ABSTRACT: Electrodiagnosis plays an important role in the early detection and characterization of inflammatory demyelinating polyradiculoneuropathies, because timely treatment reduces morbidity and disability. The challenge consists of defining electrodiagnostic criteria that are highly specific for primary demyelination but sufficiently sensitive to be useful in clinical practice. We compared 10 published sets of criteria in 53 patients with demyelinating Guillain–Barré syndrome (GBS) and 28 with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). Specificity of criteria sets was tested in 40 patients with amyotrophic lateral sclerosis (ALS) and 32 with diabetic polyneuropathy (DPN). Sensitivity ranged from 24 to 83% (mean, 54.3%) in GBS and 39 to 89% (mean, 64.9%) in CIDP. With regard to ALS, specificity was 100% for nine sets but was 97% in one. In contrast, 3–66% of DPN patients fulfilled criteria in eight of ten sets. We propose a set of criteria with 72% and 75% sensitivity in our GBS and CIDP patient series, respectively, and 100% specificity with regard to ALS and DPN. Our data illustrate that most, but not all, patients can be electrodiagnostically ascertained.

Muscle Nerve **29:** 565–574, 2004

ELECTRODIAGNOSTIC CRITERIA FOR ACUTE AND CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY

PETER Y. K. VAN DEN BERGH, MD, PhD,[1] and FRANÇOISE PIÉRET, MD[1]

[1]Service de Neurologie, Cliniques Universitaires St-Luc, Université Catholique de Louvain, 10 Avenue Hippocrate, 1200 Brussels, Belgium

Accepted 17 November 2003

Most acquired demyelinating neuropathies are of presumed inflammatory origin. They include the classic demyelinating form of Guillain–Barré syndrome (GBS), chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), and two CIDP variants: multifocal motor neuropathy (MMN) and multifocal demyelinating neuropathy with persistent conduction block, also known as Lewis–Sumner syndrome, or multifocal acquired demyelinating sensory and motor neuropathy (MADSAM). GBS and CIDP are characterized by areflexic symmetric tetraparesis, sensory symptoms and signs, and elevated spinal fluid protein concentration.[2,6] Patients with GBS reach their clinical nadir of symptoms and signs by 4 weeks, and a significant proportion present with cranial (mainly facial) nerve palsy, autonomic involvement, and respiratory failure. In contrast, patients with CIDP present with a progressive or relapsing course of at least 2-month duration; facial palsy is rare and autonomic or respiratory involvement is exceptional. The diagnosis of GBS and CIDP is based on clinical features, electrodiagnostic (nerve conduction) studies, spinal fluid examination, and, in selected cases, peripheral nerve biopsy.

There are four basic electrodiagnostic parameters of demyelination: (1) reduced motor conduction velocity; (2) motor conduction block or abnormal temporal dispersion in nerve segments not prone to compression; (3) prolonged motor distal latency; and (4) prolonged minimal F-wave latency or absent F waves. Over the last two decades, various sets of criteria have been proposed for GBS[4–6,14,16,18,19] and CIDP.[2,5,7,17,20,24] These sets of criteria are very similar because they are based on the same four basic parameters, but they differ quantitatively: (1) in the percentage of change from normal values; and (2) the number of abnormal parameters required (Table 1). Using their own sets of criteria, various investigators[4,14,18,19] have reported

Abbreviations: ALS, amyotrophic lateral sclerosis; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; CMAP, compound muscle action potential; dCMAP, distal negative-peak CMAP amplitude; DPN, diabetic polyneuropathy; GBS, Guillain–Barré syndrome; MADSAM, multifocal acquired demyelinating sensory and motor neuropathy; MMN, multifocal motor neuropathy.

Key words: chronic inflammatory demyelinating polyradiculoneuropathy; criteria for primary demyelination; electrodiagnosis; Guillain–Barré syndrome; nerve conduction studies

Correspondence to: P.Y.K. Van den Bergh; e-mail: vandenbergh@nchm.ucl.ac.be

Published online 23 February 2004 in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/mus.20022

Table 1. Comparison of published electrodiagnostic criteria for primary demyelination.

	Motor nerve conduction parameters										
	Conduction velocity slowing		Distal latency prolongation		F-wave latency prolongation		Conduction block		Abnormal temporal dispersion		Abnormal
Criteria set	% of LLN	No. of nerves	% of ULN	No. of nerves	% of ULN	No. of nerves	%	No. of nerves	%	No. of nerves	parameters required
A[4]	>5 (15)	2	>10 (20)	2	>20	2	>30	2	>30	2	1
B[5]	>10 (20)	2	>15 (25)	2	>25	1	>30	1	>30	1	3
C[2,6]	>20 (30)	2	>25 (50)	2	>20 (50)	2	>20*	1	>15	1	3
D[16]	>10 (15)	2	>10 (20)	2	>20	2	—	—	>30	2	1
E[19]	>30	2 or 1	>50	2 or 1	>50	2 or 1	>16 ulnar† >11 median† >41 peroneal†	2 or 1	>50	2 or 1	1 or 2
F[18]	>20 (30)	2	>25 (50)	2	>20 (50)	2	>30*	1	>30	1	2
G[14]	>10 (15)	2	>10 (20)	2	>20	2	>50	2	—	—	1
H[20]	>20 (30)	‡	>25 (50)	‡	>20 (50)	‡	>30*	1–3‡	>15	1–3‡	1 in 3 nerves
I[17]	>20 (30)	‡	>25 (50)	‡	>20 (50)	‡	>20*	2–3‡	>15	2‡	1 in 3 nerves
J[24]	>20 (30)	2	>25 (50)	2	>20 (50)	2	>50	1	>15	1	2

