ABSTRACT: The electrodiagnosis of carpal tunnel syndrome (CTS) is reviewed, including discussions of old and new techniques of motor and sensory nerve conduction, anomalous innervation, and needle electrode examination. A variety of sensitive nerve conduction studies (NCSs) are available for the evaluation of a patient with suspected CTS. For any particular patient, the NCS method chosen by the clinical neurophysiologist may vary for a number of reasons, including the severity of the deficit and the presence of superimposed conditions. © 1997 John Wiley & Sons, Inc. Muscle Nerve 20: 1477–1486, 1997

Key words: carpal tunnel syndrome; nerve conduction study; needle electrode examination; diagnosis

AAEM MINIMONOGRAPH #26: THE ELECTRODIAGNOSIS OF CARPAL TUNNEL SYNDROME

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The symptoms and signs caused by compression of the median nerve as it passes from the forearm to the palm are known as carpal tunnel syndrome (CTS). It is the most common entrapment neuropathy seen in electrodiagnostic laboratories. Because it has many underlying causes,97 patients with CTS are encountered by physicians in many specialties with varying skills in the diagnosis of peripheral nerve lesions. Since acroparesthesias result from lesions in the cerebral cortex to peripheral nerve terminals, electrodiagnostic confirmation of a peripheral nervous system lesion is important, particularly when the CTS is mild. This discussion concerns the electrodiagnosis of CTS and includes historical aspects and recent refinements in techniques for examination of the patient with symptoms of CTS.

MEDIAN MOTOR NERVE CONDUCTION STUDIES

The first report of the usefulness of median motor nerve conduction studies (NCSs) in the diagnosis of CTS was done by Simpson in 1956.92 Others soon confirmed his observations.25,100,101 Median motor nerve latencies are prolonged across the carpal tunnel but nerve conduction is usually normal or faster proximal and distal to the transverse carpal liga- ment. Even though less sensitive than other diagnostic methods listed below, motor nerve stimulation still plays an important role in the documentation of motor fiber involvement and can be used to localize the lesion when no sensory potentials can be recorded. Among residents of Rochester, Minnesota, with CTS, 311 (37.5%) of 829 hands examined had prolonged (>4.6 ms) median motor nerve distal latencies, and 1.9% had no response.96 When the median motor distal latency is in the normal range, it may still be prolonged compared with the ulnar motor distal latency. In the author’s laboratory, the median latency is abnormal if it is \( > 1.0 \) ms longer than the ulnar latency. The median motor latency can also be considered abnormal on the symptomatic side when it is \( \geq 1.0 \) ms longer than the median motor nerve latency on the opposite side. This comparison is rarely helpful, in part because CTS is bilateral in 58% of patients. Prolonged median motor distal latency to the abductor pollicis brevis in other series of CTS vary from 29% to 81%.45 Information about the presence or absence of conduction block can be obtained by recording the change in amplitude after stimulation of motor fibers in the palm and at the wrist.62

Occasionally, distal motor latencies are abnormal when sensory nerve latencies are normal. The cause of this unusual finding may be related to more extensive compression of the fascicles that contain motor fibers, an anatomical variation,9 or because the
motor branch can exit the carpal tunnel through a separate opening in the carpal ligament, where it may be compressed.\textsuperscript{50} When the distal motor latencies are abnormal when sensory nerve latencies are normal, extra care is required to exclude other causes, such as a C8 radiculopathy or anterior horn cell disease, by reviewing the clinical findings and by doing additional NCSs and needle electrode examination. Usually, isolated abnormalities of median motor nerve conduction with a normal median sensory NCS are not due to CTS.

Repetitive firing of motor nerve fibers in patients with CTS was first noted by Simpson.\textsuperscript{92} Such firing occurs infrequently and can be easily overlooked. It is recognized by a characteristic short burst of discharges that produces a buzzing sound after the stimulation, and by the appearance of a series of smaller potentials sometimes decreasing in amplitude following the M-wave. The cause may be demyelination of nerve fibers in the carpal tunnel or repetitive firing of hyperexcitable regenerating distal axons.\textsuperscript{63} Occasionally, a decremental response during repetitive stimulation is seen in CTS which can be confusing when testing is done for a defect of neuromuscular transmission.\textsuperscript{93}

**Conduction Velocity in the Forearm.** In approximately 10\% of patients, median motor nerve conduction velocity is slowed in the forearm, usually in association with prolongation of the distal motor latency.\textsuperscript{96} The likely cause of slowing is selective damage of large, rapidly conducting fibers in the carpal tunnel, possibly associated with retrograde nerve fiber degeneration or atrophy.\textsuperscript{41,78,101,102}

**Lumbrical and Interossei Recording.** Comparison of the median motor distal latency by recording from the second lumbrical, with the ulnar latency recording from the interossei, is a new technique that improves the sensitivity of the motor NCS.\textsuperscript{80,82} The nerves are stimulated at the wrist using identical distances and the compound muscle action potentials (CMAPs) from both muscles are recorded between the midpoint of the second and third metacarpal. Care must be taken to place the recording electrode over the second lumbrical motor point.\textsuperscript{73,81} A difference of $>0.4$ ms between the median and ulnar latencies is significant. In addition, because the second lumbrical is relatively spared compared with the thenar muscles, this technique is helpful in patients with severe CTS because a lumbrical response may be obtained when other responses are absent (Fig. 1).\textsuperscript{64}

**Other Methods.** Latencies may increase in cases of borderline CTS after 2 to 5 min of wrist flexion.\textsuperscript{67,89} Unfortunately, the latencies also increase in normal subjects to a similar extent.\textsuperscript{22} Formulas have been proposed to increase the sensitivity of the median motor nerve distal latency,\textsuperscript{59,91} however, they are rarely used because they are less sensitive than sensory NCSs.\textsuperscript{28,52}

**Forearm Median–Ulnar Nerve Communications.** Between 15\% and 30\% of normal persons\textsuperscript{39,108} have anomalous motor axons passing from the median to the ulnar nerve in the proximal third of the forearm (Martin–Gruber anastomosis). The anomaly is bilateral in 68\% and is probably inherited as an autosomal dominant trait.\textsuperscript{16,56} Anomalous axons may leave either the main trunk of the median nerve or, most often, the anterior interosseous nerve and “cross over” to the main trunk of the ulnar nerve. The communicating fibers innervate the first dorsal interosseous area, hypothenar, and least often the thenar area. Axons leaving and joining the nerves between the elbow and the wrist cause a change in the size and shape of the CMAP. With ulnar nerve stimulation, the amplitude is lower during proximal stimulation, whereas the median nerve stimulation, the amplitude is higher during proximal stimulation. In the presence of CTS, an additional clue to anomalous innervation is an initial positive dip in the thenar CMAP with stimulation at the elbow that is not present with stimulation at the wrist.\textsuperscript{40} These signs of anomalous innervation may become more prominent with the passage of time.\textsuperscript{60} In the presence of

![Figure 1](https://example.com/figure1.png)
CTS, the anastomosis provides a pathway to the thenar muscles that bypasses the carpal tunnel. This can result in a latency with elbow stimulation that is relatively shorter than appropriate for fibers that traverse the carpal tunnel (and may be similar to that obtained with wrist stimulation) producing erroneously fast median motor nerve conduction velocities (Fig. 2).

Exceptionally, other median and ulnar nerve anastomoses occur in the forearm that can confuse the clinical and electrodiagnostic diagnosis of CTS. Very rarely, motor fibers may pass from the ulnar to the median nerve. Anomalous motor nerve anastomoses are very well known; however, median-to-ulnar and ulnar-to-median sensory nerve communications have also been described. An unusual anomaly has been found in one instance in which the ulnar nerve accompanied the median nerve through the carpal tunnel, resulting in compression of both nerves. Communications between the motor branch of the median nerve and deep ulnar branch in the hand, the Riche–Cannieu anastomoses, do not usually affect the motor NCSs but can cause puzzling changes on needle electrode examination. An anomalous branch of the median nerve arising in the middle of the carpal tunnel and passing to the hypothenar muscles has been observed in two cases. In one instance, there was rare fibrillation potentials recorded in the abductor digiti quinti muscle.

MEDIAN SENSORY NERVE CONDUCTION STUDIES

Older Methods. In 1956, Dawson described the technique of orthodromic sensory nerve conduction as it is now used. Gilliatt and Sears recognized the value of this technique in the diagnosis of CTS. Antidromic sensory nerve latencies are not significantly different from orthodromic sensory nerve latencies, and antidromic stimulation has the advantage of producing sensory nerve action potentials (SNAPs) of greater amplitude. Commonly, the latencies are measured at 13 cm from the index finger or at 14 cm from the middle finger. Prolongation of the distal sensory latency or absence of the SNAP in CTS has been reported in 53% to 98% of cases. Presumably, the wide variation in the number of positive studies is the result of selection factors.

The antidromic median sensory nerve amplitudes are reduced in most patients with CTS. Unfortunately, in the absence of a prolonged distal latency, this finding has limited localizing value, unless a normal amplitude can be obtained when stimulation is distal to the carpal tunnel. Occasionally, patients have slowing limited to only one or two of the digital branches, and in rare cases it is useful to measure latencies from individual digital nerves. A prolonged finger-to-wrist latency can also be the result of a focal lesion distal to the carpal ligament, such as a digital neuropathy.

Mild slowing of median forearm sensory nerve conduction velocities occurred in 9% of the author’s patients. Buchthal and colleagues found slowing of conduction from the wrist to the elbow in only 2 of 81 forearms.

Measurement of Latency from Wrist to Palm and Palm to Wrist. Improvement in diagnostic sensitiv-

![Figure 2](image-url)

**Figure 2.** Median motor NCS in a 66-year-old man with CTS and a median-to-ulnar crossover. The distal latency after stimulation at the wrist is markedly prolonged (14.6 ms). After stimulation at the elbow there are two potentials. The first potential (arrow) is the CMAP from crossover fibers bypassing the carpal tunnel. The second potential is from fibers passing through the carpal tunnel (latency 19.6 ms, conduction velocity 54 m/s).
ity in NCS occurred in the early 1970s, when latency was measured over shorter segments from the index or middle fingers to the palm and from palm to wrist. Because the segment of nerve distal to the carpal tunnel conducts relatively normally, the inclusion of this segment in latency measurements “dilutes” the sensitivity of routine orthodromic or antidromic methods. Initial reports utilized orthodromic stimulation of the digits with recording at the palm and wrist. Subtraction of the digit-to-wrist latency from the digit-to-palm latency gives the latency or conduction velocity across the carpal tunnel. The disadvantages of this technique are the need to record at the palm with needle electrodes and troublesome shock artifact. Later, a more practical method using antidromic stimulation was reported. The segmental measurement of latencies is helpful in distinguishing CTS from peripheral neuropathy, because in CTS the maximal slowing is across the wrist rather than from palm to digit. Another advantage of using antidromic stimulation is the ability to recognize conduction block, which may be a hallmark of acute CTS. An increase in the palm SNAP amplitude of ≥50% compared with wrist stimulation suggests conduction block.

Orthodromic Palmar Stimulation. Eklund described a faster and more direct method of obtaining the palm-to-wrist latency and, with slight modification, it remains the preferred method for diagnosis of CTS in the present investigator’s laboratory. Median palmar stimulation evokes a mixed nerve action potential (NAP) because motor fibers innervating the second lumbrical muscle are stimulated in addition to digital nerve afferents from the index and middle fingers. However, the NAP recorded at the wrist is primarily generated by sensory fibers. Palmar stimulation is more sensitive than antidromic or orthodromic stimulation of digital fibers in establishing the diagnosis of CTS. Kimura found that the palm-to-wrist sensory nerve latency was prolonged in 21% of hands in which conventional latencies were normal. The median and ulnar nerves are stimulated in the midpalm at a point 8 cm distal to the wrist recording electrodes (Fig. 3). The upper limit of normal for the ulnar and median mixed nerve peak latencies is 2.2 ms. When the median nerve latency is normal, comparison of the ulnar and median nerve latencies increases the number of positive results. In the author’s laboratory, a difference of ≥0.3 ms is considered significant. Some investigators have advised a slightly larger difference to avoid false positives. Besides being more sensitive, the amplitude of the palmar NAP recording at the wrist is higher than antidromic stimulation recording from a digit. This results in fewer absent responses. Disadvantages of the technique include shock artifact. This can be reduced or eliminated by rotation of the anode. It is uncertain if normal conduction of the less affected motor fibers obscures slowing of conduction in digital sensory fibers.

Median Sensory Short Segment Stimulation across the Wrist. A high rate of abnormality is obtained with antidromic serial 1-cm stimulation of the median nerve across the carpal tunnel recording from the index or middle fingers. In half of the patients with CTS, localized slowing of conduction is found near the distal portion of the carpal tunnel, whereas in the remainder the slowing is more evenly distributed. For routine use, eight or even fewer stimulation sites are sufficient. A segmental peak latency difference of ≥0.5 ms is abnormal. Although serial stimulation is a reliable method, it has the disadvantages of being time consuming and uncomfortable because multiple sites are stimulated. In addition, serial stimulation can be difficult to perform because of stimulation artifact. In those patients with large hands, the strong stimulus intensities required...
to adequately stimulate the nerve make the exact site of stimulation uncertain.

**Median-Ulnar Sensory Latency Difference to the Ring Finger.** Because the fourth digit has median and ulnar innervation, comparison of the latencies with antidromic\textsuperscript{47,48,72} or orthodromic\textsuperscript{61,104,105} stimulation is a sensitive method of diagnosis. Antidromic stimulation at a distance of 14 cm is preferred, measuring latencies to the peak of the SNAP (Fig. 4). A significant difference between the median and ulnar nerve latencies is >0.4 ms.\textsuperscript{12} Antidromic stimulation is useful for the diagnosis of mild CTS because fibers from the fourth digit may be more subject to compression due to the position of ring finger fibers in the outer margin of the median nerve just beneath the transverse carpal ligament. More centrally located fascicles, such as those from the index finger, are less susceptible. Other clinicians believe the thumb is the most likely digit to show slowing.\textsuperscript{58}

There are a few drawbacks to antidromic stimulation. Ulnar nerve innervation of the entire ring finger is a potential source of error, but rarely seems to be encountered. Amplitude measurements with antidromic stimulation can be difficult because muscle CMAP obscures the sensory response. Last, because the SNAP amplitudes are small, the response may be lost in more advanced cases of CTS.

**Median-Radial Latency Difference.** Use of the radial nerve instead of the ulnar nerve for comparison with the median nerve is attractive because the radial nerve is less subject to entrapment.\textsuperscript{6,11,13,49,94} The normal median-radial latency difference (MRLD) with antidromic stimulation and a 10-cm distance for each nerve is <0.5 ms.\textsuperscript{9,77} It has been noted that it is more difficult to make accurate distance measurements with antidromic stimulation, and that a significant MRLD can occur in the presence of a peripheral neuropathy simply because the radial nerve may be less affected by a neuropathy.\textsuperscript{14}

**GENERAL APPROACH TO NERVE CONDUCTION STUDIES**

**Uncomplicated Carpal Tunnel Syndrome.** In all cases, median and ulnar motor nerve distal latencies and forearm NCSs should be performed. The inclusion of ulnar motor NCSs will help avoid errors caused by the presence of a peripheral neuropathy or a superimposed ulnar neuropathy. An abnormal ulnar NCS may also be a clue to anterior horn cell disease, a C-8 or T-1 radiculopathy, brachial plexopathy, thoracic outlet syndrome, or other unexpected more diffuse lesion.

Comparison of the median and ulnar orthodromic palmar latencies is usually the next study performed in the author’s laboratory. One of the other sensitive sensory nerve conduction methods discussed above could be employed instead. The method chosen may vary and will depend on the electrodiagnostic medicine (EDX) consultant’s training and experience, the availability of normal values for the laboratory, and the particular clinical situation to be investigated. It is not wise, however, to do multiple different sensitive NCSs in the same patient, because the risk of a type I error (normal patient is mistakenly called abnormal) increases with each additional technique used.\textsuperscript{84} If the median/thenar CMAP and sensory responses are absent, recording from the second lumbrical muscle is worthwhile.

When NCSs are abnormal in one limb or the symptoms are bilateral, ulnar and median sensory NCSs are done on the opposite side. If they are normal, no further NCSs are needed. If CTS if found on the opposite side, a median motor NCS should be considered, particularly if the sensory study is quite abnormal. If the symptomatic hand has normal NCSs, there is no need to perform NCSs on the opposite asymptomatic extremity. Practice parameters

*FIGURE 4. Median- and ulnar-nerve stimulation recording from the digits in a patient with CTS. The wrist-to-digit measurement is 14 cm. The latency after median nerve stimulation recording from the index finger is normal (3.4 ms). The latency recording from the ring finger after median nerve stimulation (3.6 ms) is prolonged compared with the latency after ulnar nerve stimulation (2.9 ms).*

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for an EDX examination in CTS have been published by the American Association of Electrodiagnostic Medicine.\(^3\)

**Carpal Tunnel Syndrome with a Superimposed Ulnar Neuropathy or Peripheral Neuropathy.** Interpretation of the NCS findings is problematic when the patient has an ulnar neuropathy with prolonged distal latencies, because comparison of median and ulnar latencies assumes normal ulnar function. Alternatively, the median sensory latency can be compared with superficial radial nerve latency.

Slowing of median and ulnar nerve conduction is an indication for NCSs in a lower limb. Not infrequently, entrapment of the ulnar and the median nerves is superimposed on a peripheral neuropathy. When a peripheral neuropathy is confirmed, CTS can still be diagnosed when the median motor and sensory distal latencies are disproportionately prolonged compared with the ulnar latencies. Caution is advised in interpreting the findings because the more severely prolonged median distal latencies may simply be due to more severe involvement of the median nerve by the neuropathy rather than median nerve compression in the carpal tunnel. Unfortunately, firm guidelines for interpretation of NCSs in this situation are not available. Segmental nerve conduction techniques which show slowing mainly in the transcarpal segment rather than in the palm-to-digit or forearm segments may be helpful, but still need to be interpreted with care.\(^4\) Electrophysiological abnormalities may be subclinical or of no clinical significance, particularly in diabetic patients.\(^2\) In a series of patients with mild diabetic neuropathy, in which any patient with more than mild symptoms of CTS were excluded, Albers and colleagues found 23% of their patients had NCS evidence of a median mononeuropathy.\(^2\) Because many diabetic patients with median NCS slowing do not have CTS, the EDX consultant should be cautious when interpreting the results for the referring physician.

**Hand Deformity.** The choice of the NCS method may be affected by physical deformities and trauma of the hand. For example, amputations of one or more digits may make a favorite technique impossible to use. For this and other situations noted above, it is necessary for the EDX consultant to be familiar with a variety of NCS techniques for the diagnosis of CTS.

**Nerve Conduction Studies after Surgery.** NCSs performed after surgery usually show significant improvement, correlating with relief of symptoms; however, immediate improvement in distal latencies has not been found by all investigators.\(^29,33,43\) The maximum improvement in NCSs occurs in the first 6 weeks after operation.\(^76\) It has been suggested that the almost immediate relief of symptoms after surgery is the result of a reduction in spontaneous activity generated by the compressed nerve segment rather than by recovery from the conduction block.\(^109\) Prolonged latencies do not always return to normal when symptoms are relieved, even when the study is done a year later.\(^36,70\)

**Recurrent Paresthesias in Patients Who Have Had Surgery.** Patients are sometimes referred for evaluation of possible recurrent CTS, months or years after an apparently successful carpal tunnel release. The paresthesias may be due to recurrent CTS but more often another process such as a cervical radiculopathy or a cerebral infarct is responsible. In these cases, normal median sensory NCSs make CTS unlikely. When the NCSs are abnormal, availability of preoperative NCSs are helpful for comparison. If preoperative EDX studies were not performed, or if the results are unavailable, it will be difficult to know if prolonged latencies are due to recurrent CTS. As noted above, the presence of mild median nerve conduction abnormalities may only be a residual outcome of successfully treated CTS. Severely prolonged latencies favor recurrent median nerve compression. A repeat NCS in several months can be suggested if the symptoms are worsening. Progression of the median NCS abnormalities favors recurrent CTS.

**NEEDLE ELECTRODE EXAMINATION**

The needle electrode examination helps define the severity of the lesion by indicating the presence of axonal destruction as manifested by fibrillation potentials and abnormalities of motor unit potentials. It is also necessary to distinguish CTS from proximal median nerve entrapment, cervical radiculopathies,\(^32\) and peripheral neuropathy. Prolonged median motor and sensory distal latencies are the most important predictors of an abnormal needle electromyography (EMG) examination of the abductor pollicis brevis but do not eliminate the need for the needle examination.\(^106\) Muscles examined when the findings of the NCSs are consistent with CTS may include the first dorsal intersosseous, abductor pollicis brevis, flexor pollicis brevis, pronator teres, biceps, and triceps. The severity of the abnormalities found on needle examination of the thenar muscles varies with the effort made to detect the changes and...
the severity of the cases studied. When mild CTS is found, study of the abductor pollicis brevis is optional because it is painful and unlikely to show an abnormality.

