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**Christopher T. Leffler, MD, MPH*, Shai N. Gozani, MD, PhD*♦, Zung Q. Nguyen, BS*, Didier Cros, MD+**

*From *NeuroMetrix, Inc., Cambridge, Massachusetts; ♦Harvard-MIT Division of Health Sciences and Technology, Cambridge, Massachusetts; and +Department of Neurology, Massachusetts General Hospital, Boston, Massachusetts.*

# An Automated Electrodiagnostic Technique for Detection of Carpal Tunnel Syndrome

■ We designed an automated electrophysiologic neurodiagnostic device (AEND) yielding a distal motor latency (DML) using automated stimulation and analysis, volume-conducted waveforms, and physiologic adjustments. AEND screening was studied in 75 symptomatic patients, who also had conventional electrodiagnostic studies, and 22 asymptomatic subjects. The AEND yielded a DML in 92% of hands with a conventional motor response. The correlation between AEND and conventional DML was .90 ($P < .001$). The neurologists diagnosed 62 of 129 symptomatic hands with median neuropathy at the wrist (MNW). At 90% specificity, AEND DML had a sensitivity of 82% for MNW diagnosed by the neurologist and 87% for MNW defined by symptoms plus conventional electrophysiology. DML adjustment for age, height, and temperature was associated with an odds ratio for correct diagnostic classification of 1.80 in receiver operating characteristic curve analysis. A volume-conducted latency determined by an automated technique, designed for screening for MNW in an occupational medicine or primary care setting, is highly correlated with conventional techniques. Physiologic adjustments nearly double the odds of correct diagnostic classification. ■

**Keywords:** distal motor latency (DML), carpal tunnel syndrome (CTS), median neuropathy at the wrist (MNW), volume conduction, temperature

The prevalence of hand symptoms involving the median nerve distribution is 14% in the general population (Atroshi et al, 1999). Industrial or blue-collar populations are especially susceptible, given that carpal tunnel syndrome (CTS) is associated with awkward wrist postures, repetitious or forceful hand activity, and vibratory tool use (Silverstein et al, 1987; Atroshi et al, 1999). Patients with symptoms of median neuropathy at the wrist (MNW) are frequently referred for electrodiagnostic testing. Electrodiagnosis is typically based on sensory and motor studies of multiple nerves. According to the American Association of Electrodiagnostic Medicine (AAEM), "median sensory and motor NCS's [nerve conduction studies]…confirm a clinical diagnosis of CTS in patients with a high degree of sensitivity and specificity" (1993a, p. 1390). Deciding which patients to refer for testing is complicated by the fact that MNW cannot be diagnosed reliably on clinical grounds alone (DeKrom et al, 1990; Katz et al, 1990b; Gerr and Letz, 1998). Therefore, electrodiagnostic instruments for screening patients in an occupational medicine or primary care setting may help to identify patients who require complete electrodiagnostic testing in a timely fashion. Detection of conduction abnormalities would then prompt referral to a neurodiagnostic specialist to confirm the diagnosis of CTS and fully assess the differential diagnosis, which is not possible with a screening device.

Unfortunately, there are no nerve conduction measurement technologies widely accepted for screening of median conduction abnormalities at the wrist. Existing systems have been criticized for:

1. Not providing the ability to visually audit and document the evoked compound muscle action potentials (CMAPs).
2. Using waveform analysis that measures the latency near, not at, the onset of depolarization.
3. Using nonstandardized stimulus intensity control methods that do not ensure activation of the fastest motor fibers.
4. Not accounting for important physiological variables such as skin surface temperature and patient age (Chaudhry, 1997).

We sought to address these and other limitations of existing technology. Therefore, we developed an automated electrophysiologic neurodiagnostic device (AEND) to supplement the clinical evaluation of suspected CTS in an occupational or primary care setting. We intended for this device to be user-friendly and robust enough to be used for screening purposes. This method cannot replace conventional electrodiagnostic testing, which adds accuracy in the diagnosis of subtle pa-



Address correspondence and reprint requests to Didier Cros, MD, Department of Neurology, Massachusetts General Hospital, Boston, MA 02114 (e-mail: dcros@partners.org).

thology and versatility in the assessment of anomalous innervation patterns and the delicate problems of differential diagnosis.