LLN, lower limit of normal; ULN, upper limit of normal. Numbers in parentheses show percent if distal negative-peak CMAP amplitude is <50% (sets A, B, D, E, G) or <80% (sets C, F, H, I). Absent F waves are a criterion in C, F, I, and J. Conduction block, percent of proximal-to-distal negative-peak CMAP amplitude (or area) reduction (if distal amplitude ≥20% of LLN in G). Conduction block is not considered in the posterior tibial nerve in C, F, H, and J. Temporal dispersion, percent increase of proximal-to-distal negative-peak CMAP duration. In E, either one parameter must be abnormal in 2 nerves, or two parameters must be abnormal, each in a different nerve; the posterior tibial nerve is not considered for any parameter.*

†In E, if distal negative-peak CMAP amplitude is <5 mV (<3 mV for the peroneal nerve), reduction of >1 mV is required.

‡In H, motor conduction block/abnormal temporal dispersion in 1, 2, or 3 nerves needs to be associated with 2, 1, 1 other abnormal parameters in a total of 3 nerves; in I, motor conduction block/abnormal temporal dispersion in a single nerve only is not considered.

sensitivity levels of 56–71% in individual series of GBS patients. When Alam et al.[3] applied these criteria sets as well as those reported by others[4–6,18,19] to a series of 43 GBS patients, they found sensitivity levels of 21–72% (mean, 65%). Comparing three sets of criteria for CIDP,[2,5,7] Bromberg[8] found a maximal sensitivity level of 66%. Two disease control groups, consisting of patients with amyotrophic lateral sclerosis (ALS) and diabetic polyneuropathy (DPN), were used to demonstrate 100% specifity of the three criteria sets. Nicolas et al.[20] found that only 63% of their CIDP patients fulfilled the criteria of the Ad Hoc Subcommittee of the American Academy of Neurology. They therefore proposed a revision of the latter criteria, which increased sensitivity to 90% but reduced specificity to 97% with regard to their control group of patients with axonal polyneuropathy.

We decided to test the sensitivity and specificity of 10 published sets of criteria for primary demyelination (Table 1) by reviewing nerve conduction studies from our series of patients with GBS, CIDP, ALS, and DPN. We then determined the percentage of change in nerve conduction parameters and the number of abnormal parameters necessary to obtain 100% specificity in order to establish whether a set of criteria with higher sensitivity than previously reported could be assembled.

PATIENTS AND METHODS

Patients. Patients evaluated at our Department of Neurology between 1994 and 2000, and who had a final diagnosis of GBS, CIDP, ALS, or DPN, were included. The diagnosis of GBS was based on published clinical criteria.[6] Inclusion criteria were symmetric weakness of more than one limb, progressing over a maximum of 4 weeks, and absent or reduced deep tendon reflexes. Patients with CIDP conformed to clinical criteria of the Ad Hoc Subcommittee of the American Academy of Neurology.[2] Inclusion criteria were progressive, stepwise, or relapsing symmetric proximal and distal weakness and sensory dysfunction of more than one limb, of a peripheral nature, developing over at least 2 months, and absent or reduced deep tendon reflexes. Most patients with GBS and CIDP presented with spinal fluid cytoalbuminemic dissociation and responded to immune therapy.

Exclusion criteria for the diagnosis of GBS and CIDP were a history of drug or toxin exposure, a family history of polyneuropathy or clinical features suggestive of a hereditary demyelinating neuropathy, abnormal porphyrin metabolism, and the presence of a sensory level or sphincter dysfunction. For CIDP, patients with the following concurrent diseases were excluded: diabetes, human immunodefi-

Table 2. Demographic features of the four patient groups.

Diagnosis	Patient number	Men		Women	
		Number	Mean age (range)	Number	Mean age (range)
GBS	53	33	51 (11–74)	20	52 (3–82)
CIDP	28	23	56 (14–72)	5	40 (11–59)
ALS	40	15	55 (33–78)	25	61 (34–77)
DPN	32	24	57 (41–83)	8	50 (32–76)

ALS, amyotrophic lateral sclerosis; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; DPN, diabetic polyneuropathy; GBS, Guillain–Barré syndrome.

ciency virus infection, systemic lupus erythematosus, monoclonal or biclonal gammopathy, and central nervous system demyelinating disease.

The Airlie House criteria for the diagnosis of clinically definite ALS (upper motor neuron signs in two regions and lower motor neuron signs in three regions) were met in all ALS patients.[9,25] Patients with DPN had clinical evidence of a chronic, predominantly distal, symmetric, sensorimotor polyneuropathy in a context of long-standing, overt insulin-dependent or -independent diabetes mellitus.[12]

Neurophysiological Methods. Median, ulnar, peroneal, and posterior tibial motor nerve conduction studies were performed unilaterally with percutaneous supramaximal nerve stimulation while recording the compound muscle action potential (CMAP) with 11-mm disk electrodes. Proximal stimulation sites were located at the elbow for the median nerve, below the elbow for the ulnar nerve, below the fibular head for the peroneal nerve, and at the popliteal fossa for the posterior tibial nerve. Motor conduction velocity or CMAP changes across the elbow in the ulnar nerve or across the fibular head in the peroneal nerve were not taken into account. The amplitude, duration, and area of the negative peak of each CMAP were measured. F-waves were recorded from each nerve following at least 10 distal stimuli to determine minimal F-wave latency or F-wave absence. Sensory nerve action potentials were recorded antidromically with surface ring (median and ulnar nerves) and 11-mm disk (sural nerve) electrodes. Electromyography was performed with standard concentric needle electrodes. Skin temperature was at least 33°C at the palm and 30°C at the external malleolus.

