Certainly, none of my patients with migraine had any clinical similarity with such a patient. I hope that Wilder-Smith is not suggesting that these patients with migraine should have transcranial Doppler sonography to verify the diagnosis.

Further experience and more confidence in clinical diagnosis, obtained through meticulous evaluation of symptoms in classic migraine and occipital lobe epilepsy, may be needed. This is the main message of my report.

C P PANAYIOTOPOULOS
Department of Clinical Neurophysiology and Epilepsy, St Thomas' Hospital, London SE1 7EH, UK

1 Panayiotopoulos CP. Difficulties in differentiating migraine and epilepsy based on clinical and EEG findings. In: Andermann F, Lugaresi E, eds. *Migraine and epilepsy*. London: Butterworth Publishers Inc, 1987: 31–46.
2 Panayiotopoulos CP. Basilar migraine? Seizures, and severe EEG abnormalities. *Neurology* 1980;**30**:1122–5.

Antiganglioside antibodies in the CSF of patients with motor neuron diseases and Guillain-Barré syndrome

In a recent report in this *Journal* Stevens *et al* described increased titres of antiganglioside antibodies (AGAs) in the CSF of patients with amyotrophic lateral sclerosis.[1] They concluded that patients with amyotrophic lateral sclerosis have raised CSF IgM antibodies to all gangliosides except asialo-GM1 (A-GM1), due to a chronic intrathecal immune response. The authors did not, however, evaluate other motor neuron disorders related to amyotrophic lateral sclerosis and with sometimes borderline diagnosis.[2] We have studied AGA reactivity in the CSF of 23 patients whose diagnosis included (*a*) four strictly defined patients with amyotrophic lateral sclerosis; (*b*) 13 patients with lower motor neuron signs, from which six had a syndrome of multifocal motor neuropathy with conduction block and two had overactive tendon reflexes in limbs, with weak, wasted, twitching muscles, but no Babinski sign or ankle clonus; and (*c*) three patients with Guillain-Barré syndrome and three patients with chronic inflammatory demyelinating neuropathy. Thirty three subjects were tested as controls, including 28 patients with other neurological disease and 10 people whose CSF was normal and in whom irrelevant diseases, such as migraine or tensional headache, were found after later studies (normal controls).

Serum and CSF were assayed for antibodies to gangliosides GM1, GD1b, GD1a, and A-GM1 by enzyme linked immunosorbent assay (ELISA) according to the method described by Nobile-Oracio *et al*.[3] Results were expressed as the mean absorbance obtained from the well coated with ganglioside minus the absorbance obtained from a bovine serum albumin coated well. Results were considered positive when this difference exceeded 0·1. Concentrations of AGA were considered to be increased if this titre was higher than 3 SD from the mean of the results obtained in the 10 normal controls. In patients with high antibody titres by ELISA, reactivity to gangliosides was confirmed by high performance thin layer chromatography according to the method described by Ilyas *et al*.[4] Total CSF IgM concentration was measured by ELISA.[5] Intrathecal production of IgM AGAs was determined by measuring the optical density values per unit weight of IgM in serum and CSF, and expressing results as the ratio CSF values:serum values.[5]

Mean (SD) blood and CSF variables measured in patients and control groups

	Normal control group	*Other neurological diseases group*	*Patient group*	*P value**
Albumin index	1·80 (0·50)	2·40 (3·40)	1·50 (0·90)	NS
IgG index	0·35 (0·18)	0·34 (0·18)	0·68 (0·65)	NS
IgM index	0·05 (0·02)	0·05 (0·021)	0·33 (0·61)	NS
CSF: serum ratio (GM1)	0·49 (0·08)	0·44 (0·26)	5·40 (13·03)	0·0005
CSF: serum ratio (GD1b)	0·58 (0·33)	0·36 (0·19)	1·80 (3·20)	0·05
CSF: serum ratio (A-GM1)	0·58 (0·33)	0·46 (0·28)	3·60 (7·20)	0·004

*Analysis of variance.