Infrequently, spontaneously discharging motor unit potentials are found in the thenar muscles of patients with CTS. These discharges may take the form of single, very regularly firing potentials, or doublets or triplets firing in groups in the pattern of myokymia. The potentials appear to be generated distally, probably in the carpal tunnel.

STANDARDS FOR THE DIAGNOSIS AND SEVERITY OF CARPAL TUNNEL SYNDROME

There is no universally agreed upon standard for the diagnosis of CTS or method of grading the severity of CTS. Many findings from the history and physical examination have limited diagnostic utility. A combination of clinical and EDX findings should be used rather than the clinical or EDX examination alone. The following is a grading scheme for the severity of CTS by EDX criteria that is useful when writing a consultation:

- **Mild CTS**—prolonged (relative or absolute) sensory or mixed NAP distal latency (orthodromic, antidromic, or palmar) ± SNAP amplitude below the lower limit of normal.
- **Moderate CTS**—abnormal median sensory latencies as above, and (relative or absolute) prolongation of median motor distal latency.
- **Severe CTS**—prolonged median motor and sensory distal latencies, with either an absent SNAP or mixed NAP, or low amplitude or absent thenar CMAP. Needle examination often reveals fibrillations, reduced recruitment, and motor unit potential changes.

INTERPRETATION OF ELECTRODIAGNOSTIC FINDINGS

Frequently the patient and referring physician will ask the EDX consultant for an opinion regarding the significance of the findings and the need for treatment. Prolonged latencies with reasonably preserved amplitudes or conduction block in the carpal tunnel suggests local demyelination and potentially rapid recovery after surgery. Unfortunately, the severity of symptoms does not correlate well with latencies. Some patients with slight prolongation of sensory latencies may be very symptomatic, whereas a few stoic patients with marked thenar atrophy are surprised when this is pointed out to them. The finding of sensory loss and thenar muscle weakness and wasting on physical examination usually suggests the need for more aggressive therapy. The equivalent findings from NCSs are decreased SNAP and thenar CMAP amplitudes. The presence of fibrillation potentials on needle examination, decreased recruitment, and motor units of increased size is also an indication of more severe median nerve compression and axonal loss.

The newer nerve conduction techniques are more sensitive for the diagnosis of CTS; however, there are still false negative results. It is important to emphasize the obvious—patients with a normal sensitive NCS have very mild CTS if they have it at all and if the clinical features are not typical, the benefits of surgery should be carefully considered.

CONCLUSION

In a majority of cases, a careful history and physical examination are sufficient to make a presumptive diagnosis of CTS, but as experience in the laboratory indicates, even the most seasoned clinician can mistakenly diagnose CTS when the problem is a radiculopathy, or they may be surprised when unsuspected CTS is found. An EDX examination confirming the clinical impression is reassuring for the patient and physician, gives objective evidence of the severity of the condition, is helpful in planning treatment, and will be useful in understanding new, changed, or recurrent symptoms later in the patient’s life.

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Suspected ulnar neuropathy at the elbow is commonly evaluated in the electromyography lab. In this report the anatomy and pathology of ulnar elbow lesions are reviewed. The patterns of electrophysiologic abnormality that have been reported in the literature and in the author’s own laboratory are discussed along with a suggested routine for evaluation.

Patients are frequently referred to the EMG laboratory for evaluation of suspected ulnar neuropathy at the elbow. In performing this evaluation the electromyographer undertakes to determine whether a lesion is present, to localize it along the nerve, and to gauge its severity. Localization is important, because the ulnar nerve is liable to injury at the wrist, elbow, and in the upper arm. Lower trunk plexus and root level lesions also may present similarly and must be differentiated.

Anatomy. The ulnar nerve is derived from the C8 and T1 nerve roots which form the lower trunk and medial cord of the brachial plexus. C7 also contributes a component through the middle trunk and lateral cord. The nerve descends into the upper arm in proximity to the brachial artery and median nerve. At about the midhumeral level it deviates dorsally and pierces the medial intermuscular septum to continue superficially on the medial head of the triceps. At the elbow, the nerve enters a groove formed by the medial epicondyle of the humerus and the olecranon of the ulna (Fig. 1). The flexor carpi ulnaris overlies this groove and itself arises as two heads: one from the medial epicondyle and the other from the medial margin of the olecranon. The lateral border of the groove is formed by the ulnar collateral ligament, which bridges the medial epicondyle and both the olecranon and coronoid process of the ulna. This groove has been termed the cubital tunnel by Feindel and Stratford. The nerve then continues along the medial aspect of the forearm and, proximal to the wrist, assumes a more ventral location as it enters the hand. The ulnar branches to the flexor carpi ulnaris (FCU) and flexor digitorum profundus (FDP) usually arise distal to the medial epicondyle, but in 2 of Sunderland’s 20 dissections, the FCU branches arose at, or proximal to, the epicondyle. The fascicles for these muscles may have defined themselves intraneurally for several centimeters, however, before actually forming an external branch.

There are several features of anatomy which may enhance the nerves’ susceptibility to injury at the elbow and also account for the frequently observed clinical pattern of hand muscle involvement with sparing of the ulnar forearm muscles. The number of fascicles tends to be reduced in the elbow region, as is the percentage of the total cross-sectional area of the nerve occupied by epineural tissue. These features may render the nerve more compression sensitive. The axons innervating the FCU and FDP tend to be located posterolaterally at that level, while the sensory and...
motor axons for the hand tend to be located anteromedially. The latter are said to be potentially more susceptible to compression in the cubital tunnel. The branches to the forearm muscles, being smaller than the main nerve, may be less compression sensitive as well.

The dimensions of the cubital tunnel change with elbow position, so that minimum tunnel size is present when the elbow is flexed. This is said to occur because the ulnar collateral ligament and the aponeurosis between the two heads of the flexor carpi ulnaris become taut when the elbow is flexed.

**Pathology.** Neary and Eames examined the ulnar nerves in three autopsy cases. One had obvious clinical evidence of ulnar neuropathy. A firm nodular swelling was noted in the clinically affected nerve arising just proximal to the arch of the two heads of the flexor carpi ulnaris. Histologic abnormalities were confined to the nerve segments extending 5 cm proximal and distal to the FCU arch. At the lesion’s center, increased perineural thickness and endoneural connective tissue were noted. The numbers of larger-diameter axons were decreased at that level, and both thinly myelinated fibers and clusters of regenerating fibers were noted. Bulbar myelin swellings were noted in the internodes situated centrifugally from the lesion. Even in the more severe of the material they examined, the fiber diameter histogram was normal distal to the lesion, suggesting that the predominant pathology in their patients was demyelination rather than axonal loss. In situations where the electromyographer encounters fibrillation potentials, enlarged motor unit potentials, slowed velocity, and reduced amplitude evoked responses distal to a focal lesion, varying degrees of axonal injury must have also occurred.

**Pathogenesis.** A number of pathogeneses have been suggested for elbow lesions. The tardy ulnar palsy which is said to follow an elbow fracture or dislocation by many years is probably best known. Alteration of the carrying angle of the elbow and limitation of full extension are factors postulated for the nerve being subjected to traction around the elbow. The concept of compression in the cubital tunnel was suggested by Osborne and Fiendel and Stafford to account for patients who developed idiopathic lesions and also as another explanation for tardy lesions. This is likely the most common cause of ulnar elbow lesions. Lesions that occur during general anesthesia are also well known. Although a compressive lesion is suspected, the predisposing factors are not known. Hypermobility of the nerve, with a tendency to sublux over the medial epicondyle, is another possible pathogenesis. The appearance of ulnar mononeuropathy may also herald the onset of a more generalized neuropathy.
ELECTROPHYSIOLOGIC EVALUATION
The evaluation of suspected ulnar neuropathy at the elbow has been the subject of a number of reports.\textsuperscript{1-4,6,8,11,12,14,17-19,21,22,25,29,33-35,38} There have been differences in technique between many of these, and the criteria for recognition of abnormality similarly have varied.

Parameters which have been utilized have included motor, mixed nerve, and sensory conduction velocity of the elbow segment;\textsuperscript{2-4,11,14,22,25,29,33,38} comparison of the elbow segment velocity to that of an adjacent nerve segment,\textsuperscript{1,11,33,38} latency from elbow to wrist,\textsuperscript{11} latency from above the elbow to the FCU or FDP,\textsuperscript{1,33,38} change in the size or configuration of the compound muscle action potential (CMAP) or sensory nerve action potential (SNAP) evoked proximal and distal to the elbow,\textsuperscript{4,6,25,29,33,38} and the pattern of needle examination abnormalities in ulnar-supplied muscles.\textsuperscript{11,33}

Motor Conduction Studies. Simpson first showed that conduction time could be increased across the elbow segment in a patient with ulnar neuropathy at the elbow.\textsuperscript{35} Since then a number of reports have shown applications of variations on this theme. Slowing of the elbow segment's conduction velocity has been a primary identifier of an abnormality. Comparison between the velocity of elbow segment and that of an adjacent nerve segment has been used to localize the lesion. Most authors have advocated recording from the hypothenar muscles and stimulating the nerve at the wrist, below the elbow distal to the medial epicondyle, at or just above the elbow, and in the upper arm or axilla. Velocities may then be calculated for the forearm, the elbow segment, and the upper arm. Recording from the first dorsal interosseus (FDI) in addition to the hypothenar muscles has also been advocated, since these may be differentially affected.\textsuperscript{33,38}

Conduction studies in normal subjects frequently show velocity slowing in the elbow segment when a fully extended elbow position is used.\textsuperscript{6,8,11,18,21,22,28,33} When the elbow is flexed to 45° or more, 0° being full extension, the elbow-segment slowing is eliminated when mean values are considered.\textsuperscript{1,6,17,19,21} Underestimation of the actual length of the nerve in the elbow region as assessed by surface distance measurement likely accounts for the discrepancy in velocity with the extended elbow position. Cadaver studies have shown slack and wrinkling of the nerve at the elbow with an extended position.\textsuperscript{6,17}

The length of a nerve segment which includes the elbow portion of the nerve may also be a factor in the ability of conduction studies to identify a lesion. A very short nerve segment which includes a lesion that produces local slowing should have a high chance of being abnormal. When conduction velocity is calculated over a progressively longer segment that may include normal along with the abnormal nerve, any slowing present in the abnormal segment may be diluted and normalized.\textsuperscript{4,5,20}

Short-length segments, though, may be susceptible to considerable error in velocity calculation due to inaccuracies in measuring latency and distance.\textsuperscript{24} Most authors have used a 10–12 cm distance between the below and above-elbow stimulation sites, but segments as short as 2 cm\textsuperscript{19} or as long as 19 cm\textsuperscript{17} have been reported. Longer, overlapping segments such as elbow-wrist and axilla-wrist may be used for velocity comparison with the forearm as an attempt to limit the inaccuracies encountered with shorter-length ones.

If the elbow segment velocity alone is used as the primary identifier of an ulnar elbow lesion, then the angle of the elbow may not be a consideration, since direct comparison to normal values alone is required.\textsuperscript{3} Reported lower limits of normal conduction velocity for that segment are shown in Table 1.

When attempting to localize a lesion by comparison of velocities in the elbow and adjacent segments, the tendency for elbow segment slowing, encountered with an extended elbow position, may limit the study’s sensitivity, and therefore a flexed position seems preferable. Even with the elbow flexed, some segment-to-segment conduction

<table>
<thead>
<tr>
<th>Angle</th>
<th>Segment length (cm)</th>
<th>Low-normal* velocity</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0°</td>
<td>8</td>
<td>34</td>
<td>8</td>
</tr>
<tr>
<td>0°</td>
<td>10</td>
<td>34†</td>
<td>22</td>
</tr>
<tr>
<td>0°</td>
<td>10</td>
<td>35</td>
<td>25</td>
</tr>
<tr>
<td>0°</td>
<td>10</td>
<td>38</td>
<td>11</td>
</tr>
<tr>
<td>0°</td>
<td>15</td>
<td>41†</td>
<td>18</td>
</tr>
<tr>
<td>0°</td>
<td>10</td>
<td>44†</td>
<td>33</td>
</tr>
<tr>
<td>35°</td>
<td>10–14</td>
<td>45††</td>
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<tr>
<td>45°</td>
<td>19</td>
<td>49</td>
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<td>135°</td>
<td>13</td>
<td>49</td>
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<td>52</td>
<td>4</td>
</tr>
<tr>
<td>110°</td>
<td>11.5</td>
<td>52</td>
<td>8</td>
</tr>
</tbody>
</table>

Note: 0° = full extension.
*Two standard deviations or lower range (R) if the latter is higher.
†Denotes intramuscular needle recording.

Table 1. Elbow segment motor velocity.
velocity variation will still exist due to experimental error in distance and latency measurement. A difference of up to 11 m/sec for the elbow segment velocity as compared with the forearm was found in studies of normal subjects done at 45° and 135° of flexion, while another reported that this velocity should be no more than 7.6% slower than the forearm when an 110° flexion was used. Differences of greater than 20 m/sec could be encountered if this comparison is done with the elbow in extension. The normal values used in the author's laboratory are shown in Table 2, and recording methods are described in the Appendix.

Lesions may be encountered in which the forearm velocity is also slowed. In such a situation, inappropriate elbow segment slowing might not be encountered, but comparison to a proximal segment such as axilla-elbow could be valuable. Reported normal values for axilla-elbow velocities are shown in Table 3. A very mild lesion might produce only relative slowing but leave the absolute velocity or latency normal. Such findings can be seen in mild carpal tunnel syndromes.

Several reports have demonstrated the actual types of motor conduction abnormalities that can be encountered. Payan found elbow segment motor velocity slowing in 85% of his patients. In 54%, comparison of the elbow segment and forearm velocities localized the lesion to the elbow. In patients with both sensory and motor clinical findings, Tackmann found that 65% had elbow segment slowing, and 49% localized to the elbow by slowing relative to the forearm. Fifty patients with the clinical diagnosis of an ulnar elbow lesion were studied in the Indiana University EMG Laboratory. Among these patients, 40% had both motor and sensory deficits, and of these, 86% had elbow segment motor slowing and 48% could be localized to the elbow by comparison with the forearm velocity. The remainder failed to localize because the forearm conduction was also slow. Comparing velocities between the longer elbow-wrist segment and that of the forearm was slightly less sensitive in localizing lesions. Ninety-four percent of those with a slow elbow segment velocity had elbow-
wrist slowing. Eighty-eight percent of those with a slow elbow segment velocity, both absolute and relative to the forearm, had a greater-than-normal difference between the elbow-wrist and forearm. Seventy-six percent of this group with sensory and motor symptoms had low CMAP amplitude with elbow stimulation.

In a group of patients who had sensory symptoms only, Payan still found elbow segment slowing in 71%. Tackmann found slowing in 33%, and 20% could be localized by comparison to the forearm. Twenty-three percent had a slowed forearm arm. Twenty-three percent had a slowed forearm velocity. In a similar group of patients studied in our lab, 48% had elbow segment slowing and a greater-than-normal difference when that velocity was compared with the forearm. Another 16% had normal elbow segment velocity but a greater-than-normal difference with the forearm. None had forearm slowing. The elbow segment velocity was again more often abnormal than was the elbow-wrist one. Only 40% of those with a slow elbow segment velocity had elbow-wrist slowing. Six percent of this entire group had a low CMAP with elbow stimulation. Four percent had an abnormally slow elbow segment motor velocity but had normal sensory conduction studies.

**Sensory Conduction Studies.** Sensory conduction studies may also be valuable in evaluating ulnar neuropathy. Two studies have shown that assessment of sensory conduction velocity and action potential configuration could be useful in identifying elbow lesions. Orthodromic recording with near-nerve needle electrodes were used in both reports. Elbow segment slowing was present in the normal subjects reported by Payan using the extended-elbow position. Surface recording of orthodromic SNAP's at the wrist and more proximal sites has also been reported. In our experience, orthodromic surface-recorded SNAP's may be lower in amplitude at the below-elbow site than at the elbow, even in thin subjects. This is likely due to greater distance between the nerve and the surface electrodes at the former site because of the nerve being deep to the flexor carpi ulnaris there. Antidromic recording obviates this problem, but rarely antidromic SNAP's may be difficult to distinguish from the closely trailing volume-conducted CMAP. Although Harding found segment-to-segment velocity variation of a sufficient degree to cast doubt on the utility of such studies, others found antidromic recording to be easily, reliably accomplished. Our normal values for sensory velocities and SNAP amplitude are shown in Table 2.

The types of sensory conduction abnormalities actually encountered have been reported by several authors. Payan found elbow segment slowing in 86% of his patients, 83% had forearm slowing, and 63% could be localized to the elbow. Seventy-eight percent had a low amplitude SNAP at the wrist. In a group of patients with both sensory and motor symptoms, Tackmann found elbow segment slowing in 70%, whereas 32% had forearm abnormality, and 54% could be localized to the elbow. Sixty percent had low amplitude or nonresponsive wrist SNAP's. With antidromic surface recording, 71% of our group of patients with both sensory and motor symptoms showed a nonresponsive SNAP at the wrist, and 15% more had a low-amplitude response. Of that 15%, one-third showed elbow segment slowing, one-third had no detectable response with elbow stimulation, and one-third showed normal velocities.

Our patients with sensory-only symptoms had no detectable SNAP with wrist stimulation in 3%, and 26% had low amplitude. Thirty-two percent had elbow segment slowing, and 29% had greater-than-normal slowing compared with the forearm. Another 32% had normal elbow segment velocity but showed a greater-than-normal difference when compared with the forearm. Thirteen percent were normal by all electrical criteria.

**Proximal Segment Motor Latencies.** Latency from an above-elbow stimulus site to the FCU or the ulnar-innervated FDP has been assessed in several reports and appears to be a valuable parameter. Conduction distances of 12–15 cm have been used for the FCU, and normal latencies of less than 3.7–4.0 msec have been reported for subjects 68 years or younger. One report specifies placing the recording electrode 10 cm distal to, and stimulating 2 cm proximal to, the medial epicondyle. From 44 to 82% of patients have shown abnormalities in this parameter. This may be abnormal while the elbow segment motor velocity is normal. Intramuscular needle recording has been utilized. Whether surface recording could be done has not been specified.

**Amplitude Change Between Stimulus Sites.** Change in the amplitude (Fig. 2) or configuration (Fig. 3) of the CMAP or SNAP may be useful in localizing a lesion site along the nerve. For surface electrode-recorded CMAPs, Checkles found that normals had elbow amplitudes no
more than 36% smaller than that of the below-elbow site. Brown found no more than a 5% difference in peak-to-peak amplitude, whereas another study reported a maximum decrease of 10.5% or 1.2 mV between these sites for baseline-to-negative-peak measurements. The incidence of such CMAP amplitude changes in a group of patients with ulnar neuropathy has not been specified, but we found these in 10% of patients, all of which had elbow segment slowing. The magnitude of these amplitude changes ranged from 2 to 5.6 mV.

When a greater-than-normal amplitude difference is identified between standard stimulation points such as below-elbow and elbow, then serial stimulation between those sites at intervals of 1 or 2 cm, "inching," may precisely localize a lesion by showing a point of abrupt change in the response's amplitude or additionally an abrupt prolongation of latency. This technique can usually be easily applied to ulnar stimulations in the elbow segment. Amplitude change due to a lesion must not be confused with that which can be seen in variations of normal arm innervation. Median-to-ulnar nerve cross-overs may cause a greater-than-normal difference in CMAP amplitude between the elbow and wrist stimulation sites but should not affect the elbow and below-elbow sites.

Change in SNAP configuration or amplitude may also be useful in identifying lesions. Orthodromic potentials recorded with near-nerve needle electrodes could show decreases of up to 40–50% in peak-to-peak amplitude between the below-elbow and elbow sites. Antidromic surface-recorded potentials could change by up to 53%, or 8 μV. Tackmann found that greater-than-normal amplitude change was always accompanied by slowing of sensory conduction velocity. Three percent of a group of patients evaluated in our laboratory showed a greater-than-normal SNAP amplitude change, while all other sensory parameters were normal. Tackmann noted that change in SNAP configuration was useful in localizing 13% of patients with sensory symptoms alone but only 2% of those with motor and sensory lesions. Payan found these parameters helpful in 10% of cases.

