Chronic Inflammatory Demyelinating Polyradiculoneuropathy

A Study of Proposed Electrodiagnostic and Histologic Criteria

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Objective: To examine the sensitivity of the 3 proposed electrodiagnostic (EDX) criteria for demyelination, the sensitivity and specificity of the proposed Ad Hoc Subcommittee of the American Academy of Neurology AIDS [Acquired Immunodeficiency Syndrome] Task Force histologic criteria (AAN criteria), the degree of agreement among these criteria, and the diagnostic value of sural nerve histologic criteria in patients with idiopathic chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

Design and Methods: A retrospective analysis of 24 patients with idiopathic CIDP and 12 patients with diabetic polyneuropathy (DP) who underwent comparable testing of clinical, histologic, and EDX features.

Results: We found 42%, 50%, and 79% sensitivity of the proposed EDX, AAN teased fiber, and AAN electron microscopic (EM) criteria, respectively, for demyelination in CIDP. The specificity of the proposed AAN teased fiber and EM criteria for demyelination was greater than 80% when tested against patients with DP. There was lack of agreement between the EDX and histologic criteria. Almost two thirds of patients with CIDP who met the EM criteria but none of the EDX criteria for demyelination showed a favorable response to immunomodulatory therapy.

Conclusions: Sural nerve histologic criteria offer unique sensitivity and acceptable specificity toward the diagnosis of CIDP. Sural nerve biopsy should be considered when a clinical suspicion of CIDP remains in patients who do not meet the proposed EDX criteria for demyelination.

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PATIENTS AND METHODS

PATIENT SELECTION

We reviewed medical records of all patients with a clinical and electrophysiologic diagnosis of polyneuropathy at the Medical Center Hospital of Vermont–Fletcher Allen Health Care, Burlington, between 1983 and 1997. From this group of approximately 1200 patients, we identified 24 patients who met the clinical criteria for the diagnosis of CIDP and had undergone sural nerve biopsy. The clinical criteria were modified from those first published by Dyck et al and included the following: symmetric distal and/or proximal limb involvement (predominantly motor or sensory), mainly large-fiber sensory loss when present; progressive or relapsing course of at least 8 weeks' duration; and albuminocytologic dissociation in CSF. All these patients were required to show EDX features of an acquired, multifocal, demyelinating polyneuropathy, as judged by the electromyographer. Other causes of polyneuropathy were excluded by appropriate testing.

We also reviewed the charts of approximately 300 patients with diabetic polyneuropathy (DP) diagnosed clinically. Twelve patients with DP who had undergone comparable testing (electrophysiologic and histologic), and in whom other causes of polyneuropathy were excluded, were available for comparison with patients with CIDP.

EDX STUDIES

Motor nerve conduction studies were performed using standard techniques of supramaximal percutaneous stimulation and surface electrode recording. Proximal stimulation sites for median, ulnar, and peroneal conductions were below the elbow and fibular head, respectively. The EDX data examined included compound muscle action potential amplitude, conduction block or temporal dispersion, conduction velocity, distal latency, and F-wave latency as previously described. These measurements were converted to percentage of laboratory norms for each nerve in each patient. These values were then used to determine the percentage of patients who fulfilled the proposed EDX criteria for demyelination in sets A, B, and C (Table 1). Data from nerves that did not show a response were excluded, except F-wave latency values, which were included for analysis of criteria in set B.

HISTOLOGIC STUDIES

Sural nerve biopsy was performed in all patients using standard techniques for biopsy, sample preparation, and analysis. Biopsy specimens were reviewed in a blinded fashion by 3 of us (R.U.H., W.W.P., and R.T.) who are fellowship-trained neurologists with experience in nerve and muscle histology. Plastic-embedded sections, 1-µm thick, stained with toluidine blue were reviewed for light microscopy, for morphometric analysis of nerves, and to qualitatively determine the presence of each of the AAN supportive histologic criteria for demyelination (Table 2). Selected areas of thin sections were stained with lead citrate–uranyl acetate and subjected to electron microscopy (EM). Teased fiber analysis identified pathologic conditions denoting axonal degeneration (conditions E and H) and demyelination or remyelination (conditions C, D, F, and G) as described by Dyck et al. Nerve fibers were considered to be undergoing active demyelination under EM if macrophage-mediated demyelination (myelin stripping), myelin debris-laden macrophages in the endoneurium in association with thinly myelinated fibers, or complete demyelination of fibers without evidence of remyelination (naked axons) in more than 5 fibers (AAN mandatory EM criterion) were present.

