We reviewed 180 electroneuromyographic (EMG) studies from patients with acute inflammatory demyelinating polyradiculoneuropathy. EMG criteria suggestive of demyelination were met during the first 5 weeks in 87% of patients; an additional 10% had indeterminate electrodiagnostic evaluations, and 3% demonstrated axonal degeneration only. Motor nerve conduction abnormalities initially predominated, with the nadir of abnormality occurring at week 3. Sensory nerve conduction abnormalities peaked during week 4 and were atypical for polyneuropathy, with 52% of patients having normal sural but abnormal median sensory studies, perhaps reflecting distal nerve involvement. Delayed sensory abnormalities may reflect, in part, secondary involvement related to increased intraneural edema accentuated by compression at sites of anatomic vulnerability. Fibrillation potentials and increased polyphasia appeared between weeks 2 and 5 in proximal and distal muscles simultaneously, which is consistent with either random axonal degeneration at any point along the axon or distal involvement. Resolution of conduction abnormalities began between weeks 6 and 10, with increased mean motor-evoked amplitude best reflecting functional clinical recovery.

MUSCLE & NERVE 8:528–539 1985

SEQUENTIAL ELECTRODIAGNOSTIC ABNORMALITIES IN ACUTE INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY

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A variety of electrodiagnostic findings have been reported for patients with acute inflammatory demyelinating polyradiculoneuropathy (AIDP) (acute idiopathic polyradiculoneuritis, Guillain-Barré syndrome [GBS]).[13,16,18,20,24,26] The reported abnormalities are thought to reflect both the multifocal nature of the disorder and the combination of demyelination with varying amounts of secondary axonal degeneration. In addition, the variable electrodiagnostic findings unquestionably reflect the time at which studies are performed relative to disease onset, recognizing that temporal changes occur in response to cumulative demyelination and axonal degeneration. Surprisingly, temporal findings in conventional electrodiagnosis have received little consideration.[21] Patients with AIDP frequently have multiple electrodiagnostic evaluations, either to clarify the diagnosis or to establish the prognosis. We reviewed our experience over a 5-year period with the electrodiagnostic evaluation of patients fulfilling clinical criteria for AIDP. Findings were grouped as a function of time after onset of neurologic symptoms to see if this resulted in identification of specific electrodiagnostic patterns that were not previously appreciated. In addition, we hoped that the temporal grouping would provide further understanding of the underlying peripheral nerve pathophysiology in AIDP.

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Acknowledgments: The authors wish to thank Drs. James A. Leonard, Jr, Steven R. Geiringer, and Richard D. Ball for their help in performing and interpreting the electrodiagnostic evaluation, and Cathy J. Olszewski and Andrew J. Miller for their technical assistance. We also are grateful to Pamela Stegath and Barbara C. Stanley for their skillful secretarial assistance in preparation of the manuscript.

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Presented in part at the Thirty-First Annual Meeting of the American Association of Electromyography and Electrodiagnosis, Kansas City, MO, September 22, 1984.

Received for publication August 3, 1984; revised manuscript accepted for publication November 15, 1984.

0148-639X/0806/0528 $04.00

MATERIALS AND METHODS

Clinical and electrodiagnostic records were reviewed of all patients evaluated by the Neurology Departments at the Medical College of Wis-

consin (July 1977 through June 1979) and by the Neurology and Physical Medicine and Rehabilitation Departments at the University of Michigan Medical Center (July 1978 through June 1983) and found to have a final clinical diagnosis of AIDP. Only patients 3 years of age and older who fulfilled conventional diagnostic clinical criteria[3-6,12,14,25,28] were included. Criteria required demonstration of weakness of multiple limbs (ranging from mild weakness of legs to complete paralysis of all extremity, bulbar, facial, and trunk muscles) and areflexia or definite hyporeflexia. *Progression* of weakness during the initial phase of the illness, plateauing by week 6, also was required. Features strongly supportive of a diagnosis of AIDP were identical to those described by Asbury,[5,6] including relative symmetry, mild sensory symptoms and signs, cranial nerve involvement (particularly facial), improvement after a plateau phase, autonomic involvement, and absence of fever at onset of neurologic symptoms (unless a specific cause of transient fever was identified). Patients with any suggestion of central nervous system involvement were excluded. Transient bladder impairment was not considered to be exclusionary. All patients had cerebrospinal fluid evaluations; greater than 40 mononuclear leukocytes/cu mm would have resulted in exclusion. Following the initial selection process, all records were reviewed to identify patients with other disorders known to be associated with polyneuropathy. Excluded were patients with evidence of monoclonal gammopathy (8 patients), systemic lupus erythematosus (1), lymphoma (1), diabetes mellitus (2), renal disease (1), chronic alcohol abuse (1), acute intermittent porphyria (1), and arsenic intoxication (1). Also excluded were 30 patients having a final clinical diagnosis of chronic inflammatory demyelinating polyradiculoneuropathy. No remaining patient had clinical or historical evidence of abnormal porphyrin metabolism, hexacarbon abuse, diphtheritic infection, poliomyelitis, botulism, or lead neuropathy.

All patients had one or more electrodiagnostic evaluations, and the majority of studies were performed by one of the authors. All other studies were performed by electromyographers at the University of Michigan Medical Center. Electrodiagnostic reports were reviewed, including the original data sheets, to obtain measures of temporal dispersion, limb temperature, etc., that were not included in the final reports. Because standardized techniques and protocols existed at both institutions (Table 1), data collection was relatively uniform, although not all patients had the complete evaluation as outlined in Table 1.

Motor and sensory conduction studies were performed using the standard technique of supramaximal percutaneous stimulation and surface electrode recording. Compound muscle ac-

Table 1. Inflammatory demyelinating polyradiculoneuropathy: electrodiagnostic protocol.

