Preface

Clinical Electromyography

This issue of Neurologic Clinics is devoted to clinical electromyography (EMG). Clinical EMG, also known as electrodiagnostic study, is the electrophysiological examination of peripheral nerve and muscle. It is a distinct discipline and plays a pivotal role in the evaluation and management of patients with neuromuscular disorders. Clinical EMG best serves as an extension of the neurologic examination. It is well suited to diagnose disorders of the peripheral nervous system, including the sensory nerves, the dorsal root ganglia, and the motor unit (anterior horn cells, motor nerves, neuromuscular junctions and muscles). Each study must be individualized, based on the manifestations and differential diagnosis, and modified as further information is gained.

The focus of this issue is clinical. To accomplish this task, I have assembled a group of practicing academic electromyographers with expertise in the disciplines of clinical EMG and neuromuscular disorders. All contributions emphasize the practical aspects of the electrodiagnostic studies, as encountered daily in the EMG laboratory. I have divided the subjects into two sections: Basic Concepts and Findings in Neuromuscular Diseases. The first section starts with an introduction on the discipline of clinical EMG, in which I define the scope of the examination with emphasis on the EMG laboratory’s referral process and reporting. This is followed by Asa Wilbourn’s scholarly review of the basic abnormalities of nerve conduction studies seen in peripheral nerve lesions and their localization values. This interesting article provides many of the basics to the understanding and analysis of the electrodiagnostic study in general and the nerve conduction studies in particular. Next, Morris Fisher summarizes the physiology of the
F-waves and H-reflexes and their utilities in diagnosing neuromuscular and spinal cord disorders. Finally, David Preston and Barbara Shapiro complete this section by covering, in detail, the fundamentals of needle EMG with emphasis on normal and abnormal findings.

The second section of this issue is divided into several articles discussing the electrodiagnostic findings of the most common neuromuscular diseases referred to the EMG laboratory. In his comprehensive article on radiculopathies, Kerry Levin updates the classic EMG patterns seen with cervical and lumbosacral radiculopathies and emphasizes the recently published EMG-based myotomal charts. After setting the tone of the terminology and anatomy of the various elements of the brachial plexus, Mark Ferrante and Asa Wilbourn discuss, in detail, the value of the electrodiagnostic findings in the accurate and precise localization of brachial plexopathies. Next, two articles are devoted to mononeuropathies: David Herrmann and Eric Logigian discuss the approach and findings of upper limb mononeuropathies while I review the electrodiagnostic studies of those of the lower limb. The article on peripheral polyneuropathy, by Theodore Wein and James Albers, covers, first, the clinical approach to polyneuropathies in general, and then highlights the electrodiagnostic findings in the demyelinating and axonal polyneuropathies. David Chad’s interesting article on motor neuron disease starts with a discussion of the clinical diagnosis and electrodiagnostic findings, with a healthy critique of the criteria (including the revised El Escorial criteria), and ends with a differential diagnosis of the mimickers of motor neuron disease. With Henry Kaminski, I outline the physiology of neuromuscular transmission as it pertains to the electrodiagnostic examination and highlight the findings of neuromuscular junction disorders with emphasis on myasthenia gravis, Lambert-Eaton myasthenic syndrome and botulism. Finally, David Lacomis summarizes the findings in the various myopathies presenting to the EMG laboratory and constructs practical tables summarizing their EMG patterns.

Overall, I believe that this issue of Neurologic Clinics will prove to be an extremely useful reading to practicing neurologists and physiatrists, training fellows in clinical neurophysiology, neuromuscular diseases and clinical EMG, as well as residents in Neurology and in Physical Medicine and Rehabilitation.

Finally, I want to thank all the authors for their generous contributions, and to the editors at W.B. Saunders for inviting me to be the guest editor of this issue. I am most grateful to my wife, Patricia, and my children, Linda and Michael, for their encouragement and support.

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The clinical electromyography examination
An overview

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Definitions of terms

The term electromyography (EMG) was first coined by Weddell et al., in 1943, who pioneered the clinical use of needle electrode examination of muscles. Since then, the titles EMG or Clinical EMG have been used by physicians to refer to the electrophysiologic examination of peripheral nerve and muscle, which includes nerve conduction studies (NCS) and needle EMG. Unfortunately, this continues to cause confusion among physicians and healthcare workers; some physicians refer the study as EMG/NCS, reserving the name EMG solely to the needle EMG evaluation and adding the term NCS to reflect these studies separately. Others have used the title needle electrode examination (NEE) to reflect the needle evaluation of muscles, while keeping the name EMG to describe the entire evaluation. More recently, a nonspecific term, the electrodiagnostic (EDX) examination, has gained popularity to serve as an umbrella covering both the needle EMG and NCS. Other nomenclature used worldwide includes the electrophysiologic examination (which may be confused with the cardiac electrophysiologic studies) and the electroneuromyographic (ENMG) examination (which is, in my opinion, the most accurate, yet not widely used, description of the study). Finally, the physician performing and interpreting these studies is referred to as electromyographer (EMGer), electrodiagnostician, or EDX consultant.

To minimize confusion among physicians and other healthcare providers, the designations, EDX examination, EMG examination or clinical EMG examination, are best used interchangeably to reflect the entire electrophysiologic study of nerve and muscle (NCS and needle EMG), while

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the names needle EMG or NEE are kept for the specific testing which involve needle electrode evaluation of muscle.

The practice of electrodiagnosis is a practice of medicine. EDX consultants (electromyographers) function in a similar fashion as radiologists by providing diagnostic studies directed by the patient clinical symptoms and working diagnosis. Hence, the EMG study should be as independent as possible, by providing an objective physiological assessment of the neuromuscular system [1].

**Scope of electrodiagnostic examination**

The EDX examination (EMG examination) comprises a group of tests that are usually complimentary to each other and necessary to make a final diagnosis [1–6]. The EDX examination is composed of several components:

1. **Nerve conduction studies (NCS)**, which include sensory, motor, and mixed NCS with measurements of response amplitudes, areas, distal and proximal latencies, and conduction velocities. Unfortunately, many physicians continue to refer to this test as nerve conduction velocities (NCV), reflecting the focus on velocities (and latencies) and, thus ignoring the most important data obtained with these studies, namely amplitudes and areas.

2. **Needle EMG (NEE)**. Sometimes, the terms “conventional or routine” precede needle EMG to distinguish this test from the advanced EMG studies including single fiber EMG and quantitative EMG (see below). At other times, the names “concentric or monopolar” are added to reflect the type of needle electrode used during the needle EMG study. Needle EMG includes evaluation of muscles’ spontaneous and insertional activities, and motor unit action potential (MUAP) recruitment, activation and morphology.

3. Special studies are additional tests, which often supplement the NCSs and needle EMG. Some are administered when specific neuromuscular disorders are suspected. These studies include: (a) *F-waves* are also referred to as F-responses. Because of their utilities and ease, these late responses are often incorporated during performance of the NCSs and have become an integral part of the EDX examination. (b) *H-reflexes* are also labeled as H-responses. As with F-waves, many EMG laboratories have included the tibial H-reflexes routinely when NCSs of the lower extremities are performed. (c) *Blink reflexes* are specialized studies often done in the evaluation of patients with facial nerve, trigeminal nerve, brainstem disorders or added to the armament of studies in patients with suspected peripheral polyneuropathy, particularly the demyelinating type. (d) *Repetitive nerve stimulations* are specialized tests usually done following motor NCSs and indicated in patients with suspected neuromuscular junction disorders, but may be useful in myotonic
and neurogenic disorders. (e) *Single fiber EMG* is a specialized study, which is most useful in the diagnosis and management of patients with neuromuscular junction disorders, particularly myasthenia gravis [7]. EMG is an adjunctive test in the assessment of neurogenic disorders. (f) *Quantitative EMG analyses* are a group of specialized studies usually requiring sophisticated equipment and software, used as a clinical and research tool in the assessment of the microenvironment of the motor unit. These studies include MUAP morphology analysis, turns and amplitudes analysis, macro EMG, and motor unit number estimate (MUNE) [8].

**The referral process to the EMG laboratory**

Patients are referred to the EMG laboratory for EDX studies following a clinical assessment by a physician who suspects a disorder of the peripheral nervous system. For example, a patient with intermittent hand paresthesias and positive Phalen’s signs may be referred to the EMG laboratory to evaluate a possible carpal tunnel syndrome. The background and specialty of the referring physician plays a significant role in the planning and execution of the EDX study. This usually follows one of these three scenario:

1. The referring physician is well versed with the anatomy and disorders of the peripheral nervous system and the EDX examination. The referring physician is often a neurologist or physiatrist but, occasionally, a neurosurgeon or an orthopedist. In this situation, the referral information often includes a brief, yet focused, clinical information, and a limited differential diagnosis. In these situations, the EDX consultant performs an EDX study on the symptomatic limb(s) to confirm or exclude the suspected diagnosis or, sometimes, make an alternative diagnosis, which may have not been considered by the referring physician.

2. The referring physician is also the EDX consultant (electromyographer). In other words, the patient is examined first by the EDX consultant (usually a neurologist or physiatrist) who, then, performs and interprets the EDX study. The advantage of this situation is that the neurological examination is often thorough and the differential diagnosis is limited. Hence, the selection of NCSs and the choice of sampled muscles on needle EMG are well guided by the neurological findings. Though this scenario is ideal, it is not practical in a busy EMG laboratory. A pitfall of this approach is that some electromyographers may perform a very limited and suboptimal study, or become bias by the clinical information, resulting in a significant number of diagnostic errors. Another hazard is that some EDX consultants may change the interpretation of similar findings among different studies to suit and support the clinical diagnosis. For example, a diabetic patient with denervation of quadriceps, iliacus, thigh adductors, and lumbar paraspinal muscles may be diagnosed in the EMG laboratory as consistent with lumbar radiculopathy or dia-
abetic amyotrophy depending on the temporal course of the symptoms, pain characteristics, status of diabetic control, or findings on imaging of the spine.

(3) The referring physician is not well versed with disorders of the peripheral nervous system. Often, the referral working diagnoses in these patients are vague, nonspecific or extensive. Since the EDX study has limitations related to patient discomfort, expense, and time constraints, a directed neurological history and a brief neurological examination is often mandatory before planning and executing the EDX study. Unfortunately, contacting the referring physician to extract more specific information is often, in my experience, not fruitful.

Patients referred to the EMG laboratory should have a referral from completed by the referring physician with relevant clinical information and differential diagnosis (Fig. 1). Referring physicians should describe the EDX study to their patients, particularly in regard the discomfort associated with it, without creating a significant anxiety. If unclear about the technical details of the procedure, they should encourage their patients to contact the EMG laboratory to get a verbal or written description of the procedure (Fig. 2). Such written descriptions should be widely available in all referring physicians offices.

**EMG laboratory procedures**

Upon arrival to the EMG laboratory for testing, the patient should be informed in details of the procedures planned based on the referral information and clinical manifestations. Reading a written description is useful, but a verbal description of the procedure by the EDX technologist and electromyographer are usually more comforting and reassuring to the patient.

EDX consultants must have a good fund of knowledge pertinent to the anatomy, physiology, and disorders of the peripheral nervous system. They must be familiar with the anatomy necessary for performing the NCSs and needle EMG. Although a formal training in clinical EMG is necessary, the EDX consultant skills is usually based on the number and type of patients studied.

