seen on a centrifuged specimen. Nerve conduction studies performed 10 days after admission showed absent sural nerve sensory action potential and distal slowing of motor conduction in both upper and lower limbs (ulnar nerve distal motor latency 4.7 ms and conduction velocity 46 m/s; common peroneal nerve distal motor latency 8.5 ms and conduction velocity 34 m/s). Ulnar nerve F response was 33.6 ms and no F responses were detected from common peroneal nerve stimulation. No antibodies against myelin associated glycoprotein were detected in the serum. A diagnosis of postinfectious acute inflammatory demyelinating polyradiculopathy (AIDP) prompted treatment with intravenous immunoglobulin. After six weeks without improvement treatment with 60 mg prednisolone daily was started. A sural nerve biopsy showed severe loss of large and small myelinated fibres, but no malignant infiltration or deposition of amyloid light chains or cryoglobulin. After 10 weeks without clinical improvement and still wheelchair bound, treatment with 10 mg chlorambucil daily was started. Within a week of this treatment she could lift her legs off the bed. After six cycles of combined treatment (two weeks 10 mg chlorambucil, 40 mg prednisolone daily, followed by two weeks off treatment) she was able to walk with a stick. Her white cell count had fallen to 8×10^9/l (46% lymphocytes) and her paraprotein to 8 g/l.

Chronic lymphocytic leukaemia is the most common human leukaemia but infrequently causes neurological symptoms. The predominant neurological complications of chronic lymphocytic leukaemia are due to meningeal[5] or peripheral nerve infiltration,[6] both of which were excluded in our patient. Although rare cases of axonal peripheral neuropathy have been described in patients with chronic lymphocytic leukaemia,[6] we think that this is the first case of a paraproteinaemic demyelinating polyneuropathy associated with chronic lymphocytic leukaemia. This case is not typical of the POEMS syndrome in that the neuropathy was of relatively acute onset, there was no endocrinopathy or skin changes and, in POEMS, the underlying haematological disorder is usually osteosclerotic myeloma. An autoimmune aetiology of the polyneuropathy seems likely as quantitative defects of the immunoglobulins in chronic lymphocytic leukaemia can disrupt the anti-idiotype network's regulation, resulting in autoimmune manifestations that may affect peripheral nerves. In addition, peripheral demyelination may be caused by binding of the paraprotein and complement C3b to myelin associated glycoproteins.[7] It is of interest that specific treatment of the lymphoproliferative condition in our patient resulted in a reduction in the paraprotein and a dramatic clinical improvement.

This case emphasises the diversity of haematological malignancies that can manifest as paraproteinaemic demyelinating polyneuropathy. The prognosis for neuropathies associated with paraproteinaemia is generally poor, but this case suggests that chronic lymphocytic leukaemia, in addition to POEMS, is an example in which treatment of the underlying disorder may modify the natural history of the neuropathy.

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Endovascular electroencephalography during an intracarotid amobarbital test with simultaneous recordings from 16 electrodes

Recently, Boniface and Antoun[1] reported endovascular EEG during intra-arterial amobarbital tests using an endovascular guide wire as the different electrode for bipolar recordings against an extracranial surface electrode (T3) or an average reference. They concluded that their technique was feasible to identify intracranial epileptiform discharges and was less invasive than other intracranial EEG methods with the advantage that it was possible to move the guide wire between different intracranial sides. They also mentioned "the potential to achieve more in a bipolar format when the electrical characteristics of the electrode are optimised".

Our experience with this technique[2] prompted us to use a multilead catheter developed for cardiological examinations (PathfinderTM, Cardima, 47201 Lakeview Boulevard, Fremont, CA 94538, USA) with eight pairs of electrodes (electrode length 0.5 mm, interelectrode spacing 2 mm; electrode pair spacing 6 mm). This allows bipolar recording simultaneously from each electrode to an extracranial surface electrode (FZ) (figure). Our endovascular EEG shows pulse artefacts in some leads, which are a common problem of this technique,[1–3] but they were less pronounced than other recordings.[1] Using the tip of the guide wire as the different electrode, as done by previous groups,[1–3] has the disadvantage that recordings are achieved from a single area at one time only and that the guide wire has to be moved to record from other parts of the temporal lobe. The catheter we used, however, provides simultaneous recordings from 16 different points over a length of 72 mm of the temporal lobe. Such a technique may be of interest during pharmacological activation of epileptogenic foci with short acting barbiturates,[4] and especially during the intracarotid amobarbital test, as this test is routinely performed during presurgical evaluation of patients with medically intractable temporal lobe epilepsy and is known to activate the epileptic focus in more than half of the patients.[5] The clinical use of this technique awaits further evaluation in an appropriate number of patients.