To further examine the specificity of myelin stripping and naked axons seen on EM, at least one of these ultrastructural pathologic features was required to be present in at least one section to be counted as an abnormality. For EM, a mean of 18 sections (range, 9-36) at magnifications of 1250 to 12000 was examined from each nerve.

STATISTICAL ANALYSIS

Demographic characteristics in patients with CIDP and DP were compared using the t test for continuous measures and the Fisher exact test for categorical variables. The McNemar test for correlated proportions was used to examine differences in sensitivity and specificity of the diagnostic criteria. Likelihood ratios quantified the proportion of patients with CIDP compared with patients with DP who met the criteria. The κ statistic was used as a measure of agreement between histologic and EDX criteria in patients with CIDP. Response to treatment was evaluated using t tests and Fisher exact test. P<.05 was considered statistically significant. All analyses were performed using SAS statistical software (SAS Institute Inc, Cary, NC).

RESULTS

DEMOGRAPHIC FEATURES

The demographic features of the 24 patients with CIDP and 12 patients with DP are presented in Table 3. Among the patients with CIDP, 17 were walking independently and 7 were walking with assistance at initial evaluation. The severity of motor dysfunction was measured by an ordinal scale, which we have previously described. Weakness was only distal in 7 patients, only proximal in 5 patients, and predominantly distal in 12 patients. Sensory impairment was of the large fiber type in 20 patients, of the small fiber type in 2 patients, and absent in 2 patients. There were no significant differences between patients with CIDP and DP with respect to recorded demographic characteristics.

The clinical features, including sex, duration of symptoms, clinical course and level of disability, motor and sensory involvement, and CSF protein levels, were not significantly different between patients with CIDP who met at least one set of EDX criteria and those who did not.
EDX CRITERIA FOR DEMYELINATION

At least one set of EDX criteria for demyelination (Table 1) was fulfilled by 42% of patients with CIDP. Overall, 33% of patients met criteria for demyelination in set A and set B each and 29% in set C. Differences in sensitivity among the 3 sets of criteria were not statistically significant (McNemar test, \( P > .99 \) for all comparisons). None of the patients with DP fulfilled any set of EDX criteria.

SENSITIVITY, SPECIFICITY, AND DIAGNOSTIC VALUE OF NERVE HISTOLOGIC CRITERIA

The sensitivity and specificity of the AAN histologic criteria are given in Table 4. There was a trend toward significance in the proportion of patients with CIDP who met the AAN EM criterion compared with those who met the AAN teased fiber criterion (79% vs 50%, respectively; McNemar test, \( P = .07 \)). The AAN EM criterion for demyelination was fulfilled by 79% of patients with CIDP and 9% of patients with DP (Fisher exact test; \( P = .05 \)). Among the AAN supportive histologic criteria for demyelination in patients with CIDP, endoneurial edema and subperineurial edema were more frequently present than perivascular inflammatory cells and onion bulbs (McNemar test, \( P < .05 \)). Similarly, onion bulbs were more frequently present than perivascular inflammatory cells (McNemar test, \( P = .05 \)). Subperineurial and endoneurial edema were present in significantly higher numbers of patients with CIDP than patients with DP (100% vs 67% for subperineurial edema, 94% vs 38% for endoneurial edema; Fisher exact test, \( P < .05 \) for both comparisons). Among the specific ultrastructural features of demyelination, naked axons and active myelin stripping were seen only in patients with CIDP (46% vs 0%; Fisher exact test, \( P < .05 \) for both comparisons).

Axonal pathologic condition at teasing was seen in nerves from 17 (71%) of 24 patients with CIDP. Overall, a mean of 5% of teased fibers showed axonal degeneration in CIDP nerves (range, 2%-16%). The likelihood ratio for CIDP was 8.77 for the AAN EM criterion and 2.94 for teasing (Table 4). The presence of naked axons and myelin stripping was universally predictive of the diagnosis of CIDP.