Conduction studies*

1. Test most involved site when mild or moderate, least involved if severe.
2. Peroneal motor (extensor digitorum brevis); stimulate ankle and knee. Measure F-response latency.†
3. If abnormal, tibial motor (abductor hallucis); stimulate ankle and knee. Measure F-response latency.
4. If no responses:
   a. Peroneal motor (anterior tibial); stimulate fibula and above knee.
   b. Ulnar motor (hypothenar); stimulate elbow and wrist. Measure F-response latency.
   c. Median motor (thenar); stimulate elbow and wrist. Measure F-response latency.
5. Sural sensory (ankle); stimulate 14 cm from recording electrode; perform conduction velocity unless amplitude supernormal.
6. Median sensory (index); stimulate wrist and elbow. If antidromic response is absent or focal entrapment is suspected, record from the wrist stimulating the palm.
7. Additional peripheral nerves can be evaluated if findings are equivocal. Definite abnormalities should result in:
   a. Evaluation of contralateral extremity.
   b. Proceeding to evaluation of specific suspected abnormality.
8. If prominent cranial involvement:
   a. Facial motor (orbicularis oculi); stimulate at angle of jaw.
   b. Blink reflex studies (orbicularis oculi); stimulate supraorbital nerve.

Needle examination

1. Examine anterior tibial, medial gastrocnemius, abductor hallucis, vastus lateralis, biceps brachii, interosseous (hand), and lumbar paraspinal muscles.
2. Any abnormality should be confirmed by examination of at least one contralateral muscle.

**Words in parentheses indicate recording site for conduction studies.*
†All F-response latency measurements are for distal stimulation sites only.

tion potential (CMAP) and sensory nerve action potential (SNAP) amplitudes were measured from baseline to negative peak and were reported for stimulation at distal and proximal sites. Conduction velocity was measured in the forearm or leg segment, and distal latencies were converted to "terminal conduction velocity" by dividing the distance by the terminal latency. Temporal dispersion was estimated by recording the ratio of the proximal to the distal CMAP, recognizing that a reduced proximal to distal CMAP ratio can be attributed both to temporal dispersion and/or conduction block in some fibers.[19] Measurements of CMAP duration would be useful in determining the contribution of temporal dispersion, but were not available retrospectively. F-response latencies were measured as the minimal latency in a series of 10–15 F-responses using distal (wrist or ankle) antidromic motor nerve stimulation. Skin temperatures were measured and maintained above 32°C, using either warm compresses or an infrared heater.

Needle electromyography recordings were performed using standard concentric needle electrodes. Fibrillation potentials and positive waves were graded from 0 to 4+ using conventional methods: 0, no fibrillation; 1+, persistent single trains in at least two areas away from the endplate; 2+, moderate numbers in three or more areas; 3+, many in all areas; 4+, filling the baseline in all areas. Motor unit action potential (MUAP) recruitment, amplitude, and configuration (percentage polyphasia) were graded subjectively using a 5-point interval scale (0–4+) coinciding to zero, slight, mild, moderate, or severe. For recruitment, 4+ was equivalent to normal; for amplitude recordings, 4+ was equivalent to marked increase; for spontaneous activity and configuration, 0 was equivalent to normal.

All findings were summarized as a function of time following the onset of first neurologic symtoms. Weekly intervals were used for the first 5 weeks. Thereafter, data were combined for weeks 6–10, 11–15, 16–25, 26–35, and 36–50, respectively. Data for studies performed more than 50 weeks after onset were reviewed, but these 34 studies are not included in the figures because of the variable recording intervals. Conduction study results from individual nerves were expressed as a percentage of the normal mean for each nerve and then averaged for motor and sensory studies. Needle electromyographic data were similarly combined and expressed as an average for distal and proximal muscles. All data in a given time interval (e.g., 6–10 weeks) were then averaged, recognizing that such averages tend to deemphasize abnormalities in any multifocal, nonhomogeneous disorder. In addition, individual electrodiagnostic evaluations were reviewed to determine whether or not specific criteria (Table 2) for demyelination were met. These criteria were modified from those proposed by Kelly.[15] The criteria were selected so as to be highly suggestive of demyelination, recognizing that the distinction between "demyelination" and "axonal degeneration" is not always clear. There are situations attributed to pure axonal degeneration and regeneration, during which there may be considerable slowing of action potential propagation and relative preservation of the evoked response amplitude. Nevertheless, the combined criteria were felt to have substantial consensual validity, provide consistency with prior electrodiagnostic measures of "demyelination," and insure a small likelihood of misrepresenting the data.

RESULTS

Clinical. There were 32 male and 38 female patients, having an average age of 37 years (range 3–82 years). An antecedent illness was reported by

Table 2. Criteria suggestive of demyelination in the electrodiagnostic evaluation of acute inflammatory demyelinating polyradiculoneuropathy.

Demonstrate at least one of the following in two or more nerves (exceptions noted):

A. Conduction velocity less than 95% of lower limit of normal if amplitude exceeds 50% of lower limit of normal, less than 85% if amplitude less than 50% of lower limit of normal. (1)
B. Distal latency exceeding 110% of upper limit of normal if amplitude normal, exceeding 120% of upper limit of normal if amplitude less than lower limit of normal. (2)
C. Evidence of unequivocal temporal dispersion or a proximal to distal amplitude ratio less than 0.7. (2,3)
D. F-response latency exceeding 120% of upper limit of normal. (1,2)

Exceptions:

1. Excluding isolated ulnar or peroneal nerve abnormalities at the elbow or knee, respectively.
2. Excluding isolated median nerve abnormality at the wrist.
3. Excluding the presence of anomalous innervation (e.g., median to ulnar nerve crossover).

75% of patients within the 2 months prior to onset. The interval from the onset of antecedent illness to first neuropathic symptom averaged 11 days (range 1–42 days), and the interval from first neuropathic symptom to plateau of neurologic impairment averaged 15 days (range 2–33 days). Ten patients remained ambulatory; 9 of the 10 required assistance in walking. The tenth ambulatory patient had primary bulbar involvement. Mechanical respiratory assistance was required for 34% of patients and averaged 39 days (range 1–274 days). Autonomic dysfunction (instability of blood pressure or bowel or bladder abnormalities) occurred in 36% of patients. Muscle stretch reflexes were unobtainable at some time during the illness in all but 11 patients; those 11 had trace to hypoactive reflexes. No pathologic reflexes were recorded. Cerebrospinal fluid (CSF) total protein was elevated in all but three patients. The average CSF total protein was 139 mg/dl (range 25–522). The average number of CSF white blood cells was 3.0 (range 0–38).

