covering an area between 2.4 and 19 cm² were applied to the shaved chests of Parkinsonian monkeys. Locomotor activity was increased according to the skin surface area available for transdermal absorption, and was restored to the range observed in normal, untreated monkeys through a 24 h period using a surface area of 4.9–19 cm². Comparing the minimum dose of (+)-PHNO required for restoration of locomotor activity to normal levels by the subcutaneous and transdermal routes (2.5 μg/kg/h and 4.78 cm², respectively), we would estimate the systemic availability of (+)-PHNO using the transdermal patch to be <20% of the in vitro release rate. Analysis of plasma levels of (+)-PHNO in a single animal treated with transdermal patches covering an area of either 2.4 or 9.6 cm² indicated a lag period of approximately 12 h before stable plasma levels were attained; thereafter plasma concentrations of (+)-PHNO remained stable throughout the following 36 h period until the patches were removed at 48 h. Steady state plasma levels of (+)-PHNO were proportional to the surface area of skin exposed to the transdermal delivery system (approximately 100 pg/ml using a patch size of 2.4 cm², and 500–600 pg/ml for a total patch size of 9.6 cm²). Our findings indicate that plasma levels of (+)-PHNO within the therapeutic range may be achieved and sustained for at least 24 h using rate-controlled transdermal absorption, and suggest a novel sustained release delivery system for antiparkinsonian therapy.

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Matters arising

Herpes simplex type II encephalitis with complete Kluver-Bucy syndrome in a non-immunocompromised adult

Sir: In your issue of March 1988, Baker et al reported the unexpected finding of herpes virus type II (HSVII) as the causal agent of an encephalitis occurring in a young, non-immunocompromised adult. This diagnosis was supported with relevant serological investigations. The patient was treated with intravenous acycloguanosine and gradually recovered with no neurological sequelae except for a long-term memory deficit. Whereas HSVII is the most common cause of acute encephalitis in the neonate, the authors pointed out that in adults, acute necrotising encephalitis is usually due to herpes simplex type I (HSV). They stated that their report represented "a previously unrecognised entity due to HSVII in a non-immunocompromised adult."

This last point, however, should be corrected. To our knowledge, two similar cases had already been reported.23 We had the opportunity to observe one of these.4 A 42 year old, previously well man presented with a 3 day history of fever, diffuse myalgias and intense headache with vomiting. The day prior to admission he became confused and disoriented, and experienced auditory hallucinations. Soon after admission, he became comatose and required endotracheal intubation. Computed tomography showed large areas of low density involving both temporal lobes which showed contrast enhancement. A seroconversion for HSVII was demonstrated in blood and cerebrospinal fluid (CSF) with a rising of specific IgM titre. In blood, the HSVII IgM titre was 1:80 at day 8 of the illness, and 1:1024 at day 16. In CSF, the titre was 1:16 at day 8, and 1:250 at day 16. The patient was treated with intravenous acyclovir for 10 days. His condition slowly improved, allowing formal neuropsychological testing. The typical characteristics of a complete Kluver-Bucy syndrome were demonstrated. The neuropsychological data are published elsewhere.5 Unfortunately, 8 weeks after its onset, the encephalitis recurred, and, in spite of a second course of treatment with acyclovir, the patient was left in a demented state. Neither immunocompromise nor a co-existing potentially immunodepressive disorder was able to be demonstrated in our patient. Four years later, the patient is alive and he has been otherwise well.

When we published this case, we were only able to find six other well-documented examples of HSVII encephalitis in adults reported in the literature.3,23 Usually the patients were immunodepressed and had genital herpes; however, in one case,2 as in ours, no predisposing factors were found. Since then, in spite of the increasing number of immunocompromised patients with acquired immunodeficiency syndrome (AIDS), only very few cases of HSVII encephalitis or encephalomylitis, have been reported in those patients.4 The rarity of HSVII encephalitis in both healthy and immunocompromised patients remains to be explained.

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References

Intracranial aneurysm and HLA-DR2

Sir: We read with interest the letter from Schievink et al concerning HLA antigens and intracranial aneurysms. They commented on a study by Østergaard’s group 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.

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 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.

References


An implant clamp for atlanto-axial fusion

Sir: Mills et al., in a letter to the Journal 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