We evaluated the AEND in symptomatic patients receiving standard NCSs and in asymptomatic control subjects. The objectives of the study were to compare the results obtained with the AEND with those of conventional studies and to determine the value of the AEND in diagnosing MNW.

## Materials and Methods

### *Subjects*

We studied 75 patients referred to the Massachusetts General Hospital electromyography laboratory for upper-extremity or neck symptoms and 22 asymptomatic volunteers. Once a patient finished the study, a technician enrolled the next available qualifying patient. For symptomatic patients, inclusion criteria were age 18 to 75 and symptoms for at least 1 month before examination (Bessette et al, 1997) and on most days in the past week; the exclusion criterion was median nerve injection in the past 30 days. For asymptomatic volunteers, the inclusion criterion was age 18 to 75; exclusion criteria were upper-extremity symptoms in the past month, patient-reported history of CTS in the past year, or polyneuropathy. All subjects volunteered after providing written informed consent. Subjects were asked to complete a hand symptom diagram for each hand (Katz et al, 1990b). Patients with bilateral symptoms indicated which side was more severely affected. The study was approved by the hospital Committee for the Protection of Human Subjects and was designed to conform to the recommendations for future research (with regard to CTS) of the AAEM (1993a, 1993b; Chaudhry, 1997).

### *Conventional Electrodiagnostic Methods*

Symptomatic patients received a standard electrodiagnostic evaluation. Limb temperature was maintained near 32°C. Surface stimulation and recording were used for median and ulnar NCSs. Evaluation included distal motor latencies (DMLs), sensory latencies, motor and sensory conduction velocities, mixed palm-to-wrist studies, and F-wave latencies. The mixed nerve action potentials were evoked with palmar stimulation and were recorded 8 cm proximally at the wrist. Median CMAPs were recorded over the abductor pollicis brevis (APB). The median nerve was stimulated 2 cm proximal to the proximal wrist crease. Needle electromyography was performed when indicated.

### *AEND Methods*

In all subjects, median nerve conduction was studied with an AEND (NC-Stat™, NeuroMetrix, Inc., Cambridge, MA). The device uses a standardized geometry for placement of the stimulus, recording, and ground electrodes. The stimulus cathode is placed 3 cm proximal to the distal wrist crease (Kimura, 1979). The volume-conducted thenar CMAP is detected 1 cm proximal to the wrist crease on the medial and lateral (active electrode) aspect of the wrist. The CMAP onset is negative. As the volume conductor does not low-pass-filter the rising edge of the thenar CMAP, the latency is essentially identical to that of the signal over the muscle (Lateva et al, 1996). The amplitude of the off-muscle signal is substantially less than that of the over-the-muscle signal.

The handheld, battery-operated device has two optically isolated subcircuits. Each is based on an embedded 8-bit microprocessor and is powered by a single 1.5V battery. One subcircuit controls the stimulator. The other records and analyzes the signal and displays the result. The user interface consists of 4 push-button switches and a display of messages and latencies. All waveforms and measurements (eg, stimulus intensity, gain, noise levels) are stored and can be downloaded to a computer. The device acquires and analyzes M waves and F waves. Signals are filtered with a high-pass cutoff (–3-dB point) of 1.5 Hz and a low-pass cutoff (–3-dB point) of 3 kHz. The sampling rate is 10 kHz for the M wave and 4 kHz for the F wave. The M-wave signal is usually acquired at a gain of about 1000 to 3000. The device sets the gain to optimize the dynamic range of the analog-to-digital converter. F waves are acquired at a gain of approximately 20,000. The M wave is acquired for 12.8 ms after the onset of the stimulus. The F wave is acquired for 32 ms starting 20 ms after the stimulus onset. The device generates constant current stimuli with a magnitude up to 20 mA and a duration up to 500 μs. The stimulus intensity is incremented in 2.5-mA and 100-μs steps such that the total charge delivered to the nerve increases in a monotonic fashion. The device automatically maps the stimulus-response curve and identifies stimulus intensity within 10% of the maximal intensity. This intensity was selected because we wanted to reduce patient discomfort and because the minimum motor latency occurs at these levels (Rhodes et al, 1965). The device automatically determines the DML. The prototype evaluated in this study recorded the F-wave signals but did not include automatic F-wave latency determination. Therefore, analysis of the F-wave latencies is not included in this report, although an example of the volume-conducted F-wave signals is shown (Fig. 1). The latency determination algorithm uses the raw and filtered versions of the CMAP to detect the start of the negative deflection. This determination is effectively accomplished by detecting a discontinuity in the CMAP first derivative. After 8 latencies are determined, any outliers are dis-