One patient died of a severe superimposed respiratory infection. The duration of hospitalization for the remaining patients averaged 81 days (range 13–408 days). Total recovery was reported for 64% of patients; remaining patients had evidence of mild to severe (nonambulatory) neurologic impairment at 6–36 months after onset. During this interval, two patients (3%) had an unequivocal relapse.

Electrodiagnosis. Conduction study results are shown in Table 3 and Figures 1 through 4, respectively. Of these 70 consecutive patients with AIDP, conduction abnormalities were evident in the majority of patients from the time of initial evaluation. During the first 5 weeks of illness, motor conduction study abnormalities (abnormal CMAP temporal dispersion and/or conduction block, reduced amplitude, conduction velocity or terminal conduction velocity, and prolonged or absent F-responses) were more common than sensory conduction abnormalities. Normal conduction studies were unusual, and only one patient had no abnormality of conduction during the first 5 weeks of illness. Using the pooled data in Table 3, the nadir of abnormality occurred during the third week for

Table 3. Motor and sensory conduction studies in patients with AIDP evaluated 1 week to 12 months after disease onset.

	Time (weeks) after disease onset									
	1	2	3	4	5	6–10	11–15	16–25	26–35	36–50
A. Results for given time interval (weeks) after disease onset*										
Conduction studies(*N*)	8	18	26	25	19	19	8	6	12	5
Motor conduction										
Amplitude†	46 ± 13.1	28 ± 6.1	26 ± 4.1	38 ± 5.9	32 ± 6.2	35 ± 6.9	50 ± 10.3	66 ± 15.5	62 ± 11.3	79 ± 20.1
Conduction velocity†	88 ± 5.3	87 ± 2.8	72 ± 2.6	77 ± 3.4	76 ± 2.8	72 ± 4.4	82 ± 3.9	83 ± 7.3	82 ± 4.3	95 ± 4.9
Terminal Conduction velocity†	85 ± 6.9	88 ± 6.5	64 ± 3.4	68 ± 4.7	67 ± 6.4	67 ± 6.9	79 ± 9.2	83 ± 7.3	76 ± 5.5	88 ± 7.6
F-response latency‡	94 ± 2.8	112 ± 6.9	125 ± 10.4	134 ± 18.0	132 ± 14.1	127 ± 11.2	116 ± 12.1	114 ± 8.4	105 ± 5.5	92 ± 6.9
Temporal dispersion§	77 ± 4.5	69 ± 4.1	67 ± 4.1	66 ± 6.4	76 ± 3.9	67 ± 6.1	73 ± 7.1	86 ± 4.0	79 ± 4.2	85 ± 3.2
Sensory conduction										
Amplitude†	82 ± 13.8	79 ± 10.6	50 ± 7.3	30 ± 5.6	37 ± 6.9	38 ± 10.3	45 ± 10.2	66 ± 27.0	62 ± 9.9	76 ± 10.1
Conduction velocity†	101 ± 2.1	96 ± 2.7	99 ± 3.7	90 ± 3.7	91 ± 3.2	90 ± 4.9	91 ± 6.0	99 ± 8.7	97 ± 3.3	89 ± 1.7
Terminal conduction velocity†	105 ± 3.5	103 ± 4.1	93 ± 4.0	91 ± 3.5	94 ± 2.7	84 ± 5.7	92 ± 7.2	97 ± 12.0	94 ± 4.4	94 ± 5.5
B. Percentage of patients fulfilling criteria for demyelination and percentage of patients with abnormal motor or sensory studies for given time (weeks) after onset										
Demyelination present										
Yes	50	50	85	68	63	63	63	67	25	20
No	12	28	7.5	16	11	16	37	33	50	80
Indeterminate	38	28	7.5	16	26	21	0	0	25	0
Percentage of patients with										
Abnormal motor	88	89	96	92	91	89	75	83	90	40
Abnormal sensory	25	39	73	72	68	83	43	60	60	25
Both normal	12	6	4	8	5	0	0	17	17	40

Mean ± SEM.

†*Percentage of normal mean.*

‡*Percentage of upper limit of normal.*

§*Proximal to distal CMAP amplitude × 100.*

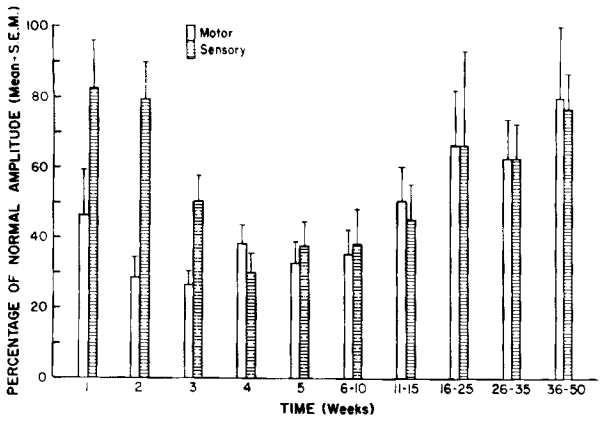

FIGURE 1. Motor (white bar) and sensory (striped bar) evoked response amplitudes expressed as a percentage of the normal mean as a function of time after disease onset in patients with acute inflammatory demyelinating polyradiculoneuropathy. The responses are significantly ($P < 0.05$) different for weeks 1, 2, and 3. No significant differences exist thereafter.

