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**Article abstract**—We compared the electrodiagnostic studies of 40 patients with chronic acquired demyelinating neuropathy and 18 patients with familial demyelinating neuropathy. Patients with acquired neuropathy had differential slowing of conduction velocity when distal latencies were compared with more proximal conduction velocities in the same nerve, when equivalent segments of different nerves were compared, and when dispersion of compound motor action potentials was examined. Conduction block was noted in some patients. Patients with familial disease had uniform conduction slowing of all nerve segments, and conduction block was not seen.

Chronic acquired demyelinating neuropathy is characterized by multifocal slowing of nerve conduction, whereas familial demyelinating neuropathy is characterized by uniform conduction slowing.

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# The electrodiagnostic distinctions between chronic familial and acquired demyelinating neuropathies

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Electrodiagnostic testing has been useful in distinguishing between neuropathies caused by primary segmental demyelination and those caused by axonal degeneration, both clinically and experimentally. However, distinctions between different demyelinating disorders have not been shown clearly. Some patients with chronic acquired demyelinating neuropathy may respond to corticosteroid therapy,<sup>1,2</sup> immunosuppressive drugs, or plasma exchange.<sup>3,4</sup> It is therefore important to distinguish familial from acquired chronic demyelinating neuropathies. This is often achieved by clinical history and examination, but sometimes the family history is unclear, the duration of the neuropathy indeterminate, and the clinical signs indistinguishable. For these patients, electrodiagnostic features might be helpful in distinguishing acquired from familial demyelinating neuropathy.

**Methods.** We examined the records of 75 patients who had a progressive neuropathy for more than 6 months in duration and whose electrodiagnostic studies were consistent with a demyelinating neuropathy as evidenced by conduction block or slowing of nerve conduction velocity greater than could be accounted for by axonal degeneration. Each of 18 patients had an autosomal-dominant inherited neuropathy, pes cavus, and peroneal muscular atrophy. Half of these patients had thickened nerves

to palpation or onion-bulb formation on diagnostic sural nerve biopsy. These patients were considered to have the hypertrophic form of Charcot-Marie-Tooth disease (CMT), also called hereditary motor sensory neuropathy type 1.<sup>5</sup>

Forty patients had no family history of affected members, slowly progressive or relapsing neuropathy, areflexia, high CSF protein, and, when performed, segmental demyelination on biopsy (with or without inflammatory cell infiltration). These patients were considered to have chronic inflammatory polyradiculoneuropathy.<sup>6</sup> Seven of the 40 had a multifocal disorder with persistent conduction block.<sup>7</sup> Fifteen patients were excluded from the study because of an unclear family history ("high-arched feet" but no clearly defined neuropathy) or because of associated illnesses that might be related to the neuropathy.

The electrodiagnostic studies of these patients were examined retrospectively. All electrodiagnostic studies were performed at the Hospital of the University of Pennsylvania, using standard EMG equipment (TECA 4) and standard techniques. A permanent record of each study was made with a fiberoptic recording system. The duration of the compound action potential was measured (figure 1) arbitrarily including all of the initial negative deflection (the portion of the action potential above the baseline). Although this pro-

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cedure might have missed motor units that merge with the positive deflection and falsely shorten the duration, this error was considered insignificant in a comparison of two groups.

Partial conduction block was suspected when the amplitude of the evoked response elicited from proximal sites was 50% or less of the amplitude evoked from distal sites of stimulation. By measuring and comparing both the amplitudes and the areas of the compound action potentials, we ensured that these differences in amplitude represented an absolute conduction block and were not simply due to increased dispersion of action potentials. In all instances of conduction block,

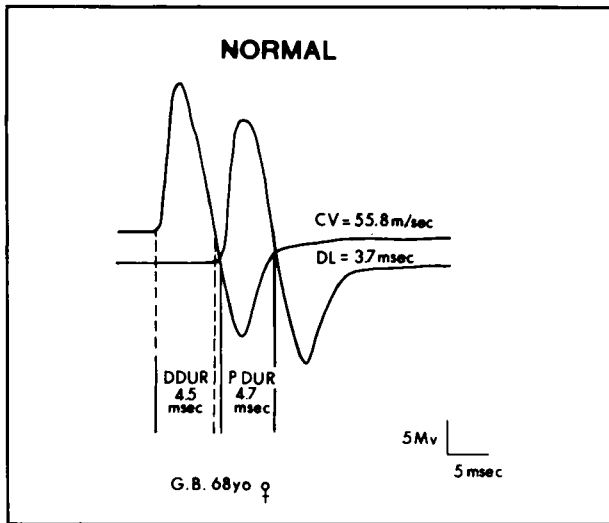


Figure 1. The duration of the compound action potential on distal (DDUR) and proximal (PDUR) stimulation. The difference in durations is 4% of the distal duration ( $\frac{PDUR-DDUR}{DDUR} \times 100$ ). MV = millivolts, msec = milliseconds, m/sec = meters per second, DL = distal latency, and CV = conduction velocity.

the total area beneath the evoked response on proximal stimulation was less than 60% of the area obtained on distal stimulation.

