Increased Beta₂-microglobulin in CSF of multiple sclerosis

Sir: Increased cerebrospinal fluid (CSF) levels of beta₂-microglobulin (B₂m) have been found in a number of primary central nervous system (CNS) diseases¹ as well as in neurological complications of systemic malignancies,^{2,3} cerebrovascular lesions⁴ and CNS infection.⁵ However, there are discrepancies in the values obtained by several authors for B₂m in CSF of multiple sclerosis patients.^{1,2,5} This may be due to the fact that these studies were performed in small series of patients without taking into account whether they were in relapse or not. We felt, therefore, that the study of CSF B₂m in relation to clinical activity in multiple sclerosis would be of interest.

We studied 30 patients with clinically definite multiple sclerosis.⁶ They were divided into two groups: Group A comprised 14 patients in a stable phase of the disease. Group B included 16 patients who were studied during an acute exacerbation of multiple sclerosis, their sera and CSF having been withdrawn within 3 weeks from the onset of the attack. Control CSF and serum data were obtained from 16 age-matched patients who did not show signs of organic neurological disease and their CSF study was unremarkable. Serum and CSF B₂m was measured by means of an ELISA developed in our laboratory.⁷ No significant difference in serum B₂m was found between the two multiple sclerosis groups and controls, being 1.77 ± 0.19 mg/l for group A, 1.86 ± 0.18 mg/l for group B and 1.80 ± 0.12 mg/l for controls (mean $\pm$ standard error of the mean).

CSF biochemical parameters studied are shown in the table. CSF IgG, IgG index,⁸ daily IgG synthesis⁹ and B₂m were found to be significantly higher in multiple sclerosis patients in relapse. The ratio CSF/serum

albumin was, however, within normal limits,⁸ thus showing a normal blood-brain barrier function.

The origin of increased CSF B₂m in multiple sclerosis patients remains unclear. Higher B₂m values in CSF compared with serum would indicate an intrathecal production and was found in every patient of group B. Whether B₂m comes from tissue destruction or from T-cell activation¹⁰ is at present unknown. Nevertheless, it seems likely that CSF B₂m may be an index of multiple sclerosis activity.

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Accepted 7 March 1987

Late onset adrenomyeloneuropathy

Sir: Adrenomyeloneuropathy is a disorder of lipid metabolism which results in accumulation of long chain fatty acids. The accumulation and associated dysfunction is most marked in those cells which depend highly on lipid metabolism: adrenal cortex, gonads, cerebral cortex and myelin sheaths of peripheral nerves. The condition is thus characterised by the association of Addison's disease and hypogonadism, with progressive peripheral and central neurological disease, and is usually familial. Inheritance is X-linked, and expression is usually confined to males, but several variants have been described.³ The best recognised form of this condition is that which occurs in children (adrenoleukodystrophy, Addison-Schilder's disease),⁴ with rapidly progressive neurological damage resulting in death within the first 15 years of life. However, a family history is not invariable, and the condition may present later.¹ In their review of 303 cases, Moser *et al*⁵ described only five patients who first developed neurological symptoms after age 21 years, and none with both Addison's disease and neurological signs who presented after 37 years of age.

In 1975 a 53 year old milkman was admitted to hospital with clinical and biochemical

Table CSF findings in multiple sclerosis patients and controls*

	Controls (n = 16)	Group A (n = 14)	Group B (n = 16)
CSF albumin (mg/dl)	19.93 $\pm$ 1.29	18.92 $\pm$ 2.19	23.18 $\pm$ 1.96
CSF/S albumin ratio	4.42 $\pm$ 0.26	4.38 $\pm$ 0.43	4.68 $\pm$ 0.55
CSF IgG (mg/dl)	2.72 $\pm$ 0.40	4.00 $\pm$ 0.57†	5.50 $\pm$ 0.62‡§
IgG index	0.45 $\pm$ 0.04	0.90 $\pm$ 0.11‡	1.15 $\pm$ 0.10‡
Daily IgG synthesis (mg/day)	3.05 $\pm$ 2.5	5.4 $\pm$ 2.15†	15.46 $\pm$ 3.38‡§
B ₂ m (mg/l)	1.49 $\pm$ 0.19	1.51 $\pm$ 0.22	3.21 $\pm$ 0.30‡

A: patients in a stable phase. B: patients in relapse.

*Values reported as mean $\pm$ SEM.

†Significantly different from control p < 0.05 (Student t-test).

‡Significantly different from control p < 0.01.

§Significantly different from Group A of patients p < 0.05.

||Significantly different from Group A of patients p < 0.01.