

the multiple sclerosis lesion increased only by a factor of 4 from normal. This contrasts with our MR findings using Gd-DTPA, in which signal enhancement is high (approximately 100%) in enhancing lesions, and negligible (<3%) in normal white matter.³ These MR findings suggest that the BBB permeability is enhanced by at least a factor of 30 in active multiple sclerosis. At 45 minutes after contrast injection MRI shows uniform enhancement, like HVD-CT.⁴ However, at shorter times (5–10 minutes) ring enhancement is usually seen in lesions >5 mm in diameter,⁴ which is consistent with pathological descriptions of active inflammation and demyelination at the perimeter of multiple sclerosis plaques.⁵ Later enhancement in the older, inner core of the lesion is probably caused by diffusion inwards from the ring enhancing edge. Using the CT scan to delineate the region of interest on the PET scan will produce a mean K_1 over the whole lesion, thus significantly underestimating the K_1 of the active ring-like part with defective BBB. The true K_1 will be greater by approximately the ratio of total lesion area to ring area, that is, as much as twenty times higher. Even if the correct region of interest was used, PET is intrinsically incapable of resolving the ring enhancement in multiple sclerosis because its spatial resolution is too poor (9 mm in the plane of a 16 mm thick slice). Our preliminary measurements of K_1 in the active part of the lesion using dynamic MRI scanning suggest values of K_1 in the range 0.012–0.06 ml g⁻¹min⁻¹ (3 lesions) that is 10–50 times higher than in the authors' table 3.

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Pozzilli *et al* reply:

We are grateful to Drs Tofts and Kermode for giving us the opportunity to rectify a typographical omission in our article. In tables 2 and 3 the V_p should have been multiplied by 10⁻², as correctly shown in our previous paper,¹ and in the summary the values of K_1 are $\times 10^4$. Clearly this omission solves a contradiction which is only too apparent. The values of V_p in the range of 3.3–4.5 $\times 10^{-2}$ ml g⁻¹ are in agreement with the values of CBV reported in the literature.^{2,3}

Drs Tofts and Kermode, on the basis of signal enhancement, reach the conclusion that BBB permeability should be increased by a factor of 30 in active multiple sclerosis. This, according to them is in contrast with the increase by a factor of four reported by us. We frankly have some difficulty in comparing the two sets of data since one originates from a signal enhancement ratio and the other from a numerical value of K_1 calculated on the basis of a kinetic model for the passage of substances across the BBB.¹

Unfortunately we are unable to comment on the value of K_1 measured with MRI since the underlying assumptions and the mathematical formulation of the method are neither reported in the letter, nor in the quoted reference. It should be pointed out, however, that K_1 approaches in magnitude the permeability-surface area product (PS) only when $PS \ll F$ (where F = blood flow).⁴ Values of K_1 as high as 0.06 ml g⁻¹min⁻¹ would suggest that PS approaches F in magnitude. In these circumstances K_1 is not only expression of PS, but would also depend upon blood flow. Thus for a correct evaluation of PS a measurement of local blood flow would be required.

Finally, our recent experience on Gd-DTPA suggest that ring enhancement in patients with multiple sclerosis is an uncommon finding. Moreover, none of the patients reported in our study showed a ring en-

hancement in the high volume delayed (HVD) CT scan.

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Encephalopathy, deafness and blindness in young women: a distinct retinocochleocerebellar arteriopathy?

Sir: The recent paper by Bogousslavsky *et al*¹ documenting three patients with developed progressive neuropsychiatric and neurological disturbances with hearing and multifocal retinal artery branch occlusions, requires some comment.

Their first patient demonstrated an abnormality of the T-helper/suppressor cells in blood suggesting an immunological disturbance. This patient also showed elevations of the CSF protein and erythrocyte sedimentation rate. Their third patient, in addition to an elevated ESR of 27 mm/hour, also demonstrated positive antinuclear antibodies (1:320) as well as positive rheumatoid factor (1:160), and low complement levels were later also discovered.

We would draw attention to the recently defined "primary" antiphospholipid syndrome.² These patients may develop multiple infarct dementia,³ and vascular occlusion occur, involving both venous and arterial circulations. Indeed there appears to be a strong association between the retinal vasculopathy described and the presence of CNS disease.^{4,5} As many as 40% of these patients may be ANA negative, and there is only a 60%–70% concordance between "lupus anticoagulant" activity and the presence of anticardiolipin antibodies (aCL). The VDRL may only be positive in 20%–30% of patients. Other immunological dis-

Matters arising

turbances, such as positive tests for rheumatoid factor, a very non-specific B-cell reaction, may also be found. However, antibodies to double stranded deoxyribonucleic acid (DNA) and extractable nuclear antigens (ENAs) are persistently negative. Histology of vessels reveals a complete absence of vasculitis with intimal thickening predominating.