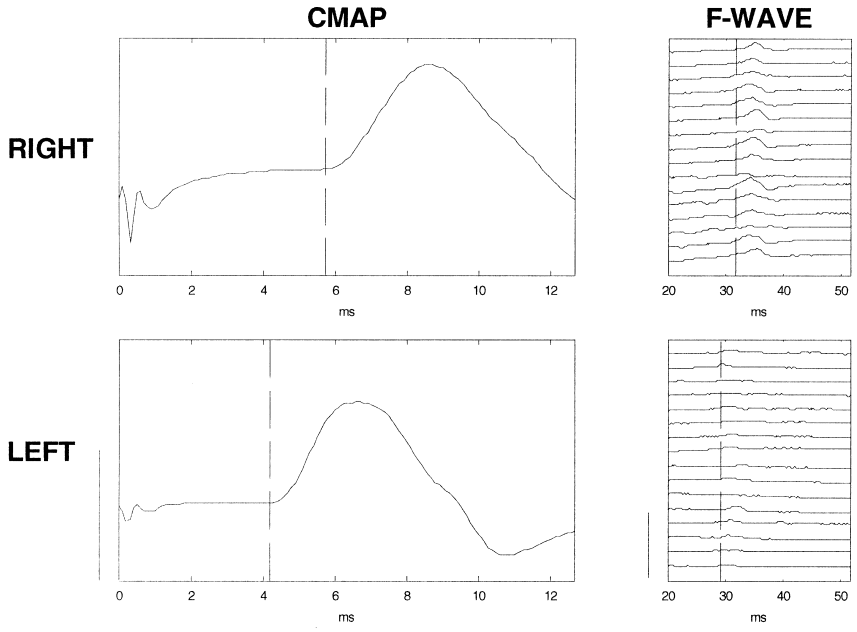


**Figure 1.** Compound motor action potentials (CMAPs) obtained with the electrophysiologic device in a 56-year-old, 163-cm-tall patient with bilateral symptoms that were worse on the right. The hand symptom diagrams were scored as "possible" bilaterally. The neurologist diagnosed a bilateral median neuropathy at the wrist that was moderate on the right and mild on the left. The unadjusted distal motor latency obtained with the automated electrophysiologic device was 5.7 ms on the right and 4.3 ms on the left. The volume-conducted F-wave signals recorded by the device are shown; the median F-wave latency by the retrospective algorithm was 31.8 ms on the right and 29.3 ms on the left. The CMAP marker on the left represents 1 μV, and the F-wave diagram marker on the right represents 250 μV.

carded, and the nerve is restimulated to obtain a replacement. In addition to outlier processing, algorithms are used to ensure that the waveforms are physiologically viable (eg, do not have excessive noise or large stimulus artifact). If this is not the case, then these latencies are discarded and replaced. Once the device has 8 acceptable latencies, it displays the mean DML. If an acceptable group of waveforms is not obtained within a fixed number of stimuli, a "retest" message is displayed. If a valid DML cannot be obtained with the first application of electrodes, the electrodes are reapplied once. The study of each hand takes approximately 2 minutes. During this study, the device did not display the latencies. This "blinding" prevented the results from influencing the procedure.

### Case and Control Hands

Case and control hands were defined in two ways: using the neurologist's final diagnosis after the conventional electrodiagnostic study and using a standardized definition based on the hand symptom diagram and conventional electrophysiologic parameters.