Increased CSF anti-GM1 IgM antibody concentrations, with intrathecal synthesis, were found in six of the 23 patients (two patients with amyotrophic lateral sclerosis, two patients with lower motor neuron signs and hyperreflexia and two patients with Guillain-Barré syndrome), and in one of 28 patients of the group of patients with other neurological diseases (Fisher's test; P = 0·037). Intrathecal synthesis of anti-A-GM1 and anti-GD1b IgM antibodies was also detected in four of these six cases. Two of these patients, one with amyotrophic lateral sclerosis and one with Guillain-Barré syndrome, also had low positive titres of anti-GM1 IgM antibodies in serum. The ratio of CSF values:serum values for the AGAs was significantly higher in the patient group than in the group with other neurological diseases and the control group (table). No intrathecal synthesis of anti-GM1 IgM antibodies was found in CSF of the patients with other neurological diseases and normal controls, even in the cases when such antibodies were present in serum. In patients with Guillain-Barré syndrome there was no correlation between CSF anti-GM1 antibody titres and the degree of blood-brain barrier disruption expressed as the CSF:serum albumin ratio. In the patients with intrathecal synthesis of anti-GM1 antibodies, no abnormalities in cell count, albumin, IgG, IgM, albumin index, IgG index, or IgM index were detected. Intrathecal synthesis of AGA was not associated with a lower functional status or clinical evolution.

According to these results CSF antiganglioside reactivity is present in some patients with specific motor neuron disorders—namely, amyotrophic lateral sclerosis and lower motor neuron signs with hyperreflexia—but not in other forms of lower motor neuron signs. It seems highly specific for these neurological disorders, excluding the acute demyelinating inflammatory polyneuropathies, the clinical pattern of which is easy to differentiate from motor neuron disorders. The reactivity against GM1, GD1b, and A-GM1 suggest that Galβ(1,3)NAcGal is the common reactive epitope. It is still necessary to clarify if cases of amyotrophic lateral sclerosis and other motor neuron disorders where CSF antiganglioside reactivity is negative, represent a different pathogenetic mechanism, a failure of detection of intrathecal AGA reactivity due to a change in antibody profile during the evolution of the disease, or an imprecise detection method.

C IÑIGUEZ
A JIMÉNEZ-ESCRIG
J M GOBERNADO
Department of Neurology, Hospital "Ramon y Cajal", University of Alcala, Madrid, Spain
M NOCITO
P GONZALEZ-PORQUE
Department of Immunology

Correspondence to: Dr A Jiménez-Escrig, Servicio de Neurologia, Hospital Ramn y Cajal, Carret de Colmenar Km 9, 28034 Madrid, Spain.

1 Stevens A, Weller M, Wiethölter H. A characteristic ganglioside antibody pattern in the CSF of patients with amyotrophic lateral sclerosis. *J Neurol Neurosurg Psychiatry* 1993; **56**:361–4.
2 Pestronk A, Adams RN, Clawson L, *et al*. Serum antibodies to GM1 ganglioside in amyotrophic lateral sclerosis. *Neurology* 1988;**38**:1457–61.
3 Nobile-Oracio E, Carpo M, Legname G, Meucci N, Sonnino S, Scarlato G. Anti-GM1 IgM antibodies in motor neuron disease and neuropathy. *Neurology* 1990;**40**: 1747–50.
4 Ilyas AA, Quarles RH, Dalakas MC, Fishman PH, Brady RO. Monoclonal IgM in a patient with paraproteinemic polyneuropathy binds to gangliosides containing disialosyl groups. *Ann Neurol* 1985;**18**: 655–9.
5 Sharief M, Phil M, Hentges R, Ciardi M. Intrathecal immune response in patients with the post-polio syndrome. *N Engl J Med* 1991;**325**:749–55.

Stevens *et al* reply:

The authors report significantly increased antibody titres and evidence of intrathecal synthesis of antibodies to asialo-GM1 (AGM1), GD1b, and GM1 in the CSF of patients with amyotrophic lateral sclerosis and lower motor neuron disease, as well as from Guillain-Barré syndrome. They conclude that CSF immunoreactivity to AGM1, GD1b, and GM1 is specific for these disorders. Although they interpret their data as affirmative for an intrathecal immunological process in motor neuron disease,[1] they report antibody spectra differing from those in our sample of patients with amyotrophic lateral sclerosis. On closer scrutiny, this seems not to be the case, as anti-AGM1 IgM antibodies do appear in CSF of nine of 35 patients of our previously reported sample. Anti-AGM1 antibodies are not, however, part of the panel of antibodies that are typically raised in this disease.

Although the comparative approach of Iniguez *et al* is up to date, due to the small sample size the results are difficult to interpret in terms of specificity and sensitivity—for example, the CSF-IGM and the IGG index of their patients are raised (which was not the case in our study) but are not reported as significant due to large within-group variation. The results within the three