**Results.** Because of the severe denervation in distal leg muscles in both acquired and familial cases, peroneal motor nerve conduction velocities were not always determined. Therefore, comparison was limited to studies of the arms. The mean distal motor latency (DML) and forearm motor conduction velocity (CV) of both the median and ulnar nerves were markedly slow in both groups (table). Median sensory latency was prolonged, and amplitude was reduced when a response was obtained. The familial group had slower motor nerve CV ( $p < 0.001$ ), more prolonged median distal sensory latencies ( $p < 0.01$ ) and ulnar DML ( $p < 0.05$ ), and lower median sensory amplitudes ( $p < 0.05$ ) than the acquired group. Because of the large variation in DML and CV in the acquired group, these differences were not of predictive value. When the median motor nerve conduction studies were examined (figure 2), it was noted that the CV and the DML of the familial cases clustered. Some acquired patients had nearly normal DML with normal or mildly abnormal motor CV, and others had both severely prolonged DML and slow motor CV. However, some had severely slow motor CV and normal DML, and a few had very prolonged DML with only minimally abnormal CV. When the patients were arbitrarily grouped into mildly, moderately and severely abnormal groups (figure 3), there was no correspondence of DML and CV in 15 cases of acquired neuropathy, but mild discrepancy was noted in only 1 familial case.

Although there was no difference in the group mean forearm motor conduction velocity of median and ulnar nerves, a discrepancy was noted in individual patients with acquired neuropathy when ulnar and median nerve CV were compared (figure 4). In all 13 familial patients who had both ulnar

Table. Motor and sensory conduction studies (mean  $\pm$  SEM)

	Familial	Acquired	Normal
<b>Motor conduction studies</b>			
Median nerve	n = 18	n = 40	n = 30
Distal latency (msec)	9.9 $\pm$ 0.5	7.9 $\pm$ 0.9	3.5 $\pm$ 0.1
Conduction velocity (m/sec)	17.6 $\pm$ 0.9	29.9 $\pm$ 2.0	56.5 $\pm$ 0.5
Ulnar nerve	n = 13	n = 40	n = 30
Distal latency	8.1 $\pm$ 0.7	6.0 $\pm$ 0.5	2.8 $\pm$ 0.1
Conduction velocity	15.6 $\pm$ 1.2	29.9 $\pm$ 1.9	54.2 $\pm$ 0.5
<b>Sensory conduction studies</b>			
Median nerve	n = 7	n = 14	n = 30
Amplitude ( $\mu$ V)	2.3 $\pm$ 0.5	7.5 $\pm$ 2.3	17.3 $\pm$ 1.2
Latency	7.1 $\pm$ 0.4	4.2 $\pm$ 0.6	2.7 $\pm$ 0.1

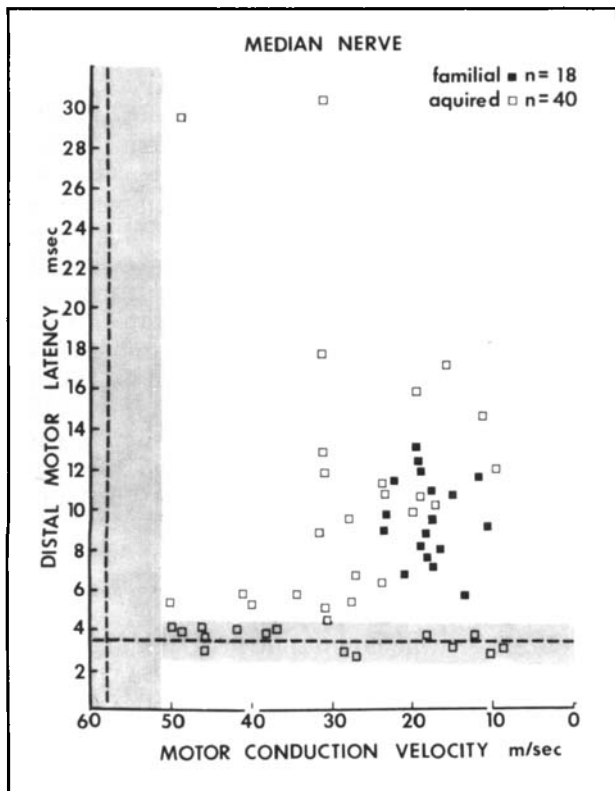


Figure 2. Scattergram of the median distal motor latency and forearm conduction velocity of familial patients (black squares) and acquired patients (open squares). Shaded areas are normal  $\pm$  2 SD.