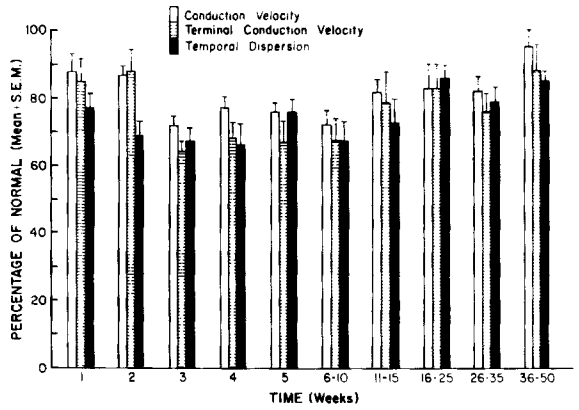

FIGURE 2. Compound muscle action potential conduction velocity (white bar), terminal conduction velocity (striped bar), and temporal dispersion (solid bar) as a function of time after disease onset in patients with acute inflammatory demyelinating polyradiculoneuropathy. The conduction velocities are expressed as a percentage of the normal mean. Temporal dispersion is expressed as a ratio of the proximal to distal compound muscle action potential amplitudes $\times 100$.

motor conduction studies and during the fourth week for sensory conduction studies. Figure 1 compares CMAP and SNAP amplitudes, expressed as a percentage of the normal mean, as a function of time after disease onset. There is a significant ($P < 0.05$) difference between the two measures, with the SNAP amplitude exceeding the CMAP amplitude during the first 3 weeks of illness. Thereafter, they are indistinguishable. Examination of the original data demonstrated that motor abnormalities within a given patient were more likely to be homogeneous, with the lower limbs showing greater involvement than the upper limbs. Sensory conduction studies, on the other hand, were more likely to demonstrate abnormalities of individual nerves, with other nerves being normal. Comparison of sural and median sensory conduction studies is shown in Table 4. At the time of initial evaluation during the first 4 weeks of illness (39 patients), the most common finding was an abnormal median sensory response (usually an absent or markedly reduced SNAP amplitude with reduced terminal conduction velocity) with normal sural conduction studies. In a smaller proportion of patients, both sensory conduction studies were either normal or abnormal. No patient had abnormal sural and normal median sen-

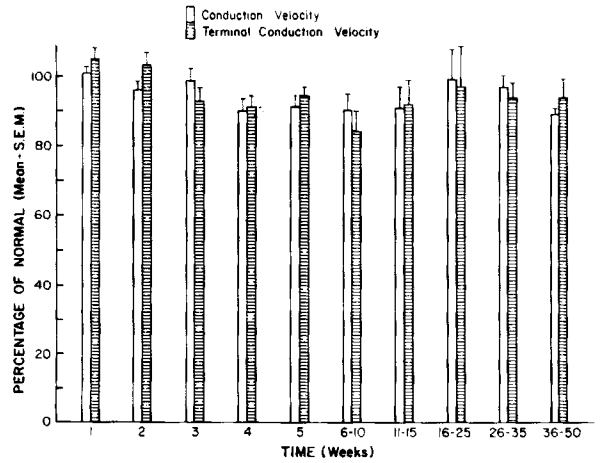

FIGURE 3. Sensory nerve action potential conduction velocity (white bar) and terminal conduction velocity (striped bar) as a function of time after disease onset in patients with acute inflammatory demyelinating polyradiculoneuropathy, expressed as a percentage of the normal mean.

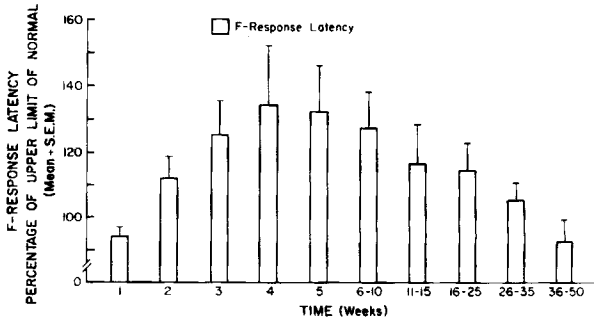

FIGURE 4. F-response latency as a function of time after disease onset in patients with acute inflammatory demyelinating polyradiculoneuropathy, expressed as a percentage of the upper limit of normal.

Table 4. Comparison of median and sural sensory conduction studies in patients with acute inflammatory demyelinating polyradiculoneuropathy. Results at the time of initial and follow-up evaluation.

	All studies (N = 86)	Initial evaluation (first 4 weeks) (39)	Follow-up (39)
Both normal	30 (35%)	11 (28%)	13 (33%)
Both abnormal	20 (23%)	9 (23%)	13 (33%)
Median abnormal and sural normal	36 (42%)	19 (49%)	13 (33%)
Median normal and sural abnormal	0 (0%)	0 (0%)	0 (0%)

sory studies, a finding that is characteristic of most mild chronic sensory polyneuropathies.

Using the criteria for the presence of demyelination, 50 (71%) patients had unequivocal electrodiagnostic evidence of a demyelinating polyneuropathy (Table 5). In addition, 11 patients (16%) fulfilled the criteria for demyelination in a single nerve, after excluding isolated ulnar, peroneal, or median abnormalities at common sites of entrapment. In all 11 patients, the electromyographer used the term "demyelinating" in the interpretation of the evaluation, although the complete protocol, as outlined in Table 1, was not completed. In all, abnormalities of conduction velocity were striking, and none could be considered borderline. Therefore, as many as 87% of the 70 patients had evidence of a demyelinating neuropathy. Seven additional patients (10%) had indeterminate evaluations, usually demonstrating isolated abnormalities, such as abnormal dispersion, borderline reduction in conduction velocity, or absent evoked responses. In these patients, it was neither possible to conclude that demyelination was present nor to exclude the possibility with a high degree of certainty. For example, one patient had completely absent CMAP and SNAP evoked responses, recording from distal and proximal extremities as well as facial muscles. These studies, performed during the fourth week of illness, do not preclude the possibility that evidence of demyelination would have been present on earlier studies. Two patients had definite evidence of axonal degeneration only, with preservation of conduction velocity (proximal and distal) and F-response latencies, without evidence of temporal dispersion. Both patients had multiple studies (5 and 8, respectively) over an interval of 1–30 weeks.

Table 5. Electrodiagnostic evidence suggestive of demyelination in 180 studies of 70 patients with AIDP.