Although a "sero-negative" group of patients with similar manifestations undoubtedly exists, we consider it mandatory that aCl antibody estimations be undertaken in all patients with obscure cerebral disease, perhaps accompanied by vascular occlusions, such as the authors describe in their patients. Therapy with anticoagulation and/or aspirin and other antiplatelet drugs is more beneficial than steroids or immunosuppression in these patients and may well prevent further deterioration.

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occlusive ocular vascular disease in systemic lupus erythematosus and the "primary" Antiphospholipid Syndrome. *Ann Rheum Dis* 1989;48:358-61.

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Dr Bogouslavsky replies:

I agree with Dr Asherson that newly developed tests should be performed in patients with obscure cerebrovascular disease. But before attributing an aetiological value to abnormal results of these tests, their significance should have been screened in well-controlled studies of unselected patients with stroke, which is not yet the case for anticardiolipin antibodies. The same remark applies to therapy, as no controlled study of anti-agregants, anticoagulants, steroids or other immunosuppressive agents has been reported.

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Book reviews

Basic Neurochemistry: Molecular, Cellular, and Medical Aspects. Edited by George J Siegel, Bernard W Agranoff, R Wayne Albers, Perry B Molinoff. (Pp 1000; \$65.00.) New York: Raven Press, 1988.

This fourth edition of an already successful publication can justifiably be regarded as a new book. More than half the chapters appear for the first time and all other contributions have been written and updated. Authors have written succinctly with only key (mainly American) references and the format has been greatly improved. Each chapter has a list of contents with italicised sentences summarising an area of text and headings which, with an index of 50 pages, facilitates information retrieval.

Basic Neurochemistry has a subtitle *Molecular, Cellular and Medical Aspects* and this gives a realistic indication of the scope of this substantial treatise. Contemporary neurochemistry is no longer restricted to descriptive biochemistry of the nervous system and indeed this aspect of the subject is not emphasised. The book is divided into six parts, the first of which is on neural membranes. This includes an introduction to cellular neuroanatomy, properties of membranes, myelin and a brief review of the molecular biology of vision and phototransduction mechanisms. The next and major topic is synaptic function and related neuropharmacology. Chapter 9 is particularly useful as there is a clear explanation of

quantitative aspects of drug-receptor interactions. A typical chapter of 28 pages is on acetylcholine with clear text and diagrams (for example the molecular species of cholinesterase, the active site, the transmembrane domain structure of the muscarinic receptor). An important concept discussed by various contributors is that of the second messenger systems (G-proteins, phosphoinositides, cyclic AMP), their regulation and neuronal function mediated through protein phosphorylation. Molecular neurobiology is dealt with in Part 3: gene expression, molecular probes and molecular genetics of inherited neurological degenerative disorders. The individual chapters in this part are short but provide an understandable basis for a difficult yet essential new area of progress. In the section on cellular neurochemistry there are authoritative reviews on metabolism and neurobiology (axonal transport, plasticity and regeneration). There are much improved chapters on development and ageing of the nervous system.

In Part 5 (biochemical aspects of neurological diseases) some chapters are descriptive (such as muscle biochemistry or diseases of oxidative metabolism) but others are more concerned with pathogenic mechanisms. Examples of the latter are an interesting general chapter on the biochemistry of neuropathy, one on ischaemia and hypoxia and another on epileptic seizures. There is a new account of positron emission tomography which interrelates with chapter 29 on circulation and energy metabolism of the brain. A chapter on clinical chemistry

could have been profitably included in this section. The final chapters are on behavioural neurochemistry and this includes schizophrenia, affective disorders and anxiety. The effects of endocrines on behaviour and a thoughtful chapter on mechanisms of learning and memory conclude this part.

The editors and the contributors are to be congratulated for producing such a splendid book although owing to its size (700g) it is likely to be primarily used for reference purposes. By present day standards it is reasonably priced and I can recommend it to both clinical and basic scientists as an essential and very readable textbook.

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Epilepsy and the Reticular Formation: The Role of the Reticular Core in Convulsive Seizures. (*Neurology and Neurobiology Vol 2.*) Edited by GH Fromm, CL Faingold, RA Browning, WM Burnham. (Pp 232; \$49.50.) New York: Alan R Liss, 1987.

The mechanism and site of seizure initiation in primary generalised epilepsies remains conjectural. Penfield and Jasper in their classic volume *Epilepsy and the Functional Anatomy of the Human Brain* (1954) proposed a centrencephalic theory that attributed synchronous cortical discharges to activity originating in the reticular core of the brain stem and midbrain. More recently