**Needle Examination.** Needle electrode examination is useful in establishing whether axonal interruption has occurred, gauging the chronology of the lesion, determining whether reinnervation is occurring, and localizing the lesion site. In concert with conduction studies it can also be very helpful in differentiating a radicular or plexus lesion from one of the ulnar nerve. The examination should include the FDI and hypothenar muscles, a forearm muscle innervated by the ulnar nerve, and the abductor pollicis brevis.

Mild lesions with sensory loss as the primary symptom may result in no needle exam abnormalities. Lesions characterized by conduction block may show reduced motor unit potential (MUP) recruitment, but little else. When axonal interruption occurs, positive sharp waves and fibrillations can be observed. Enlarged MUPs suggest that reinnervation has taken place, whereas polyphasic MUPs demonstrating moment-to-moment variation in shape indicate that reinnervation is taking place. FCU or FDP abnormalities indicate a lesion arising at or proximal to the elbow, although these muscles may be normal in the presence of elbow lesions.

Payan found hand muscle fibrillation in 57% of his cases. Eisen noted fibrillations or positive waves in the FDI in 50%, hypothenar in 37%, and FCU in 6% of patients with sensory and motor deficits. MUP abnormalities were present in hand muscles in all patients and in the FCU in 27%.

In our group of patients 47% showed needle
exam abnormalities in hand muscles. Sixty-three percent of those had fibrillations. Forty-one percent of the total group also had abnormalities in the FCU. Sixty-five percent of those with FCU abnormalities had enlarged motor unit potentials, whereas another 24% had both fibrillations and enlarged MUPs. The frequency of FCU abnormality on both needle exam and proximal segment latency testing is contrasted with the infrequent involvement of the forearm muscles detected on clinical examination.¹,¹³

Patients in our group who demonstrated needle exam abnormalities tended to have more severe lesions. Ninety-three percent of those with both fibrillations and enlarged MUPs in hand muscles had lesions producing both motor and sensory symptoms.

**Cumulative Results.** Using the combined results of the individual evaluations, Tackmann was able to localize the lesion in 95% of patients with motor and sensory deficits and 82.5% of those with sensory-only deficits.³⁸ Payan could place the lesion at the elbow in 96% of his cases.³⁹

In our patients with both motor and sensory symptoms, 48% could be localized by the finding of an elbow segment motor velocity that was slowed both absolutely and relative to the forearm. Another 5% with normal elbow segment velocity localized by a greater-than-normal difference relative to the forearm. Nineteen percent more could be localized by comparing the elbow segment and axilla-elbow velocities when the forearm was also slowed. Sensory studies did not localize any additional patients. Needle exam abnormalities in forearm muscles helped to place lesions at or proximal to the elbow in an additional 14%. Fourteen percent showed slowed elbow segment and forearm velocities, but did not have axillary stimulation done; nor did they show needle exam abnormality in proximal ulnar muscles.

In the patients with sensory-only symptoms, 48% could be localized by elbow segment motor slowing both absolute and relative to the forearm. Another 16% with a normal elbow segment motor velocity showed a greater-than-normal velocity difference compared with the forearm. Three percent showed elbow segment slowing without a
significant difference to the forearm but had a normal axilla-elbow velocity. Three percent additionally localized by absolute and relative sensory velocity slowing, whereas another 13% had normal elbow segment sensory velocity but a greater-than-normal difference relative to the forearm. Three percent more showed only an abnormal change in SNAP amplitude between the below-elbow and elbow stimulus sites. Needle examination did not provide any additional data aiding in elbow localization. Thirteen percent of these patients, 8% of the combined groups, were normal in all parameters.

**Electrophysiologic Differential Diagnosis.**

*Cervical Radiculopathy. Cervical radiculopathy at the C₈ or T₁ level could produce symptoms and signs similar to ulnar neuropathy at the elbow. Ulnar sensory conduction studies should be normal. The ulnar and median CMAP could be low and motor conduction velocity mildly slowed if axonal injury has occurred. Both ulnar and median F*

---

**FIGURE 5.** Flexed elbow position showing wrist, below-elbow, and elbow stimulus sites. Axillary site is 10–15 cm proximal to elbow site.
wave latencies could be prolonged. If needle examination abnormalities are present, they should be seen in a combination of ulnar, median, and radial innervated muscles of those myotomes and may also be present in the cervical paraspinal muscles.

Lower Trunk Plexopathy. Involvement of the lower trunk or medial cord of the brachial plexus can present similarly to ulnar neuropathy at the elbow. Because the lesion is distal to the sensory ganglion cell, ulnar sensory nerve conduction studies are often abnormal. The classic conduction study findings are an absent or low-amplitude ulnar SNAP and reduced CMAP amplitude of both the ulnar and median innervated hand muscles. Mild motor velocity slowing may be present, and prolongation of both median and ulnar F wave latencies might be seen. Again in such cases, needle exam abnormalities should be present in both median and ulnar territories that share C, and TI innervation. Cervical paraspinals should be spared in this lesion.15,39

Wrist Lesion. The ulnar nerve may suffer local trauma at the wrist as it enters the hand through Guyon's canal. Although both hypothenar and interossei involvement may occur, preferential involvement of the FDI is said to favor a wrist lesion. Distal latency to the FDI may be disproportionately prolonged as compared with the hypothenar group. The ulnar SNAP may or may not be abnormal, depending on the nature of the lesion. The dorsal cutaneous ulnar action potential should be normal, since this nerve branch arises proximal to the wrist.10,30

SUMMARY
Electrodiagnostic testing is useful in evaluating ulnar nerve elbow lesions. A flexed elbow seems preferable for conduction studies, since it eliminates the elbow segment slowing found in normals done in the extended position. Slowing of the motor velocity in the elbow segment was the most frequent abnormality in this study. Sensory conduction studies and needle examination each provided additional helpful data. Latency to ulnar forearm muscles and "inching" stimulations around the elbow are techniques that also deserve to be included in our standard armamentarium.
APPENDIX

This protocol is used in our laboratory for the evaluation of suspected ulnar neuropathy at the elbow. Ulnar motor conduction studies are performed with recording by surface electrode. The electrode placement is shown in Fig. 4. Surface temperature measured over the first dorsal interosseus must be at least 33°C. The elbow is flexed to 135° and forearm supinated (Fig. 5). Stimulation sites are at the wrist 6.5 cm proximal to the recording electrode, below the elbow 3–4 cm distal to the medial epicondyle, above the elbow 8–12 cm proximal to the below-elbow site, and in the axilla. Responses are measured from photorecorder records. CMAPs are recorded at a 5 mV per division gain and a 1.6 Hz to 16 KHz bandwidth. Onset latency and baseline-to-negative-peak amplitude are determined at each site. F wave latency is measured from the wrist. Antidromic SNAPs are recorded from the fifth digit. The recording electrode placement is shown in Fig. 6. Stimulation sites are the same as motor, except the wrist site is adjusted for an 11 cm distance to the active recording electrode. Responses are recorded at 10 μV/division gain and a 32 Hz to 3.2 KHz bandwidth. Three traces are superimposed on the photorecorder record. Electronic averaging is not used. Action potentials are considered non-responsive when no reproducible response is observable above baseline noise. Velocity calculations are done from onset latencies. The baseline-to-negative-peak amplitude of each response is also measured. Our normal values for amplitudes, segmental velocities, and difference in velocity between segments are shown in Table 2. Median nerve conduction studies are also done. These should include at least assessment of the amplitudes of CMAP and SNAP, motor and sensory distal latency, motor conduction velocity between elbow and wrist, and the F wave latency. Needle examination is done on the FDI, hypothenar, and FCU muscles as well as the abductor pollicis brevis.


REFERENCES

Electrodiagnostic evaluation of patients with suspected polyneuropathy is useful for detecting and documenting peripheral abnormalities, identifying the predominant pathophysiology, and determining the prognosis for certain disorders. The electrodiagnostic classification of polyneuropathy is associated with morphologic correlates and is based upon determining involvement of sensory and motor fibers and distinguishing between predominantly axon loss and demyelinating lesions. Accurate electrodiagnostic classification leads to a more focused and expedient identification of the etiology of polyneuropathy in clinical situations.

Key words: polyneuropathy • electrodiagnosis • nerve conduction studies • electromyography

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PERIPHERAL NERVE DISORDERS

Initial classifications of nerve disorders were based upon anatomic and clinical observations following focal nerve damage. Waller demonstrated the predictable degeneration of nerve fibers in the distal stump of a transected nerve, describing the initial discontinuities of axolemma with subsequent dissolution of axons. "Axonotmesis" was used to describe focal destruction of axons and myelin sheaths without interruption of the nerve stroma. Axonal (wallerian) degeneration occurred distal to the lesion, identical to the degeneration associated...
with nerve transection. Recovery was prolonged, occurring first in muscles closest to the site of damage, and related to regeneration of the axon via intact endoneurial tubes. "Neurapraxia" was used to define a motor paralysis not associated with axonal degeneration; recovery occurred within hours to months.

Histopathologic evaluation of experimental nerve compression has increased our understanding of "neurapraxia." Defects have been demonstrated under the edges of the compressing tourniquet without extension throughout the compressed area. Invagination of one myelin segment into the next has been associated with conduction block by occluding the node of Ranvier, resulting in ionic current blockade.

Electrodiagnostic evaluation of polyneuropathy is similar to the evaluation of focal nerve lesions. It is necessary to determine the presence of sensory and motor fiber involvement and to accurately distinguish between axon loss and demyelinating lesions. Clearly, many polyneuropathies are neither purely axonal or demyelinating, but rather a combination of both with predominance of one or the other. The results of conventional electroneuromyography usually can make this distinction.

**PHYSIOLOGIC BASIS OF ELECTRODIAGNOSTIC ABNORMALITIES**

The characteristic electrodiagnostic findings in purely axon loss lesions are best demonstrated following total axonal interruption as in nerve transection. Attention to the sequential abnormalities is useful in identifying those components of the electrodiagnostic examination most sensitive to axonal disorders. Landau demonstrated that muscle contraction could be evoked for several days with stimulation of a transected nerve; the response then diminished with complete loss of excitability after 4 to 5 days.

Clinical electrodiagnostic evaluation demonstrates similar findings. Immediately after transection, motor and sensory evoked response amplitude, conduction velocity, and distal latency remain normal with stimulation distal to the lesion. Needle electromyography demonstrates normal insertional and rest activity, although voluntary motor unit action potentials (MUAPs) cannot be activated. Within days, a progressive decrease in compound muscle action potential (CMAP) and sensory nerve action potential (SNAP) amplitude occurs. Evoked responses ultimately disappear after 3 to 7 days. Prior to disappearance, sensory and motor conduction velocities and distal latencies remain essentially normal with only minimal abnormalities at a time when amplitude is substantially diminished. Insertional and rest abnormalities on needle electromyography can be apparent within 7 to 10 days, although may not be evident for up to 3 weeks depending upon the proximity of the denervated muscle to the site of nerve section. Initial abnormality consists of prolonged insertional activity, followed by the appearance of sustained positive waves, spontaneous fibrillation potentials, and complex repetitive discharges.

With incomplete axon loss lesions, reduced recruitment is recorded rather than complete absence of voluntary MUAPs. MUAPs initially are of normal amplitude, duration, and configuration. A slight increase in the percentage of polyphasic MUAPs may appear after 10 to 14 days, presumably secondary to sprouting or collateral regeneration of surviving motor axons. Within months, MUAPs are of increased amplitude and duration with an increased percentage of polyphasic potentials.

In contrast, different electrodiagnostic results are obtained following either focal or diffuse demyelination. With a complete focal conduction block, initial findings are identical to those described for nerve transection. Motor and sensory evoked responses cannot be demonstrated with nerve stimulation proximal to the lesion; however, stimulation distal to the lesion results in normal responses. Regardless of the duration of the physiologic block, all nerve conduction studies distal to the lesion remain normal. Insertional and resting abnormalities may not develop on needle examination. If present, those abnormalities are modest, commensurate with the mild degree of axon loss often resulting from insults severe enough to produce conduction block.

The electrodiagnostic abnormalities associated with focal demyelination without conduction block are similar to those seen in chronic nerve compression, ie, substantial reduction of conduction velocity across the lesion.

In uniform demyelinating disorders, the marked reduction of conduction velocity is disproportionate to the relatively normal evoked response amplitude with distal stimulation. There is relatively homogeneous involvement of all myelinated fibers.

With multifocal demyelination, conduction velocity may also be reduced disproportionate to the relatively preserved evoked response amplitude with distal stimulation. Proximal stimulation re-
sults in abnormal temporal dispersion of the response, the proximal response being of substantially lower amplitude and longer duration than the distal response (Figure 1). Reduced conduction velocity in some fibers increases temporal dispersion by accentuating the differences in conduction of different fibers within the nerve. Partial conduction block can contribute to diminished amplitude. Distal demyelination may be associated with prolonged distal latency.

Needle electromyography demonstrates decreased recruitment (attributable to conduction block in some fibers) and MUAPs may show increased polyphasia, presumably secondary to distal demyelination. Other characteristic findings associated with denervation are not present on needle electromyography unless superimposed axon loss exists.

**ELECTRODIAGNOSTIC EVALUATION IN SUSPECTED POLYNEUROPATHY**

The collective results of nerve conduction studies and electromyography are useful in analyzing the underlying pathophysiology, and this data, together with the clinical findings, may suggest a specific diagnosis in addition to giving an approximation to the disease duration.

Complete electrodiagnostic examination of a polyneuropathy requires both motor and sensory conduction studies, preferably upon multiple nerves in upper and lower extremities. Bilateral studies should be performed on several peripheral nerves to demonstrate the characteristic symmetry of abnormality. Since individuals with polyneuropathy are susceptible to focal trauma, it is not unusual to find a clinical mononeuropathy superimposed upon a mild polyneuropathy. All individuals with mononeuropathy should be evaluated for an underlying polyneuropathy.

A relatively standardized electrodiagnostic evaluation (Table 1) is recommended for the evaluation of polyneuropathy, although the strategy may differ depending upon severity. In individuals with mild symptoms and signs, the electromyographer is advised to evaluate the most sensitive or susceptible peripheral nerves.

For example, in a typical diffuse polyneuropathy, motor and sensory nerve conduction studies of the distal lower extremity are more likely to be abnormal than those in the upper extremity. Similarly, needle electromyography of the intrinsic

**Table 1. Polyneuropathy protocol.**

<table>
<thead>
<tr>
<th>Conduction Studies</th>
<th>Test most involved site when mild or moderate, least involved if severe</th>
</tr>
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<tbody>
<tr>
<td>Peroneal motor (extensor digitorum brevis); stimulate at ankle and knee. Record F response latency following distal antidromic stimulation.</td>
<td></td>
</tr>
<tr>
<td>If abnormal, tibial motor (abductor hallucis); stimulate at ankle and knee; record F response latency.</td>
<td></td>
</tr>
<tr>
<td>If no responses: Peroneal motor (anterior tibial); stimulate at fibula and knee.</td>
<td></td>
</tr>
<tr>
<td>Ulnar motor (hypothenar); stimulate at elbow and wrist. Measure F response latency.</td>
<td></td>
</tr>
<tr>
<td>If abnormal: Median motor (thenar); stimulate at elbow and wrist. Measure F response latency.</td>
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<tr>
<td>Sural sensory (ankle): stimulate 14 cm from recording electrode; perform conduction velocity unless amplitude supernormal. If not clearly normal because of age or technical factors, consider: Needle recording. Averaging.</td>
<td></td>
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<tr>
<td>Median sensory (index); stimulate wrist and elbow. If antidromic response is absent or a focal entrapment is suspected, record from the wrist stimulating the palm. Additional peripheral nerves can be evaluated if findings equivocal. Definite abnormalities should result in: Evaluation of opposite extremity. Proceed to evaluation of specific suspected abnormality.</td>
<td></td>
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<tr>
<td>If prominent cranial involvement: Facial motor (orbicularis oculi); stimulate at angle of jaw. Blink reflex studies (orbicularis oculi); stimulate supraorbital nerve.</td>
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**Needle Examination**

Examine anterior tibial, medial gastrocnemius, first dorsal interosseous (hand), and lumbar paraspinal muscles. If normal, intrinsic foot muscles should be examined. Abnormalities should be confirmed by examination of at least one contralateral muscle.

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**Figure 1.** Ulnar motor nerve conduction study recording from the abductor digiti minimi muscle in a patient with chronic inflammatory demyelinating polyneuropathy. Marked temporal dispersion of the proximal compound motor action potential (CMAP) on elbow stimulation (B) is recorded compared with the distal CMAP on stimulation at the wrist (A).
foot muscles may demonstrate abnormality not present in upper extremity muscles. Conversely, evoked responses may be absent in the distal lower extremities in individuals with moderately severe symptoms and signs, making it impossible to determine the presence of a demyelinating component. Additional studies should be performed using proximal nerves as well as upper extremity or facial nerves.

Needle electromyography is useful in grossly defining the chronicity of an axon loss lesion, based upon the distribution and amplitude of fibrillation potentials and positive waves, as well as MUAP parameters. The distribution of needle abnormality is useful in identifying other disorders that may be confused with, or superimposed upon, an underlying polyneuropathy. For example, distal predilection of abnormality, greater in the lower than upper extremities, is characteristic of most axon loss polyneuropathies. Moderately severe, asymmetric involvement of lower extremity muscles, sparing the intrinsic foot muscles, although not completely inconsistent with a diagnosis of polyneuropathy, would be more consistent with old poliomyelitis, other motoneuron disorders, or polyradiculopathy. Similarly, marked abnormality on examination of paraspinal muscles is unusual in polyneuropathy and suggests a superimposed polyradiculopathy.

**CLASSIFICATION OF POLYNEUROPATHY BASED UPON ELECTRODIAGNOSTIC FINDINGS**

Although a universally accepted electrodiagnostic classification is improbable, a useful model can be created using the predominant electrodiagnostic abnormalities. In this classification, polyneuropathy is divided into six categories based upon the prevalence of sensory and motor as well as axon and myelin involvement. Demyelinating polyneuropathies are subdivided into uniform and segmental disorders. Discussion will be devoted to the clinical and electrodiagnostic aspects of one or two common polyneuropathies within each category; polyneuropathies with similar electrodiagnostic characteristics are listed in a table under each classification. Only polyneuropathies with documented electrophysiologic abnormalities are listed. Some etiologies are listed under more than one category as they can manifest several types of diffuse and symmetric polyneuropathy. Carcinoma, acquired immune deficiency syndrome (AIDS), and lupus erythematosus are examples of the latter.

**Uniform Demyelinating, Mixed Sensorimotor Polyneuropathy.** Hereditary motor sensory neuropathy type I (HMSN I) is a dominantly inherited hypertrophic sensorimotor polyneuropathy with insidious onset in childhood or early adult life. Associated features include firm enlarged nerves, scoliosis, pes cavus, hammer toes, distal weakness with little atrophy, abnormal vibratory and position sensation, and hyporeflexia. There is evidence of demyelination, remyelination, and onion bulb formation on nerve biopsy.

The electrodiagnostic hallmark of HMSN I is reduced maximum conduction velocity, typically less than 85% of the expected lower limit of normal. Values as slow as 25 m/s are common. Because of the uniform demyelination of all fibers, temporal dispersion usually is not a feature, although phase cancellation may cause abnormal temporal dispersion. Nevertheless, the absence of temporal dispersion is useful in distinguishing hereditary from acquired demyelinating polyneuropathies. Motor evoked responses may be reduced, but the predominant abnormality remains uniformly reduced conduction velocity. F responses, when recordable, are prolonged as are distal latencies commensurate with slowing in other segments. Sensory evoked responses are usually absent. Needle electromyography demonstrates reduced recruitment; MUAP amplitude and duration may be increased with evidence of mild to moderately severe distal denervation, proportionate to the amount of superimposed axon loss.

Hereditary motor sensory neuropathy type III (Dejerine–Sottas disease) is a rare autosomal recessive hypertrophic neuropathy with onset in infancy; associated features include enlarged nerves, kyphoscoliosis, pes cavus, weakness, ataxia, sensory loss, and areflexia. Nerve pathology is similar to that of HMSN type I, as are the electrodiagnostic findings except for greater reduction of conduction velocity. Listed in Table 2 are other
inherited or congenital diseases with similar electrodagnostic findings.

**Segmental Demyelinating, Motor > Sensory Polyneuropathy.** Acute inflammatory demyelinating polyneuropathy (AIDP, Guillain–Barré syndrome) is of unknown etiology, but is preceded by an infection in 70% of individuals, raising the hypothesis of an immunologic origin. This is supported by the efficacy of therapeutic plasma exchange in treating AIDP.

This disorder commonly presents with distal paresthesias followed by symmetric weakness of extremity and cranial muscles, usually sparing extraocular muscles and sphincters. Weakness predominates and increases for 1 to 4 weeks. Additional findings include areflexia and cytoalbuminodissociation after 1 week. An associated autonomic neuropathy may coexist. Pathologic studies verify the inflammatory and demyelinating involvement of the peripheral nerve that may be associated with severe, secondary axonal and even anterior horn cell degeneration.

