Journal of Neurology, Neurosurgery, and Psychiatry 1995;59:482–486

Electrodiagnostic criteria for polyneuropathy and demyelination: application in 135 patients with Guillain-Barré syndrome

J Meulstee, F G A van der Meché, and the Dutch Guillain-Barré Study Group

Abstract

Since the development of effective but expensive therapeutic strategies for the treatment of Guillain-Barré syndrome, early confirmation of the diagnosis has become very important. Electrodiagnostic criteria were developed for the discrimination of polyneuropathy and in particular for demyelination. The sensitivity and specificity of these criteria were determined in 135 patients with Guillain-Barré syndrome in an early stage of the disease, along with 45 healthy volunteers.

The algorithms used to develop our criteria consisted of sets of selected electrodiagnostic variables, each of them relevant to the detection of polyneuropathy. Each set was applied on all of three consecutive electrodiagnostic examinations within one month of disease onset. Application of the best set resulted in 85% of patients with Guillain-Barré syndrome fulfilling the criteria for polyneuropathy at the first examination (mean time interval six days of disease onset), whereas none of the healthy volunteers fulfilled the criteria (sensitivity 85%, specificity 100%).

The set of criteria for the detection of demyelination was fulfilled by 60% during the first examination (by 66% and 72% during the second and third examination). Application of criteria for demyelinating polyneuropathy as defined by others resulted in substantially lowered incidence (3%–46%).

It is concluded that these criteria for the electrodiagnostic delineation of polyneuropathy are the most sensitive to date, with respect to the early confirmation of the diagnosis of Guillain-Barré syndrome.

(*J Neurol Neurosurg Psychiatry* 1995;59:482–486)

Keywords: Guillain-Barré syndrome; demyelinating polyneuropathy; electrodiagnostic criteria

Department of Neurology, University Hospital Dijkzigt and Erasmus University Rotterdam, The Netherlands
J Meulstee
F G A van der Meché

Correspondence to:
Dr J Meulstee, Department of Neurology, University Hospital Dijkzigt and Erasmus University Rotterdam.
Dr Molewaterplein 40.
Room BA-402. NL 3015 GD The Netherlands.

Received 24 February 1995 and in revised form 4 July 1995
Accepted 11 July 1995

The Guillain-Barré syndrome is an acute polyradiculoneuropathy which may lead to severe tetraparesis. The precise aetiology is unknown but immune mechanisms are involved. In the recent past several therapeutic regimes have emerged, all of which help to reduce the duration and severity of the disease as well as the incidence and duration of respiratory dependency.[1 3] Therefore, it is of major importance to have a firm diagnosis as early as possible. Clinical diagnostic criteria have in general been shown to be reliable in recently conducted clinical trials.[4 5] Electrodiagnostic tests may, however, in some cases be necessary in the differential diagnosis of Guillain-Barré syndrome. Moreover, in cases of clinically defined Guillain-Barré syndrome, electrodiagnostic studies and, more specifically, nerve conduction studies may show signs of demyelination, and thus further characterise clinically defined Guillain-Barré syndrome as demyelinating Guillain-Barré syndrome. This may, in the future, prove to be of help in the selection of specific treatments. In the present study we constructed two sets of electrodiagnostic criteria, based on the findings in patients included in the Dutch Guillain-Barré study.[3] The first set can be used to prove the existence of a polyneuropathy. The second set was designed to test the presence of electrodiagnostic signs of demyelination. In addition, we tested several, previously published sets of electrodiagnostic criteria constructed for demyelinating polyneuropathies.[4 6 8]

Patients and methods

Patients tested in this study were all included in the Dutch Guillain-Barré trial which tested the efficacy of intravenous immunoglobulin *v* plasma exchange in 147 patients.[3] Patients (mean age 47·5 (SD 19·2)) entered the study if they fulfilled the criteria for acute Guillain-Barré syndrome,[4] were not able to walk 10 metres independently, and could enter the study within two weeks of onset of the polyneuropathy. The predefined outcome measure was improvement at four weeks by at least one grade on a seven point scale of motor function. Patients were followed up for six months. The main conclusion was that immunoglobulin treatment was at least as effective as plasma exchange and that immunoglobulin is a practical, safe, and effective treatment for Guillain-Barré syndrome. The results of electrodiagnostic tests were not part of the inclusion criteria. Electrodiagnostic tests were scheduled within two days of entry, one week later, and one month later.