Nerve conduction studies and repetitive nerve stimulations may be performed by the electromyographer, EDX technologist, or both (Table 1). Well-trained, preferably certified, EDX technologists should work under close supervision of the electromyographer. The EDX consultant should view all NCSs and RNS before proceeding with the needle EMG. Additional NCS may be added pending the needle EMG findings. For example, the median sensory NCS, recording the index and thumb, should be added to the routine NCS if the needle EMG examination reveals denervation in C6 innervated muscles, to confirm the presence of a C6 radiculopathy (intraspinal canal lesion) and exclude an upper brachial plexopathy.
The EDX consultant performs needle EMG, because data are obtained online and could not be repeated. A concentric or monopolar needle electrode with the smallest diameter possible should be utilized, to reduce the extent of pain. Patient should be comforted throughout the procedure; if requested, a pause should be granted in the midst of the study. Needle EMG examination protocols for common disorders seen in the EMG laboratory are shown in

Fig. 1. A sample of an EMG referral form.
Table 2. In an extremely anxious patient or in a non-sedated child, the needle EMG should focus on muscles with the highest likelihood of abnormality, since only few muscles may be ultimately sampled. For example, sampling the vastus lateralis and deltoid may be the only possible muscles examined in a child with possible proximal myopathy.
When completed, the EDX consultant should explain the findings in brief to the patient, bearing in mind that the electromyographer is often not the referring or treating physician. Discussion of a serious illness, such as amyotrophic lateral sclerosis, may be best left to the referring physician. Suggestions for clinical management should not be discussed with patient (except in general terms if necessary) unless the referring physician has requested a formal neuromuscular consultation.

The results of the EDX study should be conveyed promptly to the referring physicians. An EMG laboratory report is the best way to transmit the results of the EDX assessment to the referring physician. Occasionally, the EDX consultant should contact the referring physician if the EMG findings reflect a grave disease or if planned surgery needs to proceed or be cancelled due to these findings.

Generating a concise and understandable EMG laboratory report is an important function of the electromyographer [2]. The EDX report should

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### Table 1
Suggested nerve conduction studies for common referrals to the EMG laboratory

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Nerve tested (s = sensory, m = motor)a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical radiculopathy</td>
<td>Median (s)</td>
</tr>
<tr>
<td></td>
<td>Ulnar (s)</td>
</tr>
<tr>
<td></td>
<td>Radial (s)</td>
</tr>
<tr>
<td></td>
<td>Median (m)</td>
</tr>
<tr>
<td></td>
<td>Ulnar (m)</td>
</tr>
<tr>
<td>Carpal tunnel syndrome</td>
<td>Nerves tested for cervical radiculopathy plus one or more of the internal hand comparison studies if indicatedb</td>
</tr>
<tr>
<td>Lumbosacral radiculopathy</td>
<td>Sural (s)</td>
</tr>
<tr>
<td></td>
<td>Peroneal (m)</td>
</tr>
<tr>
<td></td>
<td>Tibial (m)</td>
</tr>
<tr>
<td></td>
<td>Bilateral tibial H-reflexes</td>
</tr>
<tr>
<td>Ulnar neuropathy</td>
<td>Nerves tested for cervical radiculopathy plus Dorsal ulnar (s)</td>
</tr>
<tr>
<td></td>
<td>Ulnar (m) recording first dorsal interosseous</td>
</tr>
<tr>
<td>Peroneal neuropathy</td>
<td>Nerves tested for lumbosacral radiculopathy plus Superficial peroneal (s)</td>
</tr>
<tr>
<td>Peripheral Polyneuropathy</td>
<td>Nerves tested for cervical and lumbosacral radiculopathy</td>
</tr>
<tr>
<td>Motor neuron disease</td>
<td>Nerves tested for cervical and lumbosacral radiculopathy</td>
</tr>
<tr>
<td>Myopathy</td>
<td>Median (s)</td>
</tr>
<tr>
<td></td>
<td>Sural (s)</td>
</tr>
<tr>
<td></td>
<td>Tibial (m)</td>
</tr>
</tbody>
</table>

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a Nerves should be tested on the symptomatic side. Contralateral studies are recommended for comparison and in patients with bilateral symptoms.

b This may include the mixed median and ulnar plantar study, median and ulnar sensory recording ring finger, or median and ulnar motor recording 2nd lumbrical and 2nd interossei respectively.
be typed (not hand written) because it constitutes an integral part of the patient’s medical records. The report should contain all the pertinent data acquired during the study, despite that many referring physicians are only interested in the final conclusion. In addition to the demographic data

Table 2
Suggested needle EMG protocol for common referrals to the EMG laboratory

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Muscle examined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical radiculopathy or carpal tunnel syndrome</td>
<td>First dorsal interosseous</td>
</tr>
<tr>
<td></td>
<td>Abductor pollicis brevis(^a)</td>
</tr>
<tr>
<td></td>
<td>Flexor pollicis longus</td>
</tr>
<tr>
<td></td>
<td>Extensor indices proprius</td>
</tr>
<tr>
<td></td>
<td>Pronator teres</td>
</tr>
<tr>
<td></td>
<td>Biceps</td>
</tr>
<tr>
<td></td>
<td>Triceps</td>
</tr>
<tr>
<td></td>
<td>Deltoid</td>
</tr>
<tr>
<td></td>
<td>Mid and low cervical paraspinal muscles</td>
</tr>
<tr>
<td>Lumbosacral radiculopathy</td>
<td>Tibialis anterior</td>
</tr>
<tr>
<td></td>
<td>Medial gastrocnemius</td>
</tr>
<tr>
<td></td>
<td>Extensor hallucis</td>
</tr>
<tr>
<td></td>
<td>Flexor digitorum longus</td>
</tr>
<tr>
<td></td>
<td>Vastus lateralis</td>
</tr>
<tr>
<td></td>
<td>Gluteus medius</td>
</tr>
<tr>
<td></td>
<td>Mid and low lumbar paraspinals</td>
</tr>
<tr>
<td>Ulnar neuropathy</td>
<td>Muscles tested for cervical radiculopathy plus</td>
</tr>
<tr>
<td></td>
<td>Abductor digiti minimi</td>
</tr>
<tr>
<td></td>
<td>Flexor carpi ulnaris</td>
</tr>
<tr>
<td></td>
<td>Flexor digitorum profundus (ulnar part)</td>
</tr>
<tr>
<td>Peroneal neuropathy</td>
<td>Muscles tested for lumbosacral radiculopathy plus</td>
</tr>
<tr>
<td></td>
<td>Peroneus longus</td>
</tr>
<tr>
<td></td>
<td>Short head of biceps femoris</td>
</tr>
<tr>
<td>Peripheral Polyneuropathy</td>
<td>Muscles tested for lumbosacral radiculopathy plus</td>
</tr>
<tr>
<td></td>
<td>Abductor hallucis</td>
</tr>
<tr>
<td></td>
<td>Extensor digitorum brevis</td>
</tr>
<tr>
<td></td>
<td>First dorsal interosseous(^b)</td>
</tr>
<tr>
<td>Motor neuron disease</td>
<td>Muscles tested for cervical and lumbosacral radiculopathy</td>
</tr>
<tr>
<td></td>
<td>in three limbs plus thoracic paraspinals</td>
</tr>
<tr>
<td>Myopathy</td>
<td>Tibialis anterior</td>
</tr>
<tr>
<td></td>
<td>Medial Gastrocnemius</td>
</tr>
<tr>
<td></td>
<td>Vastus lateralis</td>
</tr>
<tr>
<td></td>
<td>Vastus medialis</td>
</tr>
<tr>
<td></td>
<td>Gluteus medius</td>
</tr>
<tr>
<td></td>
<td>Brachioradialis</td>
</tr>
<tr>
<td></td>
<td>Biceps</td>
</tr>
<tr>
<td></td>
<td>Triceps</td>
</tr>
<tr>
<td></td>
<td>Deltoid</td>
</tr>
<tr>
<td></td>
<td>Mid and low lumbar paraspinals</td>
</tr>
</tbody>
</table>

\(^a\) Suggested in carpal tunnel syndrome only since it is extremely painful to sample.

\(^b\) More proximal muscles should be tested if first dorsal interosseous is abnormal to establish a distal to proximal gradient.
(patient name, age, birth date, sex, hospital number, date of study, and referring physician), the EMG laboratory report should include the following:

1) **Reason for referral to the EMG laboratory.** This should include a brief and pertinent clinical summary, highlighting the limbs involved, the temporal course of the illness (with date of onset if applicable) and the complicating factors, which may influence the EDX findings. These factors include diabetes mellitus, local swelling, limb deformity, history of poliomyelitis, or previous lumbar or cervical spinal surgery. An example of a note outlining the reason for referral is the following: “Acute right foot drop noted after recent craniotomy on 03/03/2001. The patient has diabetes mellitus and remote history of lumbar laminectomy. Evaluate for peroneal neuropathy and lumbosacral radiculopathy.”

2) **Nerve conduction studies table.** This segment of the report should always be a part of the EMG laboratory report, and is particularly directed to physicians who are well versed with the EDX examination. Recording and revealing limb temperature is extremely useful, since many of the NCS parameters are greatly affected by cool limbs. Since F-wave and H-reflex latencies are length-dependent, the patient’s height should be highlighted in the report. The tabulated NCS form should be detailed but not overcrowded with unnecessary numbers. Nerves stimulated, stimulation sites and recording points are extremely important. Amplitudes (distal and proximal), latencies, conduction velocities, and F-wave latencies should be noted. Contralateral findings and normal laboratory values should also be shown, preferably on the same row within the NCS table (Fig. 3).

3) **Needle EMG table.** This should list all the muscles tested with their detailed findings (Fig. 4). Several columns should follow each muscle revealing the following: Insertional activity (increased, decreased, myotonic discharges, etc.), spontaneous activity (fibrillation potentials, fasciculation potentials, complex repetitive discharges, etc.), MUAP activation (normal, fair, or poor) and recruitment (normal, decreased, early), and MUAP morphology (amplitude, duration, percentage polyphasia). A separate column should be left for additional comments such as tremor, nascent MUAPs, mixed small and large MUAPs, etc. If an advanced EMG study is done (such as quantitative MUAP analysis, MUNE), the findings should be shown in a table or outlined in details in the summary of findings.

4) **Summary of the findings.** It is good practice to recap the pertinent aspects of the EDX study in one or two paragraphs. All the data obtained should be assessed and abnormalities relevant negatives highlighted. This summary set the stage for formulating meaningful impression.
## Electromyography Laboratory Report