Presence of demyelination:	
Fulfilled criteria for demyelination (multiple nerves)	50 (71%)
Fulfilled criteria for demyelination (single nerve)*	11 (16%)
Indeterminate (isolated abnormal dispersion, borderline reduction in conduction velocity, absent evoked responses)	7 (10%)
Fulfilled criteria for axonal degeneration only†	2 (3%)

**Electromyographer diagnosed "demyelination" in all of these studies; evoked responses often absent in other nerves studied. All patients had only one study performed.*

†Both patients had five or more studies over a 30-week period.

Measures of conduction velocity, terminal conduction velocity, F-response latency, and temporal dispersion for the 70 patients with AIDP demonstrated slight variation over the evaluation period. The motor conduction velocity and terminal conduction velocity data, together with the amount of temporal dispersion, are presented in Figure 2 as a function of time after disease onset, demonstrating a maximum impairment in all measures between the third and eighth weeks. Of interest, abnormalities of conduction velocity at the 20th week after onset were similar to the impairment at week 2. In other words, conduction velocity, at a time when clinical improvement was substantial, was indistinguishable from conduction abnormalities early in the course of the disease. This is in contrast to the CMAP amplitude data that demonstrated significant improvement by the 20th week when compared to initial responses. Frequent examples of progressive slowing of conduction velocity were documented in patients who were well into their recovery stage. Sensory conduction velocity and terminal conduction velocity are shown in Figure 3, demonstrating similar, but less striking, abnormality compared to motor studies.

F-response latencies as a function of time after disease onset are shown in Figure 4. The most pro-

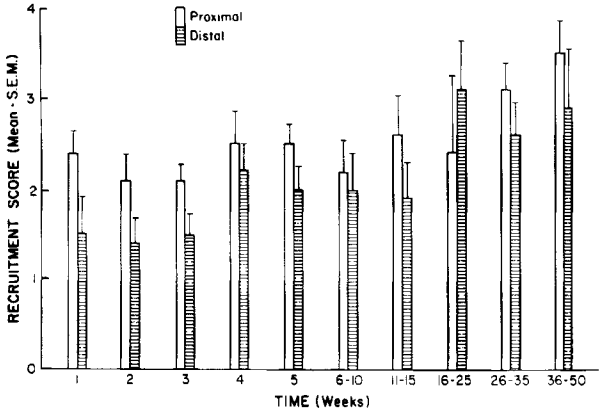

FIGURE 5. Motor unit action potential recruitment score for proximal (white bar) and distal (striped bar) muscles as a function of time after disease onset in patients with acute inflammatory demyelinating polyradiculoneuropathy. Recruitment is expressed from 0 (absent) to 4+ (normal).

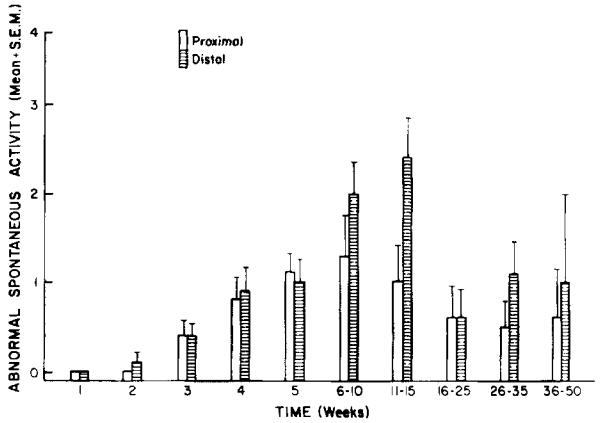

FIGURE 6. Abnormal spontaneous activity in proximal (white bar) and distal (striped bar) muscles as a function of time after disease onset in patients with acute inflammatory demyelinating polyradiculoneuropathy. Fibrillation scores range from 0 to 4+, with 0 = none and 4+ = profuse fibrillation potentials in all areas of muscle.

longed latencies were recorded during the third to fifth weeks after onset. These results are misleading, because absent F-responses were common early in the course of illness. Because of the wide range of results, the latency measurements for the different evaluation periods were not significantly different. Within a given patient, however, results were relatively uniform, and individuals with marked prolongations in one nerve usually had either absent responses or similarly prolonged latencies in other nerves.

The results of needle electromyography are shown in Figures 5 through 8. The earliest abnormality was decreased MUAP recruitment, without abnormality of configuration or evidence of abnormal spontaneous activity. Overall, recruitment abnormalities were most prominent distally (Fig. 5), although there were individual patients with profound proximal involvement of some muscles and minimal findings distally. No patient had normal MUAP recruitment at the time of initial examination. MUAP recruitment scores gradually improved, but the slow improvement did not reflect the overall clinical improvement of these patients, particularly late in the course of the disease.

Abnormal spontaneous activity appeared between the second and fourth weeks following disease onset (Fig. 6). Fibrillation potentials and

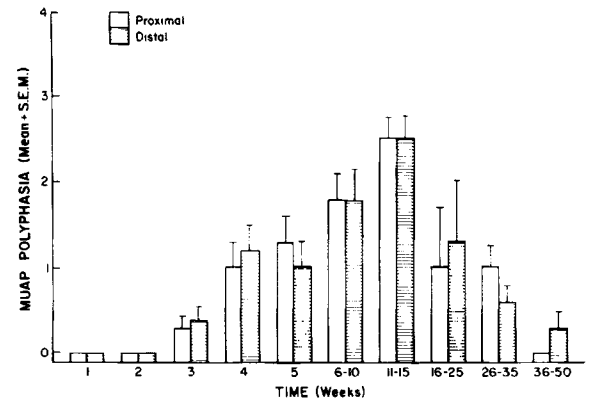

FIGURE 7. Motor unit action potential polyphasia as a function of time after disease onset in patients with acute inflammatory demyelinating polyradiculoneuropathy. The percentage of polyphasic potentials in proximal (white bar) and distal (striped bar) muscles is expressed from 0 (normal) to 4+ (marked increase).