The methods of electrodiagnostic testing have been discussed in detail elsewhere.[9] In short: motor nerve conduction studies were performed on ulnar and median nerves in the forearm. Shortest F response latencies were measured after 20 stimuli. Sensory nerve

conduction velocities of ulnar and median nerves were measured antidromically. Amplitudes and duration of the evoked motor and sensory responses were measured with surface electrodes. The peroneal and sural nerves were tested when relevant. With concentric needle electrodes, small hand muscles and anterior tibial muscles were tested for the presence of denervation potentials and the recruitment pattern on maximal voluntary effort. All tests were performed unilaterally.

Electrodiagnostic variables used for the development of criteria were: distal motor latency (DML), motor nerve conduction velocity (m-NCV), F response latency, compound muscle action potential amplitude (CMAP amplitude), and duration after distal stimulation, ratio of distal *v* proximal CMAP amplitude, ratio of distal *v* proximal CMAP duration, compound sensory nerve action potential amplitude (CSNAP amplitude), sensory nerve conduction velocity (s-NCV), recruitment pattern, and presence of denervation potentials. Some values were not scored in individual patients; however their clinical characteristics were not different. In 135 patients at least one complete electrodiagnostic examination (EMG) was performed (table 1). An electrodiagnostic variable was defined as abnormal if it fell outside our laboratory's limits of normal (outside 95th percentile). These limits of normal were obtained in 45 healthy volunteers (range of ages 37·7 (SD 11·6)) (table 2). We defined abnormal CMAP amplitude reduction as present if the observed decrease in CMAP amplitude exceeded the upper limit of normal; in cases where the CMAP amplitude after distal stimulation was < 5 mV, we defined CMAP amplitude reduction as abnormal if the difference between distal and proximal stimulation was at least 1 mV. Recruitment pattern was defined as abnormal if no pattern or a single pattern was obtained on maximal voluntary effort.

Electrodiagnostically a nerve can be defined as abnormal if a minimal number of variables exceed the normal limits; however, no consensus exists on the number of required abnormal variables per nerve and the required number of abnormal nerves with regard to the electrodiagnostic definition of polyneuropathy. Due to the nature of polyneuropathy a minimal number of two abnormal nerves would seem to be required. By varying the number of abnormal variables per nerve, and the number of required abnormal nerves, we designed different sets. An optimal set would result in a high sensitivity and specificity, yet still be feasable in clinical practice. Therefore, the number of required abnormal variables per nerve was varied between three and five out of 11 tested, and the number of required abnormal nerves was limited to two or three. The sensitivity and specificity of both polyneuropathy sets and sets for demyelination were tested in 135 patients with Guillain-Barré syndrome and 45 healthy subjects. Only the results of the first two EMGs were used to compute the sensitivity of polyneuropathy criteria, as these are of relevance for early diagnosis.

In addition to criteria for polyneuropathy in general, the following findings, characteristic of demyelination, were evaluated: severe slowing of conduction, abnormal dispersion, and abnormal reduction in CMAP amplitude.[7 9 10] We considered signs of demyelination to be present in a peripheral nerve if at least one of the aforementioned criteria was fulfilled. The polyneuropathy was considered to be demyelinating if two or more nerves showed signs of demyelination (table 3). Patients in whom less than two nerves were tested were excluded; the number of patients with at least two completely tested nerves is presented throughout the results section. In addition, we calculated the incidence of several previously designed sets of criteria for demyelinating polyneuropathy in the same group of patients. Here again, a correction for bias due to absent values was performed and true incidence was calculated as the ratio between sufficiently tested patients and patients with electrodiagnostic abnormalities.

Table 1 Variables used for the development of criteria for the electrodiagnostic delineation of polyneuropathy

1	DML > ULN
2	m-NCV < LLN
3	F wave latency >ULN if m-NCV is normal
4	s-NCV <LLN
5	Distal CMAP amplitude < LLN
6	Abnormal CMAP amplitude decay; CMAP amplitude decay > ULN if distal CMAP > 5 mV (hand) response, > 3 mV (foot), or CMAP amplitude decay of 1 mV if distal CMAP < 5 respectively 3 mV
7	Distal CMAP-duration > ULN
8	Increase of CMAP duration > ULN
9	Distal CSNAP amplitude < LLN
10	Recruitment pattern 0 or SP
11	Presence of denervation potentials

DML = distal motor latency; ULN = upper limit of normal; m-NCV = motor nerve conduction velocity; LLN = laboratory limits of normal; s-NCV = sensory nerve potential; CMAP = compound muscle action potential; CSNAP = compound sensory nerve action potential; SP = single pattern.