**Name:** [Redacted]

**Hospital No.:** 2648849

**Sex:** Male

**Height:** 71 (in)

**Referring Physician:** [Redacted]

**Date:** 9/18/01

**Birth date:** 8/6/68

**Age:** 33

**Temp:** 33 (°C) Hand

**Temp:** 35 (°C) Foot

### Reason for Referral:

### Nerve Conduction Studies

<table>
<thead>
<tr>
<th>Nerve Stimulated</th>
<th>Stimulation Site</th>
<th>Recording Site</th>
<th>Amplitude Motor = mV; Sensory = μV</th>
<th>Distal/Peak Latency msec</th>
<th>Conduction Velocity m/sec</th>
<th>F-wave Latency msec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (S)</td>
<td>Wrist</td>
<td>Index</td>
<td>28</td>
<td>3.5  &gt;3.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (S)</td>
<td>Wrist</td>
<td>Middle</td>
<td>31</td>
<td>3.4  &gt;3.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulnar (S)</td>
<td>Wrist</td>
<td>Little</td>
<td>15</td>
<td>2.6  &gt;3.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radial (S)</td>
<td>Forearm</td>
<td>Snbox</td>
<td>32</td>
<td>2.1  &gt;2.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sural (S)</td>
<td>calf</td>
<td>Ankle</td>
<td>14</td>
<td>4.0  &gt;4.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (M)</td>
<td>Wrist</td>
<td>APB</td>
<td>9.6  &gt;6</td>
<td>3.5  &gt;3.9</td>
<td></td>
<td>27.9</td>
</tr>
<tr>
<td>Median (M)</td>
<td>Elbow</td>
<td>APB</td>
<td>8.4</td>
<td>8.5</td>
<td>55  &gt;50</td>
<td></td>
</tr>
<tr>
<td>Ulnar (M)</td>
<td>Wrist</td>
<td>ADM</td>
<td>9.6  &gt;7</td>
<td>1.8  &gt;3.1</td>
<td></td>
<td>28.8</td>
</tr>
<tr>
<td>Ulnar (M)</td>
<td>B. Elb</td>
<td>ADM</td>
<td>7.6</td>
<td>6.3</td>
<td>51  &gt;50</td>
<td></td>
</tr>
<tr>
<td>Ulnar (M)</td>
<td>Ab Erb</td>
<td>ADM</td>
<td>6.6</td>
<td>8.6</td>
<td>57  &gt;50</td>
<td></td>
</tr>
<tr>
<td>Peroneal (M)</td>
<td>Ankle</td>
<td>EDB</td>
<td>4.6  &gt;3</td>
<td>3.2  &gt;5.5</td>
<td></td>
<td>50.1</td>
</tr>
<tr>
<td>Peroneal (M)</td>
<td>Ab Knee</td>
<td>EDB</td>
<td>6.9</td>
<td>13.5</td>
<td>43  &gt;40</td>
<td></td>
</tr>
<tr>
<td>Tibial (M)</td>
<td>Ankle</td>
<td>AH</td>
<td>12.2  &gt;8</td>
<td>6.8  &gt;6.0</td>
<td></td>
<td>52.6</td>
</tr>
<tr>
<td>Tibial (M)</td>
<td>Knee</td>
<td>AH</td>
<td>10.4  &gt;10</td>
<td>14.2</td>
<td>56  &gt;40</td>
<td></td>
</tr>
<tr>
<td>Tibial (H - Reflex (M))</td>
<td>Knee</td>
<td>Soleus</td>
<td>5.1  13.8</td>
<td>6.6  8.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tibial (H - Reflex)</td>
<td>Knee</td>
<td>Soleus</td>
<td>7.4  6.7</td>
<td>33.9  31.1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(NR = No Response; Rt = right; Lt = Left; APB = Abductor Pollicis Brevis; ADM = Abductor Digiti Minimi; EDB = Extensor Digitorum Brevis; AH = Abductor Hallucis).
### Needle Examination

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Insertional Activity</th>
<th>Spontaneous Activity</th>
<th>Voluntary Motor Unit Potentials</th>
<th>Comment</th>
</tr>
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<td>Fascs</td>
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<tr>
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<td>SL Decr</td>
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<tr>
<td>AHB-Abd hall brev</td>
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<td>0</td>
<td>SL Decr</td>
</tr>
<tr>
<td>EDB-Ext dig brevis</td>
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<td>MK Decr</td>
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<tr>
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<td>0</td>
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<tr>
<td>MG-Medial Gastroc</td>
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<td>0</td>
<td>MO Decr</td>
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<tr>
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<tr>
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<td>0</td>
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<tr>
<td>VM-Vastus medialis</td>
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<td>MO Decr</td>
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<td>IL-iliacus</td>
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<td>AD-Thigh adductors</td>
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<td>T9 Paraspinal</td>
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<td>0</td>
<td>N/A</td>
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<tr>
<td>AHB-Abd hall brev</td>
<td>Normal</td>
<td>0</td>
<td>0</td>
<td>Normal</td>
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<tr>
<td>EDB-Ext dig brevis</td>
<td>!+2</td>
<td>0</td>
<td>0</td>
<td>MO Decr</td>
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<tr>
<td>TA-Tib Anterior</td>
<td>!+2</td>
<td>0</td>
<td>0</td>
<td>MO Decr</td>
</tr>
<tr>
<td>VL-Vastus lateralis</td>
<td>!+2</td>
<td>0</td>
<td>0</td>
<td>MO Decr</td>
</tr>
</tbody>
</table>

(CRD = Complex repetitive discharge; N-Myoton = Neuromyotonia; SL Decr = Slightly Decreased; MO Decr = Moderately Decreased; MK Decr = Markedly Decreased; +1, +2, +3 = slightly, moderately, markedly increased; -1, -2, -3 = slightly, moderately, markedly reduced; N+1 = borderline increased; N-1 = borderline reduced).

Fig. 4. A sample of the needle EMG form in the EMG laboratory report (This is usually followed by the summary and impression which are not shown).
(5) Impression (or conclusion). This is the most important component of the EMG laboratory report because it represents the final link between the EDX consultant and referring physician. The impression should be brief, yet clear, and disclose as much information as possible. The impression should reflect the extremity tested and the extent of the EDX test (extensive or limited) if the EMG examination deviates from the standard. If the EDX examination was limited or incomplete, such as due to poor patient tolerance, this should be explicitly explained in the impression. If the EDX study is normal, the impression should also state that there was no evidence of the specific disorder for which the patient was referred. If the EDX study detects a peripheral nervous system lesion, the site of pathology with its severity, chronicity, and pathophysiology, should be delineated if possible. The EDX examination often makes an anatomic or physiologic diagnosis, but not clinical syndromes. For example, the EDX study often can diagnose a median mononeuropathy at the wrist or ulnar mononeuropathy across the elbow, but not carpal tunnel syndrome or cubital tunnel syndrome, respectively. In these situations, the electromyographer may report that the findings are consistent with or compatible with the appropriate suspected clinical syndrome. At times, a brief list of differential diagnosis may be useful. For example, if myotonia is detected on needle EMG, a list of the common inherited myotonic disorders and the drug-induced myotonias may be useful to the referring physician. Rarely, the EDX examination may be diagnostic of a specific disorder such as Lambert-Eaton myasthenic syndrome. If a repeat EMG study is needed, the report’s impression should state the proposed time frame for such a study. In situations where multiple EDX findings are detected, they should preferably be listed relevant to their individual relation to the suspected diagnosis, followed by the likely incidental or asymptomatic findings.

Finally, the EDX consultant should be as objective as possible and should not fall into the habit of using the clinical information excessively to make a diagnosis not substantiated fully by the EDX findings. For example, the EDX of a patient with a remote elbow fracture and suspected tardy ulnar palsy may show an axon-loss ulnar mononeuropathy without focal slowing or conduction block but with denervation of the ulnar innervated muscles in the forearm. The electromyographer should report that the ulnar neuropathy is localized at or above the elbow and refrain from localizing the lesion to the elbow, in order to confirm the surgeon’s suspected clinical diagnosis. Apart from some prognostication in patients with nerve injuries, the EDX report should not include treatment or management recommendations. In situations where the electromyographer is the treating physician or is asked to provide a neuromuscular consultation, a detailed neurological history, examination, diagnosis, management, and prognosis should be included in a separate neurological consultation report.
References


Nerve conduction studies
Types, components, abnormalities, and value in localization
Asa J. Wilbourn, MD

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Nerve conduction studies (NCS) are one of the two major components of the electrodiagnostic (EDX) assessment, the other being the needle electrode examination (NEE). The third, and final, component consists of a variety of procedures, grouped under the umbrella title special studies, most of which are nerve stimulation procedures similar to the NCS. There are three types of NCS, motor, sensory, and mixed (Fig. 1). Because of differing technical aspects in their performance, these must be performed sequentially, rather than simultaneously, whenever the same mixed nerve is being assessed (ie, motor and sensory NCS cannot be done on a nerve trunk at the same time). Similar to the NEE and the various special studies, all three types of NCS assess only large, heavily myelinated nerve fibers [1–3].

Nerve conduction studies: basic types

Of the three types of NCS, only the motor NCS indirectly assess the peripheral nervous system (PNS) because their endpoint is not a motor nerve action potential, but rather a compound muscle action potential (CMAP). Thus, the motor axons are evaluated by stimulating them and then recording the response this elicits from the innervated muscle. The advantage of this arrangement is the magnification effect ie, activation of a single motor axon causes the near simultaneous initiation of impulses in many individual muscle fibers (up to several hundred), the number depending upon the innervation ratio of the recorded muscle. The resulting CMAP amplitudes are of sufficient magnitude to be measured in millivolts (mV) (Fig. 1). This is the principal reason why motor NCS became a diagnostic tool several years before the sensory NCS did; they require far less amplification and all the technical problems attendant to it. This recording method, however, also has an inherent disadvantage: the low amplitude, or unelicitable CMAPs may be due to other than...
Fig. 1. Three types of nerve conduction studies performed in the electrodiagnostic laboratory: (A) motor, (B) sensory, and (C) mixed (motor and sensory). (From Isley MR, Kranss GL, Levin KH, Litt B, Shields RW, Wilbourn AJ. Electromyography/Electroencephalography. Redford, Washington: SpaceLabs Medical; 1993; with permission.)
motor nerve dysfunction because the abnormalities may reside in the neuromuscular junctions, or in the muscle fibers themselves. Motor NCS are valuable diagnostic aids for several reasons. As early as 1961, Lambert listed nine reasons for motor NCS (many also would apply to sensory NCS), including:

1. Provide objective evidence of motor unit abnormalities in patients with suspected hysteria, malingering, or upper motor neuron lesions.
2. Identify and localize focal lesions along individual nerves.
3. Separate polyneuropathies from both myopathies and motor neuron disease.
4. Detect various disorders in neuromuscular transmission and distinguish them from one another.
5. Disclose evidence of subclinical PNS disorders, both focal (eg, CTS) and generalized (eg, Charcot-Marie Tooth disease, Type I).
6. Reveal some peripheral nerve anomalies, (eg, Martin-Gruber anastomosis) [4].

To these can be added that they help differentiate familial from acquired types of demyelinating polyneuropathy [5].

In contrast to motor NCS, sensory NCS directly assess sensory axons. Thus, their endpoint is a sensory nerve action potential (SNAP). The advantage of this recording setup is obvious: if technical factors can be discounted, a sensory NCS abnormality is indicative of a lesion involving either the sensory axons assessed, or their cell bodies in the dorsal root ganglia (DRG). There is a major disadvantage, however, due to the SNAP amplitudes being so small that they must be measured in microvolts (µV) (Fig. 1). Higher amplifications result in various physiologic and technical problems, which assume a prominent, and often disruptive, role in the procedure. These are responsible for most of the limitations of the sensory NCS. These include the fact that the SNAPs:

1. are affected more by physical considerations (eg, temperature) than their motor NCS counterparts.
2. are often low in amplitude or are unelicitable because of physiologic factors (age), technical reasons (limb edema), and/or coincidental cutaneous nerve injury (minor skin lacerations) [6].
3. do not evaluate the most distal segments of the sensory nerves or the sensory receptors, even though abnormalities may begin in, or be limited to, those regions [7].

Despite their limitations, sensory NCS have become an indispensable part of the EDX evaluation for three main reasons, First, they may be the only abnormal NCS, since some PNS lesions affect only sensory axons (eg, digital neuropathy; pure sensory polyneuropathy). Second, they generally are more sensitive than motor NCS to pathophysiologic processes involving mixed nerves; thus, SNAP latencies typically are affected at an earlier stage, and then more severely, than the CMAP latencies by demyelinating lesions causing focal slowing (eg, carpal tunnel syndrome [CTS]), and the SNAP
amplitudes usually are relatively more decreased than the corresponding CMAP amplitudes for any given degree of incomplete axon loss. Third, they are extremely helpful in localizing proximal axon loss lesions of at least moderate severity to either the root or plexus level, because they are unaffected by nerve fiber damage located within the intraspinal canal, proximal to the DRG (eg, myelopathies and radiculopathies), whereas they are low in amplitude or unelicitable with those located at or distal to the DRG (eg, plexopathies); thus, along with the presence of paraspinal fibrillation potentials, sensory NCS are crucial for differentiating intraspinal canal lesions from plexopathies in the EDX laboratory [3,6].