Electrodiagnostic findings are variable. In 1965, Lambert and Mulder reported electrodiagnostic studies for 49 patients evaluated during the first 3 weeks of illness: 14% had no abnormality of conduction, 61% had conduction velocities less than 70% of the normal mean, and 25% demonstrated prolonged distal latencies with minimal or no slowing of conduction velocities. Serial evaluation of the latter group demonstrated sequential slowing of conduction velocity in some patients similar to the second group described above.

The large percentage of patients with normal conduction studies probably reflected the state of electrodagnosis at that time when motor conduction studies were emphasized and sensory conduction studies, H reflexes, and F waves were not in general use. Variability in reported electrodiagnostic findings can be explained by understanding the temporal changes following acute axonal degeneration and by recognizing this as a multifocal rather than a diffuse disorder.

We analyzed sequential electrodagnostic data for 70 consecutive patients with AIDP. During the first 5 weeks of illness, motor conduction study abnormalities (abnormal CMAP temporal dispersion and/or conduction block, reduced amplitude, slowed conventional or terminal conduction velocity, and prolonged or absent F responses) were more common than sensory conduction abnormalities. Early in the disease (weeks 1 to 2), abnormalities of motor amplitudes were much more common than slowing in distal or proximal motor conduction rates. In the case of F responses, the latency was often prolonged out of proportion to that expected when the distal motor latencies and limb conduction velocities were considered, results indicating proximal nerve involvement.

Using pooled data, the nadir of abnormality occurred during the third week for motor conduction studies and during the fourth week for sensory conduction studies. Motor study abnormalities tended to be homogeneous, while sensory study abnormalities were patchy, revealing defects of individual nerves and normalcy of other sensory nerves. Most notably, in approximately half of patients during the first 4 weeks of disease, sural studies were normal in the setting of abnormal median sensory results, findings atypical in any diffuse polyneuropathy. Normal conduction studies were unusual: only one patient manifested no abnormality of conduction during the first 5 weeks of illness. Using criterion for assessing the presence of demyelination, 87% of patients had evidence of a prominent demyelinating neuropathy in at least one nerve not localizable to a common entrapment site. Two patients were classified as having axonal degeneration only; indeterminate results were recorded in 10% of patients.

On needle electromyography, abnormal spontaneous activity appeared between weeks 2 and 4, while abnormalities of MUAP morphology (increased polyphasia and amplitude) became apparent during weeks 4 to 5. No patient had normal MUAP recruitment at the time of initial examination.

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a disorder of presumed immunologic etiology, presenting as a slowly progressive, stepwise progressive, or monophasic illness in the majority of patients. A relapsing and remitting course is seen in approximately one-third of patients. Weakness involves cranial, truncal, and extremity musculature. Pathologically, there is evidence for mononuclear cell infiltration, segmental demyelination, and hypertrophic changes most often observed in spinal roots, spinal ganglia, and proximal nerve trunks. Electrodagnostic findings in the individual patient are indistinguishable from AIDP. On occasion, sensory evoked responses are spared. Motor conduction velocity may improve concurrent with clinical remission, but disproportionately less than the degree of clinical improvement would suggest. Nevertheless, a poor correlation exists between slowing of
motor nerve conduction velocity and the severity of muscle weakness, and conduction velocity often remains severely reduced during clinical remission. Needle examination usually demonstrates distal greater than proximal limb and paraspinal muscle denervation.

Several types of polyneuropathy are associated with plasma cell dyscrasias. One type, a severe chronic demyelinating polyneuropathy, has been associated with osteosclerotic myeloma, Waldenstrom’s macroglobulinemia, and monoclonal gammopathy of undetermined significance. Clinical and electrodiagnostic features are similar to those of CIDP.

On a global scale, leprosy is the most common cause of peripheral neuropathy. It is best conceived as a mononeuropathy of superficial sensory nerve branches within cutaneous lesions, with subsequent involvement of major motor branches. A symmetric sensory and motor distal polyneuropathy should never be found, although involvement may be so widespread as to suggest a diffuse process. The neuropathy of leprosy is classified under this category because the clinical presentation of multiple mononeuropathies and the pathologic and electrodiagnostic features of segmental demyelination most mimic a motor greater than sensory demyelinating polyneuropathy.

Slowed conduction velocity and/or proximal conduction block of motor nerves across focal areas of involvement is common. Adjacent motor nerves may be normal.

Other diseases manifesting electrodiagnostically as segmental demyelinating, motor greater than sensory polyneuropathy are listed in Table 3. Multifocal demyelinating polyneuropathy with persistent conduction block of motor nerves across focal areas of involvement is common. Adjacent motor nerves may be normal.

Axon Loss, Motor > Sensory Polyneuropathy. Acute intermittent porphyria is an autosomal dominant disorder with incomplete penetrance, presentings as a classic triad of psychosis, abdominal pain, and polyneuropathy clinically resembling AIDP. Pathology of peripheral nerve reveals axonal degeneration with secondary demyelination. Nerve conduction studies demonstrate reduced motor evoked amplitudes, whereas conduction velocity slowing is spared until substantial reduction of amplitude occurs. Sensory evoked amplitudes are reduced in approximately 50% of patients. Fibrillation potentials appear in paraspinal muscles in 7 to 10 days and subsequently appear in other proximal and then distal muscles symmetrically.

Similar electrodiagnostic findings to porphyria may be observed in lead polyneuropathy, although there may be greater involvement of upper than lower extremities.

Hereditary motor sensory neuropathy type II (neuronal Charcot–Marie–Tooth disease) is a dominantly inherited sensorimotor polyneuropathy with insidious onset in the third to fourth decade; associated features include moderate to severe atrophy, pes cavus, hammer toes, and mild sensory loss. Motor evoked amplitudes are reduced with essentially normal conduction velocities. Sensory responses are absent in 50% of patients. Needle electromyography demonstrates chronic neurogenic changes, most prominent distally.

Although most pharmaceutically induced polyneuropathies present as a sensory greater than motor axonopathy, several medications produce, as an adverse effect, motor greater than sensory

<table>
<thead>
<tr>
<th>Table 3. Segmental demyelinating, motor &gt; sensory polyneuropathy.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute inflammatory demyelinating polyneuropathy.</td>
</tr>
<tr>
<td>Chronic inflammatory demyelinating polyneuropathy.</td>
</tr>
<tr>
<td>Multifocal demyelinating polyneuropathy with persistent conduction block.</td>
</tr>
<tr>
<td>Osteosclerotic myeloma.</td>
</tr>
<tr>
<td>Waldenstrom’s macroglobulinemia.</td>
</tr>
<tr>
<td>Monoclonal gammopathy of undetermined significance.</td>
</tr>
<tr>
<td>Gamma heavy chain disease.</td>
</tr>
<tr>
<td>Angiofollicular lymph node hyperplasia.</td>
</tr>
<tr>
<td>Hyperthyroidism.</td>
</tr>
<tr>
<td>Leprosy.</td>
</tr>
<tr>
<td>Diphtheria.</td>
</tr>
<tr>
<td>Acute arsenic polyneuropathy.</td>
</tr>
<tr>
<td>Pharmaceuticals</td>
</tr>
<tr>
<td>Amiodarone.</td>
</tr>
<tr>
<td>Perhexiline.</td>
</tr>
<tr>
<td>High dose Ara-C.</td>
</tr>
<tr>
<td>Lymphoma.</td>
</tr>
<tr>
<td>Carcinoma.</td>
</tr>
<tr>
<td>AIDS.</td>
</tr>
<tr>
<td>Systemic lupus erythematosus.</td>
</tr>
<tr>
<td>Glue sniffing neuropathy.</td>
</tr>
<tr>
<td>Post polonovalis anastomosis.</td>
</tr>
<tr>
<td>Neuropathy associated with progressive external ophthalmoplegia.</td>
</tr>
<tr>
<td>Ulcerative colitis.</td>
</tr>
<tr>
<td>Marinesco–Sjogren syndrome.</td>
</tr>
<tr>
<td>Cryoglobulinemia.</td>
</tr>
</tbody>
</table>

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involvement. Dapsone neuronopathy is an example of such involvement.  

Table 4 lists other polyneuropathies with electrodiagnostic features similar to porphyria and HMSN type II.

**Sensory Axon Loss Neuropathy.** Carcinomatous sensory neuronopathy is the most distinctive of the remote-effect polyneuropathies associated with carcinoma. Its onset is subacute, often preceding identification of the neoplasm by several months. A strong association exists between oat cell carcinoma of the lung and a sensory neuronopathy. Symptoms and signs include pain, paresthesias, dysesthesias, and large, more than small, fiber sensory loss. Areflexia, gait ataxia, and choreoathetoid movements are common, but strength is usually preserved. Neuropathology reveals inflammation and cell loss in dorsal root ganglia, and gliosis of the posterior column of the spinal cord. Nerve conduction studies usually reveal diminished or absent SNAP amplitudes in the setting of normal motor nerve conduction studies. Motor amplitudes and conduction may be slightly reduced in severe cases, perhaps representing disuse atrophy, axonal stenosis, or a combination of both. Needle examination is usually normal except in late, severe disease when spontaneous activity at rest may be recorded.

Friedreich's ataxia is a recessively inherited disorder characterized by ataxia, mild weakness, areflexia, and dissociated sensory loss involving modalities classically interpreted as reflecting posterior column dysfunction (abnormal vibration, two-point discrimination, and joint position sensation). Associated signs include scoliosis, pes cavus deformity, extensor plantar responses, nystagmus, and optic atrophy. Sensory responses are usually absent, although responses of markedly reduced amplitude may be recorded.

**Motor Axon Loss Neuropathy.** The majority of toxic and metabolic polyneuropathies manifest evidence of degeneration of the distal portion of the axon. In general, these polyneuropathies are electrodiagnostically indistinguishable from one another. Sensory symptoms and signs may initially predominate, and sensory evoked amplitudes may be reduced early in the course of the disease, when motor studies are normal. Conduction velocity is normal until there is a substantial reduction of amplitude, although predilection for large fibers may reduce the maximum conduction velocity slightly. Distal latency may be slightly prolonged, prior to reduction of evoked amplitude, perhaps in association with distal axonostenosis. In contradistinction to primary demyelinating disorders, appreciable temporal dispersion of the proximal, compared with distal, CMAP is not recorded (Figure 2). Fibrillation potentials and positive waves may be seen symmetri-

**Table 4.** Axon loss, motor > sensory polyneuropathy.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Porphyria</td>
<td>5</td>
</tr>
<tr>
<td>Axonal Guillain–Barré syndrome</td>
<td>79</td>
</tr>
<tr>
<td>Hereditary motor sensory neuropathy types II and V</td>
<td>68</td>
</tr>
<tr>
<td>Lead neuropathy</td>
<td>116</td>
</tr>
<tr>
<td>Dapsone neuropathy</td>
<td>2,100,239</td>
</tr>
<tr>
<td>Vincristine neuropathy</td>
<td>32,36,99</td>
</tr>
<tr>
<td>Remote-effect motor neuropathy associated with lymphoma</td>
<td>230</td>
</tr>
<tr>
<td>Remote-effect motor neuropathy associated with carcinoma</td>
<td>248</td>
</tr>
<tr>
<td>Hypoglycemia/hyperinsulinemia</td>
<td>59,175</td>
</tr>
</tbody>
</table>

**Table 5.** Axon loss sensory neuropathy or neuropathy.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hereditary sensory neuropathy types I–IV</td>
<td>24,69,191</td>
</tr>
<tr>
<td>Friedreich’s ataxia</td>
<td>96,103,200</td>
</tr>
<tr>
<td>Spinocerebellar degeneration</td>
<td>73,106,183</td>
</tr>
<tr>
<td>Abetalipoproteinemia (Bassen–Kornzweig disease)</td>
<td>112,168,244</td>
</tr>
<tr>
<td>Primary biliary cirrhosis</td>
<td>11</td>
</tr>
<tr>
<td>Acute sensory neuropathy</td>
<td>239</td>
</tr>
<tr>
<td>Cis-platinum toxicity</td>
<td>70,208,209</td>
</tr>
<tr>
<td>Carcinomatous sensory neuropathy</td>
<td>111,234</td>
</tr>
<tr>
<td>Lymphomatous sensory neuropathy</td>
<td>214</td>
</tr>
<tr>
<td>Chronic idiopathic ataxic neuropathy</td>
<td>56</td>
</tr>
<tr>
<td>Sjogren’s syndrome</td>
<td>104,140,154</td>
</tr>
<tr>
<td>Fisher variant Guillain–Barré syndrome</td>
<td>75,117</td>
</tr>
<tr>
<td>Paraproteinemia</td>
<td>66,205</td>
</tr>
<tr>
<td>Pyridoxine toxicity</td>
<td>194,219</td>
</tr>
<tr>
<td>Idiopathic sensory neuropathy</td>
<td>122</td>
</tr>
<tr>
<td>Styrene-induced peripheral neuropathy</td>
<td>18</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>181</td>
</tr>
<tr>
<td>Thalidomide toxicity</td>
<td>139</td>
</tr>
<tr>
<td>Nonsystemic vasculitic neuropathy</td>
<td>70</td>
</tr>
<tr>
<td>Chronic gluten enteropathy</td>
<td>118</td>
</tr>
<tr>
<td>Vitamin E deficiency</td>
<td>83,106,112</td>
</tr>
</tbody>
</table>
FIGURE 2. Peroneal motor nerve conduction study recording from the extensor digitorum brevis muscle in a patient with a chronic sensorimotor axonal polyneuropathy. The amplitude, shape, and duration of the compound motor action potential recorded on ankle stimulation (A) does not appreciably change on stimulation at the fibular head (B).

cally in distal extremity muscles. These abnormalities on needle examination typically precede clinical evidence of motor involvement.

A common example is the polyneuropathy associated with chronic alcoholism and secondary nutritional deficiency. The clinical features are those of a symmetric and generalized sensorimotor distal polyneuropathy. Patients complain of paresthesias and dyesthesias of the feet and distal legs, more so than weakness. Physical findings consist of absent or diminished sensation in a distal to proximal gradient in the lower extremities, absent ankle reflexes, and mild weakness of toe and ankle extension. Involvement of the proximal lower extremity and hands only occurs in severe, progressive alcoholic polyneuropathy.

A detailed list of disorders associated with an axonal sensorimotor polyneuropathy and presenting with similar electrodiagnostic findings is found in Table 6.

**Mixed Axon Loss and Demyelinating Sensorimotor Polyneuropathy.** Diabetic polyneuropathy is the most common polyneuropathy in North America. It also represents a polyneuropathy demonstrating evidence of both axonal degeneration and demyelination. Even though several classifications of diabetic neuropathy exist, this monograph will discuss only the commonly observed, diffuse, symmetric sensorimotor polyneuropathy.

Patients characteristically manifest paresthesias, disabling dyesthesias, or numbness in the distal lower extremities. Examination demonstrates reduced vibratory sensation and two-point discrimination in a distal-to-proximal gradient in the lower extremities; proprioception may also be impaired in severe cases. This apparent dissociative sensory loss relates to predilection of large fiber involvement. In more severe disease, small fi-

### Table 6. Axon loss, mixed sensorimotor polyneuropathy.

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amyloidosis</td>
<td>22,126,127</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>119,131</td>
</tr>
<tr>
<td>Nutritional diseases</td>
<td></td>
</tr>
<tr>
<td>Vitamin B12 deficiency</td>
<td>81,160,161</td>
</tr>
<tr>
<td>Folate deficiency</td>
<td>29,80</td>
</tr>
<tr>
<td>Whipple’s disease</td>
<td>50</td>
</tr>
<tr>
<td>Post-gastrectomy syndrome</td>
<td>16</td>
</tr>
<tr>
<td>Gastric restriction surgery for obesity</td>
<td>1</td>
</tr>
<tr>
<td>Thiamine deficiency</td>
<td>180</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>9,220,223</td>
</tr>
<tr>
<td>Sarcoiodosis</td>
<td>26,182,187</td>
</tr>
<tr>
<td>Connective tissue diseases</td>
<td></td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>96,174,199</td>
</tr>
<tr>
<td>Periarteritis nodosa</td>
<td>39</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td></td>
</tr>
<tr>
<td>Churg-Strauss vasculitis</td>
<td>55,186</td>
</tr>
<tr>
<td>Temporal arteritis</td>
<td>37</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>146</td>
</tr>
<tr>
<td>Behcet’s disease</td>
<td>178</td>
</tr>
<tr>
<td>Hypereosinophilic syndrome</td>
<td>171,243</td>
</tr>
<tr>
<td>Cryoglobulinemia</td>
<td>160</td>
</tr>
<tr>
<td>Toxic neuropathy</td>
<td>215</td>
</tr>
<tr>
<td>Acrylamide</td>
<td>96,147</td>
</tr>
<tr>
<td>Carbon disulfide</td>
<td>18,226</td>
</tr>
<tr>
<td>Dichlorophenoxyacetic acid</td>
<td>56</td>
</tr>
<tr>
<td>Ethylene oxide</td>
<td>62,97,157</td>
</tr>
<tr>
<td>Hexacarbons</td>
<td>147</td>
</tr>
<tr>
<td>Carbon monoxide</td>
<td>232</td>
</tr>
<tr>
<td>Organophosphorus esters</td>
<td>51</td>
</tr>
<tr>
<td>Glue sniffing</td>
<td>134,147</td>
</tr>
<tr>
<td>Metal neuropathy</td>
<td></td>
</tr>
<tr>
<td>Chronic arsenic intoxication</td>
<td>42</td>
</tr>
<tr>
<td>Mercury</td>
<td>3</td>
</tr>
<tr>
<td>Thallium</td>
<td>16,60</td>
</tr>
<tr>
<td>Gold</td>
<td>120,241</td>
</tr>
<tr>
<td>Pharmaceuticals</td>
<td></td>
</tr>
<tr>
<td>Colchicine</td>
<td>186</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>707,230</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>176</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>150</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>31,69</td>
</tr>
<tr>
<td>Misonidazole</td>
<td>96</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>10,249</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>77</td>
</tr>
<tr>
<td>Disulfiram</td>
<td>10,21,27,235</td>
</tr>
<tr>
<td>Glutethimide</td>
<td>184</td>
</tr>
<tr>
<td>Nitrous Oxide</td>
<td>107,145,216</td>
</tr>
<tr>
<td>Lithium</td>
<td>165,166</td>
</tr>
<tr>
<td>Carcinomatous axonal sensorimotor polyneuropathy</td>
<td>51</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>76,173</td>
</tr>
<tr>
<td>Giant axonal dystrophy</td>
<td>13,129,132,204,202</td>
</tr>
<tr>
<td>Olivopontocerebellar atrophy</td>
<td>44,211</td>
</tr>
<tr>
<td>Neuropathy of chronic illness</td>
<td>24,26,252</td>
</tr>
<tr>
<td>Acromegaly</td>
<td>116</td>
</tr>
<tr>
<td>Hypophosphatemia</td>
<td></td>
</tr>
<tr>
<td>Lymphomatous axonal sensorimotor polyneuropathy</td>
<td>242</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>64,156,159,201</td>
</tr>
<tr>
<td>Myotonic dystrophy</td>
<td>52,54,165,172</td>
</tr>
<tr>
<td>Necrotizing angiopathy</td>
<td>70,130,218</td>
</tr>
<tr>
<td>Lyme disease</td>
<td>19,233</td>
</tr>
<tr>
<td>AIDS, ARC</td>
<td>25,62,152,167,183</td>
</tr>
<tr>
<td>Jamaican neuropathy</td>
<td>17,217</td>
</tr>
<tr>
<td>Tangier disease</td>
<td>152,202</td>
</tr>
<tr>
<td>Gouty neuropathy</td>
<td>43</td>
</tr>
<tr>
<td>Polycythemia vera</td>
<td>250</td>
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<tr>
<td>Typical multiple myeloma</td>
<td>126</td>
</tr>
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</table>
bers are involved as evidenced by alteration of pain and temperature sensation and dysautonomia. The major pathologic abnormalities are segmental demyelination and remyelination, in addition to axonal degeneration.291

The electrodiagnostic findings in distal symmetric diabetic polyneuropathy are variable, especially in early or mild cases. In most patients, sensory conduction studies reveal diminished evoked amplitude with moderate slowing of conduction velocity, greater than expected from axonal degeneration alone. Concurrently or later in the course of disease, motor evoked responses demonstrate similar findings with the addition of temporally dispersed proximal responses.224 Occasionally, in patients with asymptomatic or mild polyneuropathy, slowing in motor conduction velocity will be the only electrodiagnostic abnormality.246 Fibrillation potentials may appear in intrinsic foot muscles symmetrically prior to clinical evidence of atrophy or weakness, or reduced CMAP amplitudes recorded from foot muscles.