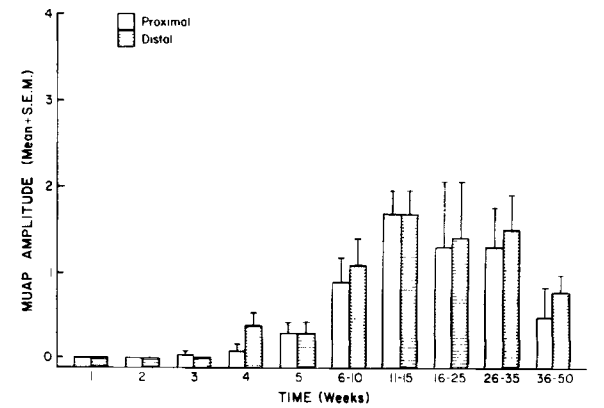

FIGURE 8. Motor unit action potential amplitude as a function of time after disease onset in patients with acute inflammatory demyelinating polyradiculoneuropathy. Amplitude in proximal (white bar) and distal (striped bar) muscles is expressed from 0 (normal) to 4+ (marked increase).

positive waves were recorded, on the average, simultaneously in distal and proximal muscles. Proximal fibrillation potentials were maximal between the sixth and tenth weeks, with distal fibrillation reaching a maximum between the 11th and 15th weeks. Thereafter, abnormal spontaneous activity slowly diminished.

MUAP configuration is described in Figures 7 and 8. The earliest abnormality was an increased percentage of polyphasic MUAPs during the fourth week for both proximal and distal muscles (Fig. 7). The greatest percentage of abnormal polyphasia was recorded between the 9th and 15th weeks of illness, with a decrease thereafter. By comparison, increased MUAP amplitude became apparent between the fourth and fifth weeks, reaching a maximum between the 11th and 35th weeks (Fig. 8). Subsequent studies showed a return toward normal in both proximal and distal muscles. The improvement was most apparent in the 34 studies performed 1–3 years after disease onset. In several patients, small low-amplitude, highly polyphasic MUAPs were reported during the second month of illness, likely representing regenerating axons.

Finally, four patients were found to have abnormal spontaneous activity, consisting of myokymic discharges, during the first 3 weeks of illness. In two, myokymic discharges were recorded from facial muscles in conjunction with clinically apparent facial myokymia. In the remaining two, myokymic discharges were recorded from limb muscles in the absence of clinical myokymia (Fig. 9). In all, the myokymic discharges were a transient finding, occurring within the first 3 weeks of illness and absent on subsequent examination.

DISCUSSION

Lambert and Mulder[16] reported electrodiagnostic evaluations on 49 patients with a clinical diagnosis of AIDP. The studies were performed during the first 3 weeks of illness, 14% of patients had no abnormality of conduction, 61% had conduction velocity less than 70% of the normal mean, and 25% had prolonged distal latencies only without substantial abnormality of conduction velocity.

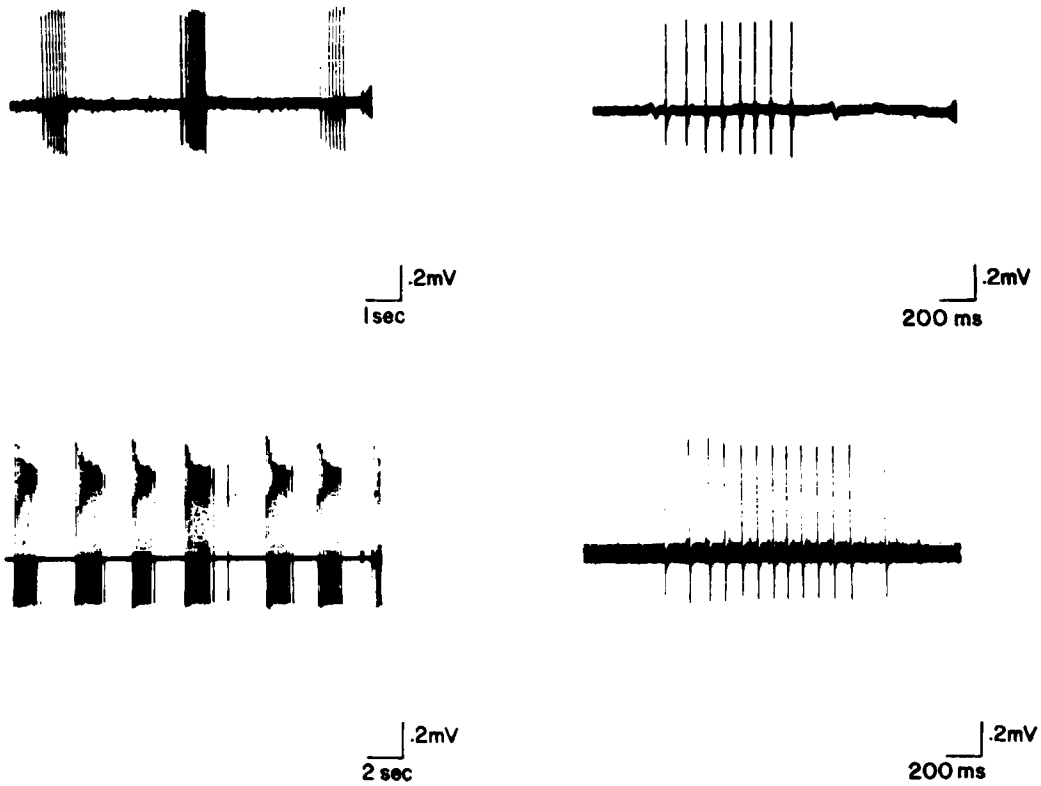

FIGURE 9. Myokymic discharges recorded from an extremity muscle during the second week of illness in two patients (top and bottom) with acute inflammatory demyelinating polyradiculoneuropathy. Clinical myokymia was not apparent. The recordings were made using a conventional concentric needle electrode. The discharges were not under voluntary control.

McLeod[20] reported similar findings in 114 patients, indicating that marked slowing of conduction velocity or an abnormally prolonged motor distal latency consistent with demyelination was found in one or more nerves in 50% of patients. Asbury[5] indicated that approximately 80% of AIDP patients have evidence of nerve conduction slowing or block at some point during their illness, although up to 20% of patients will have "normal conduction studies." The combined data for weeks 1–3 from the current study is similar to that reported above, although normal studies were less common and evidence of demyelination was more frequently present, presumably because of the increased likelihood of detecting an abnormality with repeat studies. The criteria of reporting demyelination when conduction velocity was 70% of the normal mean is approximately equivalent to our criteria using 85% of lower limit of normal. We prefer the latter because most laboratories have well-established upper and lower limits of normal; normal means are less frequently identified. Several patients had abnormal distal latency (terminal conduction velocity) without abnormality of conduction velocity in the forearm or leg segment of the extremities. Of six such patients, five subsequently demonstrated evidence of diffuse slowing of conduction velocity.