Data Analysis. All nerve conduction data were entered in a computerized database. Ten published sets of criteria for primary demyelination[2,4–6,14,16–20,24] were applied to these data in order to determine the percentage of GBS and CIDP patients meeting criteria for each set (sensitivity) as well as the percentage of ALS and DPN patients that did not (specificity). Criteria for each parameter were systematically analyzed in order to determine the percentage of change from the limits of normal values necessary to obtain maximum sensitivity together with absolute specificity for GBS and CIDP in our patient series. The results were then used to try to assemble a new set of criteria that would lead to higher scores than those obtained with the previously published sets.

Statistical Analysis. Chi-square fourfold tables were used to compare the distribution of the number of patients with GBS, CIDP, ALS, and DPN, fulfilling and not fulfilling criteria for primary demyelination. Pearson's goodness-of-fit chi-square and corresponding *P*-values were calculated for all sets of criteria, including our new one.

RESULTS

Patients. The number, age, and gender of patients in the four diagnostic categories are listed in Table 2. There was male predominance in all categories except in the ALS group. Most patients were in the fifth or sixth decades of their lives. Five GBS and 2 CIDP patients were under the age of 18 years at the time of evaluation. The mean interval between onset of symptoms and electrodiagnostic testing was 3 weeks (range, 1–7 weeks) and 4.7 years (range, 2 months to 20 years) for patients with GBS and CIDP, respectively. Thirty-six GBS patients were tested at 2–4 weeks, 8 at 1 week, and 9 at 5–7 weeks after symptom onset.

Sensitivity of Ten Published Sets of Criteria for Primary Demyelination. Sensitivity varied widely between different sets, ranging between 24% and 83% (mean, 54.3; SD, 15.8) in GBS and 39% and 89% (mean, 64.9; SD, 16.3) in CIDP (Fig. 1). Scores were higher in CIDP than in GBS for nine sets (by a mean of

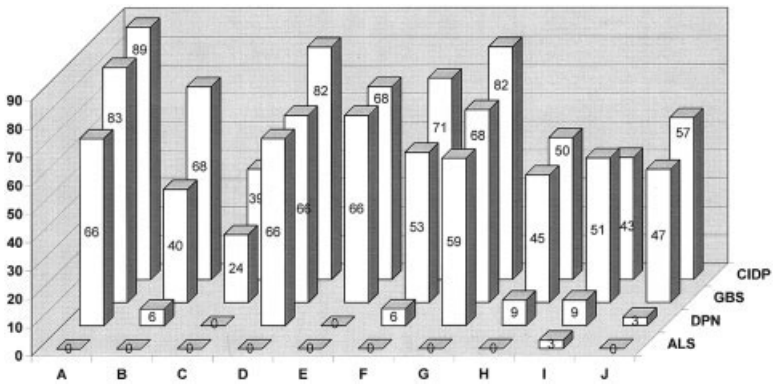

FIGURE 1. Comparison of ten sets of criteria for primary demyelination as applied to four groups of patients. The ten sets (A–J) are defined in Table 1.

11.9% and a range of 2–28%); 3% fewer CIDP than GBS patients fulfilled criteria from set I because of the requirement for motor conduction block in at least 2 nerves. Motor conduction block (>20% negative-peak CMAP amplitude reduction) was present in only 1 nerve in 11 of 28 (39%) CIDP patients and in 11 of 53 (21%) GBS patients, which explains why set I was less sensitive for CIDP. Overall, the highest scores were obtained with sets A, D, and G, the lowest scores with sets C, H and I. In GBS, sets B, F, and J yielded low scores as well. In CIDP, intermediate scores were obtained with sets B, E, and F. The requirement that more than 1 parameter should be abnormal appears to have been responsible for the low sensitivity levels obtained with sets B, C, F, and J, rather than the degree of change required for individual parameters (Table 1). This association was also clear from the results obtained with set E. Although this set was the most rigorous for individual parameter changes, the requirement for only 1 parameter to be abnormal led to a higher sensitivity level in both GBS and CIDP. As expected, loose requirements for changes in only 1 parameter in sets A, D, and G led to the highest scores.

Specificity of Ten Published Sets of Criteria for Primary Demyelination. None of the ALS patients fulfilled criteria sets A–H and J, but 3% of them did when using set I (Fig. 1). In contrast, only sets C and E were fully specific with regard to DPN. Criteria of sets A, B, D, F, G, H, I, and J were met by a variable percentage of patients with DPN (Fig. 1), indicating that they lacked specificity for primary demyelination. Interestingly, set B, which required that three parameters be abnormal, still picked up 6% of DPN patients. The lack of complete specificity was clearly related to loose criteria for motor conduction velocity and motor distal latency. Sets H and I criteria were also met by 9% of DPN patients despite the fact that criteria for individual parameters were stricter than in set B. Only sets C and E were 100% specific with respect to both ALS and DPN. The best results were obtained with set E, characterized by very strict criteria for individual parameters, only one of which was required to be abnormal.