Polyneuropathy is relatively common in chronic renal failure, and virtually all patients requiring dialysis have evidence of a distal sensorimotor polyneuropathy. In many patients, this manifests as an axon loss, mixed sensorimotor polyneuropathy with borderline-low motor and sensory evoked amplitudes.28 In other patients, nerve conduction studies demonstrate pronounced slowing in conduction velocity with preserved proximal CMAPs. These latter findings reflect the mixed components of segmental demyelination superimposed upon axon loss, verified pathologically by Dyck and colleagues.72 Fibrillation potentials are seen in distal extremity muscles, particularly the intrinsic foot muscles. Unfortunately, determination of motor nerve conduction velocities alone is probably the most widely accepted measurement of peripheral nerve function in the evaluation of and serial assessment of uremic polyneuropathy. While widely accepted as a measure of adequacy of dialysis, conduction velocity determinations alone are likely inadequate and unreliable unless changes are marked.158

For completeness, Table 7 lists the two polyneuropathies manifesting electrophysiologically as a mixed axon loss and demyelinating sensorimotor polyneuropathy.

**Sources of Error**

The primary sources of error in evaluation of patients with suspected polyneuropathy are errors of omission, ie, drawing conclusions based upon a limited data base. Another common error is overemphasizing the value of “conduction velocity.” This measure is sensitive to demyelination but may remain normal in the setting of axonal degeneration. Similarly, distal latencies, another barometer of conduction rate, are markedly prolonged only in demyelination, moderately prolonged in association with axonal stenosis, and only mildly prolonged in axonal degeneration.

Another pitfall is the failure to exclude from interpretation focal slowing of conduction velocity due to specific entrapment mononeuropathies before concluding that a generalized process of reduced conduction exists. Particularly vulnerable to entrapment are the ulnar and peroneal nerves at the elbow and knee, respectively, and the median nerve at the wrist.

Motor and sensory evoked amplitudes are extremely sensitive to axonal degeneration despite the wide range of normal values. Markedly reduced motor evoked amplitudes with normal sensory responses are unusual in polyneuropathy; further investigation usually demonstrates a polyradiculopathy, motorneuron disease, or defective neuromuscular transmission (generalized low motor-normal sensory syndrome).245

Sensitivity of conduction velocity, distal latency, and evoked response amplitude to change in temperature requires careful measurement and maintenance of proper limb temperature (32°C to 36°C, surface temperature). Warming a limb by 5°C may result in as much as a 10-m/s increase in conduction velocity, a 1-ms decrease in distal latency, and a 20% decrease in sensory and motor amplitude.

Needle electromyography of intrinsic foot muscles is a sensitive measure of potential axonal degeneration. Nevertheless, these muscles may also be subject to local trauma and false-positive studies. This situation is most commonly observed in the extensor digitorum brevis and abductor digitii minimi muscles, while the abductor hallucis and first dorsal interosseous muscles are less likely to give aberrant results.89 Careful sampling of individual muscles and documentation of bilaterality

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**Table 7.** Mixed axon loss, demyelinating sensorimotor polyneuropathy.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Mellitus</td>
<td>142, 158, 224, 231, 246</td>
</tr>
<tr>
<td>Uremia</td>
<td>20, 43, 72, 133</td>
</tr>
</tbody>
</table>

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reduces the likelihood of false positive findings secondary to local injury.

In summary, a carefully planned and performed electrodiagnostic study is useful in quantifying and defining the underlying pathophysiology in polyneuropathy. In addition, interpretation of the results of electrodiagnosis often suggests a specific diagnosis, particularly when combined with other laboratory and clinical information.

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I. INTRODUCTION

A. Who can do cranial nerve studies? Anybody who attends this lecture.

B. When and why do we study cranial nerves? To evaluate weakness, sensory loss, or spasm due to:

1. Brainstem pathology
   a. Multiple sclerosis
   b. Tumor, e.g., glioma, acoustic neuroma
   c. Vascular lesions, e.g., lateral medullary syndrome

2. Peripheral nerve pathology
   a. Bell's palsy
   b. Polyneuropathy - hereditary, acquired
   c. Myasthenia gravis
   d. Surgical grafting

3. Other
   a. Blepharospasm
   b. Hemiatrophy or hemifacial spasm
   c. Myokymia
   d. Facial synkinesis

C. Technique

1. What to record
2. Where to stimulate
3. How to interpret

D. Which cranial nerves can be studied?

1. Optic - visual evoked responses
2. Oculomotor, trochlear, abducens - EMG
3. Trigeminal - blink reflex, EMG
4. Facial - direct NCS, blink reflex, EMG
5. Acoustic - brainstem auditory evoked responses
6. Glossopharyngeal - EMG
7. Vagus - test accessory nerve
8. Accessory - NCS, EMG
9. Hypoglossal - EMG

II. ANATOMY

A. Trigeminal Nerve

1. Function
   a. Motor - masseters, pterygoids, temporalis
   b. Sensory (Figure 1)
      (1) ophthalmic, maxillary, mandibular divisions
      (2) sensation to ipsilateral face and mouth, lacrimal gland, ciliary body
(3) Ophthalmic branch gives rise to supraorbital nerve via frontal nerve
(4) Motor fibers run with mandibular division
2. Anatomy (Figure 2)
   a. Main sensory nucleus in pons receives fibers from trigeminal ganglion
      (1) pain and temperature fibers descend to spinal nucleus in lateral medulla
      (2) tactile fibers ascend to synapse in area of main sensory nucleus
   b. Mesencephalic nucleus receives ascending fibers serving proprioception which synapse in mid-pons with the trigeminal motor nucleus - basis for jaw jerk

   ![Diagram of facial nerve]

   FIGURE 2

B. Facial Nerve

1. Function
   a. Motor: facial muscles, platysma, stapedius, auricle, buccinator, scalp, stylohyoid, posterior belly of digastric
   b. Sensory: taste in anterior 2/3 of tongue; soft palate;

2. Anatomy
   a. Motor nucleus in pons - fibers wrap around VIth nerve nucleus, leave brainstem at cerebellopontine angle through internal auditory meatus
   b. Passes through facial canal (petrous portion), exits through stylomastoid foramen and branches in parotid gland into five branches: temporal, zygomatic, buccal, mandibular, cervical
   c. Geniculate ganglion in facial canal - branches to:
      (1) periphery via chorda tympani
      (2) central through acoustic meatus to enter brain between inferior peduncle and olive

C. Accessory Nerve (Figures 3 and 4)

1. Function
   a. Cranial portion: motor to pharynx, upper larynx, uvula, palate with fibers to recurrent laryngeal and cardiac nerves
   b. Spinal portion: motor to upper trapezius, sternocleidomastoid, and branches to C2,3,4 spinal nerves
2. Anatomy
   a. Cranial: fibers from nucleus ambiguous in medulla run along vagus, joined by spinal portion at jugular foramen
   b. Spinal: arises from spinal nucleus of C5-6 spinal cord segments meets cranial portion at jugular foramen and sends branches to upper trapezius and sternocleidomastoid. Contribution from C2-4 thought to be primarily proprioceptive to SCM and trapezius
III. NERVE CONDUCTION STUDIES

A. Facial Nerve

1. Record: lateral upper or lower orbicularis oculi; reference - nose, temple
2. Stimulate: anterior to mastoid- anterior to ear lobe at angle of jaw; usually 3-8 mA
3. Perform study on both sides of face with eyes open
   a. Observe:
      (1) visual twitch of facial muscles
      (2) variability in excitability from side-to-side (normal: within 2mA)
      (3) amplitude of direct response (normal: 1-5mV within 50% side-to-side)
      (4) latency (normal: 2.2-4.0 mms)
   b. Avoid:
      (1) masseter simulation
      (2) recording of volume-conducted potentials
4. Can record from orbicularis oris and oculi simultaneously in cases of facial synkinesis, hemifacial spasm

B. The Blink Reflex

1. Technique
   a. Record: lateral upper or lower orbicularis oculi bilaterally with reference on nose, temple
   b. Stimulate: supraorbital nerve or glabellar tap
   c. Observe responses (See Figure 5)
      (1) R₁: ipsilateral afferent trigeminal, pontine monosynaptic reflex including main sensory nucleus and facial nucleus, ipsilateral efferent facial components
2. Normal values
   a. Normal blink study
      (1) direct: less than 4.1 ms
      (2) $R_1$: < 13.0 ms
      (3) side-to-side latency: direct: within 0.6 ms; $R_1$: within 1.2 ms
      (4) R/D: 2.6-4.6
   b. R/D ratio
      (1) ratio of $R_1$ to direct response
      (2) Compares distal facial nerve conduction with entire reflex arc

3. Comments
   a. Glabellar tap stimulates trigeminal on both sides simultaneously
   b. Infraorbital or mental nerve stimulation can be used but results in inconsistent $R_1$ and $R_2$

4. Neurologic disorders with abnormal blink reflex (See Table I and worksheet)
   a. Trigeminal neuralgia
   b. Peratrigeminal neuralgia
   c. Bell's palsy
d. Acoustic neuroma

e. Facial synkinesis

f. Hemifacial spasm

g. Polyneuropathy
   (1) Guillain-Barre, HSMN I, CIDP
   (2) HSMN II
   (3) diabetic

h. Multiple sclerosis

i. Wallenberg syndrome

G. Spinal Accessory Nerve

1. Record: middle upper trapezius with reference on acromion

2. Stimulate: along middle posterior margin of sternocleidomastoid; measure distance if planning bilateral study

3. Normal: amplitude $\geq 4.0$ mV

4. Abnormalities seen in lesions of spinal accessory nerve following Parsonage. Turner syndrome, lymph node biopsy, surgery, head and neck injury - produces scapular winging more pronounced with shoulder abduction than protraction.
Blink Reflex Worksheet

Draw the expected appearance of the ipsilateral $R_1$ and $R_2$ and contralateral $R_2$ given ipsilateral lesions in the following areas:

1. Vth Nerve
   Ipsilateral: $\uparrow R_1 \uparrow R_2$
   Contralateral: $\uparrow R_2$

2. VIIth Nerve
   Ipsilateral: $\uparrow R_1 \uparrow R_2$
   Contralateral: $\uparrow R_1$

3. Main sensory nucleus
   Ipsilateral: $\uparrow R_1 \uparrow R_2$
   Contralateral: $\uparrow R_2$

4. Spinal Nucleus:
   Ipsilateral: $\uparrow R_1 \uparrow R_2$
   Contralateral: $\uparrow R_2$
<table>
<thead>
<tr>
<th>Disorders</th>
<th>Direct response</th>
<th>R1</th>
<th>R2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trigeminal neuralgia</td>
<td>Normal</td>
<td>Normal (95%)</td>
<td>Abnormal on both sides when affected</td>
</tr>
<tr>
<td>Paratrigeminal syndrome</td>
<td>Normal</td>
<td>Abnormal on the affected side (95%)</td>
<td>side stimulated (afferent type)</td>
</tr>
<tr>
<td>Bell's palsy</td>
<td>Normal unless distal segment degenerated</td>
<td>Abnormal on the affected side (99%)</td>
<td>Abnormal on the affected side regardless of the side of the stimulus (afferent type)</td>
</tr>
<tr>
<td>Acoustic neuroma</td>
<td>Normal unless distal segment degenerated</td>
<td>Abnormal on the affected side (85%)</td>
<td>Afferent and/or efferent type</td>
</tr>
<tr>
<td>Guillain-Barré syndrome</td>
<td>Abnormal (42%)</td>
<td>Abnormal (54%)</td>
<td>Afferent and/or efferent type</td>
</tr>
<tr>
<td>Hereditary motor sensory neuropathy Type I</td>
<td>Abnormal (79%)</td>
<td>Abnormal (85%)</td>
<td>Afferent and/or efferent type</td>
</tr>
<tr>
<td>Diabetic polyneuropathy</td>
<td>Abnormal (13%)</td>
<td>Abnormal (10%)</td>
<td>Afferent and/or efferent type</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>Normal</td>
<td>Abnormal with pontine or lateral medullary lesion</td>
<td>Afferent and/or efferent type</td>
</tr>
<tr>
<td>Wallenberg syndrome</td>
<td>Normal</td>
<td>Normal or borderline</td>
<td>Afferent type</td>
</tr>
<tr>
<td>Facial hypesthesia</td>
<td>Normal</td>
<td>Abnormal with lesions of the trigeminal nerve or pons</td>
<td>Afferent type</td>
</tr>
<tr>
<td>Comatose state, Akinetic mutism &amp; Locked-in syndrome</td>
<td>Normal</td>
<td>Abnormal with pontine lesion: reduced excitability in acute supratentorial lesion</td>
<td>Absent on both sides regardless of side of stimulus</td>
</tr>
</tbody>
</table>

Sphincters: c. tongue, blind, oth. muscles (usually not there) 
Chemical synapses are present

Spinal reflexes: 
Sphynx, nigra, myotonia
Blink reflex patterns of abnormalities. 

A. Normal pattern: Recording both orbicularis oculi muscles, stimulating the supraorbital nerve on each side results in an ipsilateral R1 (early) and bilateral R2 (late) potentials. 

B. Incomplete right trigeminal lesion: Stimulating the affected right side, there is a delay of all potentials, including the ipsilateral R1 and R2 and contralateral R2. Stimulating the unaffected side results in all normal potentials. 

C. Complete right trigeminal lesion: Stimulating the affected right side, all potentials are absent. Stimulating the unaffected side results in all normal potentials. 

D. Incomplete right facial lesion: Stimulating the affected side results in delay of the ipsilateral R1 and R2, but a normal contralateral R2. Stimulating the unaffected side results in a normal ipsilateral R1 and R2 but a delayed contralateral R2. In this pattern, all potentials on the affected side are abnormal, regardless of which side is stimulated. 

E. Complete right facial lesion: Stimulating the affected side results in absent ipsilateral R1 and R2 potentials but a normal contralateral R2. 

F. Right midpontine lesion (main sensory nucleus V and/or lesion of the pontine interneurons to the ipsilateral facial nerve nucleus, or both): Stimulating the affected side results in an absent or delayed R1 but an intact ipsilateral and contralateral R2. 

G. Right medullary lesion (spinal tract and nucleus V and/or lesion of the medullary interneurons to the ipsilateral facial nerve nucleus, or both): Stimulating the affected side results in a normal R1 and contralateral R2, but an absent or delayed ipsilateral R2. 

H. Demyelinating peripheral polyneuropathy: All potentials of the blink response may be markedly delayed or absent, reflecting slowing of either or both motor and sensory pathways.
NEUROMUSCULAR COMPLICATIONS OF CANCER

I. **Peripheral Nerve/Muscle Neoplasms**

   A. Intrinsic (primary); arise from nerve fibers.
      1. Schwann cells/fibroblasts.
      2. Traumatic neuroma.

   B. Extrinsic (secondary); arise from other structures.
      1. Common sites; central portion of neuroaxis within intraspinal canal or plexus.

   C. A normal EMG examination never excludes a peripheral nerve neoplasm, although normal studies are rare.
      1. Axonal degeneration most common pathologic abnormality.
      2. Sensory and motor evoked amplitudes are more important than conduction velocity in defining an abnormality.
      3. Needle EMG changes are consistent with partial denervation; fibrillation potentials are the most sensitive indicator of axon loss.

   D. Neoplasms involving cranial nerves; diagnostic studies.
      1. CN V (trigeminal); blink reflex; EMG masseter.
      2. CN VII (facial); blink reflex; facial motor evoked response; EMG facial muscles.
      3. CN XI (spinal accessory); evoked response; EMG of trapezius and SCM muscles.
      4. CN XII (hypoglossal); EMG tongue.

   E. Neoplastic intraspinal canal lesions (Intramedullary, intradural/extradural).
      1. Intradural tumors.
         a. Often primary neoplasms.
         b. Histologically benign.
         c. Frequent in children, middle age adults.
         d. Slow onset and progression.
      2. Intramedullary.
         a. Ependymoma.
         b. Astrocytomas.
      3. Extramedullary/intradural.
         a. Schwannoma.
         b. Neurofibroma.
         c. Meningioma.
         d. Leptomeningeal seeding (lung, breast, leukemia/lymphoma).
4. Extradural lesions commonly represent metastasis.
   a. Breast.
   b. Lung.
   c. Prostate.
   d. Lymphoma and myeloma.
5. EMG findings do not differentiate type of "polyradiculopathy".
   a. Fibrillations and MUAP changes in appropriate myotomes (including paraspinal muscles).
   b. Low motor with normal sensory evoked responses.
   c. Always evaluate contralateral limb.
   d. LaBan syndrome (paraspinal abnormalities only).
      (1) Direct invasion of posterior primary rami by tumor.
      (2) Tumor emboli via paravertebral plexus of veins to paraspinal muscle mass.

F. Facial myokymia.
   1. Multiple sclerosis.
   2. Brainstem (pontine) glioma.

G. Neoplasm of muscle.
   1. Usually arise from supporting tissues (lipoma, fibroma, angioma, desmoid).
   2. Striated muscle neoplasm.
      a. Rhabdomyoma.
      b. Rhabdomyosarcoma (2/3 in extremity muscles).

II. Plexus Neoplasms (See adverse effects)

III. Paraneoplastic Syndromes

A. Anterior horn cell.
   1. Resembles PMA but may be more symmetrical with proximal predilection.
   2. Incidence of neoplasm in ALS population about 5%.
   4. Reported with plasma cell dyscrasia.

B. Subacute motor neuropathy.
   1. Reported in patients with Hodgkin's disease or lymphoma.
   2. Better classification for the dysproteinemia associated MND (rather than anterior horn cell disease).

C. Sensory neuronopathy.
   1. First described by Denny-Brown.
   2. 75% precede discovery of malignancy by up to 4 years!
   3. Subacute onset followed by rapid progression (weeks to months).
   4. SNAPs absent.
   5. Oat cell carcinoma most common.
D. Nonspecific sensorimotor neuropathy
   1. Poorly defined
   2. Association of GBS with Hodgkin's disease

E. Polyneuropathy associated with paraproteinemia

F. Mononeuritis multiplex
   1. All reported cases associated with oat cell carcinoma of lung or lymphoma.
   2. Late in course, cannot separate from generalized polyneuropathy.

G. Neuromuscular transmission defects
   1. Lambert-Eaton myasthenic syndrome
      a. Brief exercise (5-10 seconds) in all patients with borderline-low CMAPs
      b. 2Hz repetitive motor nerve stimulation
      c. Oat cell carcinoma most commonly associated neoplasm
      d. If no neoplasm, cancer surveillance for three years
   2. Myasthenia gravis with thymoma

H. Disorders of muscle
   1. Dermatomyositis/polymyositis
      a. Any adult over age 10 without CTD should undergo reasonable search for neoplasm, especially if dermal and myopathic lesions coincide.
      b. Lung, ovary, and colon most common sites
   2. Necrotizing myopathy-carcinoid myopathy
      a. Necrotizing myopathy with vasculitis
      b. Myopathy associated with carcinoid that responds to periactin (endocrine-metabolic myopathy)

I. Neuromyopathy
   1. Most commonly reported remote effect.
   2. Arrggg!

IV. Adverse Effects of Antineoplastic Therapy

A. Plexopathy (radiation therapy, metastatic or direct spread).
   1. Clinical features of radiation vs. metastatic plexopathy.
      a. Latent interval to onset neurologic symptoms.
         (1) Average 6 years in both groups.
         (2) Long progression suggests radiation fibrosis.
         (3) Latent interval < 12 months may favor radiation injury if dose > 6000 rads.
      b. Pain more common with metastatic tumor (80%).
c. Localization
   (1) Lower trunk favors metastasis
   (2) Upper plexus favors radiation
   (3) Horner's syndrome favors metastasis
   (4) Lymphedema favors radiation
   (5) Late in course, plexus involvement becomes diffuse regardless of cause

2. Imaging features
   a. CT abnormal in 89% of patients with tumor.
   b. CT also may demonstrate tissue distortion in normal tissue planes without discrete mass with radiation fibrosis.
   c. May be difficult to differentiate infiltration from fibrosis.

3. Electrodagnostic evaluation of brachial plexus
   a. Differentiate radiculopathy from plexopathy
      (1) SNAPs normal with root lesions because sensory cell body located in DRG.
      (2) Paraspinal muscles involved in root lesions.
      (3) Roots may be involved in some radiation plexopathies (radiation myeloradiculoplexopathy).
   b. Lower trunk plexopathy
      (1) Ulnar and median CMAPs of low amplitude because of axonal loss
      (2) Ulnar SNAP usually absent
      (3) Median SNAP normal (fibers transverse middle trunk, later combining with motor fibers from lower trunk).
   c. Brachial plexopathy protocol (Table I)
   d. Myokymic discharges (see Figure 1 and Table II).
      (1) Semirhythmic bursts of potentials
      (2) Present in extremity muscles in 50% of patients with radiation plexopathy.
      (3) Rare findings in other disorders
      (4) Related to spontaneous discharge from degenerating axon (unlikely) or focal demyelination with ephaptic transmission.