*Mixed NCS*, in which the motor and sensory components of mixed nerves are simultaneously assessed, are direct studies, similar to sensory NCS. Their endpoints, therefore, are summated mixed nerve action potentials (MNAPs), which are reported in microvolts (µVs). Because they represent concomitant activation of both sensory and motor axons, their amplitudes typically are higher than the SNAP amplitudes recorded along the same nerve segment. The classical mixed NCS assess conduction along nerve trunks, such as in the forearm or leg. Initially, they were used principally as indirect methods for evaluating sensory axons. However, the technical problems inherent to the recording method required to obtain them were soon apparent. Mixed NCS are performed by stimulating a mixed nerve distally while recording from it at a more proximal location. Concerning main nerve trunks, this means that the recording electrodes are situated near the elbows or knees (if not more proximal), body regions in which often considerable tissue is interposed between the nerve and the electrode, particularly with obese patients. Low amplitude or unelicitable MNAPs frequently are the result. Unfortunately, the stimulation and recording setup cannot be reversed, with the recording electrodes placed more distally, because proximal stimulation of the mixed nerve generates CMAPs in the distal muscles, which obliterate the relatively tiny MNAPs. Consequently, mixed NCS along nerve trunks were mostly abandoned after sensory NCS were introduced and rendered them redundant. They were subsequently used, however, for evaluating nerves in the more distal portions of the limbs (eg, hands and feet). One of these, palmar NCS, has proven to be highly sensitive for detecting CTS [2,3].

The type of recording electrodes used during the NCS is very important. Although needle electrodes, compared to surface ones, are superior under certain conditions, they have serious limitations in regard to providing useful, reproducible CMAP and SNAP amplitudes. Thus, during motor NCS, the recording range of the needle electrode is so limited that it essentially is assessing conduction along individual axons (ie, the one or few motor units whose muscle fibers are very near its recording surface), rather than along all of those that innervate the recorded muscle. During sensory NCS, the recording surface of the near nerve electrode cannot be placed at exactly the same distance from the nerve from one assessment to the next and yet, this distance is critical for amplitudes; consequently, the results are not reproducible. For these and
other reasons (eg, convenience and noninvasiveness) probably the majority of electrodiagnosticians prefer to use surface recording electrodes [2,6,8].

Technical aspects

In the first textbook devoted solely to NCS, published in 1982, K. Hammer observed that “The performance of nerve conduction studies is deceptively simple”, but accomplishing this so that the results obtained are reliable is something else again [9]. In fact, what superficially appears an easy task, is actually encumbered with a myriad of potential pitfalls—anatomic, technical, procedural, and interpretative in nature—that present a formidable barrier to the performance of accurate, reproducible, and therefore, clinically reliable NCS. Standardization of each NCS is vital. This must extend not only to various EMG machine factors (eg, amplification and filter settings), but also to physiologic factors (eg, limb temperature), certain patient characteristics (eg, age), and the procedures employed (eg, the interelectrode distances used). This standardized approach must be used to obtain reliable laboratory normal values, because very little is accomplished if a technically superb NCS is performed, but no dependable standards of normalcy are available to which the results can be compared. The major sources of error in the performance of NCS are shown in Box 1

<table>
<thead>
<tr>
<th>Box 1</th>
<th>Major sources of error in the performance of nerve conduction studies</th>
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<tbody>
<tr>
<td>Nerve anomalies</td>
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<td>Limb temperature variations</td>
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<td>Age of patient</td>
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<td>Instrumentation inaccuracies</td>
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<td>Technical problems:</td>
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<tr>
<td>Lack of standardization</td>
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<tr>
<td>Electrode placement mistakes</td>
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<tr>
<td>Variation in inter-electrode distances</td>
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<td>Stimulation inaccuracies:</td>
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<td>Submaximal stimulation</td>
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<td>Excess stimulation</td>
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<td>Cathode-anode reversal</td>
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<tr>
<td>Movement artifact</td>
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<td>Measurement mistakes:</td>
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<tr>
<td>Skin marking variations</td>
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<tr>
<td>Limb position changes</td>
<td></td>
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<tr>
<td>Errors in measuring</td>
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<tr>
<td>Calculation mistakes (for CV)</td>
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</table>

\[ CV = \text{Conduction velocity. (Adapted from Wilbourn [3]; with permission.)}\]
These are not discussed in detail because many comprehensive reviews of them are readily available [8,10–12]. It is pertinent to note, however, that each EDX laboratory must have its own normal values. With unilateral lesions, moreover, often the best source of comparison—frequently more sensitive than laboratory normal values—are the results obtained when the same NCS is performed on the contralateral, uninvolved limb. Such side-to-side comparisons are mandatory whenever an unfamiliar NCS is performed, for which no laboratory based normal values are available [2]. Characteristically, the same nerves (eg, median) in contralateral limbs yield NCS results that are very similar [2,3]. Concerning NCS amplitudes, many electrodiagnosticians independently over the years have concluded that a response which is 50% or less than that obtained in the corresponding limb is abnormal, regardless of how it compares to laboratory values. Although this is a very conservative number, computer simulation has validated its worth in regard to detecting conduction block [13].

Components assessed

Each time an NCS is performed, several different components that can be analyzed result. As Lambert noted many years ago, “Every aspect of the response may be useful in diagnosis.” [4]. To obtain maximal value from a NCS, all of its components must be scrutinized, with attention paid to the information each is conveying about the physiology of the nerve being assessed. These components, amplitude, duration, latency, conduction velocity (CV), and area, will now be reviewed.

Amplitude

This is the height of the evoked response, expressed in mVs or μVs; it is measured from baseline to negative peak for CMAPs and for some SNAPs, and from negative to positive peak for the other SNAPs (Fig. 2). Whenever surface recording electrodes are used, amplitudes are semi-quantitative measures of the number of axons conducting impulses from the stimulating to the recording points. They also are a function of several other factors eg, the relative conduction rates along the axons, the distance between the recording electrodes and the fibers (nerve or muscle) generating the impulses. The CMAP amplitudes, in addition, are indicative of the efficiency of neuromuscular transmission, and the number of muscle fibers composing the recorded muscle that can generate action potentials [1–3]. Of the various NCS components, the amplitudes undoubtedly are the most neglected; in many EDX laboratories, even currently, they are neither recorded nor reported. Such an attitude is inexplicable, considering that, overall, they are the single most important component of the NCS: when all the different types of neuromuscular disorders are considered collectively, amplitudes are by far the most informative. Moreover, regarding neurogenic lesions, amplitudes are the only components that have a direct relationship to clinical
symptoms (ie, muscle weakness and sensory deficits affecting large fiber modalities). Finally, they are indispensable components; if a response is unelicitable (ie, has zero amplitude), then none of the other measurements can be performed [3].

**Duration**

This is the time interval during which the evoked response occurs, expressed in milliseconds (ms) (Fig. 2). For CMAPs the duration typically is that period extending from the beginning to the end of the initial negative phase. The durations of the CMAPs and SNAPs mainly reflect the relative conduction rates of the impulses as they travel along the various axons between the stimulating and recording points. Duration and amplitude are closely related: as the duration becomes more prolonged (ie, the response becomes dispersed), the amplitude decreases. The durations of the evoked responses seldom are formally measured and recorded currently, as they were formerly in many EDX laboratories. Nonetheless, determining whether responses are dispersed or not, particularly when they are of low amplitude, remains an important task. This is because low amplitude responses can result from different pathophysiologic processes. As will be discussed below, those that are of normal latency are indicative of conduction failure or conduction block, whereas those that are prolonged in latency denote differential slowing [1–3].
Latency

Latency is a time measurement, expressed in ms. Thus distal latency is the time interval between the moment of nerve stimulation at the distal stimulation point and the onset of the resulting CMAP or SNAP (Fig. 2). Customarily, motor nerves, whenever possible, are stimulated at two points along their course. The latency obtained on distal stimulation is one of the reported components of the NCS, whereas the latency obtained on proximal stimulation (proximal latency) is used to calculate a CV along the nerve segment between the two stimulation points. The motor latencies reflect the time required not only for passage of impulses along motor nerves, but also for neuromuscular transmission, and for the initiation of muscle action potentials. In contrast, the sensory latencies reflect exclusively the time required for nerve impulses to travel between the stimulating points and the recording sites. These can be measured from the instant of nerve stimulation to either the onset of the SNAP (onset or distal latency) or to its peak (peak latency). Conversely, for motor nerves, all measurements are to the onset of the CMAP (ie, on distal stimulation a motor distal latency is recorded). A latency recorded by assessing a particular nerve in a given limb can be directly compared to that recorded while assessing the same nerve in another limb, if both are obtained using standard, fixed distances between the stimulating and recording points. It is noteworthy that latencies provide no information regarding the number of nerve fibers conducting impulses, beyond the fact that at least a few of them must be doing so for latencies to be determined [2,3].

Conduction velocity

Similar to latency, this is a measure of the speed of impulse conduction. Most often, Conduction Velocity (CV)s are obtained by stimulating the nerve at two points along its course, subtracting the distal latency from the proximal latency, and then dividing that difference into the distance (as determined by surface measurements) between the two stimulating points. Thus, with CVs, the rate of conduction is expressed as the distance traveled per unit of time, in M/S (Fig. 3). Determining the speed of transmission of action potentials in this manner allows direct comparison of the rapidity of impulse propagation along different nerves, regardless of the lengths of the nerve segments assessed. Motor and sensory CVs, like latencies, are merely rate measurements. Thus, they reveal nothing about the number of axons conducting impulses, except that at least a few must be doing so for them to be calculated. Of all the various NCS components, the CVs undoubtedly are the most over-rated. Although they are the NCS component least likely to be abnormal with the great majority of neuromuscular disorders, they have received by far the most attention over the years, to the extreme that some physicians refer to NCS as nerve conduction velocities. They thereby imply that what actually is the most insignificant portion of the NCS in most instances (as far as providing positive information) is the only important component [3].
This is a function of both the amplitude and duration of the evoked response; it is measured in mVms (motor) or µVms (sensory) (Fig. 2). Compared to amplitude, it more accurately reflects the number of axons being activated. Nonetheless, it requires more technically sophisticated equipment and it can be compromised, just as the amplitude can be, by such factors as interphase cancellation. Although area will not be discussed further, alterations in area can be presumed to be present whenever there are significant changes in amplitude without concomitant changes in duration [3,11].

**Nerve conduction studies: standard and nonstandard**

More nerves can be assessed by NEE than by NCS. Nonetheless, a fairly large number of NCS can be performed, especially because they can be done on different axons composing the same nerve, as well as on different segments of the same mixed nerve. Some NCS are performed so regularly in most EDX laboratories that they are referred to as standard, or basic. These are listed in Table 1. Although in most instances they provide an adequate general survey of a limb, they are not sufficient in many specific situations; hence, other, less common, so-called nonstandard NCS must be available to be performed whenever clinical circumstances dictate. Many of these are listed in Table 2. In certain instances, the most important information obtained during the entire EDX examination is provided by such supplementary NCS [2,3,12,14].
A great variety of mechanisms—compression, traction, laceration, thermal, chemical, etc.—can injure the axons that comprise the PNS. However, the different pathologic reactions of these axons to such focal injuries is quite limited, as are their pathophysiologic responses. Regarding large myelinated nerve fibers, most focal injuries causing symptoms that persist more than a few hours are manifestations of axon loss (also known as axon degeneration), demyelination, or a combination of both. The most defining difference between an axon loss and a focal demyelinating lesion is that focal demyelination remains strictly localized to the segment of nerve initially injured. Thus, the axon does not die at the lesion site nor degenerate distally from that point, and all the supporting structures of the nerve, including the myelin, remain intact along the distal length of nerve. With axon loss, in contrast, regardless of how minute the nerve segment initially damaged, the

### Table 1

<table>
<thead>
<tr>
<th>Upper limb</th>
<th>Lower limb</th>
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<tbody>
<tr>
<td>Sensory</td>
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<tr>
<td>Median (D2 or D3)</td>
<td>Sural</td>
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<tr>
<td>Ulnar (D5)</td>
<td></td>
</tr>
<tr>
<td>Motor</td>
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<td>Median (thenar)</td>
<td>Peroneal (EDB)</td>
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<tr>
<td>Ulnar (hypothenar)</td>
<td>Tibial (AH)</td>
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</table>

( ) = Stimulating or recording sites; D2 = index finger; D3 = middle finger; D5 = little finger; EDB = extensor digitorum brevis; AH = abductor hallucis.