Systematic Analysis of Criteria for Primary Demyelination. Sensitivity and specificity of criteria for motor conduction velocity, motor distal latency, F-wave latency or absence, and motor conduction block or abnormal temporal dispersion were tested by using nerve conduction data from the four patient groups (Tables 3 and 4). Whereas full specificity with regard to ALS was readily obtained, stringent criteria were needed in at least 2 nerves with regard to DPN for all parameters except motor conduction block. No patient with DPN or ALS presented with motor conduction velocity slowing of >30% of the lower limit of normal in 2 nerves or with prolongation of motor distal latency of >150% of the upper limit of normal in 2 nerves. Prolongation of F-wave latency of >120% (>150% if the distal negative peak CMAP amplitude was <80% of the lower limit of normal values) or F-wave absence in the presence of a distal negative peak CMAP amplitude of ≥20% of the lower limit of normal in 2 nerves was required to obtain full specificity. Under these stringent conditions, the sensitivity of individual parameters of motor conduction velocity, motor distal latency, and F-wave latency or F-wave absence was rather low (Table 3). Prolonged motor distal latency was the most frequent abnormality in GBS (38%), followed by F-wave absence (26%), slowed motor conduction velocity (21%), and prolonged F-wave latency (13%). In CIDP, prolonged F-wave latency (39%) was the most common abnormality, followed by

Table 3. Effect of severity of criteria for motor conduction velocity, motor distal latency, and F-wave latency or absence on percentage of patients fulfilling criteria.

	GBS	CIDP	ALS	DPN
Motor conduction velocity (1 nerve)				
<95 (85)% [A]	79	89	13	94
<90 (85)% [D, G]	72	86	5	91
<90 (80)% [B]	72	86	5	91
<80 (70)% [C, F, H–J]	51	79	0	38
<70% [E]	38	68	0	13
Motor conduction velocity (2 nerves)				
<95 (85)% [A]	55	79	0	78
<90 (85)% [D, G]	42	71	0	66
<90 (80)% [B]	43	71	0	62
<80 (70)% [C, F, H–J]	23	36	0	6
<70% [E]	21	32	0	0
F-wave latency (1 nerve)				
>120% [A, D, G]	36	93	5	34
>125% [B]	32	82	5	22
>120 (150)% [C, F, H–J]	30	86	5	19
>150% [E]	15	54	5	0
F-wave latency (2 nerves)				
>120% [A, D, G]	17	46	0	3
>125% [B]	11	36	0	0
>120 (150)% [C, F, H–J]	13	39	0	0
>150% [E]	2	18	0	0
Motor distal latency (1 nerve)				
>110 (120)% [A, D, G]	74	75	18	56
>115 (125)% [B]	68	71	10	47
>125 (150)% [C, F, H–J]	62	68	3	19
>150% [E]	47	61	0	3
Motor distal latency (2 nerves)				
>110 (120)% [A, D, G]	57	57	0	6
>115 (125)% [B]	51	54	0	3
>125 (150)% [C, F, H–J]	40	39	0	3
>150% [E]	38	25	0	0
F-wave absence (1 nerve)				
Absence [C, F, I, J]	68	75	40	34
Absence*	53	54	28	25
F-wave absence (2 nerves)				
Absence [C, F, I, J]	45	54	10	12
Absence*	26	21	0	0

See Table 2 for abbreviations. Bracketed criteria sets as in Figure 1 and Table 1.
**Distal negative-peak CMAP amplitude ≥20% of lower limit of normal. Numbers in parentheses show percent if distal negative-peak CMAP amplitude is >50% (sets A, B, D, E, G) or >80% (sets C, F, H, I).*

slowed motor conduction velocity (32%), prolonged motor distal latency (25%), and F-wave absence (21%).

Motor conduction block was highly specific for GBS and CIDP. In our series, negative-peak CMAP amplitude reductions as small as 20% were not observed in any nerve of ALS and PDN patients. Reductions of >20% in 1 nerve were observed in 70% and 93% of GBS and CIDP patients, respectively. A significant drop in sensitivity was noted only when >50% amplitude reduction was required in 1 nerve (30% in GBS and 50% in CIDP) and in 2 nerves (23% in GBS and 25% in CIDP) (Table 4). The parameter of abnormal temporal dispersion, defined as >30% increase in proximal negative-peak CMAP duration, was fully specific when abnormal in 2 nerves, but sensitivity was low in CIDP (25%) and extremely low in GBS (2%).

Assembly of a New Set of Criteria for Primary Demyelination. Based on the aforementioned results, the diagnosis of GBS or CIDP can be supported by: (1) >150% prolongation of motor distal latency above the upper limit of normal values; (2) <70% slowing of motor conduction velocity below the lower limit of normal values; (3) >125% (>150% if the distal negative-peak CMAP amplitude was <80% of the lower limit of normal values) prolongation of F-wave latency above the upper limit of normal values; or (4) abnormal temporal dispersion (>30% negative-peak CMAP duration increase) in 2 or more nerves (Table 5).

F-wave absence in 2 or more nerves is a fully specific criterion if the distal negative-peak CMAP amplitude is ≥20% of the lower limit of normal values. However, since F-wave absence can only provide indirect evidence of demyelination, we added abnormality of at least one other parameter in 1 other nerve as a requirement for F-wave absence to be a valid criterion.

