Matters arising

Histocompatibility antigens on astrocytoma cells

Sir: We have read with interest the article on histocompatibility antigens on astrocytoma cells by Hirschberg et al recently published in your journal. The authors state that dissociated cells from astrocytommas of various degrees of malignancy do not express HLA-D/DR determinants. We recently demonstrated that monoclonal anti-HLA-DR antibodies react with glioma cells from several established lines, as shown in an antibody-binding radioimmunoassay. Monoclonal anti-HLA-DR antibodies were shown to lyse specifically 51 Cr-labelled glioma cells in the presence of complement. Absorption of anti-HLA-DR antibodies by glioma cells abolished their cytotoxicity against blasts isolated from a common acute lymphoblastic leukemia (c-ALL) line. Immuno-precipitation of solubilised 125 I-labelled membrane proteins from glioma cells by monoclonal anti-HLA-DR antibodies revealed two polypeptide chains of 28 and 33 kilodaltons characteristic of HLA-DR antigens. It must be stressed, however, that not all glioma cell lines tested expressed HLA-DR antigens (three of eight tested). Hirschberg et al point out that cell lines derived from solid tumours are probably not as suitable as primary tumour cell cultures in the study of representative antigenic determinants on the cell surface. This is true, but primary cultures are already a selection of the original cells. We have stained frozen glioma tissue with anti- HLA-DR monoclonal antibodies in an indirect immunoperoxidase assay and found that neoplastic cells were heavily stained, thus demonstrating that the antigen is also present on the tumour cells in vivo.

It may be noteworthy that Hirschberg et al have published the same results, with the same figures, same tables and identical summary in Tissue Antigens, at the same time as in the Journal of Neurology, Neurosurgery and Psychiatry.

References


Training for clinical practice

Sir: The editorial commentaries by Dr Hopkins and Professor Marsden (December, 1981) raise issues of relevance to clinical neurosciences education. Dr Hopkins records that established clinical training is founded on specific nosological entities, which his target show to be uncommon in practice. Moreover, as he and Dr Fitzpatrick report in their accompanying article, patients present to neurologists with complaints of disorders form and function. Professor Marsden concludes from Dr Hopkins' figures that the majority of common neurological problems in the United Kingdom will be managed by primary care physicians; it is important to know, therefore, whether current training equips practitioners with the requisite proficiencies to execute these responsibilities.

As part of a study to define educational objectives in undergraduate neurosciences and to establish competencies in clinical neurology relevant to future activities...
of the graduating student, a questionnaire was designed to analyse the neurological disorders seen in general practice and the difficulties experienced in their management. Replies were received from 47 practitioners. Of the 710 consultations for neurological problems, 70% comprised headaches and facial pain (35%), vertigo and dizziness (16-5%), seizures (8%) and neuropsychiatric (7%) and cerebrovascular disorders (3-5%). Of all difficulties experienced by practitioners, 20% involved undertaking the neurological examination and interpreting physical signs and 57-5% the evaluation and treatment of headache and facial pain (20-5%), vertigo and dizziness (20-5%), seizures (5-5%) and neuropsychiatric (7%) and cerebrovascular disorders (4%). These results are in accord with Murray's findings and support his conclusion that teaching programmes are failing to provide the knowledge and teach the basic skills for practitioners to evaluate and manage effectively patients with common neurological problems.

How can process and outcome be more appropriately and efficaciously matched? The design of undergraduate and postgraduate programmes must be based on defined educational objectives that reflect practical experiences and societal needs, with relevant teaching strategies directed to the acquisition of problem solving skills through education in pathophysiological processes, rather than emphasising the pattern recognition conveyed by instruction. The preparation of students for practice as primary care physicians will also necessitate structuring undergraduate training to take greater account of the need for attaining competence in the diagnostic process. This additional emphasis could be accommodated through more rigorous selection of items of knowledge the student should know. Notable in this respect is the opinion that most basic and clinical undergraduate neurology could be covered through discussion of problems presented by patients with 13 selected disorders. Such adjustments would also contribute towards rationalising the undergraduate curriculum, now critically overloaded with information to the point of manifestly declining standards of patient management.

The degree of success of programmes depends to a large extent on the calibre of the teachers. Contemporary career prospects in academic medicine are highly geared to research achievement which, as a result, dominates higher training leading to graduates manifesting a significant short-fall in competencies deemed necessary for a credible educator. As a consequence, the effectiveness of any innovations is likely to remain problematic until such time as expertise in educational methods and teaching skills receives formal recognition and comparable status in institutional terms.

References
5. Education Committee Sub-Committee on Objectives in Relation to Basic Medical Education. London: General Medical Council, 1975.

Methylprednisolone therapy in multiple sclerosis

SIR: It is evident that there is some interest in neurological circles regarding the place of intravenous therapy with methylprednisolone in multiple sclerosis patients who are in acute relapse. A recent letter in this Journal from the London Hospital (1982;45:179-80) was enthusiastic about the response in six cases, and this form of treatment was the subject of some discussion at the April meeting of the Association of British Neurologists. In 1976, one of us (MS) began to use intravenous methylprednisolone in selected multiple sclerosis cases, and since that time this Department has acquired considerable experience with this therapy. We would like to record our earlier findings which have been gathered by a retrospective analysis of our case notes.

Data were available on 61 patients who had received a total of 98 courses of treatment. The response was judged to be good in 32, fair in 47 and absent in 19. Classification of response into these three categories was by clinical observation at the end of the course of treatment or at early follow-up, coupled with the subjective views of the patient. All patients had definite multiple sclerosis according to the McAlpine criteria, and all had suffered a recent deterioration in their symptoms. In most cases, methylprednisolone was given as a slow intravenous injection of one gram, and courses of treatment were for five or seven days, tailing off with a further week of oral prednisolone.

It would be naive to over emphasise the benefits of steroids in multiple sclerosis, but accepting the limited expectations of treatment, we would like to make the following points. The natural history of relapse in multiple sclerosis does tend towards resolution and this is particularly so in patients admitted to hospital where they have rest and skilled physiotherapy. Nevertheless, we have been greatly impressed by the rapidity and extent of improvement that we have observed in our methylprednisolone treated patients, a significant number having responded dramatically within twenty-four hours of the first injection. Adverse effects have been minimal, a transient metallic taste follows most injections, a reversible facial reddening is frequently seen and mild ankle oedema has occasionally been noticeable. These reactions are much less evident than in conventionally steroid treated patients and we have not had any serious complications. The fact that several patients have had multiple courses of intravenous methylprednisolone, as many as five in three cases, testifies to the fact that such treatment appears safe, but also suggests that this therapy of acute relapse does not influence the next relapse or the continuing progression of the disease.

In addition to a study comparing this form of treatment with standard ACTH therapy, we are also exploring the use of shorter and smaller intravenous courses of treatment leading to better control of acute relapse.