### Focal nerve lesion pathophysiology: NCS recognition

A great variety of mechanisms—compression, traction, laceration, thermal, chemical, etc.—can injure the axons that comprise the PNS. However, the different pathologic reactions of these axons to such focal injuries is quite limited, as are their pathophysiologic responses. Regarding large myelinated nerve fibers, most focal injuries causing symptoms that persist more than a few hours are manifestations of axon loss (also known as axon degeneration), demyelination, or a combination of both. The most defining difference between an axon loss and a focal demyelinating lesion is that focal demyelination remains strictly localized to the segment of nerve initially injured. Thus, the axon does not die at the lesion site nor degenerate distally from that point, and all the supporting structures of the nerve, including the myelin, remain intact along the distal length of nerve. With axon loss, in contrast, regardless of how minute the nerve segment initially damaged, the

### Table 2

<table>
<thead>
<tr>
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<th>Lower limb</th>
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<tbody>
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<td>Sensory</td>
<td></td>
</tr>
<tr>
<td>Median (D1)</td>
<td>Super. peroneal sensory</td>
</tr>
<tr>
<td>Dorsum radial (thumb base)</td>
<td>Saphenous</td>
</tr>
<tr>
<td>Lat. antebrach. cutaneous</td>
<td>Lat. femoral cutaneous</td>
</tr>
<tr>
<td>Med. antebrach. cutaneous</td>
<td>Post. femoral cutaneous</td>
</tr>
<tr>
<td>Post. antebrach. cutaneous</td>
<td></td>
</tr>
<tr>
<td>Motor</td>
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<tr>
<td>Ulnar (FDI)</td>
<td>Peroneal (tibialis anterior)</td>
</tr>
<tr>
<td>Median (pronator quad.)</td>
<td>Tibial (gastrocnemius)</td>
</tr>
<tr>
<td>Radial (brachioradialis; EIP/EPB)</td>
<td>Femoral (quadriceps)</td>
</tr>
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<td>Musculocutaneous (biceps)</td>
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<tr>
<td>Axillary (deltoid)</td>
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</tbody>
</table>

( ) = Stimulating or recording sites; D1 = thumb; lat. = lateral; med = medial; post. = posterior; antebrach = antebrachial; FDI = first dorsal interosseous; EIP = extensor indicis proprius; EPB = extensor pollicis brevis.
adverse effects always are more extensive, including not only the entire length of nerve distal to the lesion site, but also the structures (sensory receptors; neuromuscular junctions and muscle fibers) to which the degenerated axons are linked [1–3]. A total of four distinct pathophysiologic patterns, and combinations thereof, can be produced by these two pathologic processes. These and their clinical correlations will now be reviewed. Note that the various components of the evoked responses are altered by these patterns as follows: amplitude, three of the four; duration, one of the four (along with amplitude, if severe); distal or peak latency, one; and CV, one [3].

Conduction failure pattern

With this NCS presentation, all the amplitudes are affected and in a characteristic manner: at all stimulation points, the evoked responses are either unelicitable or uniformly low in amplitude, but not dispersed (Fig. 4) When all categories of PNS lesions are considered, this is by far the most common type of NCS presentation encountered, because it is the pattern seen with all axon loss lesions of more than 7–10 days duration. Although termed conduction failure pattern, the title is not completely accurate because unelicitable, or uniformly low amplitude, responses at all stimulation sites can be seen with demyelinating lesions that are causing conduction block and which are situated distally along the nerve, between the most distal stimulating point and the recording site (discussed below). In contrast, whenever the conduction failure pattern is due to axon loss, a far more common situation, the responsible lesion may be located anywhere along the axon (ie, proximal, at, or distal to any stimulation point). Uniformly unelicitable or low amplitude CMAPs and SNAPs can be caused by axon loss injuries that are affecting the nerve fibers at any point, from either the anterior horn cells (AHCs) or the DRG cells distally. Because of this, although this pattern detects all but mild axon loss lesions, it does not localize them. Whenever the conduction failure is incomplete, and low amplitude responses can still be evoked, rate measurements (ie, latencies; CVs) can be ascertained. These are not materially affected, however, even when measured across the lesion site, because the speed of impulse propagation is being determined along the surviving axons, which are conducting at their normal rates. The latter point is quite important, because there is a widely held misconception that all focal nerve lesions can be localized well by NCS because all cause focal slowing. Unfortunately, this is a very inaccurate and misleading concept. Regrettably, there is no biologic law that requires all incomplete axon loss lesions to produce focal slowing along the surviving fibers at the lesion site, even though such would be a godsend for electrodiagnosticians. In fact, pure axon loss lesions cannot be localized by a single NCS, once conduction fails along the distal stump, at 7–10 days after injury [2,3]. The NCS amplitude reductions observed with the conduction failure pattern correlate well with clinical symptoms, specifically, weakness and loss of all sensory modalities.
Thus, if the recorded CMAPs are quite low in amplitude, the recorded muscle generally is very weak on clinical testing [3,15].

Conduction block pattern

With this NCS presentation, there is a substantial decrease in the amplitude of the evoked response on proximal, compared to distal, stimulation, that is not due to dispersion, nerve anomalies, or technical factors. This pattern results when some, or all, of the nerve impulses cannot traverse the lesion site, resulting, respectively, in a partial, or total, conduction block. A pertinent point is that with a partial conduction block, impulse transmis-

![Diagram](image-url)
sion is stopped at the lesion site along some of the axons, but not others. (Figs. 4 and 5) Unlike the conduction failure pattern, which produces diffuse abnormalities along the nerve distal to the lesion, the conduction block pattern causes a very focal conduction change, restricted to the site of injury. Hence, if the nerve is stimulated only distal to it, while recording still more distally, no abnormalities are seen. For a conduction block to be detected the nerve must be stimulated proximal to it; for it to be localized well, it must be bracketed by two stimulation points. Most conduction blocks seen in the EDX laboratory are due to either axon loss or focal demyelination, mainly the latter. This pattern is seen with axon loss lesions only when NCS are performed within the first week or so following a nerve injury, at a time when all, or at least some, of the nerve fibers comprising the distal stump are still capable of transmitting impulses. Thus, conduction blocks due to axon loss are transitory in nature, being replaced within 7–10 days by the conduction failure pattern [2,3] (Figs. 4 and 6). The time to conduction

Fig. 5. The nerve conduction pattern seen when focal demyelination causes conduction block along some or all of the motor axons of a nerve is shown. Lesion location along ulnar nerve at the elbow marked with an asterisk.
failure along the distal stump axons varies somewhat for motor and sensory fibers, not because of intrinsic differences in their conduction properties but, rather, because of the different methodologies used to assess them. Axon degeneration is most advanced along the most distal segment of the nerve; as a result, nerve terminals degenerate before the preterminal portions of the axons. Because motor, but not sensory, NCS require nerve impulses to traverse these most distal portions, CMAPs become unelicitable several days before SNAPs do so [16]. For motor fibers, the CMAPs on distal stimulation remain normal for the first 2–3 days postinjury, then fall rapidly, reaching approximately 15% of their normal amplitude by day 5 and their nadir (ie, zero for complete lesions), by day 7. For sensory fibers, the SNAP amplitudes begin to drop by day 5 after injury, and reach their nadir by days 10–11 [2,3]. Thus, a conduction block pattern is never seen with a pure axon loss lesion studied more than 9–10 days after onset (Fig. 6). This type of conduction block has had a number of names bestowed upon it (several by this author alone), including axonal, axon noncontinuity, early axon loss, and axon discontinuity conduction block [2,3,14,17]. The last designation will be used subsequently.

Even though an axon discontinuity conduction block is indistinguishable in its NCS appearance in every respect from that resulting from focal
demyelination, many investigators have displayed a curious reluctance to concede that it merits the name conduction block. Thus, it has been referred to, in various publications, as *pseudo* and *apparent* conduction block. It also has been described as *mimicking* a conduction block [10,12,18–20]. In one textbook, it is always bracketed by quotation marks, and is referred to as a *conduction block-like* pattern [12]. The two major causes for various investigators to deny the obvious (ie, that this is undoubtedly a conduction block) appear to be that many of them: (1) consider the term should be restricted to those instances in which the pattern results from focal demyelination; (2) are disturbed by the fact that conduction is not being determined along intact axons [21–25]. However, both of these arguments appear highly arbitrary. Granted that in most instances focal demyelination is the pathology underlying the conduction blocks detected in the EDX laboratory, nonetheless, equating virtually all conduction blocks to demyelination is unwarranted, since there are several causes for conduction block that have nothing to do with focal demyelination. (Box 2) [11,22]. Similarly, the status of the axons along which a conduction block is detected is irrelevant, because conduction block, similar to conduction slowing, is defined by its NCS presentation, not its cause, (ie, it is merely a generic label for a specific neurophysiologic presentation, the underlying basis of which is quite variable).

An axon-discontinuity conduction block is seen with every axon loss lesion assessed with motor NCS during the first 5 days or so after onset. For this reason, electrodiagnosticians are generally discouraged from performing NCS during this *hyperacute* [12] phase of nerve injury, unless the major limitation of doing so is clearly understood: even though the lesion can be localized, its underlying pathophysiology cannot be determined. Thus,

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**Box 2**

**Causes of conduction block**

- Focal demyelination
- Conduction block
- Conduction slowing (frequency-dependent)
- Early axon loss (<6 days duration)
  - (“axon-discontinuity conduction block”)
- Local anesthetics
- Cold
- Ischemia
- Electroporation
  - (due to electrical injury)

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Depending on the circumstances, any one cause could be responsible for conduction block seen on NCS in the EDX laboratory.

*See Refs. [11,19,23,25,26].*
the conduction block pattern at this very early stage does not have the same optimistic connotation it does when lesions are studied later in their course, because it may be due to axon-discontinuity, rather than to demyelination. (If caused by the former, however, localization will be far more exact than it will be after the conduction failure pattern supervenes) [3,23].

Demyelinating conduction blocks usually are found with abrupt onset PNS processes (eg, traumatic injuries resulting from moderate compression or traction; acute inflammatory demyelinating polyradiculoneuropathies (AIDP) (ie, most cases of Guillain Barré syndrome). Clinically, the conduction block pattern due to axon discontinuity, when substantial, causes clinical weakness and loss of all sensory modalities identical to that seen later, after it transmutes into the conduction failure pattern. Thus, it is impossible to determine clinically when one pattern becomes the other. The demyelinating conduction block pattern manifests clinical changes (weakness, sensory loss) indistinguishable from the two patterns that result from axon loss, except that the sensory deficits are restricted to large fiber modalities (position, vibration, and light touch) [3,15].

Conduction block has some confusing aspects. The term block often is used as a synonym for nerve lesion or injury, especially, curiously enough, one causing focal slowing. The literature is replete with this muddled terminology. If peripheral nerve fibers can be stimulated only proximal to the lesion site (ie, not distal to it), then the conduction block pattern mimics a conduction failure pattern of equally low amplitude or unelicitable responses, regardless of the site of stimulation. With such distal lesions, differentiating those due solely to severe axon loss from those due to mild axon loss with substantial coexisting demyelinating conduction block cannot be done in the EDX laboratory. This frustrating situation often is encountered when nerves to proximal muscles such as deltoids or quadriceps are injured. It can be a potent source for EDX prognostic error if it is not considered whenever lesions of recent onset (<6 weeks duration) are studied. Finally, not all demyelinating conduction blocks are benign in nature. Although most result from either trauma or AIDP, and resolve within a few weeks of onset, not all do so. Rather, some persist for months, while still others last indefinitely, and usually ultimately convert to axon loss [2,3,26].