The neurologist's diagnosis was based on the conventional electrodiagnostic evaluation, supplemented by history and physical examination. Symptomatic hands were included as cases if the neurologist diagnosed MNW and there were no other electrodiagnostic abnormalities (Sander et al, 1999) that might explain the symptoms. Symptomatic hands were included as controls if the neurologist did not diagnose MNW or polyneuropathy in the patient. Analyses were conducted for all qualifying hands and for each patient's most symptomatic hand.

According to the standardized definition, case hands had a "classic/probable" hand symptom diagram (Katz et al, 1990a) and a median-ulnar palm-to-wrist mixed nerve action potential latency difference (MUPWLD) of 0.5 ms or greater (Redmond and Rivner, 1988; Uncini et al, 1993). Although some authors have found a MUPWLD of 0.4 ms to be abnormal (Jackson and Clifford, 1988), others have observed a difference of 0.4 ms in normal subjects (Stetson et al, 1992; Redmond and Rivner, 1988; Uncini et al, 1993) and have recommended that 0.5 ms be considered the first abnormal value (Redmond and Rivner, 1988; Uncini et al, 1993). If the median or ulnar mixed response was unobtainable, a median DML of 4.2 ms or greater satisfied the electrophysiologic component of the case definition.

According to the standardized definition, control hands were symptomatic hands from patients with bilateral "possible" or "unlikely" hand symptom diagrams and a MUPWLD of 0.2 ms or less. Electrophysiologic assessment of the ulnar nerve was used to eliminate subjects with polyneuropathy (Hansson, 1995). In particular, the ulnar-digit-V-to-wrist sensory conduction velocity had to be at least 48 m/s (Stetson et al, 1992) on at least one side for any of the patient's hands to be included in the control group.

We conducted analyses with all affected hands, with each patient's most severely affected hand (Sander et al, 1999), and with each asymptomatic subject's nondominant hand. Using each qualifying hand as a separate unit of analysis has been done frequently (Nathan et al, 1992; Uncini et al, 1993; Gunnarsson et al, 1997; Garfinkel et al, 1998; Gerr and Letz, 1998; Sander et al, 1999). This method reflects the fact that evaluation of all symptomatic hands is clinically relevant.

Mean DML was nearly identical in the asymptomatic subjects (3.56; SD, 0.33) and in the symptomatic

control subjects (3.55; SD, 0.35 for the neurologist case definition). We therefore included asymptomatic subjects in the control group (Sander et al, 1999). Analyses that excluded these subjects were not meaningfully different.

### *Calculations*

The AEND parameters were evaluated by percentage of values obtained and by the product-moment correlation coefficient with standard nerve conduction studies (Armitage and Berry, 1994).

Electrophysiologic data were adjusted for standard covariates. DML was corrected to 32°C by applying an adjustment of 0.1 ms/°C. Reciprocal transformation of DML was applied to improve distribution normality (Stetson et al, 1992). The reference population percentile for the subject's age and height was then determined (Stetson et al, 1992). The DML corresponding with this percentile in a population of average age (40 y) and height (172 cm) was analyzed. It should be emphasized that, although we used published corrections for physiologic variables, the control mean and variance were derived from our own reference population.

Using Systat 8.0 (SPSS, Chicago, IL), we performed logistic regression with a neurologist diagnosis of symptomatic MNW as the dependent variable.

DML accuracy was also assessed by the sensitivity at a fixed specificity (Zweig and Campbell, 1993) of 90%, calculated for binormal distributions of the transformed variables. We felt that a 90% specificity was appropriate for a primary care setting because this value exceeds the specificity of accepted clinical parameters (Katz et al, 1990b). The area under the nonparametric receiver operating characteristic (ROC) curve was determined. This area is recommended as an overall summary of diagnostic accuracy (Swets, 1988; Zweig and Campbell, 1993; Henderson, 1993) and is interpreted as the probability that a randomly selected affected patient will have a more abnormal result than a randomly selected unaffected control (Swets, 1988; Henderson, 1993). This probability can be converted to an odds so that two ROC curves can be compared by the odds ratio (OR) describing the likelihood of correct diagnostic classification. Ninety-five percent confidence intervals (CIs) for the sensitivity area under the curve of the ROC, and the ORs, were determined with the bootstrap method (Mossman, 1995; Manly, 1997) in Matlab 5.3 (MathWorks, Natick, MA).