Motor conduction block, defined as >20% negative-peak amplitude reduction of the proximal CMAP in 1 nerve, yielded 100% specificity in our patient series. However, amplitude reductions of up to 45% in the median, 30% in the ulnar, 50% in the peroneal, and 50% in the posterior tibial nerve have been reported in normal control subjects.[19,21,27,28] This has led to the publication of consensus criteria for the diagnosis of partial conduction block by the American Association of Electrodiagnostic Medicine.[22] Our new criteria set introduces two levels of confidence for the diagnosis of primary demyelination. The diagnosis is probable in the presence of an amplitude reduction of >30% if the distal negative-peak CMAP amplitude is >20% of the lower limit of normal values in the median, ulnar, or peroneal nerves. The diagnosis is definite if, in accordance with the published consensus criteria for the diagnosis of partial conduction block,[22] there is an amplitude reduction of >50% if the distal negative-peak CMAP amplitude is ≥20% of the lower limit of normal values in the median, ulnar, peroneal, and posterior tibial nerves. Motor conduction block in at least 2 nerves or its presence in 1 nerve together with

Table 4. Effect of criteria for motor conduction block and abnormal temporal dispersion on percentage of patients fulfilling criteria.

	Percentage of patients fulfilling criteria			
	GBS	CIDP	ALS	DPN
Motor conduction block (1 nerve)				
>20% [I]	70	93	0	0
>20% (posterior tibial nerve excluded) [C]	60	82	0	0
>30% [A, B, D]	60	82	0	0
>30% (posterior tibial nerve excluded) [F, H, J]	57	64	0	0
>50%	30	50	0	0
>50% (dCMAP ≥20% of LLN) [G]	28	46	0	0
Motor conduction block (2 nerves)				
>20% [I]	57	57	0	0
>20% (posterior tibial nerve excluded) [C]	38	36	0	0
>30% [A, B, D]	45	43	0	0
>30% (posterior tibial nerve excluded) [F, H, J]	30	28	0	0
>50%	23	25	0	0
>50% (dCMAP ≥20% of LLN) [G]	13	25	0	0
Abnormal temporal dispersion (1 nerve)	15	39	0	3
Abnormal temporal dispersion (2 nerves)	2	25	0	0

All values for motor conduction block are percent of negative-peak CMAP amplitude reduction. Abnormal temporal dispersion defined as >30% increase in negative-peak CMAP duration. dCMAP, distal negative-peak CMAP amplitude. LLN, lower limit of normal. See Table 2 for other abbreviations. Bracketed criteria sets as in Figure 1.

Table 5. Proposal for a new set of criteria for primary demyelination with two levels of confidence (probable, definite) as compared with four selected published sets.

					New set	
	Set C	Set J	Set I	Set E	Probable	Definite
Parameter						
Conduction velocity	20 (30)% in 2 N	20 (30)% in 2 N	20 (30)% in 1 N	30% in 2 N	30% in 2 N	
Distal latency	125 (150)% in 2 N	125 (150)% in 2 N	125 (150)% in 1 N	150% in 2 N	150% in 2 N	
F-wave latency	120 (150)% in 2 N	120 (150)% in 2 N	120 (150)% in 1 N	150% in 2 N	120 (150)% in 2 N	
F-wave absence	Yes in 2 N	Yes in 2 N	Yes in 1 N	No	Yes in 2 N (if dCMAP ≥20%) + other parameter in other N	
Conduction block	20% in 1 N	50% in 1 N	20% in ≥2 N	16% (ulnar N), 11% (median N), 41% (peroneal N) in 2 N	30% in 2 N or in 1 N (posterior tibial excluded) + other parameter in other N (dCMAP ≥20%)	50% in 2 N or in 1 N + other parameter in other N (dCMAP ≥20%)
Abnormal temporal dispersion	15% in 1 N	15% in 1 N	15% in ≥2 N	50% in 2 N*	30% in 2 N	
Abnormal parameters	3	2	CB in ≥2 N + other parameter in other N or 3 other parameters in 3 N	1 or 2 different parameters in 2 N	1	
Sensitivity GBS	24%	47%	51%	66%	72%	64%
Sensitivity CIDP	39%	57%	43%	68%	75%	75%
Specificity ALS	100%	100%	97%	100%	100%	100%
Specificity DPN	100%	97%	91%	100%	100%	100%

N, nerve(s). Numbers in parentheses are percent if distal negative-peak CMAP amplitude is <50% (E) or <80% (C, new set). dCMAP, distal negative-peak CMAP amplitude. CB, conduction block. See Table 2 for other abbreviations. Designation of sets as in Table 1.
**If dCMAP is <5 mV (<3 mV for the peroneal nerve), reduction of >1 mV is required.*

Table 6. Results of Pearson's goodness-of-fit chi-square fourfold table statistical analysis, comparing GBS and CIDP patients with DPN patients.

	GBS vs. DPN			CIDP vs. DPN		
Criteria set	Chi-square	*P*-value	Rank	Chi-square	*P*-value	Rank
A	3.235	0.0670	10	4.673	0.0306	10
B	11.259	0.0007	8	24.914	<0.0001	5
C	9.266	0.0023	9	15.394	<0.0001	7
D	0.002	0.9689	12	2.084	0.1488	12
E	35.925	<0.0001	2	31.777	<0.0001	3
F	18.957	<0.0001	4	27.319	<0.0001	4
G	0.639	0.4242	11	3.686	0.0548	11
H	11.87	0.0005	7	12.137	0.0004	8
I	21.428	<0.0001	6	15.747	<0.0001	9
J	18.231	<0.0001	5	21.459	<0.0001	6
New set (definite)	34.214	<0.0001	3	36.923	<0.0001	1 = 2
New set (probable)	41.493	<0.0001	1	36.923	<0.0001	1 = 2

When ranked according to chi-square value, the new set for probable demyelination obtains the highest score for both GBS and CIDP. The new set for definite demyelination obtains the highest score for CIDP and a slightly lower score than set E for GBS. Statistical significance ($P < 0.05$) not reached for sets D and G (GBS and CIDP vs. DPN) and A (GBS vs. DPN). See Table 2 for abbreviations.

one other abnormal parameter in at least 1 other nerve was used in the definition of our criteria set.