and median nerve conduction studies, CV was almost identical in the median and ulnar nerves. However, 19 of the 35 patients of the acquired group had conduction velocities that differed by more than 5 meters per second, and 8 of the 35 had CV differences exceeding 10 meters per second. The ulnar CV was slower in 7 of 11 with differences between 5 and 10 meters per second, and in 4 of 8 with differences greater than 10 meters per second.

When the degree of dispersion of the compound motor action potentials was examined, other differences were found (figures 5 and 6). The duration of the compound motor action potentials elicited by stimulation at the wrist were somewhat longer than normal in both familial and acquired cases. This was consistent in all familial and most acquired cases. In normals, the duration of the compound action potential did not increase more than 10% on proximal stimulation (mean  $\pm$  SD =  $5 \pm 2\%$ ) (figure 1). The degree of dispersion, or increase, in duration of the action potential of the familial group was also minor, with the increase in duration on proximal stimulation never more than 25% of that on wrist stimulation ( $13 \pm 4\%$ ). In the acquired group, two-thirds had an increased duration of 40% or more ( $55 \pm 46\%$ ). Many had a 100% increase in duration, with severe dispersion and breakup of the action potential. Besides this marked dispersion, 12 patients in the acquired group had conduction block, either complete or partial. In all

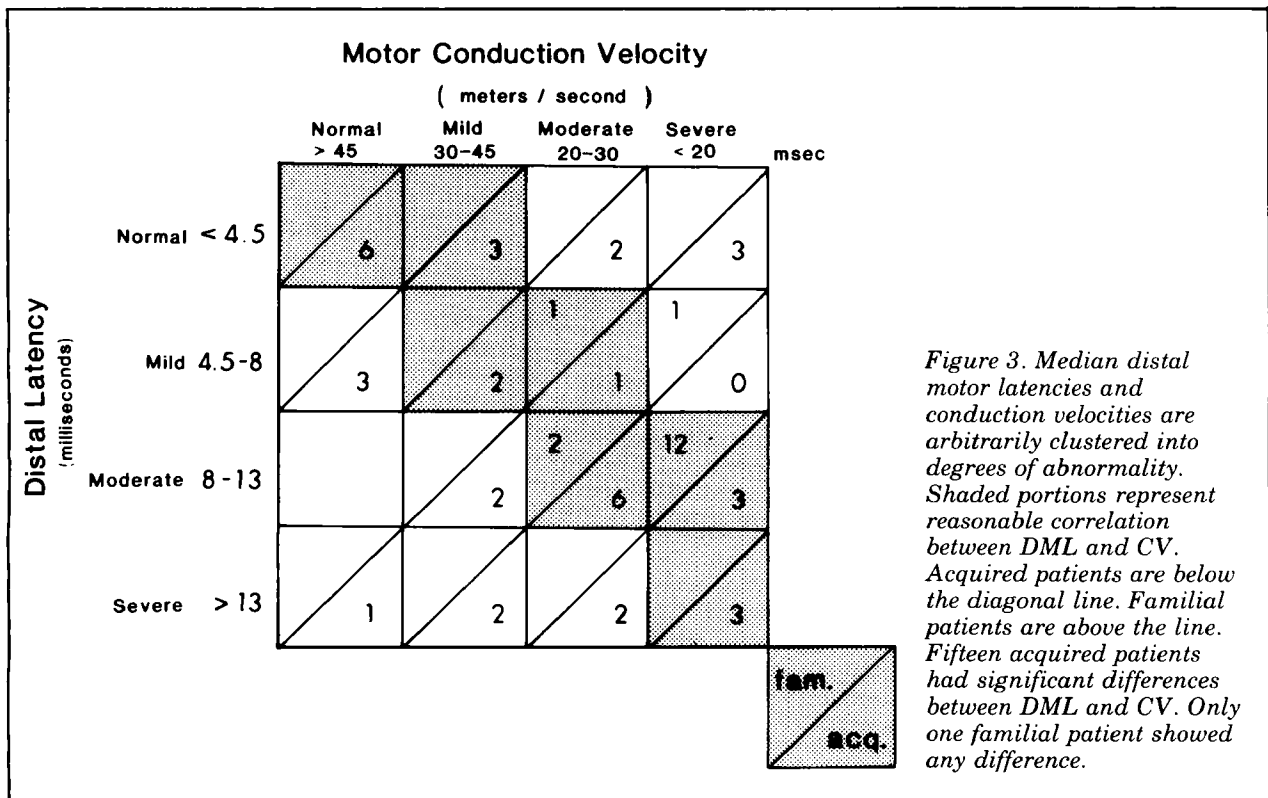


Figure 3. Median distal motor latencies and conduction velocities are arbitrarily clustered into degrees of abnormality. Shaded portions represent reasonable correlation between DML and CV. Acquired patients are below the diagonal line. Familial patients are above the line. Fifteen acquired patients had significant differences between DML and CV. Only one familial patient showed any difference.