Various types of demyelinating conduction block, classified by duration:
Rapid resolution (within 4–6 weeks)
- Acute trauma, single episode (clinically labeled “neurapraxia”)
- Guillain Barré syndrome (ie, AIDP)
Prolonged (6–12 months)
- Acute trauma, recurrent episodes (ie, repeated renewal of conduction block (CB))a

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a Seen mostly with ulnar and peroneal nemopathies, in chronic “elbow leaners” and “leg-crossers.”
Differential slowing (desynchronized slowing) pattern

This presentation is manifested as dispersed evoked responses (CMAPs or SNAPs of increased duration) on all stimulations proximal to the lesion, with nondispersed responses on stimulations distal to it (Fig. 7). When substantial, the responses are low in amplitude as well. The differential slowing pattern is due to the speed of impulse transmission being reduced along a variable number of the average conducting or slower conducting axons at the lesion site. By definition, however, at least some of the fastest conducting axons are not affected. Hence, although the evoked responses elicited on all stimulations proximal to the lesion are dispersed, and often of low amplitude, the rate of conduction (the latencies or CVs) through the lesion is not reduced. For the differential slowing pattern to be detected, nerve impulses must traverse the lesion site. Moreover, if the nerve can be stimulated immediately proximal and distal to the lesion, then very precise localization is possible. If the responsible focal nerve damage is distal to the most distal stimulating point, then all responses are equally dispersed.

Fig. 7. Nerve conduction pattern when focal demyelination causes differential slowing along a nerve. Lesion location along the ulnar nerve at the elbow marked with an asterisk.
Of various NCS patterns, the differential slowing presentation probably is the least encountered with localized nerve injury; in contrast, it is seen with some frequency when chronic demyelinating polyneuropathies, familial or acquired, are assessed. Although the underlying pathophysiology typically is focal demyelination, occasionally it is axon regeneration following remote, very severe, axon loss injury. Whenever differential slowing affects motor fibers, the dispersed, low amplitude CMAPs that result have few clinical correlations; specifically, they are not associated with weakness, because all the motor axons are conducting through the lesion site, although their relative rates of conduction are quite dissimilar. Whenever it affects sensory fibers, however, certain formal neurological testing procedures (vibration sense and deep tendon reflexes) are compromised because they require nerve impulses to travel along the axons in compact volleys [3,15].

**Focal slowing (synchronized slowing) pattern**

With this NCS presentation, the rate of conduction along all the large myelinated fibers is slowed, and to essentially the same degree (Fig. 8). The slowing is manifested as either prolonged distal or peaked latencies, or slowed CVs, depending upon whether the lesion lies between the distal stimulating point and the recording site, or between two stimulating points. Because focal slowing does not affect configuration (the amplitude or duration) of the evoked response, it is only detected when conduction rate is determined through the locus of injury. A relatively unappreciated point concerning focal slowing is that for it to be present, virtually all the large myelinated fibers, which are capable of conducting impulses, must be involved at the lesion site, and to essentially the same degree. Otherwise, if some axons conduct normally through the damaged area, then their rates of conduction determine the latencies and CVs, and the pattern becomes one of differential slowing, rather than focal slowing. Focal conduction slowing essentially is an electrophysiologic phenomenon, which usually lacks a clinical counterpart. Thus, it does not cause clinical weakness, because all the impulses are traversing the lesion site, albeit at a slower than normal rate [3]. Moreover, whenever it affects a short segment of nerve, it also does not alter any portion of the formal neurological examination, because the relative conduction rates of the individual axons are unaltered [3,15]. However, when it involves long nerve segments, such as with generalized demyelinating polyneuropathies, it causes such a marked increase in the normal temporal dispersion that it manifests as differential slowing on motor NCS (E. Stalberg, personal communication) and compromises vibration and deep tendon reflex testing. Conceivably, a localized focus of demyelination could convert from conduction slowing to conduction block because of exaggerated hyperpolarization. Little is known about these so-called frequency-dependent conduction blocks in regard to their clinical manifestations, if any. Nonetheless, in a recently published textbook (2001), they are reported to cause “fatigue after mild but
The focal slowing pattern can be seen when NCS are performed on regenerated nerves following remote, severe axon loss; under these circumstances, it usually coexists with the differential slowing pattern. Far more often, however, it is due to demyelination. Although it is the characteristic pattern of few PNS disorders—most CTS, some ulnar neuropathy (UN) at the elbow segment (ES), and some (mostly chronic) demyelinating polyneuropathies—and polyradiculopathies, it is probably the pattern sought by the majority of electrodiagnosticians when they perform NCS. Unfortunately, it is the only pattern sought by some electrodiagnosticians. This is because the incidence of CTS, and, to a lesser degree, UN-ES, is so high, compared to that of all other focal PNS disorders [3].

Fig. 8. The nerve conduction patterns seen when focal demyelination causes uniform synchronized slowing along (a) the ulnar motor axons at the wrist, producing a prolonged distal latency and (b) at the elbow, producing a slowed conduction velocity, are shown. Lesion locations marked with asterisks. Note: The prolonged distal latency demonstrated here at (a) is solely for illustration purposes; in fact, prolonged motor distal latencies rarely are seen with ulnar neuropathies at the wrist, because most lesions at this location cause conduction failure or conduction block, not conduction slowing.
Combined patterns

With several kinds of PNS lesions, only one type of NCS pattern is characteristic (e.g., focal slowing with mild-to-moderate CTS and conduction failure with acute severe trauma). However, two, or even more, NCS patterns may coexist (e.g., conduction block and conduction failure with common peroneal neuropathies at the fibular head (CPN-FH)). Of all focal nerve lesions, UN-ES notoriously demonstrates the greatest variety of patterns, sometimes several simultaneously. This occurs among approximately 40% of such lesions, which are neither solely conduction failure, nor solely focal conduction slowing (Fig. 9). In these instances, usually the different patterns present can be discerned, by first assessing the amplitude obtained on stimulating distal to the lesion, to determine the presence of axon loss (assuming the lesion is of greater than 10 days duration) and then assessing the proximal responses (and CV) to detect the pattern resulting from focal demyelination. Distinguishing demyelinating conduction block from demyelinating differential slowing has been the topic of much debate in the literature, probably too much, considering that the same pathological process, demyelination, underlies both and the central question usually is whether demyelination is present. If such differentiation is considered essential and the CMAP amplitudes are substantially low, the distinction is made by assessing the strength of the recorded muscle; if it is normal, differential slowing is the cause, whereas if it is impaired, conduction block is responsible.

Fig. 9. The nerve conduction pattern seen when multiple types of pathophysiology affect a nerve. Lesion location along the ulnar nerve at the elbow is marked with an asterisk.
Nerve conduction study interpretation: an approach

Each NCS contains a great deal of useful information about the very limited portion of the neuromuscular system that has been assessed. Unfortunately, much of this often is lost because the NCS results are not examined in a systematic fashion. It is probable most experienced electrodiagnosticians evaluate a NCS by progressing through an orderly sequence of steps (probably unconsciously), reaching tentative conclusions at each consecutive point. However, the exact reasoning process used in such analysis apparently has not been described in detail. One such approach, easily learned, is now provided, which can be employed whenever a NCS is evaluated.

First, assess the distal amplitude. If it is normal and the NCS is a motor NCS, then no substantial axon loss has occurred along the motor nerve fibers innervating the recorded muscle, from the AHCs distally, if the injury is of more than 3–4 days duration. (This would not necessarily be accurate if the lesion were of just 1 or 2 days duration, because an axon-discontinuity conduction block could be present proximal to the stimulating point.) Although some axon loss may have occurred that is too minimal to be detected by the CMAP, if it is present, it will be revealed on the subsequent NEE of the recorded muscle. Also, there is no evidence of (1) a disorder causing demyelinating conduction block or significant differential slowing between the stimulating and recording points; (2) a defect in neuromuscular transmission; or (3) a significant abnormality of the muscle fibers composing the recorded muscle. If the NCS is a sensory NCS, and the lesion is of more than 6–7 days duration, then the normal amplitude indicates that substantial axon loss has not occurred along the sensory fibers being assessed, from their DRG of origin distal to the stimulating or recording points (whichever is more distal). Moreover, nothing suggests that a demyelinating conduction block or differential slowing lesion is situated between the stimulating and recording sites.

Second, check the distal response duration. If it is normal, then there is nothing indicative of even minimal amounts of differential slowing occurring between the distal stimulation point and the recording site, due to either focal demyelination or to axon regeneration following remote, severe, denervation. (Note that substantial differential slowing would have been detected earlier, when the distal amplitude was assessed, because it would have produced a low amplitude response).

Third, consider the distal or peak latency. If it is normal, then there is no evidence of either a demyelinating lesion causing focal slowing between the distal stimulating point and the recording site, or a remote, severe axon loss injury with subsequent nerve regeneration.

Fourth, if two-point stimulation was performed, now shift attention to the proximal response, and the CV that was calculated using it, and perform the same reasoning sequence again. However, the entire purpose of assessing the proximal evoked response (and the CV) is to detect focal demyelinating
abnormalities situated between the proximal and distal stimulation points, because the possibility of substantial axon loss having occurred along the nerve has already been eliminated by the normal distal amplitudes (assuming the lesion is of >5–8 days duration).

Considering each NCS with an approach such as this will ensure that little useful information is overlooked [3].

**Localizing focal nerve injuries by nerve conduction studies**

*Focal demyelinating lesions*

Those demyelinating injuries causing solely conduction slowing, either focal or differential in nature, must be localized exclusively by NCS, and this occurs only if the recording site and at least one of the stimulation points bracket the lesion. This is because neither focal slowing nor differential slowing has any effect on the NEE. Thus, just direct NCS localization of demyelinating conduction slowing is possible. In contrast, demyelinating conduction block can be localized directly by NCS, and indirectly by using a combination of NCS and NEE. Directly, if the recording site and at least one of the stimulating points bracket the focal lesion; indirectly (for motor fibers) if the CMAP amplitude recorded from a weak muscle is disproportionately preserved, compared to the reduced motor unit action potential (MUAP) recruitment seen on NEE of the same muscle (as well as the degree of weakness it manifests on clinical examination). Under these circumstances, the conduction block must be situated along the nerve at a location proximal to the most proximal stimulating point [2,3].

*Axon loss lesions*

These injuries are on a continuum of severity, ranging from mild to total, and it is the severity of a given one that principally determines how satisfactory localization will be and what portion of the EDX examination will be of benefit in this endeavor. Concerning mixed and solely motor nerves, mild axon loss injuries cause only fibrillation potentials, evident on NEE; they do not affect any component of the NCS. More substantial axon loss along mixed nerves reduces the SNAP amplitudes, as well as causing fibrillation potentials. Even more severe axon loss also produces decreased CMAP amplitudes on NCS and reduced MUAP recruitment on NEE [2]. Axon loss injuries assessed very early in their course, while an axon-discontinuity conduction block is still present, can be localized both directly and indirectly, similar to demyelinating conduction blocks. Once the distal stump fibers have degenerated, however, single motor and sensory NCS serve principally to detect axon loss lesions, not to localize them. In this regard, the CMAP amplitudes are a rather reliable indicator of the amount of axon loss the recorded muscle has undergone (if amplitude is 50% of normal, then
approximately 50% of the motor axons innervating the recorded muscle have degenerated). However, if substantial muscle reinnervation occurs via collateral sprouting, thereby considerably altering the innervation ratio of the recorded muscle, then the CMAP amplitudes are less trustworthy than certain NEE findings, specifically, the severity of reduced MUAP recruitment, linked to the amount of chronic neurogenic MUAP change. The SNAP amplitudes characteristically overestimate the amount of axon loss that has occurred, often becoming unelicitable with mixed nerve injuries even though the CMAP amplitudes and NEE findings suggest that only approximately 60–75% of nerve the fibers have degenerated [2,3].