## Results

### *Electrophysiologic Groups*

Seventy-five symptomatic patients entered the study. Mean age was 49 years (SD, 12 y), and 72% had bilateral upper-extremity discomfort.

In 34 patients (45%), the neurologist diagnosed the most symptomatic upper extremity as having an isolated MNW. Mean age of these patients was 50 years (SD, 12 y), mean height was 164 cm (SD, 8 cm), and mean limb temperature was 32.2°C (SD, 1.4°C). Seventy-seven percent of these patients had bilateral symptoms, and in 79% the right side was most symptomatic.

Of the 25 patients with normal median nerve function at the wrist on the most symptomatic side, the diagnoses on this side after neurodiagnostic testing were normal (20), brachial plexopathy (2), cervical radiculopathy (1), radial neuropathy (1), and ulnar neuropathy (1). Mean age of these patients was 46 years (SD, 12 y), mean height was 169 cm (SD, 10 cm), and mean limb temperature was 31.7°C (SD, 1.8°C). Sixty percent had bilateral symptoms, and in 76% the right side was most symptomatic.

In the remaining 16 symptomatic patients, the most symptomatic side could not be included in the MNW group because of coexisting cervical radiculopathy (3), ulnar neuropathy (3), or polyneuropathy (3), or could not be included in the control group because of coexisting polyneuropathy (3) or contralateral median neuropathy (4).

In the 22 asymptomatic control subjects, mean age was 45 years (SD, 11 y), mean height was 178 cm (SD, 11 cm), and mean limb temperature was 31.7°C (SD, 1.8°C).

Of 129 symptomatic hands, 62 (48%) were classified as MNW cases, and 40 (31%) were controls based on neurologist diagnosis. Of these 129 hands, 33 (26%) were MNW cases and 15 (12%) were controls by the standardized definition.

### *AEND Function*

In symptomatic patients, the AEND yielded a DML in 136 (92%) of the 148 hands that had a recordable motor response in conventional testing. The volume-conducted waveforms are illustrated in Figure 1. In linear regression analysis, the correlation between the conventional and AEND DMLs was .90 ($P < .001$, Fig. 2).

The mean normalized DML obtained with the AEND was 3.55 ms (SD, 0.34 ms) in 74 control hands and 4.84 ms (SD, 1.02 ms) in 54 hands with an isolated MNW. Each 1-SD increase in the normalized DML was associated with an OR for MNW of 8.81 (95% CI; range, 4.04–19.21). At a specificity of 90%, the sensitivity of the normalized AEND DML for the standardized definition of MNW was 87% (range, 78%–96%, Table 1). Including only the most symptomatic hand resulted in a sensitivity of 89% (range, 78%–98%). Sensitivity for neurologist-defined MNW was 82% (range, 73%–90%, Table 1). The area under the ROC curve was 0.93 (range, 0.89–0.97) for a neurologist diagnosis of MNW and