4. Other forms of plexopathy or mononeuropathy

B. Cancer chemotherapy (Discussed elsewhere).
TABLE I
Brachial Plexopathy Protocol

A. Conduction Studies *

1. Ulnar motor (hypothenar); stimulate at wrist, elbow, axilla, and Erb-point. Record F-response latency.

2. Ulnar sensory (fifth digit); stimulate wrist and elbow.

3. Median motor (thenar); stimulate wrist and elbow. Record F-response latency.

4. Median sensory (index); stimulate wrist.

5. Musculocutaneous (biceps brachii); stimulate at axilla and Erb point.

6. If any abnormal responses:
   a. Evaluate opposite extremity.
   b. Check technical factors, temperature or anomalous innervation as appropriate.
   c. Proceed with evaluation with specific suspected abnormality (e.g., superimposed carpal tunnel syndrome or other)

B. Needle Examination †

1. Examine biceps brachii (musculocutaneous N, upper T, C5-6), triceps (radial N, posterior C, C6-7), deltoid (axillary N, posterior C, C5-6), pronator teres (median N, upper and middle T, C5-7), brachioradialis (radial N, posterior C, C5-6), first dorsal interosseous (ulnar N, lower T, C8-T1), infraspinatus (supraclavicular N, upper T, C5-6), extensor digitorum (radial N, posterior C, C6-7-8), abductor pollicis brevis (median N, lower T, C8-T1), cervical and upper thoracic paraspinous muscles.

2. If one root, portion of plexus, or individual peripheral nerve is suspected clinically, or if any abnormality is found, examine two or more muscles in an identical distribution (proximal and distal, if possible) and demonstrate normal muscles above and below the suspected peripheral level.

3. If any are abnormal, proceed with evaluation of the suspected abnormality

* (Indicate recording site for conduction studies)
† (Indicate peripheral nerve, plexus trunk, and root innervation for muscles listed)
<table>
<thead>
<tr>
<th>Patient</th>
<th>Neurologic diagnosis</th>
<th>Muscle</th>
<th>Spikes per burst*</th>
<th>Spike frequency in burst (Hz)*</th>
<th>Burst duration (msec)*</th>
<th>Bursts per min*</th>
<th>Spikes per min*</th>
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<tr>
<td>1</td>
<td>Brachial plexopathy</td>
<td>Deltoid</td>
<td>30 (19–37)</td>
<td>38</td>
<td>760</td>
<td>30</td>
<td>900</td>
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<tr>
<td>2</td>
<td>Brachial plexopathy</td>
<td>Flexor carpi</td>
<td>31 (19–39)</td>
<td>41</td>
<td>730</td>
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<td>3</td>
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<td>Extensor indicis</td>
<td>18 (13–15)</td>
<td>13</td>
<td>1,300</td>
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<td>Deltoid</td>
<td>37 (18–58)</td>
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<td>Pronator teres</td>
<td>14 (4–21)</td>
<td>15</td>
<td>860</td>
<td>30</td>
<td>420</td>
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<tr>
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<td>Triceps</td>
<td>6 (2–9)</td>
<td>21</td>
<td>210</td>
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<td>Levator scapuli</td>
<td>40 (17–84)</td>
<td>11</td>
<td>3,600</td>
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<td>Brachial plexopathy</td>
<td>Abductor pollicis brevis</td>
<td>9 (6–10)</td>
<td>13</td>
<td>640</td>
<td>30</td>
<td>270</td>
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<td>9</td>
<td>Brachial plexopathy</td>
<td>First dorsal interosseus</td>
<td>16 (14–19)</td>
<td>42</td>
<td>380</td>
<td>42</td>
<td>672</td>
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<td>Biceps</td>
<td>73 (54–104)</td>
<td>60</td>
<td>1,200</td>
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<td>876</td>
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<tr>
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<td>Biceps</td>
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<td>47</td>
<td>900</td>
<td>23</td>
<td>989</td>
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<td>Biceps</td>
<td>13 (12–16)</td>
<td>18</td>
<td>700</td>
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<td>Brachioradialis</td>
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<td>270</td>
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<td>Biceps</td>
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<td>70</td>
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<td>660</td>
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<td>Myelopathy</td>
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<td>49 (21–87)</td>
<td>15</td>
<td>3,200</td>
<td>13</td>
<td>637</td>
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<td></td>
<td></td>
<td>Vastus medialis</td>
<td>8 (5–9)</td>
<td>38</td>
<td>170</td>
<td>49</td>
<td>392</td>
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<td></td>
<td>Anterior tibialis</td>
<td>4 (2–6)</td>
<td>16</td>
<td>190</td>
<td>88</td>
<td>352</td>
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<td>Vastus lateralis</td>
<td>4 (2–6)</td>
<td>27</td>
<td>110</td>
<td>132</td>
<td>528</td>
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<td>Rectus femoris</td>
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<td>38</td>
<td>80</td>
<td>200</td>
<td>800</td>
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</tbody>
</table>

Mean ± SEM (range)

\[
21.9 ± 4.4 \quad 29.0 ± 3.5 \quad 918 ± 233 \quad 58.3 ± 14.3 \quad 583 ± 55
\]
\[
(3–73) \quad (11–60) \quad (70–3,600) \quad (6–220) \quad (222–989)
\]

*Mean (range).
Figure 1. Examples of myokymic discharges from 4 patients with radiation plexopathy. From top to bottom: biceps muscle, vastus lateralis muscle, biceps muscle, and pronator teres muscle. Note that each discharge is shown at a faster sweep speed on the right. Reprinted with permission. (Muscle & Nerve 4:494-504, 1981).
AN APPROACH TO THE DIAGNOSIS OF NEUROMUSCULAR DISEASE
IN THE FLOPPY INFANT

I. Introduction
A. Definitions.
   1. Infant - first month after birth.
   2. Hypotonia.
      a. Increased joint range of motion.
      b. Decreased resistance to passive range of motion of joints.
      c. Bizarre or unusual postures - "frog-leg" appearance.
   3. Weakness.
      a. Unable to move extremities against gravity.
      b. Lack of spontaneous movements.
      c. Respiratory and/or swallowing difficulties.
      d. Decreased muscle bulk.
B. Assumptions.
   1. Non-neuromuscular disorders have been ruled out.
      a. Infectious.
      b. Toxic.
      c. Metabolic/endocrine.
      d. Central nervous system disease.
      e. Chromosomal disorders.

II. Clinical Assessment
A. History.
   1. Pre-natal course.
      a. Illnesses.
      b. Medications.
      c. Fetal movements.
   2. Labor/Delivery - prolonged or difficult.
   3. Post-natal course.
      a. Onset of weakness.
      b. Progressive.
      c. Developmental milestones.
   4. Family history.
      a. Siblings: birth history, level of activity, deformities, SIDS.
      b. Adults: weakness, deformities, cataracts, diabetes mellitus, mental retardation, miscarriages.
B. Physical Examination.

1. Tone.
   a. Head lag.
   b. Ventral suspension.
   c. Recoil: upper and lower extremities.
   d. Traction: upper and lower extremities.
   e. Popliteal angle.

2. Weakness.
   a. Observe spontaneous movements.
   b. Limb movement against gravity.
   c. Respiratory/feeding difficulty.

III. Laboratory Evaluation

A. Nerve Conduction Studies and EMG in Normal Infants.

1. Sensory nerve conduction.
   a. Conduction velocity: half of adult mean value.
      (1) Increases by 0.8 m/s/week.
      (2) Double peaks: faster vs. slower fibers.
      (3) Reaches adult values by age 3 years.
   b. Amplitude: close to adult value. Reaches adult values by age 3 months.

   a. Conduction velocity: slightly less than 1/2 adult mean value.
      (1) Parallels myelin development.
      (2) Myelination begins during 15th week in utero.
      (3) Direct relationship between conceptual age and NCV.
      (4) Reaches adult values by age 3-5 years.
   b. Amplitude: 1/3 to 1/2 adult value.
      (1) Reaches adult values by age 12 years.

3. Needle examination.
   a. Motor units similar to adults.
   b. MUAP evaluation technically difficult.
   c. Fibrillation potentials away from the end-plate region are an abnormal finding two to three days after birth in a term infant.
   d. Thorough evaluation of one or two muscles preferable to limited study of many muscles.

B. Creatine kinase: essentially normal or mildly elevated in SMA and most myopathies.

C. Muscle biopsy: most important.
IV. Differential Diagnosis

A. Hypotonia.
   1. With weakness: neuromuscular disorder; always consider SCI.
   2. Without weakness: CNS disorder or benign congenital hypotonia common.

B. Neuropathic NCS/EMG.
   1. Infantile Spinal Muscular Atrophy (Werdnig-Hoffman).
      a. Onset: in utero; abruptly within 2-3 months.
      b. Clinical picture:
         (1) Frog posture.
         (2) Legs (immobile) > arms; proximal > distal; absent DTRs.
         (3) Bulbar findings: poor suck, swallow, tongue fasciculations.
         (4) Face spared: bright, alert.
         (5) Weak cry: bell-shaped chest, diaphragmatic breathing.
         (6) Arthrogryposis: "seal flipper", "jug-handle" extremity.
      c. Course: respiratory failure, progresses but plateaus by age 1 year; most die within one year.
      d. EMG: spontaneous activity, neuropathic, may see decrement.
      e. Biopsy: large groups of atrophic fibers, fiber type grouping.
   2. Other.
         (1) Central core disease; no spontaneous activity.
         (2) Pompe's Disease/Acid Maltase Deficiency.
            (a) Spontaneous activity.
            (b) May see myotonic bursts.
      b. Poliomyelitis: usually more focal.

C. Myopathic EMG.

1. Central core disease.
   a. Onset: birth to adult.
   b. Clinical picture:
      (1) Proximal or generalized; legs > arms.
      (2) Associated with malignant hyperthermia.
      (3) Congenital hip dislocation.
   c. Course: mild or no progression.
   d. EMG: no spontaneous activity, mixed myopathic/neuropathic picture.
   e. Biopsy: Type I fiber predominance; decreased stain with oxidative enzymes; zig-zag Z lines; amorphous, compact, myofibrils = "core".
   f. Multicore disease similar.

2. Nemaline myopathy.
   a. Onset: infancy or later.
b. Clinical picture:
   (1) Dysmorphic features: long, slender face and trunk.
   (2) Diffuse weakness: sucking, swallowing difficulty.
   (3) Kyphoscoliosis, pigeon chest, pescavus, high arched palate.

c. Course: nonprogressive; variable, may die of respiratory failure at birth.

d. EMG: no spontaneous activity; myopathic.

e. Biopsy: rods/thread-like structures under sarcolemma. EM: dense, rectangular, lattice-like; contain actin.

3. Myotubular (centronuclear) myopathy.
a. Onset: 2/3 at birth, 1/3 later.
b. Clinical picture:
   (1) Ptosis, external ophthalmoplegia, facial weakness.
   (2) Proximal $\geq$ distal.
   (3) Sucking, swallowing, respiratory difficulties.
   (4) Sex-linked form: Dutch families, up to 100% newborn fatality.

c. Course: slowly progressive; most cases reported are under age 10.

d. EMG: spontaneous activity, myotonic discharges have been reported, myopathic motor units.

e. Biopsy: central nuclei, fatal tubules, increased stain with oxidative enzymes type I fiber predominance.

4. Congenital fiber type disproportion (Type I Fiber Predominance).
b. Clinical picture:
   (1) Proximal = distal, legs $\geq$ arms.
   (2) Improves with age.
   (3) Respiratory failure.
   (4) Congenital hip dislocation, arthrogryposis, torticollis, kyphoscoliosis, pes planus or cavus.

c. Course: occasionally die from respiratory failure; usually improve.

d. EMG: mild myopathic changes, rarely spontaneous activity.

e. Biopsy: atrophied type I fibers (similar to early Werdnig-Hoffman and myotonic dystrophy).

5. Type II Glycogenosis (Pompe's/Acid Maltase Deficiency).
a. Onset:
   (1) Pompe's: infancy.
   (2) AMD: 3rd and 4th decade.
b. Clinical picture:
   (1) Large tongue.
   (2) Severe hypotonia, weakness.
   (3) Looks like SMA with cardiomegaly and hepatomegaly.
   (4) Affects anterior horn cells and muscles, multiple organs: kidneys, liver, heart, CNS.
   (5) EKG: gigantic QRS, short P-R interval.
   (6) Mild cases: resemble polymyositis, limb-girdle dystrophy.

c. Course: Pompe's fatal in infancy.

d. EMG: myopathic/neuropathic; myotonic bursts, spontaneous activity.

e. Biopsy: vacuolar, filled with glycogen, lysosomal glycogen.
   b. Clinical picture:
      (1) Mild hypotonia.
      (2) Poor suck, swallow:
      (3) Trunk, extremities, face: weak.
      (4) Arthrogryposis.
   c. Course: improve over time.

D. Neuromuscular Junction Defect.

1. Neonatal myasthenia gravis.
   a. Onset: birth up to 1 week (usually not apparent day of birth).
   b. Clinical picture:
      (1) Ptosis, facial weakness.
      (2) Poor suck, swallow, respiration.
      (3) Respond to anticholinesterase medications.
      (4) Higher incidence in mothers who have not had thymectomy.
   c. Course: transient.
   d. EMG: decrement to repetitive stimulation.

2. Congenital myasthenia gravis.
   a. Onset: birth to 2 years.
   b. Clinical picture:
      (1) Ptosis, external ophthalmoplegia.
      (2) Poor swallowing, respiration: grunting, weak cry.
      (3) Generalized weakness (later).
   c. Course: slowly progressive.
   d. EMG: decrement on repetitive stimulation.

   a. Onset: infancy.
   b. Clinical picture:
      (1) Acute hypotonia.
      (2) Weakness, ptosis, poor swallowing.
   c. Course: resolves over time.
   d. EMG: small initial evoked amplitude with incremental response.

E. Normal EMG.

1. Hereditary Motor Sensory Neuropathy Type III (Dejerine-Sottas).
   a. Onset: infancy.
   b. Clinical picture:
      (1) Usually not hypotonic.
      (2) Delayed milestones.
   c. EMG: slowed conduction velocities. Check parents.

2. CNS disorders with polyneuropathy.
   a. Metachromatic leukodystrophy: age 1-2 years.
   b. Krabbe's: age 1-2 years.

b. Clinical picture:
   (1) General hypotonia.
   (2) Poor suck, swallow, respiration.
   (3) Polyhydramnios, decreased fetal movements.
   (4) Facial diplegia (can't close eyes), triangular (tented) "fish" mouth.
   (5) Mental retardation.
   (6) Kyphoscoliosis, equinovarus, thin ribs, hypoplastic diaphragm (elevated on x-ray)

c. Course: gradual improvement after 8-10 months. Death: respiratory failure.

d. EMG: normal. Check parents and siblings.

e. Biopsy: type I fiber atrophy, mild.

4. Type III Glycogenosis (Debrancher Enzyme Deficiency).
   a. Onset: infancy.
   b. Clinical picture:
      (1) Weakness.
      (2) Hypoglycemia, ketosis, hepatomegaly.
   c. Course: improves over time.
   d. EMG: normal.
   e. Biopsy: normal or increased glycogen deposits.

V. Conclusion
**SUMMARY TABLES**

### NEUROMUSCULAR DISEASE IN INFANTS

#### GENETICS

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<th>AUTOSOMAL DOMINANT</th>
<th>SEX-LINKED</th>
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<td>Congenital Myopathies</td>
<td>Metabolic Myopathies</td>
<td>Duchenne’s</td>
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<tr>
<td>HMSN Type III</td>
<td>Myotubular Myopathy</td>
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<tr>
<td>Congenital Myasthenia</td>
<td>HMSN Type I</td>
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<td>Werdnig-Hoffman SMA</td>
<td>Myotonic Dystrophy</td>
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<td>Kugelberg-Welander SMA</td>
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### NEUROMUSCULAR DISORDERS IN INFANTS

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<th>PROGRESSIVE</th>
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<td>Infantile SMA</td>
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<tr>
<td>Juvenile SMA</td>
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<tr>
<td>Poliomyelitis</td>
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<td>MLD</td>
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<td>Krabbe’s</td>
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<td>Neonatal Myasthenia Gravis</td>
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<td>Congenital Myasthenia Gravis</td>
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<th>PROGRESSIVE</th>
<th>NON-PROGRESSIVE</th>
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<td>Congenital Myopathies</td>
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<td>Dystrophies</td>
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### CONGENITAL MYOPATHIES

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<tr>
<th>STRUCTURAL</th>
<th>METABOLIC</th>
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<tbody>
<tr>
<td>Central Core</td>
<td>Glycogenoses</td>
</tr>
<tr>
<td>Nemaline</td>
<td>Lipid disorders (late onset)</td>
</tr>
<tr>
<td>Myotubular</td>
<td>Mixed</td>
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</table>
NORMAL EMG
- Hereditary Motor Sensory Neuropathy
- Congenital Myotonic Dystrophy
- Debrancher Enzyme Deficiency (Type III Glycogenosis)

NEUROPATHIC EMG
- Infantile Spinal Muscular Atrophy (Werdnig-Hoffman)
- Congenital Myopathy – mixed neuropathic and myopathic
  - Central Core – no spontaneous activity
  - Acid Maltase Deficiency (Pompe’s)
    - spontaneous activity
    - myotonic bursts - ? infancy
- Poliomyelitis – usually more focal

MYOPATHIC EMG
- Congenital Myopathies
  - Central Core
  - Nemaline
  - Myotubular (Centronuclear) – spontaneous activity
  - Mitochondrial
  - Congenital Fiber Type Disproportion
  - Acid Maltase Deficiency / Pompe’s
- Congenital Muscular Dystrophy

NEUROMUSCULAR JUNCTION DEFECT ON REPETITIVE STIMULATION
- Infantile Spinal Muscular Atrophy
- Neonatal Myasthenia Gravis
- Congenital Myasthenia Gravis
- Botulism
References


<table>
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<tr>
<th>DISEASE (GENETIC)</th>
<th>ONSET</th>
<th>CLINICAL PICTURE</th>
<th>CONTRACTURES</th>
<th>PROGNOSIS</th>
<th>EMG</th>
<th>MUSCLE BIOPSY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infantile Spinal</td>
<td>In uero 2-3 months</td>
<td>Frog posture; legs (immobile); trunk; distal; no DTH; face spared; bell-shaped chest; poor suck; dysphagia</td>
<td>Arthrogryposis; &quot;jug-handle&quot; or &quot;seal-flipper&quot; arms</td>
<td>Most die within one year; respiratory failure; progressive weakness, but plateau</td>
<td>$Spontaneous activity\footnote{Faculations rare; low amplitude CMAP}; Normal CV; may see decrement</td>
<td>Large groups of atrophic fibers; type grouping</td>
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<tr>
<td>Muscular Atrophy</td>
<td>(AD)</td>
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<tr>
<td>Juvenile Spinal</td>
<td>5-15 years</td>
<td>Less proximal</td>
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<td>Less progressive</td>
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<td>Muscular Atrophy (AD)</td>
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**CONGENITAL MYOPATHIES - STRUCTURAL**

