indirect immunofluorescent test for Lyme disease (Institut Pasteur, Paris), Rose Bengal Plate test, immunoelectrohoresis and IgG secretion index. After the last episode electrophysiological studies (motor conduction velocity and F wave latency in the legs, brainstem auditory evoked responses, visual evoked responses) and a cerebral and whole spinal cord MRI scans were all normal.

Our patient had recurrent meningomyelitis and latterly encephalitis, in which each episode was preceded by fever and myalgia and developing severe neurological deficits requiring, on one occasion, mechanical ventilation. In spite of the severity of the motor and sensory dysfunction there was always complete recovery. The initial CSF inflammatory profile was the only abnormality found. All the other repeated investigations were normal or negative. We can only find one similar report in the literature.1


Creutzfeldt-Jacob disease following cadaveric dura mater graft

There have been three previous reports of Creutzfeldt-Jacob disease (CJD) following repair of dural defects by surgical grafting of commercially prepared, lyophilised cadaveric dura mater, one each from USA,1 New Zealand2 and Italy.3 We have recently seen the first case of CJD in the United Kingdom presumed to have been transmitted by cadaveric dura mater graft.

In October 1985 a 26 year old man had a foramen magnum decompression and cervical laminectomy for syringomyelia and cervical myelopathy. During the procedure a dural graft was stitched from the level of the third cervical vertebra to the occiput. Postoperatively he had a spastic gait and an ataxic left arm with spinothalamic sensory loss, but he remained independent and worked as a builder. In August 1989, at the age of 30, he became increasingly withdrawn: he had difficulty recognising people, and his speech, comprehension and balance became disturbed. On admission to hospital in September 1989 he was alert but severely dysphasic and dysarthric. He had a spastic tetraparesis and ataxia of all four limbs. He was unable to feed himself or walk unaided. Haematological and biochemical investigation and enhanced CT brain scan were normal. The cerebrospinal fluid was acellular with protein 0.9g/l and normal glucose. He deteriorated and became drowsy, then confused and finally comatose. Brain biopsy and three subsequent MRI scans showed widespread spongiform degeneration with gliosis and neuronal loss involving the neocortex, striatum and cerebellum.

This patient’s illness began 46 months after insertion of the dural graft, compared with intervals of 19, 31, and 44 months for the other three reported cases who were 28, 25 and 27 years old respectively. All four patients are considerably younger than the mean age of 63 years for sporadic cases occurring in the UK in whom no aetiological factors have been identified.4 They had all received the same type of lyophilised human cadaveric dural graft. “Lyodura”, manufactured by B Braun Melsungen AG, Germany, and all the grafts were inserted within a 20 month period between May 1985 and November 1986. The transmissible agent thought to be responsible for CJD is resistant to inactivation by boiling, 10% formoldehyde and ultraviolet or ionising radiation, but it can be inactivated by autoclaving at 134C for 18 minutes, or by immersion in 1 mol NaOH for one hour. The latter treatment has been incorporated into the manufacture of “Lyodura” since 1987.3 Since its introduction in 1969, over half a million packages of “Lyodura” have been used but only four cases of CJD in this group of patients have been reported to date: the risk of CJD related to “Lyodura” therefore seems low.

The implications arising from these cases are clear: autologous graft material should be used where possible. Appropriate standards should be applied in selection and preparation of donor material and physicians should be alert to this relationship in patients with a previous history of neurosurgery who develop a demyelinating illness.

H J WILLISON AN GALE JE MCLAUGHLIN
Departments of Neurology and Histopathology, Royal Prince Alfred Hospital, Sydney, NSW


2 Nisbet TJ, MacDonald I, Bishara SN. Creutzfeldt-Jacob disease in a second patient who received a cadaveric dura mater graft. JAMA 1989;291:1118.


5 Olson D. Creutzfeldt-Jacob disease associated with cadaveric dura. J Neurol Neurosurg Psychiatry 1987;47:149.

Matters arising

Ticlopidine, a new anti-thrombotic drug

In your editorial1 Charles Warlow answers the question: “Ticlopidine, a new anti-thrombotic drug: but is it better than aspirin for long term use?” The editorial gives a lot of important background, but, however, like to make several comments:

1) Professor Warlow says that there has been no large trial of aspirin alone in major ischaemic stroke. In one of the large secon-
dary prevention trials of ischaemic lesions of the nervous system, in the European Stroke Prevention Study 1 (ESPS 1), where the prevention was due to the association dipiyridamole-aspirin, the patients were included after major stroke (that is, a stroke with neurological symptoms lasting more than seven days). The results obtained can be an important improvement to the remarks made in the editorial.

2) In the ESPS 1, side effects were mainly due to the high dose of acetylsalicylic acid (900 mg per day), but toxic effects were almost non-existent. This is not the case with ticlopidine treatments.

In conclusion, we can say that secondary prevention of ischaemic lesion of the nervous system is possible thanks to anti-aggregating agents. Among the anti-aggregating agents, the association dipiyridamole and acetylsalicylic acid gives the ESPS 1 the best results. This association also works after major stroke and gives less side effects than ticlopidine.

LLOWenthal
Algemene Ziekenhuizen Middelheim, Lindendreef, 1, Antwerp, Belgium

Warlow replies:

I am relieved that Dr Lowenthal agrees with me that there were no large trials of aspirin alone in major ischaemic stroke and I certainly do not disagree with him that the European Stroke Prevention Study 1 (ESPS 1) trial recruited a large number of stroke patients. The ESPS I trial does not, of course, tell us anything about aspirin alone since it tested the combination of aspirin with dipiyridamole against placebo. So far, in the Antiparacetamol Trial, there is no indirect or direct evidence that this combination of drugs is more or less effective than aspirin alone.1 If Dr Lowenthal really believes that the combination of aspirin and dipiyridamole gives the best results then he should certainly prescribe it, whatever I or anyone else believe to be the correct interpretation of the data; it would be unethical not to do so. However, since he coordinates the ESPS II trial, I presume that he considers it ethical for other physicians to randomly allocate patients in that trial to placebo, aspirin alone and dipiyridamole alone as well as to the combination of aspirin and dipiyridamole.

I am not too sure what the difference is between “side effects” and “toxic effects” but I, like Dr Lowenthal, emphasised that the adverse effects of ticlopidine were considerably more common than those of aspirin.

Charles Warlow
Department of Neurosciences, Western General Hospital, Edinburgh, UK

1 The ESPS Group. The European Stroke Prevention Study (ESPS) principal end-points. Lancet 1987;i:1351-4.