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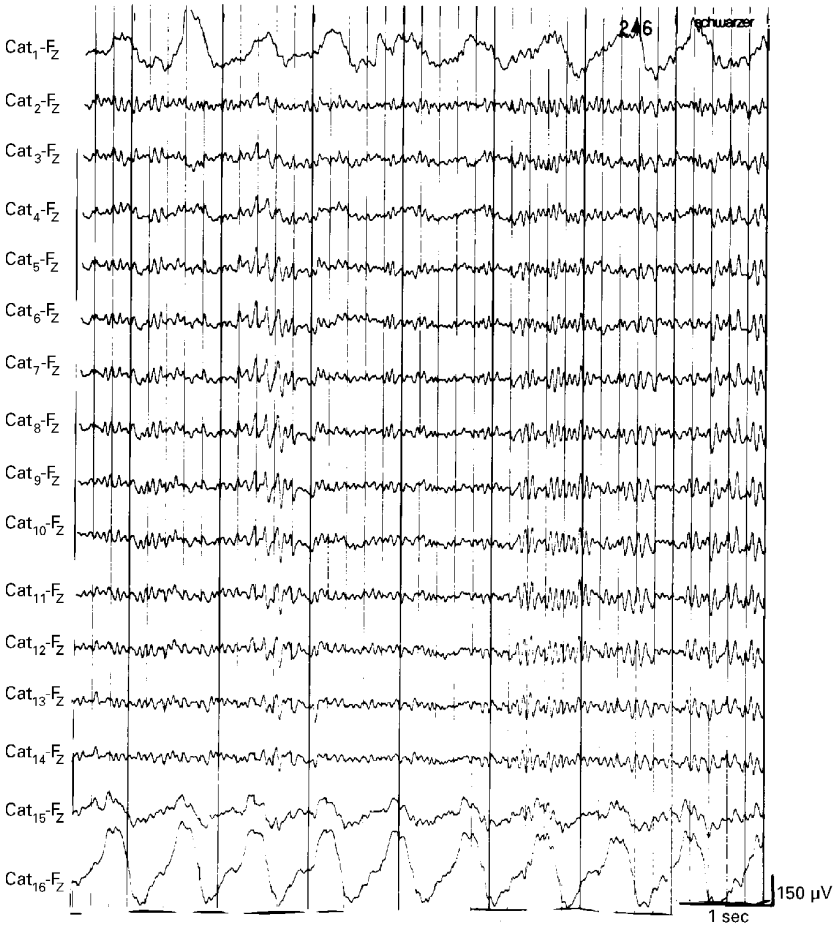

Endovascular EEG using a catheter with 16 electrodes. Bipolar recording between every single electrode and an extracranial surface electrode at FZ. (The electrodes were placed one after another over a length of 72 mm, Cat1 refers to the distal electrode at the tip of the catheter and Cat16 to the proximal electrode at the end of the line of electrodes.)

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Standardising care and clinical trials

In his editorial on the Brain Trauma Foundation guidelines for the management of severe head injury, Kirkpatrick argues that standardisation of care is a prerequisite for the conduct of multicentre randomised trials.[1] A similar concern seems to have motivated the European Brain Injury Consortium to develop its "expert opinion" based guidelines.[2] This is not the case. Providing that a trial is large enough, randomisation will ensure that the intervention and control groups are identical with regard to known and unknown confounders. It is conceivable that the size of the intervention effect may vary a little depending on the other aspects of care given, but not the direction of the effect. Patients in the future will almost certainly receive different forms of care than they do today, and treatments shown to be effective today may be more or less effective in the future, but the direction of the effect will be the same. Rather than standardise care, it would be more useful to make sure that clinical trials were large enough to detect reliably moderate but clinically important treatment effects. Even though thousands of patients each year are treated with hyperventilation, barbiturates, mannitol, and steroids, clinical trials of these interventions, even in aggregate, have involved less than a few thousand patients, and for hyperventilation, mannitol, and barbiturates, existing trials comprise less than a few hundred patients. It is not surprising that the Brain Trauma Foundation was unable to define evidence based standards of care.

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