Assessment of Our New Set of Criteria. Our new set of criteria picked up 64% and 72% of patients with GBS (probable and definite primary demyelination, respectively) and 75% of patients with CIDP (probable and definite primary demyelination). Considering full specificity, these results are superior to those obtained with the ten published sets of criteria as demonstrated by chi-square fourfold table statistical analysis (Tables 5 and 6). All sets, including our new one, differentiated GBS and CIDP patients from ALS patients ($P < 0.0001$, data not shown). When comparing GBS and CIDP patients with DPN patients, the highest chi-square values were obtained with our new set. When using our criteria set for definite primary demyelination in GBS, slightly lower sensitivity levels (64%) were obtained than with set E (66%), in which criteria for motor conduction block in upper extremity nerves were quite loose (Tables 1 and 5). Sets D and G failed to differentiate GBS and CIDP from DPN patients and set A GBS from DPN patients. The clinical characteristics of 15 GBS and 7 CIDP patients, who failed to meet our proposed criteria, were analyzed to determine whether they differed from those of patients who did meet them. Among the patients with GBS, 6 had at least 1 inexcitable motor nerve, 5 were studied at ≤2 weeks after disease onset, and 4 had mild GBS. Among the CIDP patients, 4 had at least 1 inexcitable motor nerve and the other 3 had mild symptoms and signs. It appears, therefore, that, in our database, GBS and CIDP patients with either mild or severe disease and GBS patients, studied early in the disease course, did not fulfill the criteria.

DISCUSSION

Except for the difference in temporal progression, diagnostic criteria for both GBS and CIDP are very similar.[2,6] Electrodiagnostic criteria play a crucial role because slowing of motor conduction, abnormal temporal dispersion of the CMAP, and motor conduction block provide evidence of primary demyelination, which is the underlying pathophysiological process. Defining electrodiagnostic criteria for primary demyelination is not straightforward. There not only exists a wide range of normal values for the different parameters of motor nerve conduction, but also primary axonopathies may present with secondary demyelination. Therefore, electrodiagnostic criteria have to be sufficiently stringent to be predictive of primary demyelination. They are empirically based on comparative studies in patient populations representing well-defined diagnostic categories.

We tested 10 published sets of electrodiagnostic criteria for primary demyelination for sensitivity and specificity in 4 unselected groups of patients with definite diagnoses of GBS, CIDP, ALS, and DPN. The most important finding is that only 2 sets (C, E) were fully specific. Sets A, D, and G failed to distinguish GBS from DPN, and sets D and G did not distinguish CIDP from DPN. The reason is that criteria for conduction slowing (motor distal latency, motor conduction velocity, F-wave latency) were too loose in these sets. In set I, a small number of patients with ALS did fulfill criteria, mainly because

F-wave absence, which is a nonspecific finding, was considered an independent criterion. Sets H and I picked up a small but significant number of patients with DPN. The two sets offering full specificity (C and E) had in common that criteria for motor distal latency, motor conduction velocity, and F-wave latency were more stringent than in other sets. Although one might expect their sensitivity to be lower than that of the other sets, this was only so for set C. Since criteria for individual parameters were more stringent in set E, the difference in sensitivity relates to the requirement that only one parameter needed to be abnormal as opposed to three parameters in set C. The finding that set B, which also required that three parameters were abnormal but proposed less stringent criteria, was neither very sensitive nor fully specific with regard to DPN, further demonstrates that: (1) stringency of values for abnormality of individual parameters is of primary importance for specificity; and (2) sensitivity is inversely proportional to the required number of abnormal parameters.

We found that motor conduction velocity slowing of >30% below the lower limit of normal, prolongation of motor distal latency of >150% of the upper limit of normal, and prolongation of F-wave latency of >120% of the upper limit of normal (>150% if the distal negative peak CMAP amplitude was <80% of the lower limit of normal values), each in 2 nerves, were specific for primary demyelination (Table 5). These findings are in accordance with those reported in motor neuron disorders, such as ALS, and in predominantly axonal polyneuropathies. In these conditions, mild slowing of motor conduction velocity (<30% of the lower limit of normal) and mild prolongation of distal motor latency and F-wave latency (<130% of the upper limit of normal) may occur.[9] The mechanism includes degeneration of the largest, fastest-conducting myelinated axons and slow conduction in regenerating, immature axonal sprouts. Distal motor latency may therefore be prolonged out of proportion to motor conduction slowing. Motor conduction velocity, motor distal latency, and F-wave latency abnormalities are proportional to the severity and the chronicity of the causative disorder.[11] Herrmann et al.[15] studied conduction slowing in ALS and DPN. In both conditions, distal CMAP amplitude-dependent slowing occurred, most likely due to selective loss of large myelinated fibers. In addition, amplitude-independent slowing in intermediate nerve segments was found only in DPN, most likely due to secondary demyelination–remyelination.