### Table 1. Proposed Electrodiagnostic Criteria for Demyelination*

**Set A**
- Must demonstrate 3 of the following abnormalities in motor nerves:
  1. Reduced conduction velocity in 2 or more nerves to <75% of LLN
  2. Partial conduction block or abnormal temporal dispersion in 1 or more nerves to <70% P/D ratio
  3. Prolonged distal latency in 2 or more nerves to >130% of ULN
  4. Prolonged F-wave latency in 1 or more nerves to >130% of ULN

**Set B**
- Must demonstrate 3 of the following abnormalities in motor nerves:
  1. Reduced conduction velocity in 2 or more nerves of <80% of LLN if CMAP amplitude >80% of LLN or <70% of LLN if CMAP amplitude <80% of LLN
  2. Partial conduction block or abnormal temporal dispersion in 1 or more nerves (median, ulnar, or peroneal):
    - Partial conduction block of <80% P/D ratio if duration of negative peak of proximal CMAP is <115% of distal CMAP duration
    - Abnormal temporal dispersion and possible conduction block of <80% P/D ratio if duration of negative peak of proximal CMAP is >115% of distal CMAP duration
  3. Prolonged distal latency in 2 or more nerves of >125% of ULN if CMAP amplitude is >80% of LLN or >150% of ULN if CMAP amplitude is <80% of LLN
  4. Prolonged F-wave latency in 2 or more nerves of >120% of ULN if CMAP amplitude is >80% of LLN or >150% of ULN if CMAP amplitude is <80% of LLN or absent F-waves after 10 to 15 trials

**Set C**
- Must demonstrate the following abnormality in motor nerves:
  1. Reduced conduction velocity in 2 or more nerves to <70% of LLN

* LLN indicates lower limit of normal; P/D, proximal-distal; ULN, upper limit of normal; and CMAP, compound muscle action potential.

### Table 2. Pathologic Criteria for Demyelination Proposed by the Ad Hoc Subcommittee of the American Academy of Neurology AIDS* Task Force (AAN Criteria)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Patients With CIDP (n = 24)</th>
<th>Patients With DP (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Mandatory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nerve biopsy specimen showing unequivocal evidence of demyelination and remyelination:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Demyelination by either electron microscopy (&gt;5 fibers) or teased fiber studies (&gt;12% of 50 teased fibers, minimum of 4 internodes each, demonstrating demyelination or remyelination)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B. Supportive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Subperineurial or endoneurial edema</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Mononuclear cell infiltration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Onion bulb formation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Prominent variation in the degree of demyelination between fascicles</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C. Exclusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Vasculitis, neurofilamentous swollen axons, amyloid deposits, or intracytoplasmic inclusions in Schwann cells or macrophages, indicating adrenoleukodystrophy, metachromatic leukodystrophy, globoid cell leukodystrophy, or other evidence of specific pathologic condition</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*AIDS indicates acquired immunodeficiency syndrome.

### Table 3. Demographic Characteristics of Study Patients*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients With CIDP (n = 24)</th>
<th>Patients With DP (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at initial evaluation,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (range), y</td>
<td>54 (27-78)</td>
<td>61 (28-78)</td>
</tr>
<tr>
<td>Disease duration at initial</td>
<td></td>
<td></td>
</tr>
<tr>
<td>evaluation, mean (range),</td>
<td>29 (2-120)</td>
<td>21 (2-72)</td>
</tr>
<tr>
<td>mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Functional disability†</td>
<td>4 (1-10)</td>
<td>5.3 (2-12)</td>
</tr>
<tr>
<td>Highest CSF protein level,</td>
<td>114 (22-640)</td>
<td>NA</td>
</tr>
<tr>
<td>mean (range), mg/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical course</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progressive</td>
<td>20</td>
<td>12</td>
</tr>
<tr>
<td>Relapsing</td>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>

* CIDP indicates chronic inflammatory demyelinating polyradiculoneuropathy; DP, diabetic polyneuropathy; CSF, cerebrospinal fluid; and NA, not applicable.
† Grading system from Donofrio et al.**
patients with normal CSF protein levels (Fisher exact test, \( P = .07 \)). A favorable response to treatment was seen in 75% of patients, irrespective of whether they fulfilled the AAN teased fiber criterion (6 of 8 in each group). A favorable response was seen in 12 (86%) of 14 patients who fulfilled the AAN EM criterion (Fisher exact test, \( P = .05 \)).