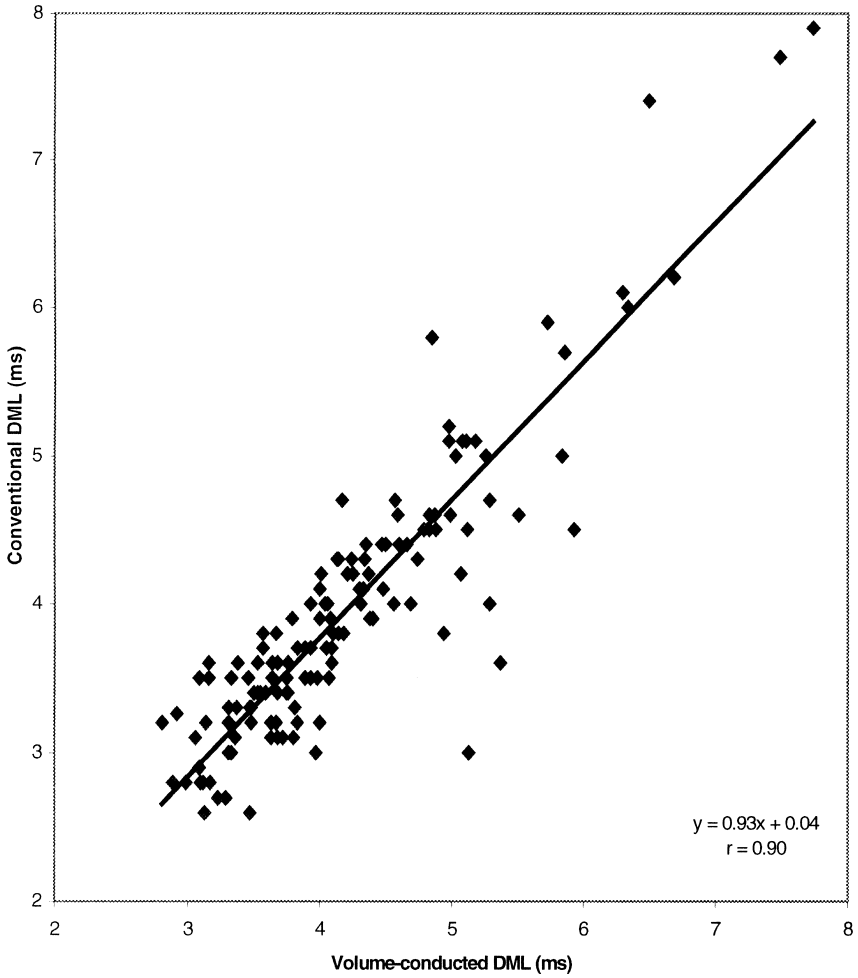


**Figure 2.** Scatter plot of the unadjusted distal motor latency (DML) by conventional techniques versus the automated, volume-conducted technique. The diagonal line represents the best least-squares fit.

0.95 (range, 0.90–0.99) for the standardized definition of MNW. The OR for correct diagnostic classification by ROC analysis associated with age, height, and temperature correction was 1.80 (range, 1.12–2.84). Including only the most symptomatic hand resulted in an OR of 1.95 (range, 1.07–3.83).

## Discussion

It is difficult to accurately diagnose MNW on clinical grounds (DeKrom et al, 1990; Katz et al, 1990b; Gerr and Letz, 1998). This study demonstrated that the DML provided by an AEND is highly correlated with the DML obtained by conventional testing. The DML had a sensitivity of 87% for MNW based on a standardized case definition. For the DML, the area under the ROC curve was 0.93 for a neurologist diagnosis of MNW and 0.95 for the standardized definition of MNW. A value over 0.90 is considered indicative of a highly accurate test (Swets, 1988). The OR of 8.8 associated with each increase of 1 SD in the normalized DML enables interpretation of the DML as a continuous variable. For instance, a patient in the upper 2.5 percentile has an OR of approximately 70 (= $8.8^{1.96}$) for MNW, relative to a patient with an average DML.

Although most clinical tests for CTS rely on a subjective response from the patient (Katz et al, 1990a), the AEND provides objective electrodiagnostic data. The system was designed to address technical and clinical limitations of prior technologies (Chaudhry, 1997). In particular, the system automatically determines the maximal stimulus intensity; analyzes the CMAPs to yield the DML using standardized signal processing algorithms; adjusts measured data for age, height, and temperature; and allows review of the waveforms.

The thenar CMAP is generally recorded with the active electrode over the motor point of the APB and the reference electrode just distal to the metacarpophalangeal joint of the thumb. However, the CMAP field extends well beyond the immediate vicinity of the activated muscle. Although the waveform morphology depends on the recording site, the waveform onset is the same whether recorded over the motor point or as a volume-conducted signal (Wee and Ashley, 1990; Lateva et al, 1996). The instrument described in this report measures intermediate-field (Lateva et al, 1996) volume-conducted potentials proximal to the wrist. This configuration has a number of important advantages. First, it is

**Table 1** Accuracy of Distal Motor Latency in Median Neuropathy at the Wrist*

| *Case Definition*[a] | *Physiologic Correction*[b] | *Hands (n)* | | *Sensitivity*[c] | *Area Under ROC*[d] *Curve* |
|---|---|---|---|---|---|
| | | *Control* | *Case* | | |
| Neurologist, all | No | 74 | 54 | 70 (58 to 82) | 0.88 (0.82 to 0.94) |
| Neurologist, all | Yes | 74 | 54 | 82 (73 to 90) | 0.93 (0.89 to 0.97) |
| Standardized, 1 | Yes | 29 | 22 | 89 (78 to 98) | 0.96 (0.90 to 0.99) |
| Standardized, all | Yes | 52 | 33 | 87 (78 to 96) | 0.95 (0.90 to 0.99) |

* Values are estimates (95% confidence intervals in parentheses).