Motor fibers are clinically involved more frequently than sensory fibers,[4,14,25,28] and sensory evoked responses may be entirely normal in patients having prominent motor abnormalities. Nevertheless, median or ulnar SNAPs have been reported to be absent in 58% of patients,[11] with abnormalities of sensory conduction (abnormal SNAP amplitude or evidence of demyelination) reported in 76% of patients.[20] The largest electrodiagnostic discrepancy between motor and sensory abnormalities occurs during the first 2 weeks after disease onset, as judged by either evoked response amplitudes or percentage of patients having abnormal motor or sensory studies. Interestingly, SNAPs may be abnormal or absent in certain nerves (e.g., median), yet normal in others (e.g., sural).[22] The relative sparing of sural responses in the presence of abnormal median sensory responses is atypical of any diffuse polyneuropathy. This finding, in association with an appropriate clinical syndrome, suggests the diagnosis of AIDP.

Several possibilities exist that can explain the discrepancy between motor and sensory studies, as well as the discrepancy between sural and median sensory conduction studies. If the size of the myelinated fiber or the amount of myelin were somehow protective in AIDP, either by protecting the axon or preserving conduction, the large myelinated sensory fibers could be preserved relative to the smaller motor fibers. This could explain prolonged function in sensory compared to motor fibers, as well as the apparent distal fiber predilection. Similarly, it could explain prolonged sural nerve function as compared to median sensory function, considering the size of the sural nerve at the ankle recording site as compared to the terminal fibers of the median sensory nerve at the digit recording site. The apparent distal predilection is consistent with previous reports describing a centripetal pattern of demyelination in some patients occurring first in the distal nerve and progressing to the spinal root.[30] These findings also are consistent with the experimental observations of Sumner,[29] who studied humorally induced demyelination in rat sciatic nerve. Smaller diameter myelinated fibers were affected earlier and more completely than larger diameter fibers. In addition, nerve roots were highly permeable to antiserum, and distal motor nerve twigs and common compression sites were identified as potential areas of vulnerability because of an impaired blood–nerve barrier.

Conversely, a model can be proposed in which sensory fibers are initially unaffected, with the disease involving motor fibers only. In any mixed nerve, an inflammatory response involving motor fibers could be associated with intraneural edema and compression of sensory fibers only as an epiphenomena. In such a model, sensory fibers could hypothetically be compressed at known sites of anatomic vulnerability. This would be consistent with the known sensitivity of diseased nerve at common compression sites, but would not explain the observation that sensory evoked potentials may demonstrate proximal slowing (between Erb's point and the cervical cord) at a time when sensory conduction is normal more distally.[9] Secondary sensory involvement also would not explain the sequential abnormalities reported on sural nerve biopsy in AIDP.[23] Of importance, however, is the demonstration that a single screening sural sensory conduction study, as is commonly done in the evaluation of chronic sensory polyneuropathies, is inadequate in the evaluation of patients with suspected AIDP.

As reported by others,[8] partial conduction block and increased temporal dispersion of motor evoked responses were helpful in establishing the presence of demyelination, particularly early in the

disease when maximum conduction velocities were often within the normal range or only slightly reduced.[8,17] Abnormal temporal dispersion can be explained by multifocal demyelination of individual axons, resulting in some fibers having little or no demyelination and other fibers having multiple areas of demyelination. These differences are accentuated by measuring conduction over sequentially longer distances. With short stimulation to recording site distances, the differences may be small and the CMAP may appear normal. With longer stimulation to recording distances, the increased range of conduction velocities results in the initial component of the CMAP (representing the fastest fibers) being greatly separated from the trailing portion of the CMAP (representing the slowest conduction in the most demyelinated fibers). This results in both a prolonged response and a markedly reduced CMAP amplitude with proximal stimulation. The amplitude may be reduced even further with progressive conduction block. The likelihood of continuous signal propagation along the nerve decreases with increasing nerve length. Temporal dispersion alone cannot always account for the observed decrease in CMAP amplitude; progressive conduction block with longer stimulation to recording distances may account for much of the amplitude reduction.

Needle electromyography findings are not frequently reported in AIDP. The initial findings in any patient with AIDP who has clinical weakness may consist only of abnormal recruitment, with the degree of abnormality being proportional to the degree of clinical weakness. Reported needle electromyography abnormalities 3–4 weeks after onset are similar to our findings and range from evidence of reduced recruitment only to extensive denervation with profuse positive waves and fibrillation potentials.[18] Axonal degeneration presumably may occur at any time during the progression of the disease, which averages 2–3 weeks and rarely exceeds 4 weeks.[4] If degeneration of an individual axon occurred proximally, it could then take an additional 3 weeks for the appearance of fibrillation potentials in distal muscles innervated by that axon. The simultaneous appearance of fibrillation potentials, on the average, in proximal and distal muscles can best be explained by a model where axonal degeneration occurs randomly along the axon or at the distal nerve ending. These findings are different from those associated with the polyneuropathy of acute intermittent porphyria, a disorder felt to have initial involvement at the anterior horn cell.[2] In porphyric neuropathy, fibrillation potentials appear within 2–3 weeks in paraspinal muscles and then subsequently appear in more distal muscles over the next several weeks. Similar findings are associated with any proximal axonal lesion. Fibrillation potentials first appear in those muscles closest to the lesion and later occur in more distal muscles. The subsequent decrease in the amount of abnormal spontaneous activity probably reflects reinnervation from either collateral sprouting[31] or even axonal regeneration, when the initial axonal damage occurred close to the muscle being reinnervated. A reduced number of fibrillation potentials in proximal, compared to distal, muscles can be explained both by the smaller probability that a long segment of axon would have regenerated and by the higher mean recruitment in proximal compared to distal muscles, increasing the likelihood of collateral reinnervation. Again, the figures represent overall averages, there being many patients who demonstrated only minimal abnormal spontaneous activity throughout the course of their disease, and other patients who had 4+ fibrillation potentials in both proximal and distal muscles for prolonged periods.