Patients who responded to treatment but did not meet EDX criteria showed the following characteristics: symmetric distal weakness, predominantly large-fiber sensory loss, elevated CSF protein level, motor conduction velocity of less than 80% of lower limit of normal in at least one nerve, and conduction block of more than 20% in at least one nerve. All these patients’ nerves demonstrated histologic demyelination that fulfilled the AAN EM criterion.

The results of our retrospective analysis in patients with idiopathic CIDP show several interesting findings. These include (1) similar sensitivity of the 3 proposed EDX criteria for demyelination; (2) similar sensitivity of the proposed EDX criteria for demyelination and the AAN teased fiber criterion; (3) greater sensitivity of the AAN EM compared with the proposed EDX and teased fiber criteria; (4) similar specificity of the AAN teased fiber and EM criteria; (5) ability of nerve biopsy to identify significant demyelinating pathologic conditions even in patients who did not meet EDX criteria for demyelination; (6) lack of agreement between the proposed EDX and histologic criteria for demyelination; (7) universal response to immunomodulatory therapy in patients who met at least one set of EDX criteria and response in most patients who fulfilled the AAN EM criterion; and (8) successful response to immunomodulatory therapy in 50% to 75% of patients who did not fulfill EDX or AAN teased fiber criteria.

**Table 4. Sensitivity and Specificity of AAN Histologic Criteria and Likelihood Ratio for Positive CIDP Test Result**

<table>
<thead>
<tr>
<th>AAN mandatory histologic criteria</th>
<th>Sensitivity† (n = 24)</th>
<th>Specificity‡ (n = 12)</th>
<th>Likelihood Ratio§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teased fiber</td>
<td>0.50</td>
<td>0.83</td>
<td>2.94</td>
</tr>
<tr>
<td>AAN EM</td>
<td>0.79</td>
<td>0.91</td>
<td>8.77</td>
</tr>
</tbody>
</table>

**Table 5. Agreement Between the Proposed Electrodiagnostic and Histologic Criteria in Patients with Chronic Inflammatory Demyelinating Polyradiculoneuropathy**

<table>
<thead>
<tr>
<th>Teased Fiber Criterion</th>
<th>AAN EM Criterion</th>
<th>No</th>
<th>Yes</th>
<th>( k )</th>
<th>No</th>
<th>Yes</th>
<th>( k )</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least 1 set of electrodiagnostic criteria met</td>
<td></td>
<td>7</td>
<td>7</td>
<td>0.00</td>
<td>5</td>
<td>9</td>
<td>0.32</td>
</tr>
<tr>
<td>Set A</td>
<td></td>
<td>5</td>
<td>5</td>
<td>0.00</td>
<td>0</td>
<td>10</td>
<td>0.32</td>
</tr>
<tr>
<td>Set B</td>
<td></td>
<td>8</td>
<td>8</td>
<td>0.00</td>
<td>5</td>
<td>11</td>
<td>0.23</td>
</tr>
<tr>
<td>Set C</td>
<td></td>
<td>4</td>
<td>4</td>
<td>0.17</td>
<td>0</td>
<td>8</td>
<td>0.23</td>
</tr>
</tbody>
</table>
| Teased fiber criterion of more than 12% fibers with demyelination; AAN EM criterion (6 of 8 in each group). A favorable response was seen in 12 (86%) of 14 patients who fulfilled the AAN EM criterion (Fisher exact test, \( P = .05 \)).

**Table 5. Agreement Between the Proposed Electrodiagnostic and Histologic Criteria in Patients with Chronic Inflammatory Demyelinating Polyradiculoneuropathy**

### AGREEMENT BETWEEN EDX AND HISTOLOGIC CRITERIA

There was lack of agreement between the EDX and histologic criteria for demyelination (\( \kappa \) range, \(-0.08\) to \(0.32\); Table 5). Comparing EDX criteria (any one set fulfilled) with the AAN teased fiber criterion revealed that the discrepancy was nondirectional, ie, patients were no more likely to fulfill one criterion than the other (Table 5). However, the discrepancy between the EDX criteria (any one set fulfilled) and the AAN EM criterion corresponded to patients who met the EM but not the EDX criteria (Table 5).