[a] Neurologist = neurologist diagnosis of median nerve neuropathy at the wrist (MNW); standardized = standardized symptoms plus electrophysiology defines MNW; all = all affected hands included in analysis; 1 = 1 affected hand per patient included in analysis.

[b] Yes = distal motor latency corrected for age, height, and temperature; no = uncorrected distal motor latency.

[c] All sensitivites determined at fixed specificity of 90%.

[d] Receiver operating characteristic curve.

readily implemented as an integrated montage that makes electrode placement rapid, accurate, and reproducible. Second, off-muscle recording of the CMAP eliminates the need to locate the motor point of the stimulated muscle (Lateva et al, 1996).

DML has been noted to be useful in diagnosing CTS (AAEM, 1993b). When comparing diagnostic accuracy of electrophysiologic parameters, it is important that sensitivities be evaluated at an equivalent specificity using clinically defined case and control populations (AAEM, 1993b). The sensitivities of the DML (61%, Kimura, 1979; 74%, Jackson and Clifford, 1988) and of the distal sensory latency (63%, Kimura, 1979; 66%, Jackson and Clifford, 1988) were comparable in the only two studies identified by the AAEM (1993b) as meeting all six quality criteria and evaluating both parameters. The low test-retest variation of motor parameters and the fact that sensory parameters are more likely to be absent in severe cases (Aulisa et al, 1998) make motor parameters sufficiently robust for screening in occupational or primary care settings.

The accuracy of electrophysiologic evaluation of the median nerve is often increased by comparison with ulnar parameters. Median-ulnar motor comparative techniques have been found to be quite sensitive (Kimura, 1978; Preston et al, 1994; Sander et al, 1999). Comparison with the ulnar responses accounts, to some extent, for variations in patient size, age-related conduction slowing, and temperature. Our technique approaches this problem in a different manner—by measuring these parameters and explicitly adjusting for them. Despite calls to control electrophysiologic studies for temperature (Chaudhry, 1997), age (Stetson et al, 1992; Chaudhry, 1997; Rempel et al, 1998), and height (Stetson et al, 1992; Rempel et al, 1998), most groups have not quantified the effect that this combination of adjustments has on diagnostic accuracy. Controlling for these factors nearly doubled the odds of correct diagnostic classification in our study (OR, 1.80). This result is consistent with a previous study showing that these adjustments doubled the fraction of uremic patients with abnormal lower limb nerve conduction velocity (Lang et al, 1977). The improvement in accuracy will be more substantial in individual patients at the extremes of age, height, and temperature and in a screening setting in which warming of limbs is not practical.

### *Limitations*

The present study identified some areas in which the AEND could be improved. First, several CMAPs were analyzed incorrectly because of particularly complex waveforms or an initial positivity (presumably caused by coactivation of the ulnar nerve). The analysis algorithms have been modified to detect these conditions. Second, a number of patients had stimulus-response curves that did not increase monotonically but rather had local plateaus. As a result, the physiological model underlying the stimulus intensity determination routine has been enhanced to account for these outliers.

Even when the DML confirms a clinical diagnosis of MNW, other neurologic and rheumatologic conditions may coexist. Practitioners will still require a detailed clinical evaluation and must use judgment in pursuing formal electrodiagnostic, serologic, and imaging studies. The automated technique does not detect the on-muscle amplitude, which helps to assess axonal loss. Moreover, the technique does not permit stimulation at proximal and distal sites along the nerve, which confirms the location of entrapment. The definitive standard for the diagnosis of median nerve entrapment will remain the comprehensive electrodiagnostic evaluation.

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