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<tr>
<th>DISEASE</th>
<th>ONSET</th>
<th>CLINICAL PICTURE</th>
<th>CONTRACTURES</th>
<th>PROGNOSIS</th>
<th>EMG</th>
<th>MUSCLE BIOPSY</th>
</tr>
</thead>
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<tr>
<td>Central Core</td>
<td>Birth-adult</td>
<td>Legs $\ddagger$ arms; proximal $\ddagger$ distal; DTH present, but face spared; malignant hyperthermia</td>
<td>Congenital hip dislocation</td>
<td>Mild or no progression</td>
<td>Mixed myopathic/neuropathic</td>
<td>Amorphous, compact myofibrils; $\ddagger$ mitochondria; cores - $\ddagger$ stain with oxidative enzymes; $\ddagger$ stain ATPase</td>
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<tr>
<td>Hemaline</td>
<td>Birth or &quot;later&quot;</td>
<td>Proximal and distal; legs and arms; long, slender face and body</td>
<td>Kyphoscoliosis, pigeon chest, pecavus, high-arched palate</td>
<td>Non-progressive; die of cardiac and/or respiratory failure at birth</td>
<td>No spontaneous activity; myopathic</td>
<td>Rods - thread-like, under sarcomeres; red-trichrome EM: dense, rectangular, lattice-like</td>
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<tr>
<td>(AD or sporadic)</td>
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<tr>
<td>Myotubular Centronuclear</td>
<td>2/3 birth 1/3 later</td>
<td>Hypotonia, external ophthalmoplegia; facial weakness; proximal $\ddagger$ distal</td>
<td>Slowly progressive; most reported cases; are $\leq$ age 10</td>
<td>$\ddagger$ Spontaneous activity; motor unit discharges($?) myopathic</td>
<td>Central nuclei, fetal tubules; type I fiber predominance; central area - $\ddagger$ stain-oxidative enzymes; $\ddagger$ stain ATPase</td>
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<td>(AD-variable penetrance)</td>
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<td></td>
<td>Newborn</td>
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<td>Up to 100 mortality; respiratory failure</td>
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<tr>
<td>Mitochondrial Myopathy</td>
<td>Later Childhood</td>
<td>(Kearns-Sayre); proximal $\ddagger$ distal; external ophthalmoplegia; retinopathy, deafness, ataxia; heartblock; $\ddagger$ CSF protein</td>
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<td>Hyopathic-mild</td>
<td>Ragged red fibers; EM-abnormal mitochondria</td>
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<td>(Sporadic)</td>
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<tr>
<td>Congenital Fiber Type Disproportion</td>
<td>Birth</td>
<td>Proximal $\ddagger$ distal; legs $\ddagger$ arms; respiratory failure</td>
<td>Congenital hip dislocation; torticollis; pes planus or cavus</td>
<td>Reaches worst point by age 2 years; improves with age</td>
<td>Myopathic, rarely shows some spontaneous activity</td>
<td>Type I fiber atrophy (like myotonic dystrophy and early SMA)</td>
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**CONGENITAL MYOPATHIES - METABOLIC**

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<th>DISEASE</th>
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<th>CLINICAL PICTURE</th>
<th>CONTRACTURES</th>
<th>PROGNOSIS</th>
<th>EMG</th>
<th>MUSCLE BIOPSY</th>
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<tbody>
<tr>
<td>Type II Glycogenosis</td>
<td>Infancy</td>
<td>Large tongue; severe hypotonia, weak; cardiac and respiratory failure; looks like SMA with hepatomegaly and cardiomegaly</td>
<td></td>
<td>Frequently fatal</td>
<td>Hyopathic/neuropathic</td>
<td>Vacuolar with $\ddagger$ glycogen; $\ddagger$ glycogen in lysosomes</td>
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<td>(Pompe's) (AR)</td>
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<tr>
<td>(Acid Malate Deficiency)</td>
<td>3rd-4th decade</td>
<td>Anterior horn cells and skeletal muscle; liver, heart, CNS, kidneys; mild cases; proximal $\ddagger$ distal; resembles limb-girdle or polymyositis; EMG: gigantic QRS, $\ddagger$ P-R</td>
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<tr>
<td>Type III Glycogenosis</td>
<td>Infancy</td>
<td>Hypoglycemia; ketosis; Hepatomegaly; mild</td>
<td></td>
<td>Improve over time</td>
<td>Normal</td>
<td>Normal or $\ddagger$ glycogen</td>
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<td>(Debranching Enzyme) (AR)</td>
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<td>DISEASE (GENETIC)</td>
<td>ONSET</td>
<td>CLINICAL PICTURE</td>
<td>CONTRACTURES</td>
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<td>EMG</td>
<td>MUSCLE BIOPSY</td>
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<tr>
<td>Type V Glycogenosis (McArdles) (AR or AD)</td>
<td>Adolescence</td>
<td>Exercise intolerance; cramps, pain; myoglobinuria</td>
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<tr>
<td>Type IV Glycogenosis (Branching enzyme deficiency)</td>
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<td>? effect on skeletal muscle</td>
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<tr>
<td>Congenital Myotonic Dystrophy (AD)</td>
<td>Birth</td>
<td>General hypotonia; dysphagia; polyhydramnios; triangular mouth; facial diplegia; can't close eyes; mental retardation</td>
<td>Kyphoscoliosis; equinovarus; thin ribs</td>
<td>Early death from respiratory failure; hypoplastic diaphragm; gradual improvement after 8-12 weeks</td>
<td>Normal; check mother</td>
<td>Type I fiber atrophy mild changes</td>
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<tr>
<td>Congenital Muscular Dystrophy (AR)</td>
<td>Birth</td>
<td>Mild hypotonia; ? suck, swallow; face, trunk involved arms-legs</td>
<td>Arthrogryposis</td>
<td>Improve over time</td>
<td>Hyopathic</td>
<td>Muscle replaced with adipose and connective tissue</td>
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<td>Duchenne's (X-linked)</td>
<td>Early Childhood</td>
<td>?CPK; proximal weakness</td>
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**NEUROMUSCULAR JUNCTION DISORDERS**

| Neonatal MG | Birth, up to 1 week | Transient; ACh receptor Ab passed across placenta; ptosis; facial weakness; ? suck, swallow, breathing | Responds to anticholinesterase medications; ? incidence in mothers who haven't had thymectomy | Decrement | |
| Congenital MG (AR) | Birth to first 1 to 2 years | Ptosis, ophthalmoplegia; later-general weakness; ? swallow, cry, grunting | | Decrement | |
| Botulism | Infant | Acute hypotonia; ptosis; dysphagia; weakness | Resolves with treatment; continues as long as GI tract colonized | Small Initial evoked CNAP; may see increment | |

**PERIPHERAL NEUROPATHIES**

| RHSN Type III DeJenne-Sottas (AR) | Infancy | Delayed motor milestones; usually not hypotonic | | $CV$; check parents | |
What is the purpose of electromyography instrumentation? A first thought is that the electromyograph should accurately display the electric signal present at the active electrode. Wrong. Most of the electric signal at the electrode is useless. The electric signals emitted by nerve and muscle are only tiny perturbations superimposed on mountains of noise. The purpose of electromyography (EMG) instrumentation is to accurately record and display the nerve and muscle signals that are physiologically relevant. Another way of expressing the same goal is that the EMG machine must discard everything that is not physiologically relevant—it must throw out 99% of the total signal. Understanding EMG electronics is important because small changes in an instrument can produce large alterations in the display, particularly when the instrument is discarding such a large proportion of the original signal.

The topics in this monograph are discussed at an introductory level to provide understanding for readers with no electronics background, and intuitive insight for more experienced readers. Basic principles of electricity include the concepts of voltage, current, charge, and impedance that allow discussion of filters, amplifiers, electrodes, digital electronics, stimulators, and patient safety. The appendix provides an intuitive introduction to voltage, current, and impedance.

ELECTRICITY

The basis of electricity is charge and charge flow. Charge is a concept that was originated to explain experimental results. Benjamin Franklin performed the experiment of rubbing a glass rod with silk and noted that the rod subsequently attracted the silk. If a second glass rod is rubbed with silk, the two rods repel each other. Presumably, two substances that were initially balanced in both the glass and the rod were somehow separated, so that more of one ended up on the glass and more of the other ended up on the silk. Franklin arbitrarily named the charge on the glass rod positive and the charge on the silk negative. The electric field was invented to explain the force between the two objects.

The movement of charges corresponds to current flowing from one object to the other. The
Current (amperes or amps) is defined as the amount of charge (coulombs) flowing per unit of time (seconds). Positive charges flowing from silk to rod are added to negative charges flowing in the opposite direction, from rod to silk, to determine the total current flow. Current has a direction, and the direction could be defined as either the net rate of flow of negative charges or the net rate of flow of positive charges. The arbitrary convention is that current is the net rate of flow of positive charges. This convention is why diagrams are drawn showing current flowing from positive (+) leads to negative (-) leads. The fact that the usual charge carriers are negative (electrons), and that flow is in the opposite direction to the one indicated, can cause confusion, but is irrelevant for circuit design. In the rod—silk example, the convention implies that current flowed from silk to rod. Physical reality is that electrons flowed from rod to silk.

The three parameters that form the basis of instrument design are voltage, current, and impedance. Voltage (V) corresponds to potential energy per unit of charge (joules/coulomb), current (I) is charge flow (coulombs/second), and impedance (Z) is, for most signals, simply the ratio of voltage to current (ohms) (Equation 1). An intuitive approach to understanding these parameters is presented in Appendix A.

\[ V = I*Z \]  

Equation 1 implies that if two of the three parameters are known, then the third can be calculated. A simple measurement of current is obtained by making an electromagnet. Current flowing through a wire produces a magnetic field. The current can be measured by determining the strength of its magnetic field, e.g., by measuring the force exerted on a piece of iron. Voltage between two locations can be measured by measuring the force on a charged object when the object is placed at one of the locations and comparing that force to the force measured when the charged object is placed at the other location. A simpler method utilizes equation 1. The two locations are connected with a known impedance, and the resulting current's magnetic field is used to deflect a piece of iron (Fig. 1).

Measuring a fixed current flow or direct current (DC) provides a straightforward answer (e.g., 10 A). How does one describe current flow that varies with time? Describing the entire waveform is cumbersome, and just reporting the peak-to-peak amplitude is misleading in the cases of currents containing occasional, short-duration, large transients. A convenient measure of current flow or of voltage is the root-mean-squared (RMS) value of the waveform (Equation 2). The RMS value of current is the value displayed by almost all alternating current (AC) voltmeters. This complicated-looking value is useful because it is a measure of the power contained in the signal. For sine waves, the RMS value is simply 0.707 times the amplitude of the sine wave. A familiar example is the wall voltage of 120-V RMS—the amplitude of the voltage is actually 170 V (120/0.707) and the peak-to-peak amplitude is 340 V.

\[ I_{rms} = \sqrt{\frac{1}{T} \int_0^T (i(t))^2 dt} \]  

where \( t \) = time, \( T \) = total time the signal exists, \( i(t) \) = current at time \( t \), and \( I_{rms} \) = root mean squared current.

Descriptions of electric signals frequently refer to the frequency content of the waveform. These descriptions rely on the fact that any arbitrary waveform can be represented as a sum of sine waves of various frequencies, amplitudes, and phases (Fig. 2). If very high-frequency sine waves are needed to obtain a good match between the waveform and the sum of sine waves, then the waveform has high-frequency components. Such a waveform is characterized by rapid fluctuations in time; the rapid fluctuations correspond to the high-frequency components. High-frequency potentials decrease in amplitude with distance from muscle fibers much more than low-frequency potentials. Tissue acts as a low-pass filter, i.e., selectively removes the high-frequency components of the signal. This explains the familiar finding that motor units recorded from far away appear
amounts of copper wire to minimize the resistance of the cord. Design criteria such as cost, size, safety, and convenience often result in compromise, allowing filtering to become significant. Recording routine conduction studies with surface electrodes instead of needles is an example of appropriate compromise. Also, EMG needles and amplifiers have filtering effects that reflect design compromises.

Some devices are designed to perform specific filtering actions. Examples are the low-pass and high-pass filters on EMG machines. The high-pass filter is the one typically set to a low frequency, e.g., 20 Hz, since it allows high frequencies through and stops low frequencies. For this reason, the high-pass filter is sometimes called the low-linear frequency filter, while the low-pass filter is sometimes called the high-linear frequency filter—a confusing set of terms. The purpose of these devices is to eliminate the frequency components of a signal that corresponds to noise while preserving the frequency components that correspond to the actual physiologic signal. Figure 5 shows the effect of introducing high- and low-pass filters inappropriately.

Most filters are designed with capacitors and resistors. Capacitors are devices that impede current flow by an amount that depends on the frequency content of the current. Capacitors completely block direct current (DC or zero frequency) signals, completely pass signals of infinite frequency, and partially impede signals of finite frequency, the impedance decreasing as frequency increases (Equation 3).

$$|Z_{\text{cap}}| = \frac{1}{2\pi fC}$$  \hspace{1cm} (3)

where $|Z_{\text{cap}}|$ = magnitude of the capacitive impedance, $f$ = frequency, and $C$ = capacitance.

Think of capacitors as valves that only let high frequencies through. A high-pass filter is created by placing a capacitor in the signal path. Only high-frequency components get through. A low-pass filter is created by connecting a capacitor between the signal path and ground. The high-frequency components leave the signal path and go to ground, leaving only the low-frequency components to travel further down the path. Capacitors also change the phase of a signal. A sine wave is shifted by 90° in phase when it passes through a capacitor. Resistors provide a constant impedance to current flow, regardless of frequency, and do

**FILTERS**

Every device that conducts an electric signal changes the signal, i.e., filters it. Most devices are designed to minimize their filtering effect. An example is the power cord connected to the wall; quality power cords are made with generous

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**FIGURE 2.** Any waveform can be represented as a sum of sine waves. (A) Waveform to be represented. (B) Sine wave: 60 Hz, 0 phase, 1 V. (C) Sine wave: 90 Hz, 45° phase, 0.5 V. (D) Sine wave: 120 Hz, 90° phase, 0.5 V. (E) Sine wave: 200 Hz, 0 phase, 0.25 V. (F) Sum of (B) and (C). (G) Sum of B, C, and D. (H) Sum of (B), (C), (D), and (E).
not produce any phase shift. The combination of resistance and capacitance determines the cutoff frequency of the filter (Equation 4).

\[ f_{co} = \frac{1}{2\pi RC} \]  

(4)

where \( f_{co} \) = cutoff frequency, \( R \) = resistance, and \( C \) = capacitance.

The cutoff frequency is the frequency at which the output signal amplitude is only about 70% (actually \((1/2)^{1/2}\)) of the input signal amplitude. The cutoff frequency is also the frequency at which half of the maximal phase shift occurs. Note that setting a 2-kHz low-pass filter does not imply that all frequency components below 2 kHz pass through unscathed. There is a smooth transition from frequencies mostly passed to frequencies mostly blocked, with 2-kHz frequency components being reduced to 70% of their input amplitude. The abruptness or “sharpness” of the cutoff varies with different designs. Often, a compromise is made between the sharpness of the cutoff and distortion from phase changes produced by the filter. The effect is similar to phase distortion in an amplifier (Fig. 5D).

Digital filters provide a simple technique for optimizing filter performance under varying conditions without expensive hardware. To change filters, one simply runs a different computer program rather than physically switching to different hardware components.

INPUT IMPEDANCE

Devices are frequently joined in series so that the output of one is the input to the next (Fig. 3). Each device can be considered independently as a filter, or “system,” with certain input/output characteristics. The input/output characteristics of the group are determined entirely by combining only the input/output characteristics of each device, without regard to the internal workings or structure of the device. This approach works for simple devices, such as resistors, and for more complicated devices, such as amplifiers or computers.

Connecting resistances in series produces a device with resistance equal to the sum of the individual resistors (Equation 5).

\[ R_{tot} = R_1 + R_2 \]  

(5)

where \( R_{tot} \) = total resistance, and \( R_1, R_2 \) = individual resistances.

For a given voltage, the current that will run through the device can be calculated using equation (1). Since there is only one pathway in the device, the same current will go through each resistor. Knowing the current passing through the whole device allows calculation of the voltage that appears across individual resistors (Fig. 3, Equation 6).

\[ V_R = \frac{R}{R_1 + R} V \]  

(6)

Note that equation 6 is easily derived from equations 1 and 5. A consistency check is made by adding the voltages across individual resistors; the sum must equal the total voltage across the device. For example, if there are only two resistors in the circuit, and they have the same resistance value, then the voltage across each resistor must be half the total voltage applied to the circuit.

Series resistors provide an illustration of the benefit of high-input impedance. The input impedance of a device is a measure of how much current flow is needed to produce a particular voltage (see Equation 1) across the input terminals of the device. Consider the case of an electrode attached in series to an amplifier (Fig. 3B). The electrode is placed in a muscle and a voltage is imposed between the active electrode and the reference. The current that flows is determined by the sum of the electrode and amplifier impedances. The sum of the voltage across the electrode...
and the voltage across the amplifier will equal the total voltage imposed between the active electrode and reference. As illustrated in Figure 3B, if the electrode impedance is high, then most of the voltage will drop across the electrode, leaving little to drop across the amplifier. Only the voltage that drops across the amplifier, however, can be detected by our apparatus and go on to be recorded and displayed. If the amplifier is to detect 99% of the voltage appearing at the electrode, then the amplifier input impedance must be 99 times greater than the electrode impedance. This is why an EMG amplifier must have an input impedance that is much higher than the needle electrode impedance.

**AMPLIFIERS**

An ideal amplifier converts a low-voltage waveform to a higher-voltage copy of the same waveform. To accomplish such a transformation, the ideal amplifier has an infinite input impedance, infinite frequency response, introduces no noise, is perfectly linear, and has an infinite dynamic range. Real amplifiers, with finite parameters, filter the signal as they amplify it. A good design only minimally filters waveforms encountered in normal operation. One can think of a real amplifier as an ideal amplifier coupled to filters that are permanently set to reflect the actual performance of the amplifier (Fig. 4).

The dimensionless ratio of the output voltage to the input voltage is the gain of the amplifier. Amplifier sensitivity relates the input voltage to a display scale, e.g., 1 mV/cm. If the amplifier sensitivity is too low, then small deviations from baseline will be unapparent, resulting in artifactual longer latencies to takeoff in nerve conduction studies, and apparent decreased duration of motor unit action potentials.

An inadequate amplifier will distort the waveform. If the amplifier’s frequency response is limited, then high- or low-frequency components may be lost (Figs. 5A, 5B, and 5C). Frequencies near the cutoff frequency can produce distortion due to a poor phase response (Fig. 5D). If the amplifier’s gain varies with the level of input voltage, then the amplifier is nonlinear and can produce bizarre distortions. A familiar nonlinearity occurs when the input voltage is too large, and the output saturates or blocks.

When a small signal is embedded in environmental electric noise, two amplifiers can be combined to create a differential amplifier that will dramatically improve the signal-to-noise ratio (Fig. 6). The “trick” is to place the input leads of the two amplifiers very close to each other so that the environmental noise will be the same on both leads. Then the leads are attached so that the desired signal will appear as a voltage between the two leads. Ideally, the leads will carry the same noise, but only the active lead will carry the signal. The differential amplifier will invert and amplify the signal from one lead (reference lead), and
then add it to the amplified signal from the other lead (active lead). If the two amplifiers are identical, then the noise, common to both leads, will cancel but the signal will be preserved. If the amplifiers are not identical, then one will amplify the noise more than the other and the sum of the two signals will no longer completely cancel.

The common mode rejection ratio (CMRR) is a measure of how identical two amplifiers are (Fig. 6). As an example, suppose the amplifiers are not identical; let amplifier 1 have a gain of 100, and amplifier 2 have a gain of 99.9. A 2.0-V signal common to both inputs will result in 200 V from amplifier 1 and negative 199.6 V from amplifier 2. Summing the two voltages yields an output of 0.4 V from the differential amplifier. The common mode gain is the ratio of the output to the common input voltage. In this example, the common input is 2.0 V and the output is 0.4 V, so the common mode gain is 0.2. If 2.0 V had been applied differentially, perhaps as +1 V to amplifier 1 and −1 V to amplifier 2, then the output would be 200 V + 196 V, or 396 V, for a “differential gain” of 396 V/2 V or 198. The CMRR is the ratio of differential gain to common mode gain, in this case, 198/0.2, or 960. Expressed in decibels [20 log10 (ratio)], a ratio of 960 is 59.6 dB.

ELECTRODES

Three electrodes are always attached to the patient during nerve conduction studies (NCS) and EMG: an active electrode, a reference electrode, and a ground electrode. As discussed above, the displayed signal will be the voltage difference between the active and reference electrodes. The ground electrode serves as a safety feature and a low impedance path to drain electric noise away from the signal electrodes.

For sensory NCSs, the two signal electrodes are both placed over the nerve or around a finger, about 4 cm apart. The 4-cm distance is appropriate because a typical action potential duration of 0.8 ms and a typical velocity of 50 m/s produces a depolarization that extends for 4 cm (500 cm/s × 0.008 seconds). Note that the differential recording produces a biphasic signal when a positive, monophasic signal appears first at the active lead and then at the reference lead. If the leads are too close together, the signal may be distorted as the beginning of the signal appears in the reference lead before the end of the signal has passed the active lead. Motor NCSs use electrodes placed over the muscle motor point and a tendon. The compound muscle action potential (CMAP) is large enough so that some of the signal will generally appear in the reference electrode.

Needle electrodes record extracellular voltages in muscle. The voltages reflect membrane current as it flows through extracellular fluid. Recall that the current flows in a loop across the muscle fiber membrane into the extracellular fluid, through the extracellular fluid longitudinally along the axon, back across the muscle fiber membrane into the cell, and through the cytoplasm back to the starting point. Note that voltages across the membrane, resting potentials, and action potentials, are not measured by the electrode. The electrode records the voltage between two extracellular locations; this voltage depends on membrane current, not membrane voltage.