### RESPONSE TO TREATMENT

Response to conventional treatments used in CIDP was deemed successful if patients were cured, significantly improved, or able to return to their previous occupation and were functioning independently for a minimum of 6 months. Sixteen of the 24 patients were treated, and in 8 patients, it was mutually decided not to treat because of mild or stable disease. Prednisone was used alone in 12 patients, with plasmapheresis in 1 patient, and with intravenous immune globulin in 2 patients; 1 patient received all 3 modalities during illness. A favorable response to treatment was seen in 12 (75%) of 16 treated patients.

Response was universal in the 8 patients who fulfilled at least one set of EDX criteria and was seen in 4 (50%) of 8 patients who did not meet any set of EDX criteria for demyelination (Fisher exact test, \( P<.05 \)). A favorable response was seen in 7 (88%) of 8 patients with elevated CSF protein levels compared with 1 (25%) of 4 patients with normal CSF protein levels (Fisher exact test, \( P=.07 \)). A favorable response to treatment was seen in 75% of patients, irrespective of whether they fulfilled the AAN teased fiber criterion (6 of 8 in each group). A favorable response was seen in 12 (86%) of 14 patients who fulfilled the AAN EM criterion (Fisher exact test, \( P = .05 \)).

Patients who responded to treatment but did not meet EDX criteria showed the following characteristics: symmetric distal weakness, predominantly large-fiber sensory loss, elevated CSF protein level, motor conduction velocity of less than 80% of lower limit of normal in at least one nerve, and conduction block of more than 20% in at least one nerve. All these patients’ nerves demonstrated histologic demyelination that fulfilled the AAN EM criterion.

### COMMENT

The results of our retrospective analysis in patients with idiopathic CIDP show several interesting findings. These include (1) similar sensitivity of the 3 proposed EDX criteria for demyelination; (2) similar sensitivity of the proposed EDX criteria for demyelination and the AAN teased fiber criterion; (3) greater sensitivity of the AAN EM compared with the proposed EDX and teased fiber criteria; (4) similar specificity of the AAN teased fiber and EM criteria; (5) ability of nerve biopsy to identify significant demyelinating pathologic conditions even in patients who did not meet EDX criteria for demyelination; (6) lack of agreement between the proposed EDX and histologic criteria for demyelination; (7) universal response to immunomodulatory therapy in patients who met at least one set of EDX criteria and response in most patients who fulfilled the AAN EM criterion; and (8) successful response to immunomodulatory therapy in 50% to 75% of patients who did not fulfill EDX or AAN teased fiber criteria.
SENSITIVITY OF THE PROPOSED EDX CRITERIA FOR DEMYELINATION

The overall sensitivity of the 3 proposed EDX criteria for primary demyelination is not significantly different in our patients, suggesting that the stringent requirements of criteria in set B may not add to the diagnosis of CIDP compared with the less complex criteria in sets A and C. The sensitivity of these 3 proposed criteria is lower in our patients than that reported from another center, perhaps because the latter series included only patients with CIDP who responded to immunotherapy. We, on the other hand, included patients with a clinical diagnosis of CIDP regardless of their eventual response to immunotherapy. Although a successful response to immunotherapy aids in the diagnosis of CIDP, others have shown a lack of response in 21% to 47% of patients given an adequate trial of high-dose steroid therapy. We therefore agree with Bromberg that these proposed EDX criteria for demyelination are restrictive, and since these criteria fail to identify patients with CIDP who exhibit lesser degrees of demyelination yet show a favorable response to immunotherapy, they need to be reconsidered.

SENSITIVITY AND SPECIFICITY OF PROPOSED TEASED FIBER CRITERION FOR DEMYELINATION AND REMYELINATION

Our study shows similar sensitivity of the AAN teasing criterion and the proposed EDX criteria for demyelination in CIDP. The sensitivity of teasing is identical in patients who fulfill and those who do not fulfill any EDX criteria for demyelination, thus corroborating the value of nerve histologic criteria, beyond the information gained from electrophysiology, in the diagnosis of CIDP. These results are at variance with those recently reported by Molenaar et al., who showed no additional diagnostic value of sural nerve biopsy in 23 patients with CIDP. Their study was biased toward including a higher proportion of patients who met the modified set A EDX criterion for demyelination (87% of patients); furthermore, EM was not performed in almost half their patients’ nerves, and demyelinating pathologic conditions were not quantitated. Thus, with an already high sensitivity of electrophysiologic studies and a lack of quantitative pathologic conditions in nerves, the likelihood of additional diagnostic yield of sural nerve histologic criteria was not surprisingly small. Higher than 80% specificity of the AAN teased fiber criterion in our study, when examined against nerves of patients with DP, suggests that pathologic conditions detected by teasing adds to the certainty of diagnosis of CIDP.