Table 2 Normal values

	Ulnar	*Median*	*Peroneal*	*Sural*
DML*	2·2 ms	3·0 ms	4·3 ms	—
m-NCV†	60 m/s	60 m/s	50 m/s	—
CMAP amplitudes†‡	15·5 mV	12·3 mV	6·0 mV	—
Reduction*§	16%	11%	41%	—
CMAP surface†‡	33 mV/ms	29 mV/ms	11 mV/ms	—
Reduction*§	11%	8%	34%	—
CMAP duration*‡	8·1 ms	7·2 ms	6·7 ms	—
Increase*§	12%	12%	19%	—
F-latency*‡	32·3 ms	31·2 ms	59·6 ms	—
s-NCV†‡	60 m/s	60 m/s	—	50 m/s
SNAP†‡	10 μV	10 μV	—	10 μV

*Upper limits and †lower limits based on 5th and 95th percentile values in 45 healthy volunteers; ‡after distal stimulation; §in the trajectory of forearm—lower leg. Skin temperature 35°C.

Table 3 Criteria for primary demyelination

Proposed and tested set: one of the following abnormalities in at least two nerves should be demonstrated.

1	DML > 150% of ULN
2	m-NCV < 70% of LLN
3	F wave latency > 150% of ULN
4	Abnormal CMAP amplitude decay > ULN
5	Abnormal distal temporal dispersion: distal CMAP duration > 300% ULN
6	Abnormal temporal dispersion: distal to proximal CMAP duration ratio > 150% of ULN

DML = distal motor latency; ULN = upper limit of normal; m-NCV = motor nerve conduction velocity; LLN = laboratory limits of normal; s-NCV = sensory nerve potential; CMAP = compound muscle action potential; CSNAP = compound sensory nerve action potential; SP = single pattern.

Table 4 Duration of weakness (days) at the moment of EMG

	Range 5%–95% (days)	Median (days)
EMG I	2–15	6
EMG II	9–22	13
EMG III	29–49	34

Results

The median duration of weakness was 6, 13, and 28 days respectively, at the moment of the three subsequent EMGs (table 4). No electrodiagnostic differences were found between the two treatment modalities.

Over 25 criteria sets were applied to all three EMGs. In these sets the definition of an abnormal nerve was varied by changing the number of required abnormal variables (three to five). The definition of a polyneuropathy was varied by changing the number of abnormal nerves (two or three). The best results were obtained when an abnormal nerve was defined by the presence of at least three abnormal variables, and polyneuropathy when at least two nerves were abnormal. Within this set the criteria were met in 85% after the first EMG and in 93% after the second EMG. In none of the healthy volunteers were these criteria met (table 5). Theoretically, bias towards a reduced sensitivity could be expected from insufficiently tested nerves. Therefore, we defined a nerve as sufficiently tested when at least five, six, or seven variables were tested. It seems that missing values did not significantly influence sensitivity when at least five variables per nerve were tested (table 5).

At the first EMG most nerves were abnormal: ulnar nerve 88%, median nerve 90%, and peroneal nerve 70%. The same trend was observed in the second EMG, but here the incidences were higher. In the 45 normal subjects these percentages were always zero.

Evidence for demyelination, as defined by the proposed criteria, was seen in 54%, 72%, and 51% in the ulnar, median, and peroneal nerves respectively, in the first EMG. In 60%, signs of demyelination were present in at least two nerves simultaneously (table 6). In subsequent EMGs these incidences increased maximally with an additional 17%. None of 45 healthy volunteers had signs of demyelination in more than one nerve according to the proposed set.

Applying previously published criteria for primary demyelinating polyneuropathies, yielded low incidences, varying from 3% to 36% at the first EMG, 8% to 39% at the second EMG, and 13% to 46% at the third EMG (table 7).

Discussion

We designed a set of electrodiagnostic criteria for detection of polyneuropathy and a set for detecting signs characteristic of demyelination, and applied these in 135 patients with clinically defined Guillain-Barré syndrome. This is the first study in which such a large group of patients has been followed up prospectively according to a standard EMG protocol. During follow up, the clinical diagnosis of Guillain-Barré syndrome was not changed in any patient; it is assumed, therefore, that in the patients the diagnosis was correct.