The earliest abnormality of MUAP configuration was an increased percentage of polyphasic MUAPs during the fourth week in both proximal and distal muscles. The greatest percentage of abnormal polyphasia was recorded between the 9th and 15th weeks of illness, with a decrease thereafter. By comparison, increased MUAP amplitude became apparent between the fourth and fifth weeks, reaching a maximum between the 11th and 35th weeks. Subsequent studies showed a return toward normal. Again, abnormalities were recorded in both proximal and distal muscles. In several patients, small low-amplitude, highly polyphasic MUAPs were reported during the second month of illness, likely representing regenerating axons. The findings are comparable to those described by Ballantyne and Hansen[7] and are consistent with a model in which surviving axons reinnervate denervated muscle fibers and then undergo a process of remodeling as regenerating axons reach the muscles. They further demonstrated that some patients showed evidence of poor reinnervation, whereas others had motor unit studies that returned to normal during that time. Unlike conventional experience with illnesses involving the motor neuron (e.g., prior polio, slowly progressive motor neuron disease), MUAP configuration and amplitude were shown to progressively improve, and they suggested that ongoing

remodeling of previously large motor units resulted in return to normal size as reinnervation progressed. Their sequential studies indicated a slow increase in MUAP area 2–4 months after onset, at a time when there was a modest increase in MUAP recruitment. Thereafter, the number of motor units stayed constant while there was evidence of increased MUAP area, which is consistent with ongoing collateral reinnervation. New axons also may reinnervate surviving muscle fibers that have been denervated, in addition to innervating those fibers shed by giant units in the process of muscle fiber turnover. Using such a model, it is easy to predict that total remodeling can occur over time, with the electrophysiologic characteristics returning to normal. In the 34 studies performed 1–3 years after disease onset, it was not uncommon to identify profuse spontaneous activity and MUAP abnormalities, most notably, reduced recruitment and increased amplitude, particularly in patients who previously had evidence of extensive axonal degeneration. This would support the suggestion that many patients with extensive axonal degeneration have failure of axonal regeneration or anterior horn cell death.[4]

The earliest abnormal spontaneous activity consisted of myokymic discharges recorded in four patients. Patients with AIDP often develop a characteristic persistent quivering of facial muscles, unilaterally or bilaterally. The term "myokymia" has been used to describe these facial movements. Myokymic discharges may be recorded from muscles of such patients.[10] These discharges consist of spontaneous, semirhythmic bursts of potentials that individually resemble MUAPs. Discharge rates within the involuntary bursts of normal-appearing MUAPs are typically 30–60 Hz, with discharges in bursts of 3–10, recurring regularly at intervals of 0.5–3.0 seconds.[10] Myokymic discharges have also been identified in the absence of clinical myokymia in limb muscles of patients with AIDP.[1] Myokymic discharges are present only in the acute phase of AIDP, and neither myokymic discharges nor clinical myokymia has been reported chronically in patients who have had AIDP. The results of local ischemia, peripheral nerve block, and percutaneous stimulation in patients with limb myokymia suggest that myokymic discharges arise focally at the site of a focal nerve lesion, most likely involving focal demyelination with underlying axonal damage.[1] Although several explanations have been proposed to account for the generation of myokymic discharges, none have been demonstrated unequivocally and different mechanisms may play a role in different patients. Possibilities have included transaxonal, ephaptic excitation through an "artificial synapse" formed after focal nerve damage and alternatively, damaged axons may serve directly as rhythmic, oscillating generators of action potentials.[1,27] Focal demyelination also may increase nerve excitability.[19]

Whether or not a pure axonal form of AIDP exists is uncertain. It is clear that all reported series of AIDP patients have included patients without electrodiagnostic evidence of demyelination. Similarly, it is often difficult to identify evidence of primary demyelination on nerve biopsy, further complicating the issue. Electrodiagnostic evaluation of additional nerves, including proximal extremity and/or facial nerve or blink reflex studies, may provide evidence suggestive of a demyelinating component to the neuropathy. In other instances, complete evaluation, and even sequential studies over many weeks, demonstrate only findings compatible with axonal degeneration alone. In our study, patients who fulfilled criteria suggestive of demyelination had an average of 2.4 electrodiagnostic studies, with less than half having only a single evaluation. By comparison, patients fulfilling the criteria for demyelination in a single nerve had an average of 1.4 studies, with 90% having a single evaluation. Patients with indeterminate evaluations had an average of 1.4 studies, with 71% of them having a single study. As anticipated, the likelihood of demonstrating evidence of demyelination or excluding its presence increased with increasing data, which was acquired both during a single evaluation and during repeat studies. It is possible that the 11% of patients with indeterminate evaluations could have been more completely categorized given additional evaluation. Nevertheless, a small percentage of patients had evidence of axonal degeneration only. In the two patients described who had no electrodiagnostic evidence of demyelination, adequate axonal function remained to record CMAP responses. It would seem unlikely that primary demyelination was the initial event, with complete destruction of all fibers involved, leaving only normal surviving axons with no evidence of demyelination.

Patients with acute porphyric polyneuropathy are often clinically indistinguishable from patients with AIDP; in many of them, abnormal porphyrin metabolism is not identified until the second episode of polyneuropathy. That these patients are clinically indistinguishable from patients with AIDP would seem the most compelling evidence

that this or similiar disorders may be included in most series of AIDP patients. Interestingly, porphyric neuropathy was initially felt to be demyelinating polyneuropathy with superimposed axonal degeneration. Recently, the demyelination has been identified as secondary to axonal degeneration, with electrodiagnostic studies demonstrating evidence of only axonal degeneration without demyelination. Patients with presumed AIDP who do not have electrodiagnostic evidence of demyelination should be evaluated thoroughly to exclude the possibility of another disorder.

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