12, the loss of amplitude on proximal stimulation could not be accounted for by dispersion. Seven of the 12 were patients with persistent multifocal conduction block, in which the conduction block was virtually the only electrodiagnostic evidence of demyelinating neuropathy; other nerve segments were normal or nearly normal.<sup>7</sup> None of the familial group had conduction block.

Distal sensory latencies were in agreement with the corresponding distal motor latencies in both familial and acquired cases. F-wave latencies were

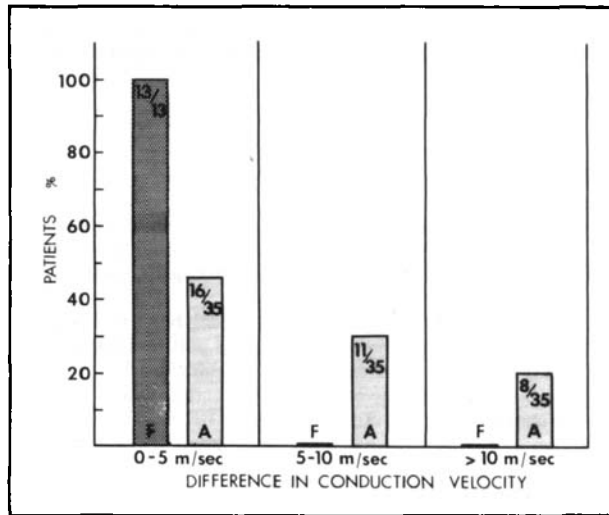


Figure 4. Bar graph comparing forearm motor CV between ulnar and median nerves.

not performed systematically and could not be used for comparison.

**Discussion.** The electrodiagnostic findings in patients with familial demyelinating neuropathy revealed a pattern of slowing of motor and sensory conduction velocities, indicating that the slowing of conduction velocity was uniform in all segments of nerve studied. In contrast, the acquired group usually showed variable degrees of abnormality. Distal latencies did not necessarily correspond to forearm conduction velocities, corresponding segments of different nerves were sometimes affected unequally, and there was increased dispersion of compound action potentials on proximal stimulation, suggesting that intermediate conducting fibers were variably affected. In addition, conduction block was noted in some of the acquired cases but never in the familial group. Of the 40 patients with acquired neuropathy, all but 4 showed at least one feature of differential slowing.

These findings are similar to the one previous attempt to differentiate acquired from familial demyelinating neuropathies.<sup>8</sup> They imply that chronic acquired demyelinating neuropathies behave electrophysiologically as if there were a multifocal attack on peripheral nerve, which may ultimately become diffuse. Some patients have a generalized disorder of all nerve segments, whereas others, despite a long history of neuropathy, have multifocal abnormalities with other segments relatively spared. It remains unclear whether the same pathophysiologic mechanisms are involved in pa-