The first set for the diagnosis of polyneuropathy was compiled from electrodiagnostic variables available from the test protocol. Because the normal limits for these variables are based on 95th percentiles, the application of individual variables would have a false positive rate of 5%, by definition. Therefore, the major advantage of requiring a minimal number of three abnormal variables per nerve in several nerves was that the false positive rate was reduced to zero in all 45 healthy subjects and therefore the specificity was 100%. The sensitivity of this set was tested in two EMGs, performed at the moment of entry (EMG I) and one week later (EMG II)—that is, at an early stage of the disease. The number of variables per nerve required for nerve to be scored as abnormal was chosen rather arbitrarily; however, different combinations all yielded a high incidence of polyneuropathy. The set which scored best was the one that required three abnormal variables in two different nerves (85% in EMG I and 93% in EMG II) (table 5). Ulnar and median nerves contributed slightly more than the peroneal nerve (about 88%, 90%, and 70% respectively in EMG I, table 5). No such sets of criteria are as yet available in the medical literature for comparison.

Electrodiagnostic criteria, usually applied for the detection of demyelination, are DML, m-NCV, F response latency, and CMAP reduction and duration of CMAPs, because these variables are related to nerve conduction slowing and conduction block.[6 7 9–11] In the present study, the threshold value that would discriminate had to be chosen arbitrarily, as has been done by others[4 7 8] Nevertheless, the proposed set yielded a high incidence of signs of demyelination (60%, 66%, and 72% in consecutive EMGs) (table 5). Again, ulnar and median nerves contributed most (table 2). The best explanation of the lower yield, compared with those for polyneuropathy,

Table 5 Incidence of abnormal nerves related to the required number of abnormal variables within a nerve

	EMG I				EMG II			
	Ulnar (% (n))	Median (% (n))	Peroneal (% (n))	> One nerve (% (n))	Ulnar (% (n))	Median (% (n))	Peroneal (% (n))	> One nerve (% (n))
3 out of 5*	88 (124)	90 (125)	70 (57)	85 (127)	93 (124)	93 (126)	77 (64)	93 (128)
4 out of 5	71 (124)	78 (125)	39 (57)	64 (127)	81 (123)	85 (126)	20 (55)	78 (127)
5 out of 5	50 (124)	50 (124)	27 (56)	40 (126)	63 (123)	66 (125)	33 (51)	50 (125)
5 out of 7	53 (116)	52 (122)	30 (50)	42 (118)	64 (122)	68 (120)	37 (46)	53 (121)

*The first number gives the required number of abnormal variables, the second the required number of evaluated variables; n = number of adequately tested patients.

Table 6 Incidence of motor nerves with at least one sign of demyelination according to the proposed set of criteria

	Normal controls (% (n))	EMG I (% (n))	EMG II (% (n))	EMG III (% (n))
Ulnar nerve	9 (45)	54 (124)	69 (121)	74 (109)
Median nerve	7 (45)	72 (120)	75 (130)	68 (130)
Peroneal nerve	11 (45)	51 (53)	52 (50)	56 (39)
Two or more nerves	0 (45)	60 (124)	66 (124)	72 (109)

n = number of adequately tested patients.

Table 7 Incidence of demyelination according to previously published sets of criteria applied to the present patients with Guillain-Barré syndrome

	EMG I (% (n))	EMG II (% (n))	EMG III (% (n))
Barohn *et al*[6]	3 (119)	8 (116)	13 (101)
Albers and Kelly[7]	5 (122)	11 (117)	15 (104)
Asbury and Cornblath[4]	22 (74)	39 (57)	46 (63)
Albers *et al*[11]	36 (72)	28 (64)	41 (59)
This study	60 (124)	66 (124)	72 (109)

n = number of adequately tested nerves.

lies in the fact that many patients with Guillain-Barré syndrome have (near) normal m-NCVs[12 13] and, as a consequence, will escape detection if the limiting value of NCV is set at a lower value. We think, however, that the proposed set is reasonable to use for the detection of demyelination, but a firmer conclusion can only be drawn if this set of criteria is tested in a group of patients with pure axonal disorders. In some patients with Guillain-Barré syndrome an "axonal form" may exist, as reflected by excitable nerves. In the present study there were seven such patients. This may be the result of severe demyelination, but a primary axonal form probably also exists. Obviously, these patients did not fulfil the proposed set of criteria for demyelination.

