Matters arising

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Creutzfeldt-Jacob like syndrome due to lithium toxicity

Sir: Recently in this Journal Smith and Kocen reported on EEG abnormalities in lithium neurotoxicity,¹ stating that periodic sharp waves have not been described in the EEG of patients with lithium intoxication. However, there exists literature since 1971 about this subject.^{2,3} Recently we described some patients.⁴

One of them was a 72 year old woman with lithium intoxication (serum lithium level 2.3 mmol/l). The EEG showed periodic sharp waves, triphasic waves and diffuse slowing. These EEG abnormalities decreased the weeks thereafter.

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Intracranial aneurysm and HLA-DR2

Sir: We read with interest the letter from Schievink *et al*¹ concerning HLA antigens and intracranial aneurysms. They commented on a study by Østergaard's group² which provided some evidence in support of a genetic predisposition to intracranial aneurysms, namely an increased incidence of HLA-DR2 amongst aneurysm patients.

Dr Schievink and his colleagues could not substantiate this hypothesis when they analysed the frequency distribution of HLA-DR2 in a retrospective study of 31 cases of death associated with subarachnoid haemorrhage (SAH) following rupture of intracranial aneurysms. Quite correctly, they emphasise the selective nature of both Østergaard's data and their own and they point to the need for larger studies of unselected patients to include those with ruptured and unruptured aneurysms.

We fear that there will inevitably be some selection despite implementation of the above suggestions. Referral to neurosurgical centres of patients after SAH will depend upon local policy but in general neurosurgeons will only be notified of the fittest patients. Furthermore, even patients with unruptured aneurysms will have been selected in that of necessity they will present with symptoms which justify the use of angiography needed to demonstrate their aneurysms.

In the light of the foregoing, the results of an investigation recently completed by us may be of interest. We conducted a pilot study concerning the possible implication of HLA antigens in the pathogenesis of non-haemorrhagic deterioration following aneurysmal SAH. The results of this study, full publication of which is in preparation, were recently announced in a preliminary communication.³

Forty patients (28 females, 12 males) of mean age 44 years (SD 13.8) who had sustained an aneurysmal SAH were followed to death or discharge. Tissue typing was performed using standard methods. The table compares the frequency of HLA-DR2 amongst controls, the total SAH study population and patients grouped according

Group	n	%HLA-DR2
Control	381	28.8
SAH group	38	28.9
ACoA	17	41.2
MCA	11	36.4

ACoA—anterior communicating artery aneurysm; MCA—middle cerebral artery aneurysm. The incidence of multiple aneurysms (20%) or aneurysms at other sites was too small for valid comparison.

to aneurysm site. Technical difficulties precluded typing for HLA-DR2 in two patients (one male and one female). No statistical significance could be observed between the several groups (chi square with Yates's correction).

On the basis of the above, we agree with Schievink *et al* that the overall frequency of HLA-DR2 does not differ significantly between control groups and the aneurysmal SAH population. However, the slightly higher incidence of HLA-DR2 in those patients with anterior communicating artery aneurysms suggests that a weak genetic predisposition for the development of this type of aneurysm may exist.

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An implant clamp for atlanto-axial fusion

Sir: Mills *et al*, in a letter to the Journal¹ describe an implant clamp for the surgical stabilisation of C1-C2 instability. The clamp is a unique device and obviously appears to render substantial stability to the spine. We, however, have several concerns regarding the utilisation of such a device. First, the Brooks and Gallie fusions, as mentioned by Mills *et al*, are widely accepted. They, in addition, have a low complication rate and an acceptable fusion rate. Furthermore, the sublaminar wires used with these fusions offer a minimal risk of spinal cord compression because of the small volume occupied by these wires in the capacious upper cervical spinal canal. On the other hand, the photographs accompanying the letter by Mills, *et al*, demonstrate a rather bulky device. The hooks of this device appear to be

significantly compromising the dorsal spinal canal at the C1 level.

If the clinical situation dictates a need for such a device for internal fixation, the Halifax interlaminar clamps have a proven safe and efficacious track record.² Cybulski *et al.*, have demonstrated their usefulness for C1–C2 instability. Furthermore, the Halifax clamps appear to cause less encroachment on the spinal canal (compare the lateral radiographs in Mills, *et al.*, and Cybulski, *et al.*).

Although the described device may have appropriate applications, we caution its widespread use.

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- The frequency, characteristics and prognosis of epileptic seizures at the onset of stroke**
- Sir: The occurrence of epileptic seizures prior to or at the onset of stroke has recently been reassessed in two reports by Shinton *et al.*^{1,2} Both investigations (which are based on the same group of patients) seem to support the case that cerebrovascular disease can be implicated not only in seizures occurring in the acute stage of the stroke but also prior to it. While the first point is well established, the problem of epilepsy preceding stroke deserves some further comments.
- Firstly, in both reports the diagnosis of ischaemic and haemorrhagic strokes was mainly based on a scoring system, CT find-
- ings being available only in a minority of cases. This could be relevant to the actual incidence of seizures prior to haemorrhagic stroke since, apart from case no 2 of Shinton *et al.*,² only three cases of heralding epilepsy related to a primary intracerebral haemorrhage (PIH) have so far been recorded.³
- Secondly, the existence of a “vascular precursor epilepsy”,³ as reported over the last decades,⁴ is not universally accepted,^{5,6} particularly when epilepsy and stroke are obviously unrelated (for instance case nos 4 and 7 of Shinton *et al.*).
- Thirdly, even a retrospective case-control investigation can be affected by several potential sources of bias, as pointed out by Starkey and Warlow.⁷
- In an unpublished series of 82 consecutive cases of PIH confirmed by CT, we have never found seizures preceding the stroke, while in 6.7% of patients with angiographically proved carotid occlusive disease, epileptic seizures were the presenting symptom.^{8,9}
- The pathophysiology of the rare (if any) epileptic seizures heralding PIH is hard to explain. On the contrary, an aetiological relationship between cerebral ischaemia and epilepsy could be accounted for by at least two pathophysiological mechanisms. In fact seizures may arise from small clinically silent infarctions,¹⁰ thus being not basically different from seizures occurring as a sequel of ischaemic stroke;⁴ or as a direct consequence of “low-grade” cerebral ischaemia, as suggested by some neurophysiological evidence.¹¹ The latter hypothesis has been challenged by Yanagihara *et al.*¹² who demonstrated that epileptic movements of extremities resulting from transient haemodynamic ischaemic episodes are associated with slow waves over the contralateral hemisphere, thus suggesting a release phenomenon of subcortical structures.¹³ Actually, transient cerebral ischaemia could be responsible either for release or epileptic phenomena, at least in principle.⁴
- The availability of high resolution neuroimaging techniques can provide guidelines for a more factual approach to the whole matter. A protocol for a prospective study should be worked out, to investigate patients who had their first epileptic seizure after the age of 40 yrs,¹⁰ with no detectable lesions at CT and MRI at the time, separately considering partial and generalised epilepsy. The risk factors for a cerebrovascular accident should be investigated as well, although their relevance to late onset epilepsy has recently been challenged (Neufeld *et al.*, Abstracts of 17th International Epilepsy Congress, 1987:85). If follow-up indicates that ischaemic strokes occur more frequently in either group than in a matched population, this could be regarded as proof that seizures may sometimes reveal an otherwise clinically silent cerebral ischaemic disease and therefore herald a major cerebrovascular event. By the same token, epileptic seizures could be included among the possible manifestations of TIAs, as already suggested.⁴

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