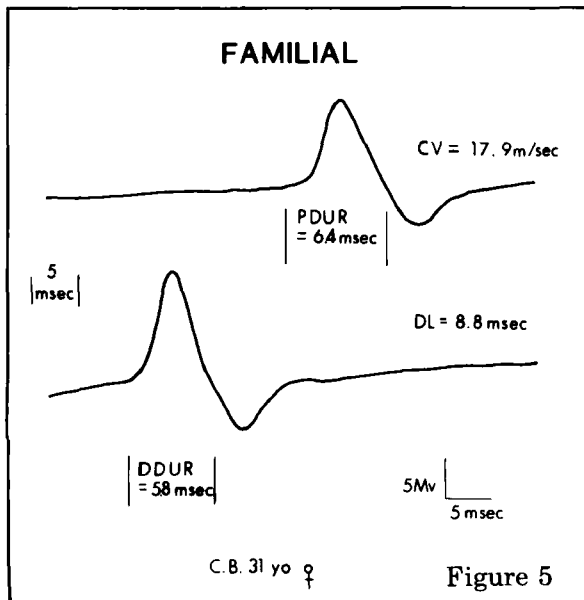


Figure 5

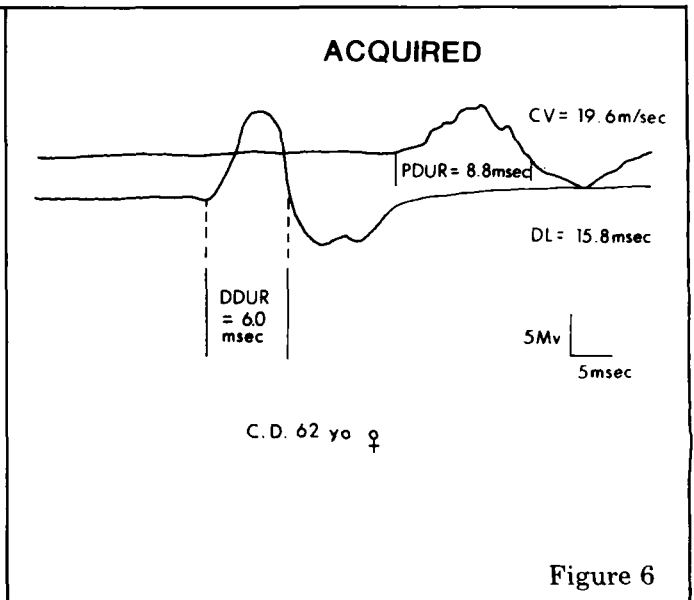


Figure 6

Figures 5 and 6. Representative median motor nerve conduction studies showing increased duration of compound action potential on proximal stimulation in an acquired patient. The familial patient had an increase in duration of 11%, whereas the acquired patient had dispersion of 47%. See figure 1 for comparison with normal.



tients with diffuse disease and those with multifocal abnormalities. The more multifocal the disease, the easier it is to distinguish from the familial diseases. However, even patients with diffuse changes have some evidence of differential slowing that distinguishes them from familial patients.

The familial neuropathy behaves electrophysiologically as if there were uniform slowing of conduction velocity in all nerve segments at all times. There have been few previous attempts to correlate nerve conduction studies of different nerves or different nerve segments in familial demyelinating neuropathy. Mongia et al<sup>9</sup> compared proximal (axilla to elbow) CV and forearm CV of the ulnar nerve in 11 family members with hypertrophic CMT. They noted slower CV in the proximal segment, but the differences were not striking. We did not systematically examine upper arm CV, and it remains unclear whether the correlation between upper arm and lower arm CV is as close as the correlation of distal latency and forearm CV.

Buchthal and Behse<sup>10</sup> compared sural nerve, superficial peroneal nerve, and median nerve sensory CV; peroneal motor nerve CV; and distal latencies to the anterior tibialis, peroneus longus, and abductor pollicis brevis in 23 patients with hypertrophic neuropathy. In each patient there was some variability, but despite the number of different measurements of sensory and motor functions in legs and arms, the correlation was good in the majority. Only three patients had values that varied by more than 30%. Kimura<sup>11</sup> noted F-wave conduction velocities of proximal segments of nerve that were comparable to distal CV in hypertrophic CMT patients. It remains to be determined whether uniform conduction slowing is found in all patients with familial demyelinating neuropathy, but this seems to be true in the great majority.

Uniform conduction slowing suggests a generalized dysfunction of Schwann cells or myelin. However, these electrodiagnostic features could also be due to the chronicity and indolence of the neuropathy. Pathologic studies have indirectly suggested that the primary abnormality may be in the neuron or axon,<sup>12-14</sup> but other evidence points to a primary defect of myelination, because Schwann cells from a CMT patient, when transplanted into immune-suppressed mice, failed to myelinate the normal mouse axons.<sup>15</sup>

Whether both axon and Schwann cell are involved in the inheritable disorder remains unclear. The electrodiagnostic findings will not provide the answer, since they cannot easily be related to the morphologic studies. The nerve conduction studies relate only to those nerve fibers that are functionally viable and do not take into account fibers that have undergone axonal degeneration. Given the chronicity of the neuropathy, the finding of uniformly slow nerve conduction velocities does

not necessarily point to the underlying pathophysiological mechanism.

Nevertheless, the electrodiagnostic distinctions between the familial and acquired demyelinating neuropathies are clear. Patients who have conduction block or evidence of differential slowing of nerve conduction should be suspected of having acquired neuropathy that may be responsive to various forms of therapy.

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