In the present study, negative-peak CMAP amplitude reduction of >20% was not observed in ALS and DPN. In contrast, it occurred in at least 1 nerve in 70% of GBS and 93% of CIDP patients. Brown and Feasby[10] reported that a >20% amplitude decrease and >15% duration increase did not occur in median, ulnar, and peroneal nerves of normal control subjects, and that in about 75% of motor nerves in GBS amplitude reductions exceeded 50%. Because motor conduction block as defined above was associated with pathological evidence of demyelination in patients with inflammatory demyelinating polyradiculoneuropathies,[13] negative-peak amplitude decline of >20% and duration increase of <15% were proposed as diagnostic criteria of motor conduction block in GBS[6] and CIDP.[2] However, various investigators have found amplitude reductions of up to 45% in the median, 30% in the ulnar, 50% in the peroneal, and 50% in the posterior tibial nerve, and a duration increase of up to 30% in normal control subjects.[19,21,27,28] Moreover, amplitude reductions of 21–40% have been reported in DPN.[1]

Combined in vivo measurements of motor unit action potentials and computer simulation of temporal dispersion and conduction block in rat sciatic nerve have indicated that broadening of the range of conduction velocities between stimulation sites may lead to negative-peak CMAP area and amplitude reductions of up to 50% and >50%, respectively.[23] These reductions were entirely due to interphase cancellation between overlapping components of opposite polarity of the motor unit action potentials, which constitute the CMAP. Moreover, the degree of motor conduction block was found to be related not necessarily to the percentage of axons with conduction block, because conduction block in the largest axons exerts disproportionately large effects on CMAP size with consequent overestimation of motor conduction block; the reverse is true for conduction block in the smallest axons. Because of these findings and because the phenomenon of interphase cancellation also occurs in axonal polyneuropathies and in ALS, criteria for motor conduction block have become much more restrictive. Consensus criteria for the diagnosis of motor conduction block, including amplitude reduction of >50% and duration increase of <30% of the negative peak of the CMAP in the presence of a distal CMAP amplitude >20% of the lower limit of normal values, have been published[22] and were adhered to in designing our proposed new criteria set for definite primary demyelination.

Since the definition of values for abnormality of each of the four parameters of motor nerve conduction in our proposed criteria set is based on full specificity with regard to ALS and DPN, it is clear that abnormality of one single parameter in a given patient is predictive of primary demyelination. However, combination of two abnormal parameters was deemed necessary with regard to F-wave absence and motor conduction block. As F-wave absence in 2 nerves inherently represents a nonspecific finding and only provides indirect information on primary demyelination, we added an abnormality of 1 other parameter in 1 other nerve for F-wave absence to be a valid criterion. Motor conduction block represents the single most specific indicator of demyelination. Because of the restrictive nature of criteria for motor conduction block, sensitivity is low when it is required in 2 nerves. To improve the yield, motor conduction block in 1 nerve together with another abnormality in 1 other nerve was included in the criteria. Considering full specificity, our new criteria set produces higher sensitivity levels for both GBS and CIDP than those obtained with the ten published sets we have studied. Our data indicate, however, that electrodiagnostic evidence of primary demyelination can be obtained in the majority of patients, but not all.

The question may arise as to whether separate criteria should be applied in GBS and CIDP. In fact, sets B, C, H, I, and J were specifically designed for CIDP, whereas the other five sets were developed for GBS. Figure 1 shows that sensitivity levels were systematically lower in GBS than in CIDP, regardless of their original intent. The main reason for this discrepancy appears to be the difference in time course between the two conditions. Motor nerve conduction abnormalities in GBS have been reported to increase progressively, with a peak at 3 weeks after onset. Albers et al.[4] found evidence of demyelination in 50%, 50%, and 85% of patients at 1, 2, and 3 weeks, respectively, after disease onset. In the study by Meulstee et al.,[19] 60%, 66%, and 72% of patients fulfilled criteria at 1, 2, and 4 weeks, respectively. These findings indicate that sensitivity levels in GBS at 3–4 weeks after onset are comparable to those in CIDP. In our study, slightly lesser sensitivity of criteria in GBS as compared with CIDP may be explained by the fact that electrodiagnostic studies were performed within the first 2 weeks of the disease course in 21 (40%) of the 53 GBS patients. Indeed, 6 of our 15 GBS patients not fulfilling criteria were studied within the first 2 weeks.

Besides the timing of electrodiagnostic studies in GBS, two factors were associated with failure to meet criteria: motor nerve inexcitability and mild disease. These findings suggest that studying GBS patients at 3–4 weeks after disease onset and studying more nerves (e.g., 8 motor nerves in 4 limbs) in both GBS and CIDP may increase sensitivity. Assessment of distal CMAP duration has been proposed as a novel criterion for primary demyelination in GBS[19] and in CIDP.[26] Dispersion of the distal CMAP was found to be significantly increased in CIDP but not in DPN and ALS.

In conclusion, the results presented herein indicate that 8 of 10 published sets of criteria for primary demyelination lack specificity, particularly with regard to DPN, and that sensitivity of one of the two fully specific sets is low because more than one parameter is required to be abnormal. Our results show that it is possible to design a criteria set wherein the combination of stringency for individual parameters and requirement for one abnormal parameter yields high sensitivity and full specificity. Our new criteria set needs to be validated by testing in patient databases from other investigators and by prospective studies, controlling for potential selection bias and investigating whether bilateral electrodiagnostic studies are helpful and also whether distal CMAP dispersion is a useful adjunct criterion for primary demyelination.

The authors thank Ph. Jacquerye, MD, for assistance in reviewing patient files and C. Beguin, MD, for statistical advice.