The metal of a needle electrode interacts with the extracellular fluid to create a charge separation similar to Franklin’s glass and silk. The resulting voltage is called a tip potential or polarization potential. These potentials can be large but generally are not noticed since they are DC signals and the amplifiers are AC coupled. Dirt or frayed Teflon, however, can cause the tip potentials to be unstable and can produce artifacts that can be mistaken for spontaneous muscle fiber activity.

The two most common EMG electrodes are the monopolar and concentric electrodes. The monopolar electrode is combined with a reference electrode placed subdermally nearby. Monopolar electrodes have much greater separation between active and reference sites than concentric needles. The increased separation increases noise and motor unit action potential (MUAP) size compared to concentric needle recordings. If the Teflon tip
frays, more of the needle is used for recording, the impedance drops, and the signal is averaged over a wider volume of muscle. The result is a reduction in amplitude and polyphasia of MUAPs that can seriously distort the waveform. Electrodes have capacitance so the electrode impedance decreases with increasing frequency. Weichers demonstrated an average impedance of monopolar electrodes of 1.4 MΩ at 10 Hz, compared with 4.7 Ω for concentric electrodes at 10 Hz. Thin concentric needles (<0.03 square millimeter area) may have high enough impedances to compromise the performance of amplifiers that have adequate input impedances for monopolar and larger concentric needles. Although concentric needles do not have the problem of Teflon fraying, there is considerable variation in electrode characteristics among manufacturers.

DIGITAL ELECTRONICS

The essence of digital storage is that any waveform can be characterized by a list of numbers. The waveform and the number list are completely equivalent; however, computers are confined to working with lists of numbers while humans have the capability to visualize and understand information presented as a waveform. The process of converting a waveform to a number list is called analog-to-digital or A-to-D conversion. The reconstruction of the waveform from numbers is D-to-A conversion.

Number list representations are frequently used as a simple method of saving the waveform for later inspection. For example, without storage, the CMAP appears as a quick transient event on the oscilloscope screen. By storing the CMAP as a list of numbers, it can be repeatedly displayed, providing the visual impression of a fixed image.

The details of digitization determine the quality and accuracy of the reconstructed and displayed waveform. If the digitization rate is too slow, then the time between two numbers on the list will be too long. The result is poor resolution in time, so that sharp spikes appear blunted or may be missed entirely. Since time is displayed along the horizontal axis, slow digitization rates produce poor horizontal resolution. Inadequate horizontal resolution prevents most digital signal processing from working properly. Poor vertical resolution occurs when the range of numbers allowed is too small. For example, if the numbers are restricted to 0, 1, 2, or 3, then each integer covers 25% of the entire range of vertical resolution. The reconstructed waveform will have only four possible voltages and will look choppy, like a staircase with high vertical steps. Since numbers in a computer are always represented in binary format, the range of allowed numbers is expressed in bits. For example, the four integers from 0 to 3 represent 2-bit resolution (00, 01, 10, 11). Twelve-bit resolution allows 2^12 or 4096 possible numbers (000000000000, 000000000001, 000000000010, 000000000011, 000000000100, ..., 111111111111), so that each number covers only 0.02% of the entire range.

The number list can be used to determine amplitude between two points by subtracting the number corresponding to one point of the waveform from the number corresponding to another point. Averaging is used to improve the signal-to-noise ratio. Averaging is accomplished by combining several number lists; the lists are added and the sum is divided by the number of lists to produce a single, averaged list. Similarly, all of the analog operations of filtering can be accomplished through appropriate manipulation of the number list.

Delay lines are made by continually updating a number list that represents the most recent waveforms recorded. The delay line allows inspection of events that occurred prior to a particular event of interest. For example, when isolating a MUAP, one usually triggers on the portion of the MUAP near the peak. Without a delay line, inspection of the MUAP waveform is limited to the portion occurring at and after the time the trigger is activated. The delay line contains data that occurred just before the trigger was activated, allowing inspection of the entire MUAP even if triggering occurs at the peak.

Digital representation of waveforms allows signal processing techniques to be used to interpret the waveforms. Computer programs can automatically determine latency and amplitude values of evoked potentials. Many algorithms exist to help interpret interference patterns and MUAP characteristics, such as turns and amplitude ratios.

STIMULATORS

Stimulators are used to induce action potentials in nerve fibers. Current flows from the anode (+ pole) of the stimulator to the cathode (− pole). Some current will flow inside each axon, from the site under the anode toward the site under the cathode. With the membrane at rest, only a few charges actually flow across the membrane, and
the membrane potential is linked to membrane current flow primarily through the capacitive properties of the membrane. Positive charges accumulating inside the axon, under the cathode, cause a depolarization as the capacitive charge is reduced (positive charges accumulating on the inside cancel the negative charges that are sustaining the membrane potential).

Current also flows just outside the axon from the anodal region to the cathodal region. Why don’t these two current transfer the same amount of charge, both inside and outside the axon, so that the net effect is zero? The difference is that the charges inside the axon are confined, but the charges outside the axon can flow toward or away from the stimulator. Positive charges outside the axon flow toward the axon under the anode, replacing the charges that flowed toward the cathode. Positive charges outside the axon flow away from the axon under the cathode, draining the charges that flowed away from the anode. The net result of all these current flows appears as a current that is flowing out into the axon under the anode and out of the axon under the cathode, resulting in depolarization of the axon under the cathode. The initial depolarization opens regenerative channels, sodium ions flow in, and an action potential is created under the cathode. The action potential is capable of propagating in both directions of the axon; however, the part of the nerve under the anode is hyperpolarized, so the action potential may fail to propagate past the anode (anod al block).

Myelinated axons are easier to stimulate than unmyelinated axons because essentially all the stimulus current exits the axon at the tiny nodes of Ranvier. Since the current flows out of a small area of membrane, the current is very concentrated and small currents produce significant local depolarization. Large axons are easier to stimulate than small axons for a similar reason. As the radius of an axon increases, the ratio of membrane area to cross-sectional area decreases. Also, the current flow produced by the stimulator in an axon is proportional to the cross-sectional area of the axon. Therefore, the stimulus current flowing through the membrane of a large axon will be more concentrated than in smaller axons.

Stimulators can provide either constant current or constant voltage stimulation. The constant voltage mode creates a voltage across the anode and cathode; the voltage is determined by a dial setting. Current flow is determined by the impedance of the skin, fluid, and tissues between the two poles. If the poles are held in the open air, essentially no current flows. If the poles are connected by a good conductor, such as a wire, then the current is only limited by safety features in the machine (i.e., buy a new fuse). Constant current stimulators provide a specific current that is selected by a dial setting. In this case, the voltage across the poles is determined by the impedance between the poles. If the poles are connected by a wire, the selected amount of current flows (with very little voltage across the poles). If the poles are held in the open air, then the maximum voltage allowed by the machine will appear across the poles and, in a good design, an indicator will inform the operator that the impedance limit was exceeded and the desired current did not flow. Constant current stimulators are much more useful than constant voltage stimulators in determining thresholds to stimulation. Variations in skin impedance alone will produce apparent threshold changes when using constant voltage stimulators.

Stimulators can develop large internal charges and voltages. Also, the discharge of a stimulator can introduce transients into other equipment, producing artifacts and, sometimes, damage. Stimulus isolation units typically use transformers or optical circuits to isolate the patient and other equipment from the stimulator circuitry.

**PATIENT SAFETY**

Where there is voltage, there is current, i.e., there is no such thing as an infinite impedance. Stray currents from apparatus are termed leakage currents and patients must be protected from them (Table 1). Electric currents can be induced in materials that are simply a nearby power source. Current flows from a metal chassis to ground because voltages are created on the chassis from power cords and transformers inside or near the chassis. Ground receptacles are not all at the same voltage so current will flow between ground leads of devices that happen to be plugged into different wall sockets. Extension cords should not be used since they increase the differences between receptacles and can induce unacceptable levels of current.

Precautions include using only a single grounding point on the patient and tying all equipment grounds to a common place that is grounded. Patients must be kept away from ungrounded surfaces or devices that could produce excessive currents when the EMG electrodes are attached. Examples include an electric bed with a metal frame and broken ground lead or a lamp with a two-prong power plug.
Table 1. Summary of risk current requirements in RMS microamperes (DC to 1 kHz).

<table>
<thead>
<tr>
<th>Category of electromedical apparatus</th>
<th>Patient risk current</th>
<th>Chassis source current</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Source current</td>
<td>Sink current</td>
</tr>
<tr>
<td>With isolated patient connection</td>
<td>10</td>
<td>10*</td>
</tr>
<tr>
<td>With nonisolated patient connection</td>
<td>50</td>
<td>NA†</td>
</tr>
<tr>
<td>Likely to contact patient</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>No patient contact</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

*The allowed sink risk current is 20 μA RMS for isolated electromedical apparatus with patient cables, when measured at the patient end of the cable (see §4.4 of the ANSI/AAMI Standard).
†Not applicable.


Very small electric currents are capable of inducing ventricular fibrillation, particularly if the skin resistance is eliminated by a needle. The American National Standards Institute (ANSI) approves test methods and safety standards that set limits on current flow for electromedical apparatus used in patient areas (Table 1).

The highest safety category is termed "isolated" patient connection. Isolated equipment is used in situations where the skin is not intact, so a pathway can conduct current to the heart. Isolated conditions require the equipment to generate less than 10 μA RMS from contact leads to ground (source current). It must also not allow more than 10 μA (sink current) to flow through the device to ground if patient leads come in contact with a 120-V, 60-Hz source. The sink current requirement helps to protect a patient who is inadvertently exposed to the wall voltage while being attached to an electromedical device. Up to 100 μA of current is allowed between the chassis and ground, tested both with the ground intact and with the ground disconnected.

The use of electrosurgical units (ESUs) for cutting and coagulating during surgery creates a very high-frequency electric field that can result in substantial current flow if devices are not adequately protected. The very high frequencies of ESUs can cause damage to solid state devices and can bypass standard safety measures designed to protect against 60-Hz risks. For example, the cables used as patient leads may have very low impedances at the frequencies used by ESUs. Some ESUs provide digital outputs to communicate to other devices when the ESU is activated, and the devices can be designed to disconnect during ESU operation.

**SUMMARY**

Electrodiagnostic instrumentation is designed to accurately measure and display tiny physiologic signals. The straightforward principles of voltage, current, and impedance provide an adequate base to understand design criteria such as wideband frequency responses, variable gains, high-input impedances, good signal-to-noise ratios, and large common mode rejection ratios. The accuracy and interpretation of test results, the selection of appropriate equipment for purchase, and patient safety are all enhanced by an understanding of fundamental electronics. Furthermore, these principles provide insight into the physiologic events being measured in electrodiagnostic studies.

**APPENDIX: INTUITIVE APPROACH TO ELECTRIC PARAMETERS**

The concepts of voltage, current, and impedance are easily related to more intuitive parameters, allowing basic understanding to grow from a conceptual basis as well as from quantitative analysis. Mechanical systems, fluid flow, heat transfer, and electric systems are all described by the same differential equations. To understand any one of these processes is equivalent to understanding them all. The only difference is the parameters. Substituting voltage for pressure and electric current for fluid flow allows an electric engineer to work in fluid mechanics.
Voltage is a measure of electric potential energy just as height is a measure of gravitational potential energy in the approximately constant gravitational field near the earth’s surface. The gravitational potential energy of an apple is realized when it drops from the tree. The apple’s velocity, when it hits your head, depends on the difference between the original height of the apple and the height of your head. Both height and voltage are measured as a difference between two locations, rather than as absolute numbers. Note that height is frequently expressed as an absolute value such as the height of Mt. Everest, or an individual’s height. The reference height could be general, such as mean sea level, or local (e.g., the ground the individual is standing upon). Absolute voltage values (e.g., 120 V) are frequently referenced to a metal post buried in the ground near the power transformer outside the building. Test equipment, however, measures voltages with respect to a very local reference such as the ground receptacle in a wall plug. One should be aware that there are frequently measurable voltages between the different ground receptacles in a single room.

Current is a measure of flow. A river current corresponds to the volume of water that flows in some amount of time (e.g., liters per second). The current is determined by the steepness of the river grade (“voltage”) and the friction of the water and river bed (“resistance”). A wide river flowing from a steep mountain passes huge amounts of water, just as a small resistor and a large voltage results in a huge electric current.

For direct currents (DC), impedance is the same as resistance, and simply corresponds to friction in a mechanical system. When alternating currents (AC) are used, however, some of the energy from one cycle can be stored for use in later cycles. This concept of energy storage forms the basis of impedance. A classic example of mechanical impedance is the mass-spring-friction system. If friction is eliminated, starting the mass and spring bouncing results in their bouncing forever. This is impedance without resistance. Energy is simply shifted back and forth between the mass and spring. For a while, the moving mass (kinetic energy) compresses the spring (potential energy), then, for a while, the compressed spring moves the mass. The frequency of bouncing is termed the resonant frequency of the mass-spring system and is determined by the spring constant and the mass. If friction is introduced, then energy is dissipated as heat and, over time, the bouncing subsides. Similarly, an ideal capacitor and inductor will pass electric energy back and forth forever oscillating between energy storage in an electric field (capacitor) and a magnetic field (inductor). Including a resistor causes the oscillations to die away as energy is dissipated as heat.

REFERENCES

INTRODUCTION TO MUSCLE PATHOLOGY

I. Introduction

A. Muscle biopsy may show evidence of:
   1. Myopathy.
   2. Neurogenic atrophy.
   3. A specific disease.

B. Biopsied muscle must be clinically affected but not severely weak or highly atrophic.

C. Complete biopsy includes:
   1. Paraffin sections.
   2. Fresh-frozen sections stained with hematoxylin and eosin, trichrome, or histochemically.
   3. Electron microscopy in selected instances.

II. Pathologic Changes Commonly Assumed to be Myopathic

A. Abnormal variation in fiber diameter.

B. Internally placed fiber nuclei.

C. Structural changes in fibers.
   1. Focal loss of striations.
   2. Cloudy, granular, or floccular changes.
   3. Vacuoles.
   4. Fiber splitting.
   5. Ring fibers.

D. Phagocytosis of degenerating fibers.

E. Regenerating fibers.

F. Endomysial fibrosis.

G. Specific examples.
   1. Normal adult muscle, trichrome stain, transverse section.
      a. Uniform fiber diameters.
      b. Sparse connective tissue between fibers (blue staining).
      c. Wide separation of fascicles are artifactual.
      d. Nuclei subsarcolemmal.
   2. Abnormal variation in fiber diameter and abundant internally located nuclei.
3. Normal adult muscle, trichrome stain, longitudinal sections.
   a. Alternating light and dark bands (I and A bands, respectively).
   b. Empty slit-like spaces in fibers are artifactual.
4. Focal loss of cross striations.
   a. H&E section.
   b. I bands are dark, A bands are light.
5. Degenerating fibers with internal nuclei filled with floccular material; excessive green-staining endomysial connective tissue.
7. Vacuolar degeneration, abnormal variation in fiber diameter, endomysial fibrosis.
8. Fiber splitting (note split fibers remain molded in shape of parent fiber).
9. Ring fibers, named for aberrantly coursing myofibrils that form ringlets at the fiber periphery.
10. Degenerating fiber invaded by macrophages.
11. Central regenerating fiber with rows of prominent nuclei.
    a. Nuclei are vesicular and display prominent nucleoli.
    b. Basophilic material in fibers due to abundant ribosomes.
12. Endomysial fibrosis; perimysial connective tissue between fascicles also is increased.

III. Histochecmistry of Muscle Biopsy

A. General observations.

1. Histochemical features of a muscle fiber are determined by its innervation.
2. All muscle fibers innervated by a single anterior horn cell have identical histochemical features.
3. Two major histochemical fiber types exist in human muscles.
   a. Type I (red); aerobic, high oxidative, "slow".
      1. Glycogen content low.
      2. Glycolytic enzymes low.
      3. Oxidative enzymes high.
   b. Type II (white); anaerobic, low oxidative, "fast".
      1. Glycogen content high.
      2. Glycolytic enzymes high.
      3. Oxidative enzymes low.
      4. Myofibrillar ATPase high.
      5. The myofibrillar ATPase staining listed is for pH 9.2; the staining inverses at pH 4.5.

B. Examples.

1. Succinic dehydrogenase stain (oxidative enzyme).
   a. Type I fibers (aerobic) stain dark.
   b. Striations due to orderly arrangement of mitochondria adjacent to I bands.
2. Longitudinal section reacted for phosphorylase.
   a. High in type II (glycolytic enzyme).
   b. Type II fiber dark.
3. Transverse section reacted for phosphorylase; note checkerboard pattern.
4. Transverse section for myofibrillar ATPase.
   a. ATPase high in Type II fibers.
   b. Note distribution of muscle fibers innervated by a single anterior horn cell.
   c. In normal muscles, the territories of different motor units overlap.

IV. **Pathologic Changes Associated with Neurogenic Atrophy**

A. Transaction of motor nerve results in muscle fiber atrophy.

B. Injury (by any pathogen) of a small fraction of all nerve fibers to given muscle results in small groups of atrophic fibers.

C. Degenerated fibers can become reinnervated by collateral sprouting of surviving axons; the territory of surviving motor units becomes larger.

D. When a reinnervated axon is injured, a large group of fibers undergoes atrophy.

E. Specific Examples.

   1. Small group of atrophic fibers secondary to loss of only a few axons; note hypertrophy of nonatrophied fibers.
   2. Chronic neurogenic atrophy in HMSN I.
   3. Large group of atrophied fibers, likely secondary to loss of reinnervated axon.
   4. Reinnervated muscle reacted for ATPase.
      a. Type II fibers dark.
      b. Type group (loss of checkerboard pattern).
   5. Target formations.
      a. Sometimes seen in reinnervated type I fibers.
      b. Decreased oxidative enzymes and glycogen in center of fiber and increase at margin.
      c. Center displays loss of striations.
      d. NADH-dehydrogenase stain (oxidative enzyme, stains Type I fibers).
   6. PAS-stained section.
   7. Trichrome-stained paraffin section.
      a. Target formations.
      b. Small groups of atrophic fibers and endomysial fibrosis.
      c. Denervation and reinnervation may proceed side-by-side in chronic neurogenic diseases.

V. **Does the Biopsy Suggest a Specific Disease?**

A. General Comments.

   1. Core formations in central core disease.
   2. Rod formations (nemaline structures) in nemaline myopathy.
3. Large central vacuoles in primary periodic paralysis.
5. Massive degenerations and regeneration of fibers, recent attack of paroxysmal myoglobinuria; rhabdomyolysis.
6. Selective degeneration and atrophy of fibers at periphery of fascicles; dermatomyositis.
7. Fibrinoid necrosis of arterioles plus neurogenic atrophy; periarteritis nodosa.
8. Perivascular collection of chronic inflammatory cells and myopathic changes in muscle fibers; polymyositis.
10. Encapsulated trichinoma which may calcify; trichinosis.

B. Specific clinical and pathologic examples.

1. 18 year old with static, diffuse weakness.
2. NADH dehydrogenase - reacted section.
   a. Core formations resembling target fibers.
   b. Central core disease.
3. Nemaline (rod) myopathy, trichrome stain.
   a. Rods stain purple.
   b. EM shows that rods arise from abnormal proliferation of Z-disks.
   a. Vacuoles develop after many paralytic attacks.
   b. Vacuoles communicate with the extracellular space via transverse tubules.
5. PAS stain for glycogen.
   a. Increased staining in Type 2 glycogen storage disease due to acid maltase deficiency.
6. Degenerating and regenerating fibers in paroxysmal rhabdomyolysis.
7. Perifascicular atrophy in dermatomyositis.
8. Marked inflammation in polymyositis.
9. Central arteriole showing fibrinoid necrosis, surrounded by an inflammatory exudate; periarteritis nodosa.
10. Small granula in sarcoidosis with giant cells.
11. Calcified encapsulated trichinella due to ancient trichinosis.
12. Trichinella in clinically active disease.

VI. The Muscle Fiber

A. Normal fiber diameter 30-60 microns.
B. Each fiber contains myofibrils (0.5 to 1 micron).
C. Each myofibril made up of repeating units.

1. Units are called sarcomeres.
D. Thin filaments are attached to the Z disk.

E. Thick filaments are attached to each other in midsarcomere region (m line).
   1. Thick filaments have side projections.
   2. Made up of myosin.

F. Thin filaments contain actin, tropomyosin, and troponin.

G. During contraction:
   1. Thin filaments from opposing ends of a sarcomere slide into the A band and the sarcomere becomes shorter.
   2. The propulsion of thin filaments toward the center of the sarcomere is dependent upon activity of the cross bridges.
   3. The length of individual thick and thin filaments does not change.
   4. The force exerted is proportional to the number of cross bridges formed.

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