Various sets of electrodiagnostic criteria for the detection of demyelination have been developed by others.[4 6-8] When possible we applied these criteria to our patient population (table 7). The criteria developed by Barohn *et al*[6] and Albers and Kelly[7] were designed for patients with chronic inflammatory demyelinating polyradiculoneuropathy. Application to our data resulted in a much lower yield. This may be explained by the fact that characteristics of demyelination are often far more pronounced partly due to the longer duration of the disease. The criteria developed by Albers *et al*[11] and Asbury and Cornblath,[4] and designed for Guillain-Barré syndrome are less stringent and therefore give a higher yield (table 7). Albers *et al* reported criteria for demyelination derived from a retrospective study on patients with Guillain-Barré syndrome.[11] Their patients were examined electrodiagnostically at weekly intervals, which enables comparison with our group. Electrodiagnostic examination at time points comparable with consecutive EMGs (I, II, and III) yielded incidences of 50%, 50%, and 68% in eight, 18, and 25 patients respectively. The study of McLeod is less comparable in this respect (duration of illness 1–125 days), but an incidence of 50% was reported.[14]

Several studies have shown the demyelinating nature of nerve pathology in Guillain-Barré syndrome.[10 15-17] Feasby *et al*[18] were able to relate conduction block to pathological demyelination in nerve biopsies. Also, experimental conduction block—whether induced mechanically[19] or immunologically[20]—is associated with demyelination. These studies suggest that significant demyelination will be revealed by conduction block and conduction slowing. In some nerves, however, these electrodiagnostic signs of demyelination are not found, despite the fact that demyelination is suspected on the basis of clinical findings. This may occur when lesions are patchy along the nerve outside the segment which can be tested in routine studies. Furthermore, conduction block in the thinner segment of motor fibres may be difficult to detect, as long as a few large motor units with thick axons—the principal constituents of the CMAP—are free from demyelination. This has been shown by morphological and physiological studies.[12 18] Another reason why patients with demyelination may pass undetected using the proposed criteria is that many patients with Guillain-Barré syndrome have a very low distal CMAP amplitude.[9] As other causes, such as axonal degeneration or motor end plate dysfunction, cannot be discriminated from distal demyelination, low CMAP amplitudes cannot be applied as a criterion of primary demyelination. Therefore, the patients with predominant distal demyelination will escape detection and may, in any set, cause a serious underestimation of the incidence of demyelination.

In conclusion, in the 135 patients with Guillain-Barré syndrome studied, the proposed set of criteria for polyneuropathy had a sensitivity of 85% and a specificity of 100%. The polyneuropathy was demyelinating in 72% or 36% respectively, using two sets of criteria for demyelination. This set should be tested in other categories of demyelinating and pure axonal neuropathies.

1 Guillain-Barré Syndrome Study Group. Plasmapheresis and acute Guillain-Barré syndrome. *Neurology* 1985;35: 1096–104.
2 French Cooperative Group on plasma exchange in Guillain-Barré syndrome. Efficiency of plasma exchange in Guillain-Barré syndrome: role of replacements fluids. *Ann Neurol* 1987;22:753–61.
3 Van der Meché FGA, Schmitz PIM and the Dutch Guillain-Barré Study Group. A randomized trial comparing intravenous immune globulin and plasma exchange in Guillain-Barré syndrome. *N Engl J Med* 1992;326:1123–9.
4 Asbury AK, Cornblath DR. Assessment of current diagnostic criteria for Guillain-Barré syndrome. *Ann Neurol* 1990;27(suppl):S21–4.
5 Van der Meché FGA, Meulstee J, Kleyweg RP. Current diagnostic criteria for Guillain-Barré syndrome. *Ann Neurol* 1991;30:851–2.
6 Barohn RJ, Kissel JT, Warmolts, Mendell JR. Chronic inflammatory demyelinating polyradiculoneuropathy. *Arch Neurol* 1989;46:878–84.
7 Albers JW, Kelly JJ. Acquired inflammatory demyelinating polyneuropathies: Clinical and electrodiagnostic features. *Muscle Nerve* 1989;12:435–51.
8 Bromberg MB. Comparison of electrodiagnostic criteria for primary demyelination in chronic polyneuropathy. *Muscle Nerve* 1991;14:968–76.
9 Van der Meché FGA, Meulstee J, Vermeulen M, Kievit A. Patterns of conduction failure in the Guillain-Barré syndrome. *Brain* 1988;111:405–16.
10 Brown WF. In: Brown WF, Bolton, eds. *Clinical electromyography*. 2nd ed. Boston: Butterworth-Heinemann, 1993.