SENSITIVITY AND SPECIFICITY OF PROPOSED EM CRITERIA FOR DEMYELINATION

Our findings show that the AAN EM criterion is almost twice as sensitive as the 3 sets of proposed EDX criteria and the AAN teased fiber criterion in idiopathic CIDP. The specificity of the EM criterion, when compared against nerves from patients with DP, is greater than 90%. Although 9% of nerves from patients with DP showed acute demyelination that fulfilled the AAN EM criterion, the absence of myelin stripping and naked axons in these nerves could have been due to our small sample size and the retrospective nature of the study. We believe that the EM criterion for demyelination and presence of myelin stripping and naked axons offers unique sensitivity and specificity toward the diagnosis of CIDP.

AGREEMENT BETWEEN THE PROPOSED EDX AND HISTOLOGIC CRITERIA IN CIDP

The number of patients fulfilling the AAN teased fiber criterion was similar regardless of whether the proposed EDX criteria for demyelination were met (Table 5). In 56 patients with CIDP, Barohn et al. found that slow motor conduction, whether less than 70% or greater than 70% of normal laboratory value, did not predict demyelination or remyelination in teased fibers from sural nerves. These data imply a lack of correlation between demyelination identified electrophysiologically and demyelination identified by teased fiber analysis. Our results also show lack of agreement between the EDX and histologic criteria for demyelination and are similar to those reported by Barohn et al.

This lack of agreement between EDX and histologic criteria in CIDP is probably multifactorial. First, the EDX criteria for demyelination examine motor nerves, whereas the histologic criteria pertain to a sensory nerve. Second, the biopsy site in the sural nerve is usually distal, whereas most of the EDX criteria for demyelination (F-wave latency, conduction velocity, conduction block, temporal dispersion) measure abnormalities either in more proximal segments of motor nerves in the legs or in the arms. Third, pathologic alterations in nerves of patients with CIDP are patchy, both within and between nerves, and may thus involve individual nerves to different degrees.

VALUE OF NERVE HISTOLOGIC CRITERIA IN CIDP

We believe that patients who did not meet the EDX criteria for demyelination in our study had CIDP, for several reasons. Data from our study show similar clinical features in patients who did not meet EDX criteria for demyelination and in those fulfilling these criteria. Furthermore, half of the patients who did not fulfill EDX criteria for demyelination responded favorably to immunotherapy. Since a larger number of patients in our study fulfilled the histologic criteria for demyelination compared with the EDX criteria, nerve histologic criteria added significantly to the diagnosis of CIDP. Among the 7 of 14 patients who met the AAN teased fiber criterion but none of the EDX criteria for demyelination, 3 patients treated adequately with steroids (without or with intravenous immune globulin) responded, 2 received an insufficient trial (60 mg of prednisone daily for 4 to 6 weeks only) and showed no improvement, and 2 were not treated because of mild disease. Similarly, among the 9 of 14 pa-
tients who fulfilled the AAN EM criterion but none of the EDX criteria for demyelination, 4 patients treated adequately with immunomodulators responded, 2 were insufficiently treated (as above) and did not improve, and 3 were not treated because of minimal involvement. The polyneuropathy in patients who did not meet EDX criteria for demyelination, but responded to immunotherapy, could have been misdiagnosed as idiopathic were it not for the unequivocal histologic evidence of demyelination in their nerve biopsy specimens.

In view of the low sensitivity of the proposed EDX criteria and higher sensitivity and specificity of histologic criteria in CIDP, we suggest that valuable information can be obtained from nerve biopsy specimens, particularly when EDX studies show equivocal features of demyelination based on existing criteria.

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REFERENCES