**Localization by electrodiagnostic examination**

Determining the site of focal PNS damage has been one of the main functions of the EDX examination since its two major components first came into clinical use. How successful it is depends on a number of factors concerning the lesion, including (1) its location; (2) the type of axons (motor, sensory, or mixed) injured; (3) its underlying pathophysiology; (4) its severity; and (5) its duration, if it is axon loss in type and static in nature.

Based upon the length of the section of nerve determined by the EDX examination to contain the focal lesion, four types of localization are possible in the EDX laboratory: (1) point, (2) segment, (3) nerve fiber, and (4) pathway (Fig. 10). In general, point or segment localization is necessary for the procedure to have clinical utility; positioning the lesion by nerve fiber or pathway localization implicates such extensive portions of the involved nerve that these are of little value in identifying the site of focal PNS damage.

**Point localization**

This is the most accurate type of lesion positioning possible. The injury is shown to involve a circumscribed portion of the length of the nerve. Precise localization of this nature can be obtained only with NCS, and specifically with lesions that (a) affect only a very restricted section of the nerve (those due to compression, as opposed to traction); (b) are causing focal conduction abnormalities (conduction block or conduction slowing); and (c) are situated along the injured nerve fibers at sites where stimulations can be applied immediately proximal and distal to them. Examples of point localization are the demonstration, on motor NCS, of conduction blocks with radial neuropathies at the spiral groove, UN-ES, and CPN-FH through progressive stimulation—using inching techniques or the more formal short segment studies—along the nerve immediately proximal to, at, and distal to the lesion site [8,17]. Other examples are the detection of conduction slowing with chronic median neuropathy at the wrist (CTS), and UN-ES, by demonstrating an abrupt change in latency at the lesion site, using the same stimulation techniques described above [8,11]. Although point localization precisely
Fig. 10. Four types of localization possible with focal nerve lesions: (1) point, (2) segment, (3) nerve fiber, and (4) pathway. While the entire motor axon is assessed with motor nerve conduction studies and needle electrode examination, the complete sensory axon is not assessed during sensory NCS (Panel 3). Instead, the most peripheral portion is not included in the assessment because the latter ends at the cathode or the active recording electrode, whichever is most distally situated along the nerve.
fixes the injury along the nerve and is, therefore, the ideal type of localization, often it is not achieved, simply because of the time expenditure required to do so. Thus, although it is possible to pinpoint the exact site of the conduction block on every patient who manifests such with a CPN-FH, in most instances the nerve stimulations are limited to just two points, popliteal fossa and below fibular head. Typically, more accurate localization is not considered necessary for clinical purposes because, assuming the duration of symptoms is more than 7 days, the pathophysiology and the severity of the damage have been established, and the section of the nerve along which the lesion resides (that portion between the two stimulation points) has been identified [17].

**Segment localization**

Segment localization is by far the most common localization realized in the EDX laboratory. Whether it is satisfactory or not in the individual case depends upon the linear extent of nerve, which is ascertained to include the focal injury. This type of localization can be accomplished with both NCS and NEE; it is the most precise type achievable with the NEE. One possible exception is the occasional ulnar neuropathy in the hand, in which NEE reveals abnormalities in some lateral intrinsic hand muscles, but not more medial ones, innervated by the deep motor nerve; in these instances, the NEE places the injury along such a short portion of nerve that it can be designated point localization, for practical purposes. This is the localization effected on NCS whenever the nerve injury has caused a focal conduction abnormality, but stimulations cannot be applied immediately proximal and distal to it. Thus, with some brachial plexopathies, supraclavicular stimulation of those motor axons that innervate intrinsic hand muscles reveals a conduction block, whereas stimulation of those same axons in the distal axilla does not. The lesion therefore can be localized to certain brachial plexus elements (the mid-distal portion of the lower trunk, the lower anterior division, or the medial cord), but not to any particular one of them. Similarly, whenever conduction blocks are detected along the ulnar nerves in the forearms of patients with multifocal motor neuropathy, the best localization possible (unless needle stimulating electrodes are used and much time expended) essentially is to some place between the wrist and elbow stimulation sites.

Even when focal conduction abnormalities are not present (ie, the conduction failure pattern pertains), segment localization is still possible by NCS if two or more NCS are performed and the results are compared to one another. This method of localization, called *pairing*, requires that NCS be performed on nerve fibers that are contiguous with each other at various portions along their course, while separate at others. If a lesion occurs at a site where they are contiguous, then the NCS that assess both groups of nerve fibers will yield low amplitude or unelicitable responses. Conversely, if the lesion is situated at a site where they are not contiguous, only one or the other NCS will manifest abnormally low amplitudes [3]. Successful pairing of NCS
requires some knowledge of anatomy. For example, the median CMAP can be paired with both the ulnar CMAP and the ulnar SNAP, because all three traverse the lower trunk and medial cord of the brachial plexus; consequently, with lesions at either of these sites, the amplitudes of all three NCS characteristically are diminished. Conversely, with lesions of the ulnar terminal nerve in the axilla or more distally, although the ulnar CMAP and SNAP amplitudes are affected, the median CMAP amplitude is not. Distal to the cords, the median CMAP can be paired with the median SNAP because the axons assessed by both NCS are contiguous from the axilla (where the lateral and medial heads of the median nerve converge to form the terminal median nerve) throughout the entire arm, forearm, and wrist, only separating in the hand after traversing the carpal tunnel. One of the most helpful instances of pairing, which permits substantial proximal axon loss lesions to be localized to either within the intraspinal canal or in the proximal plexus, has been available for EDX localization for nearly 50 years, since Gilliatt and co-workers first reported that the upper extremity SNAPs are not altered by cervical intraspinal canal lesions (those affecting the spinal cord or primary roots), whereas they are low in amplitude or unelicitable with those involving the trunks of the brachial plexus [27,28]. In contrast, corresponding CMAPs are equally affected by lesions at either location. Consequently, by pairing the appropriate CMAP and SNAP amplitudes, the lesion can be localized to either the intraspinal canal or the plexus. Nonetheless, evidence of a severe axon loss plexopathy does not exclude a coexisting severe root lesion.

Although NCS can be used to localize both focal demyelinating and axon loss, the NEE is of value almost solely with axon loss, because the only focal demyelinating injuries it detects are those that are producing demyelinating conduction block and which are rather severe in degree (those causing reduced MUAP recruitment). Often the best localization is achieved by a combination of both NCS and NEE but, depending upon exactly where the focal lesion is situated, such segment localization may still be clinically suboptimal. Consider, for example, a situation in which the median CMAPs and SNAPs are unelicitable, whereas other NCS in the limb are normal, and NEE reveals fibrillation potentials and severely reduced MUAP recruitment in all the muscles innervated by the median nerve, including the pronator teres and flexor carpi radialis. The focal injury can be definitely localized only to the linear extent of the median nerve situated between the elbow (where the motor branch to the pronator teres arises) and the origin of the terminal median nerve in the axilla (ie, to the distal axilla, entire arm, and elbow portions). Thus, in this instance, the best segment localization possible only narrows the possible lesion site to approximately 40% of the entire length of the nerve.

Localization by NEE is achieved in essentially the same manner as it is by muscle strength testing on clinical examination. With the latter, the lesion is assumed to lie somewhere along that portion of the nerve which is (1) distal to the origin of the motor branch supplying the most distal muscle that retains normal strength, while (2) proximal to the origin of the motor branch
supplying the most proximal muscle that is weak (Fig. 11). The same approach is used for NEE localization except that, instead of muscle weakness, physiologic abnormalities are sought, including reduced MUAP recruitment (the electrical counterpart of clinical weakness), chronic neurogenic MUAP changes and, particularly, fibrillation potentials, which can be produced by axon loss lesions that are much too mild in degree to cause either muscle weakness or MUAP abnormalities (Fig. 11). Unfortunately, several problems can be encountered when attempting to localize an axon loss injury by NEE, none of which is under the control of the electrodiagnostician, and most of which result in the lesion being falsely displaced distally along the affected nerve. These are a function of three factors: (1) nerve anatomy; (2) fascicular involvement of nerve fibers; and (3) duration of lesion. Because the second factor has two dissimilar presentations, it will be considered under two separate headings, severity, and nerve fascicles, in the following discussion.

Fig. 11. How axon loss lesions are localized by the needle electrode examination. The lesion is assumed to be situated at some point along the nerve segment between the origin of the motor branches that innervate: the most distal muscle that appears normal, and the most proximal muscle that appears abnormal.
Anatomy factor. The segment of nerve to which the lesion can be localized by NEE depends in large part on the anatomy of the particular nerve that has been injured—specifically, on the number and exact site of origin of the motor branches that supply the muscles which can be assessed on NEE, and on the position of the lesion along the nerve. The ideal circumstance is to have multiple motor branches arising from the nerve, at fairly regular intervals, and to have the lesion situated between the origins of two of these branches (Fig. 12A). The consummate nerve, in this regard, is the radial nerve, which essentially is the only major peripheral nerve trunk in the human body that meets these requirements. Far more common is the situation encountered whenever either the median or ulnar nerve is assessed: both have very long segments (axillary and arm; forearm) from which no motor branches arise (Fig. 12B). Consequently, as already described in the example above, segment localization along these nerves, just as along the sciatic nerve in the thigh, may be of relatively little assistance to the clinician, simply because of the excessive length of nerve along which the focal lesion may reside, as determined in the EDX laboratory.

Fig. 12. The anatomy of the injured nerve, specifically, the number of the motor branches that arise from it, in relationship to the lesion site, may have adverse effects on localization by needle electrode examination as shown. Note that the segment of nerve that encompasses the focal nerve lesion can vary substantially (B) from the ideal nerve (A).
Severity factor. The number of axons injured also can play a role in how accurate segment localization is by NEE. The model condition, in this regard, for the electrodiagnostician, although obviously not for the patient, is for the axon loss to be severe. Whenever this is the case, usually it is a relatively easy task to localize the lesion, simply by determining which muscles innervated by the damaged nerve show substantial neurogenic abnormalities and which do not (Fig. 13, left panel). In contrast, with mild and sometimes even moderate axon loss lesions, localization often is much less satisfactory, because NEE abnormalities all-too-frequently are found only in the more distal muscles innervated by the affected nerve; the more proximal muscles appear normal, despite the fact that the motor branches supplying them arise distal to the site of injury, and the symptoms are of relatively recent onset, so that the duration factor (discussed below) cannot be operative (Fig. 13, right panel). The obvious culprit in these instances is selective involvement of nerve fascicles at the lesion site a trait which this factor shares with the nerve fascicle factor described below. However, the number of axons injured also plays a substantial role: the severity factor is

Fig. 13. The effect the severity of a focal axon loss lesion, specifically one killing only a few fascicles, has on localization by needle electrode examination.
encountered almost exclusively when only mild-to-moderate numbers of axons have been killed, compared to when a substantial number have been destroyed. Moreover, nearly always the abnormalities are restricted to distal limb muscles.

