indirect immunofluorescent test for Lyme disease (Institut Pasteur, Paris), Rose Bengal Plate test, immunoelectrophoresis 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]

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1 Tippet DS, Fishman PS, Panitch HS. Relapsing transverse myelitis (abstr). *Ann Neurol* 1988; 24:143.

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 Zealand[2] 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 cerebellar ectopia. 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 In August 1989, at the age of 30, he became increasingly withdrawn: he had difficulty recognising people, and his speech, comprehension and balance became disturbed.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, mute, increasingly ataxic, and developed frequent myoclonic jerks. The electroencephalogram evolved into a pattern of intermittent repetitive triangular wave complexes on a background of generalised irregular slow-frequency activity characteristic of CJD. He died in December 1989, four months after the onset of symptoms.

Histological examination of the brain 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 lyophylised 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% formaldehyde and ultraviolet or ionizing radiation, but it can be inactivated by autoclaving at 134C for 18 minutes, or by immersion in 1 molar NaOH for one hour. The latter treatment has been incorporated into the manufacture of "Lyodura" since 1987.[3,5] 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 dementing illness.

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1 Thadani V, Penar PL, Partington J, *et al.* Creutzfeldt-Jacob disease probably aquired from a cadaveric dura mater graft. *J Neurosurg* 1988;69:766-9.
2 Nisbet TJ, MacDonaldson I, Bishara SN. Creutzfeldt-Jacob disease in a second patient who received a cadaveric dura mater graft. *JAMA* 1989;261:1118.
3 Massulo C, Pocchiari M, Macchi G, Alema G, Piazza G, Panzera MA. Transmission of Creutzfeldt-Jacob disease by dural cadaveric graft. *J Neurosurg* 1989;71:954.
4 Harries-Jones R, Knight R, Will RG, Cousens S, Smith PG, Matthews WB. Creutzfeldt-Jacob disease in England and Wales, 1980-1984: a case control study of potential risk factors. *J Neurol Neurosurg Psychiatry* 1988; 51:1113-9.
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MATTERS ARISING

Ticlopidine, a new anti-thrombotic drug

In your editorial[1] 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 information. I would, 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 secondary 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 dipyridamole-aspirin, two thirds of the patients were included after major stroke (that is, a stroke with neurological symptoms lasting more than seven days). The results obtained can add some information to the remarks made in the editorial.

Seven hundred and thirty eight post-stroke patients were included in the placebo group and 764 in the group receiving the active drug or 75 mg dipyridamole and 330 mg acetylsalicylic acid three times daily. In the first group, there were 196 end-points (a new stroke or death) and in the active arm, there were only 138 end-points, a reduction of 29·6%, which is highly significant ($p < 0.001$).

2) In the ESPS 1, side effects were mainly due to the high dose of acetyl-salicylic acid (990 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 of dipyridamole and acetylsalicylic acid gives the ESPS 1 the best results. This association also works after major stroke and gives less side-effects than ticlopidine.

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1 Warlow C. Ticlopidine, a new anti-thrombotic drug: but is it better than aspirin for long-term use? (Editorial). *J Neurol Neurosurg Psychiatry* 1990;53:185–7.

Warlow replies:

I am relieved that Dr Lowenthal agrees with me that there have been no large trials of aspirin alone in major ischaemic stroke and I certainly do not disagree with him that the European Stroke Prevention Study I (ESPS I)[1] trial recruited a large number of major stroke patients. The ESPS I trial does not, of course, tell us anything about aspirin *alone* since it tested the combination of aspirin with dipyridamole against placebo. So far, in the Antiplatelet Trialists' Collaboration, there is no indirect or direct evidence that this combination of drugs is more or less effective than aspirin alone.[2] If Dr Lowenthal *really* believes that the combination of aspirin and dipyridamole 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 dipyridamole alone as well as to the combination of aspirin and dipyridamole.

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.

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1 The ESPS Group. The European Stroke Prevention Study (ESPS) principal endpoints. *Lancet* 1987;ii:1351–4.