11 Albers JW, Donofrio PD, McGonagle TK. Sequential electrodiagnostic abnormalities in acute inflammatory demyelinating polyradiculoneuropathy. *Muscle Nerve* 1985;**8**:528–39.
12 Brown WF, Feasby TE. Conduction block and denervation in Guilain-Barré polyneuropathy. *Brain* 1984;**107**: 219–39.
13 Arnason BGW. Acute inflammatory demyelinating polyradiculoneuropathies. In: Dijck PJ, Thomas PK, Lambert EH, Bunge RP, eds. *Peripheral neuropathy*. Vol 2. 3rd ed. Philadelphia: WB Saunders 1993:1437–97.
14 McLeod J. Electrophysiological studies in Guillain-Barré syndrome. *Ann Neurol* 1981;**9**:20–7.
15 Asbury AK, Arnason BG, Adams RD. The inflammatory lesion in idiopathic polyneuritis. *Medicine* 1969;**48**: 173–215.
16 Saida K, Saida T, Brown MJ, Silbergberg DH. In vivo demyelination induced by intraneural injection of anti-galactocerebroside serum. *Am J Pathol* 1979;**95**:99.
17 Sumner AJ. The physiological basis for symptoms in Guillain-Barré syndrome. *Ann Neurol* 1981;**9**(suppl): 28–30.
18 Feasby TE, Brown WF, Gilliatt JJ, Hahn AF. The pathological basis for conduction block in human neuropathies. *J Neurol Neurosurg Psychiatry* 1985;**48**:234–44.
19 Denny-Brown D, Brenner C. Paralysis of nerve induced by direct pressure and by tourniquet. *Archives of Neurology and Psychiatry* 1944;**51**:1–26.
20 McDonald WI. The effects of experimental demyelination on conduction in peripheral nerve: a histological and electrophysiological study. II Electrophysiological observations. *Brain* 1963;**86**:502–24.

NEUROLOGY IN LITERATURE

Migraine

Descriptions of migraine in the literature have proved remarkably elusive. Even where the term has been used, for example with Mrs Ordyntsev, doubt arises as to the certainty of the diagnosis. Madame Goesler, in Phineas Redux, feigns an attack to avoid an uncomfortable situation; perhaps a device neurologists should recall when dealing with an intractable case! At least present day sufferers have the consolation of more effective remedies than Hoffman's drops.

George Eliott, 1858, Scenes of clerical life
Just before the appointed hour of eleven, Caterina came down into the drawing-room, looking so unusually ill as to call forth an anxious inquiry from Lady Cheverel, who, on learning that she had a severe headache insisted that she should not attend service, and at once packed her up comfortably on a sofa near the fire, . . .

"Well, my dear Miss Sarti, and how do you feel now?—a little better, I see. I thought you would be, sitting quietly here. These headaches, now, are all from weakness. You must not overexert yourself, and you must take bitters. I used to have just the same sort of headaches when I was your age, and old Dr Samson used to say to my mother, "Madam, what your daughter suffers from is weakness."

Fedor Dostoyevsky, 1868, The idiot
Mrs Odyntsev, I was told, had migraine, was running a temperature, and was delirious.

Leo Tolstoy, 1868–9, War and peace
The countess had a headache brought on by all the noise and turmoil, and was lying down in the new sittingroom with a vinegar compress on her head . . .

Natasha ran into the house, and went on tiptoe through the half-open door into the sitting-room where there was a smell of vinegar and Hoffman's drops.

Anthony Trollope, 1874, Phineas Redux
She almost plotted some scheme of a headache, by which she might be enabled not to show herself till after dinner. "I am so blind that I can hardly see out of my eyes," she said to the maid, actually beginning the scheme.

Saki, 1911, The way to the dairy
They contrived, whenever possible, to excuse themselves from participation in their aunt's deplored gaieties; the Brimley Bomefield headaches became famous . . .

"It's time you went home and had those headaches seen to by a specialist," was her comment on the situation.

Arnold Bennett, 1918, The pretty lady
"Do not be vexed. I have my migraine—am good for nothing. But I gave the order that thou shouldst be admitted."

Thomas Mann, 1947, Dr Faustus
Adrian had not asked for a physician, because he wanted to interpret his sufferings as familiar and hereditary, as merely an acute intensification of his father's migraine. It was Frau Schweigestill who at last insisted on calling in Dr Kürbis, the Waldshut district physician, the same who had once delivered the fräulein from Bayreuth. The good man would not hear of migraine, since the often excessive pains were not one-sided as is the case with migraine but consisted in a raging torment in and above both eyes, and moreover were considered by the physician to be a secondary symptom.

G D PERKIN
Regional Neurosciences Centre, Charing Cross Hospital, Fulham Palace Road, London W6 8RF, UK