REFERENCES

1. Abu-Shakra SR, Cornblath DR, Avila OL, Chaudhry V, Freimer M, Glass JD, Reim JW, Ronnett GV. Conduction block in diabetic neuropathy. Muscle Nerve 1991;14:858–862.
2. Ad Hoc Subcommittee of the American Academy of Neurology AIDS Task Force. Research criteria for diagnosis chronic inflammatory demyelinating polyneuropathy. Neurology 1991;41:617–618.
3. Alam AT, Chaudhry V, Cornblath DR. Electrophysiological studies in the Guillain–Barré syndrome: distinguishing subtypes by published criteria. Muscle Nerve 1998;21:1275–1279.
4. Albers JW, Donofrio PD, McGonagle TK. Sequential electrodiagnostic abnormalities in acute inflammatory demyelinating polyradiculoneuropathy. Muscle Nerve 1985;8:528–539.
5. Albers JW, Kelly JJ Jr. Acquired demyelinating polyneuropathies: clinical and electrodiagnostic features. Muscle Nerve 1989;12:435–451.
6. Asbury AK, Cornblath DR. Assessment of current diagnostic criteria for Guillain–Barré syndrome. Ann Neurol 1990; 27(suppl):S21–24.
7. Barohn RJ, Kissel JT, Warmolts JR, Mendell JR. Chronic inflammatory demyelinating polyradiculoneuropathy. Arch Neurol 1989;46:878–884.
8. Bromberg MB. Comparison of electrodiagnostic criteria for primary demyelination in chronic polyneuropathy. Muscle Nerve 1991;10:968–976.
9. Brooks BR, Miller RG, Swash M, Munsat TL. World Federation of Neurology. Research Group on Motor Neuron Diseases. El Escorial revisited: revised criteria for the diagnosis of amyotro-

phic lateral sclerosis. A consensus conference held at Airlie House. www.wfnals.org/oldsite/Articles/elescorial1998.htm.
10. Brown WF, Feasby TE. Conduction block and denervation in Guillain–Barré polyneuropathy. Brain 1984;107:219–239.
11. Daube JR. Electrodiagnostic studies in amyotrophic lateral sclerosis and other motor neuron disorders. Muscle Nerve 2000;23:1488–1502.
12. Dyck JB, Dyck PJ. Diabetic polyneuropathy. In: Dyck PJ, Thomas PK, editors. Diabetic neuropathy, 2nd ed. Philadelphia: W. B. Saunders; 1999. p 255–278.
13. Feasby TE, Brown WF, Gilbert JJ, Hahn AF. The pathological basis of conduction block in human neuropathies. J Neurol Neurosurg Psychiatry 1985;48:239–244.
14. Hadden RDM, Hughes RAC, Cornblath DR, Zielasek J, Hartung H-P, Toyka KV, Swann AV. Electrophysiological classification of Guillain–Barré syndrome: Clinical associations and outcome. Ann Neurol 1998;44:780–788.
15. Herrmann DN, Ferguson ML, Logigian EL. Conduction slowing in diabetic distal polyneuropathy. Muscle Nerve 2002;26: 232–237.
16. Ho TW, Mishu B, Li CY, Gao CY, Cornblath DR, Griffin JW, Asbury AK, Blaser MJ, McKhann GM. Guillain–Barré syndrome in northern China. Relationship to *Campylobacter jejuni* infection and antiglycolipid antibodies. Brain 1995;118:597–605.
17. Hughes R, Bensa S, Willison HJ, Van den Bergh P, Comi G, Illa I, Nobile-Orazio E, van Doorn P, Dalakas M, Bojar M, Swan A, and the INCAT Group. Randomized controlled trial of intravenous immunoglobulin versus prednisolone in chronic inflammatory demyelinating polyradiculoneuropathy. Ann Neurol 2001;50:195–201.
18. Italian Guillain–Barré Study Group. The prognosis and main prognostic indicators of Guillain–Barré syndrome. Brain 1996;119:2053–2061.
19. Meulstee J, van der Meché F, and the Dutch Guillain–Barré Study Group: Electrodiagnostic criteria for polyneuropathy and demyelination: application in 135 patients with Guillain–Barré syndrome. J Neurol Neurosurg Psychiatry 1995;59:482–486.
20. Nicolas G, Maisonobe T, Le Forestier N, Léger JM, Bouche P. Proposed revised electrophysiological criteria for chronic inflammatory demyelinating polyradiculoneuropathy. Muscle Nerve 2002;25:26–30.
21. Oh SJ, Kim DE, Kuruoglu HR. What is the best diagnostic index of conduction block and temporal dispersion? Muscle Nerve 1994;17:489–493.
22. Olney RK. Guidelines in electrodiagnostic medicine: consensus criteria for the diagnosis of partial conduction block. Muscle Nerve 1999;22(suppl):S225–S229.
23. Rhee EK, England JD, Sumner AJ. A computer simulation of conduction block: effects produced by actual block versus phase cancellation. Ann Neurol 1990;28:146–156.
24. Saperstein DS, Katz JS, Amato AA, Barohn RJ. Clinical spectrum of chronic acquired demyelinating polyneuropathies. Muscle Nerve 2001;24:311–324.
25. Swash M. Clinical features and diagnosis of amyotrophic lateral sclerosis. In: Brown RH Jr, Meininger V, Swash M, editors. Amyotrophic lateral sclerosis. London: Martin Dunitz; 2000. p 3–30.
26. Thaisetthawatkul P, Logigian EL, Herrmann DN. Dispersion of the distal compound muscle action potential as a diagnostic criterion for chronic inflammatory demyelinating polyneuropathy. Neurology 2002;59:1526–1532.
27. Taylor PK. CMAP dispersion, amplitude decay, and area decay in a normal population. Muscle Nerve 1993;16:1181–1187.
28. Weber F. Conduction block and abnormal temporal dispersion—diagnostic criteria. Electromyogr Clin Neurophysiol 1997;37:305–309.