**Nerve fascicle factor.** Occasionally, selective fascicular involvement at the site of injury reputedly is responsible for EDX presentations which are quite different from those characteristic of the severity factor, in that (1) the axon loss has been very substantial or even total, rather than mild or minimal; (2) the abnormal muscles are not necessarily located in the distal portion of the limb. Thus, with a severe focal axon loss injury, some muscles innervated by the affected nerve show massive denervation on NEE, whereas others appear normal, even though they definitely should not, based on the site of the nerve damage (Fig. 14). Classic examples of this perplexing phenomenon are (a) some UN-ES that cause severe denervation of the ulnar nerve-innervated hand muscles (ie, very low amplitude ulnar CMAPs, recording hypothenar and first dorsal interossseous, along with very substantial reduced MUAP recruitment in those same muscles on NEE), while completely sparing those in the forearm; (b) the occasional CPN-FH that produces near total axon loss along the proximal deep peroneal fibers, while leaving intact the superficial peroneal ones [2,17]. The explanation advanced for these peculiar patterns of denervation, which are strikingly different from those seen with the typical severe axon loss lesions, is unconvincing: The nerve fascicles that innervate the uninvolved muscles are unscathed because they occupy a protected location in the cross section of the nerve at the lesion site. Generally unstated is exactly how this possibly can occur, considering the extent of denervation found in the affected muscles. Thus, the cause of these patterns remains somewhat of an enigma. Nonetheless, regardless of its validity, the explanation proposed does serve to assuage the electrodiagnostician’s unease when confronted with such inexplicable findings.

**Duration factor.** How long a static axon loss lesion has been present can play a significant role in localization. Although conceivably all muscles innervated by nerve branches originating from the injured nerve distal to the lesion site initially may manifest neurogenic changes (eg, fibrillation potentials; MUAP loss), as time passes the more proximally involved ones are reinnervated, by proximo-distal regeneration of nerve fibers from the site of the injury, by collateral sprouting, or both. As a result, the longer the duration of a static lesion, the more likely the NEE abnormalities will be restricted to progressively fewer, and more distal, muscles of the limb [2] (Fig. 15). In many instances, reinnervation has been so efficient in the initially denervated proximal muscles that it is impossible to determine, by NEE, that they were ever involved.
Nerve fiber localization

With this type of localization, which is quite unsatisfactory for clinical purposes, the focal damage can only be determined to be situated along a very long length of nerve extending, for motor fibers, from the AHCs to a single muscle, and for sensory fibers, from the DRG to a single cutaneous nerve (Fig. 10) (panel 3). Thus, whenever only one CMAP or SNAP is abnormally low in amplitude or unelicitable during NCS, or just one muscle shows abnormalities on NEE, or F-wave abnormalities are restricted to a single nerve, only nerve fiber localization is possible.

Pathway localization

This is the only lesion positioning possible whenever abnormalities are restricted to the H-response (ie, it is either prolonged in latency or, far more
often, low in amplitude or unelicitable). In the lower limb in these instances, if the traditional NCS and NEE reveal no abnormalities, then it can only be said that the lesion resides in the S1 segment of the spinal cord, or somewhere along the very long sensory and motor pathways extending distally from that spinal cord segment (Fig. 10) (panel 4). Therefore, it may be involving sensory fibers, motor fibers, or both, as well as the spinal cord itself. Consequently, even though a definite abnormality is detected on EDX examination, it is of very little localizing value.

Conclusions

The NCS are an integral component of the EDX examination, in large part because, unlike the NEE, they can assess sensory axons, and they can detect focal demyelinating lesions. However, to yield reliable information, they must be performed in a standardized fashion, with meticulous attention paid to detail. Of the various components of the NCS, the amplitudes are by far the most important, overall, especially with any lesion causing clinical weakness or static large fiber sensory deficits. They also are by far the component most often abnormal, if all neuromuscular disorders are considered. In contrast, the CVs are the least important, yielding posi-
tive diagnostic information essentially only with some UN-ES and with many (mainly chronic) demyelinating polyneuropathies.

References


H reflexes and F waves
Fundamentals, normal and
abnormal patterns
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H reflexes and F waves are frequently used for similar clinical problems. They are found at comparable latencies, reflect conduction to and from the spinal cord, and involve motor neuron activation. Therefore, H reflexes and F waves, although physiologically quite distinct, are commonly discussed together.

H reflex

Physiology

H reflexes are named after Paul Hoffman, who, in 1918, described a reflex response in calf muscles that followed stimulation of the tibial nerve and was comparable in latency to the Achilles’ reflex [1,2]. Because H reflexes involve conduction from the periphery to and from the spinal cord, they occur at latencies considerably longer than the direct motor response. H reflexes—as well as F waves—have therefore been called “late” responses (Figs. 1 and 2). A necessary condition for establishing an H reflex with certainty is that the “late” response must be larger than the preceding direct motor response. This can occur only if there is central amplification of the motor response due to reflex activation of motor neurons. H reflexes involve afferent conduction in large-fast conducting Ia fibers; subsequent reflex activation—possibly monosynaptic—of motor neurons in the anterior horn of the spinal cord; and efferent conduction in alpha motor fibers. In that sense, the H reflex is similar
to the phasic myotatic (deep tendon) reflex produced by muscle stretch. Unlike the phasic myotatic reflex, however, the H reflex does not involve muscle spindle activation. This difference may at times explain the presence of calf H reflexes in the absence of Achilles’ reflexes, and vice versa.

H reflexes are inhibited as the stimulus intensity is increased from submaximal to that required for eliciting a maximal direct (M) response. This is best explained by increasing central inhibition as the stimulus intensity is increased. Large H reflexes are obtained from calf muscles, even with supramaximal stimulation, if the stimuli are timed appropriately with phasic contractions of the muscles [3]. This indicates that H-reflex inhibition is dependent on central motor neuron pool excitability states rather than fixed peripheral conduction times. Recent studies in normal subjects versus patients with spastic symptoms are consistent with central inhibition of H reflexes as the stimulus intensity is increased [4].

There are inhibitory mechanisms in the spinal cord, such as Renshaw cells, that could explain H-reflex inhibition with increasing stimulus inten-
Renshaw cells are inhibitory interneurons activated by antidromic stimulation [5]. They are distributed widely throughout the motorneuron pool [6] and discharge more strongly and with a shorter latency as stimulus intensity increases [7]. H reflexes may be monosynaptic, whereas H-reflex inhibition by Renshaw cells would involve two synapses. Any resulting difference in the onset of inhibitory and excitatory effects may be as brief as 0.3 milliseconds [6] and therefore well within a reasonable physiologic range given potential motor neuron excitatory postsynaptic rise times of at least 3 milliseconds [8]. Single-fiber electromyographic (EMG) studies of H reflexes support a process of active inhibition involving inhibitory synapses with stimuli of increasing intensity [9]. H-reflex studies have been used to demonstrate prominent central inhibition following supramaximal nerve stimulation consistent with Renshaw cell activation [10].

In children younger than 2 years, H reflexes are widely distributed. Beyond infancy, H reflexes are regularly found in calf muscles, primarily the...
soleus, and homologous forearm flexors. They are also frequently present in the quadriceps and occasionally in plantar foot muscles. This restricted distribution of H reflexes reflects physiologic, not structural, changes associated with maturation of the central nervous system (CNS).

The fraction of the soleus motor neuron pool activated in an H reflex is usually about 50% but can be as high as 100% [11]. The ratio of the peak-to-peak maximum H reflex to maximum M amplitude (H/M) provides a measure of motor neuron pool activation and therefore of excitability. The H/M ratio for calf H reflexes is normally less than 0.7 [12].

H reflexes are enhanced by maneuvers that increase excitability of the motor neuron pool, such as the Jendressik maneuver [13] and teeth clenching [14]. Facilitated by contraction or post-tetanic potentiation, H reflexes may be elicited in muscles where they are not usually present, such as in small hand muscles [3, 15].

Vibration activates large afferent fibers. H reflexes are inhibited by vibration caused by peripheral “busy line” interference, presynaptic inhibition of afferent input, and the activation of spindles in antagonistic muscles [16, 17].

Reproducible patterns of changes in H-reflex amplitude can be defined if test stimuli are given at varying intervals after a conditioning stimulus [18]. These excitability or recovery curves vary with the level of stimulation [19].

H reflexes have been used to investigate motor control in humans [20]. H-reflex studies, for example, have shown patterns consistent with the reflex effects of both group Ia and group II afferents [3, 11, 21–23]. Changes in presynaptic inhibition of Ia fibers in a functionally meaningful pattern have been demonstrated [24]. The methodology for analyzing reciprocal inhibition in the forearm using H reflexes has been described [25].

**Recording technique**

H reflexes are readily obtained using percutaneous stimulation and surface recording techniques. The stimulating cathode is placed proximally to avoid the theoretical possibility of anodal block. Stimulus pulses of long duration (1 ms) are used to preferentially activate large sensory fibers [26, 27]. The stimulus frequency should be 1 per 3 seconds or less to allow full recovery of the H reflex from a prior stimulus. By starting with submaximal stimuli and increasing to supramaximal stimulation, one should determine that: (1) the “late” response can be larger than the preceding direct motor response, (2) the H reflex with the largest amplitude, and (3) the inhibition of the H reflex with increasing stimulus intensity. A “late” response larger than the associated M wave can only occur if there is reflex activation of motor neurons. Latencies should be measured to the onset of the responses—either negative or positive—and amplitudes are probably best measured peak to peak. H reflexes should be stable for similar conditions of stimulation and recording.
For calf H reflexes, the tibial nerve is stimulated in the popliteal fossa. Bipolar stimulation is usually adequate. Use of an anode with a large surface area at the patella may help ensure selective activation of Ia fibers [28]. Surface recordings are made from the soleus muscle. Although techniques for recording H reflexes vary, a standard and convenient location for the active electrode is medial to the tibia at a point that is one half the distance between the stimulation site and the medial malleolus, with the indifferent electrode placed on the Achilles’ tendon.

H reflexes in the forearm are recorded from the flexor carpi radialis muscle [29]. Surface muscle belly recordings are usually adequate, with the recording electrode placed at the junction of the upper one third and lower two thirds of the distance between the medial epicondyle and the radial styloid. The median nerve is stimulated percutaneously in the cubital fossa.

H reflexes are routinely recorded with the muscle at rest. Contraction of the recording muscle will enhance H reflexes by facilitating the motor neuron pool. Such contraction can help identify H reflexes in muscles where H reflexes are normally present as well as elicit H reflexes in muscles where they are not normally found [26].

Normal findings

The upper limit of normal latency for the soleus and flexor carpi radialis H reflexes are 35 and 21 milliseconds, respectively. H-reflex latencies are directly related to leg or arm length and height and, to a lesser degree, age [30–33]. H-reflex latencies are best predicted if these parameters are considered. Normal values for infants and children have been reported previously [34,35]. For routine clinical work, and consistent with a criterion of 3 standard deviations from the mean, 2 milliseconds should be allowed for side-to-side differences when recording from the calf and 1.5 milliseconds when recording from the forearm. Using a carefully defined technique, the upper limit of normal of the interside ratio of H-reflex amplitudes for calf muscles has been reported as 2 [36]. Given the potential variability in H-reflex amplitude due to variation in motor neuron pool excitability [37], a preferable figure for general clinical work is closer to 3 [38], which is similar to that for H reflexes in the forearm.

Calf H reflexes are usually present in normal subjects. As with phasic myotatic reflexes, however, this is not always true, and the percentage of absent responses increases in elderly persons [39].

Clinical uses

H reflexes are a sensitive test for polyneuropathies, and may be abnormal even in mild neuropathies [40,41]. H reflexes involve conduction in proximal fibers, and these studies can therefore define proximal nerve injury and may be abnormal even when distal studies are unremarkable. Absent H reflexes, for example, are a characteristic and early finding in acute idiopathic
polyneuropathy (Guillain-Barré syndrome). The absence of calf H reflexes following distal (popliteal fossa) but their presence with proximal stimulation (gluteal fold) has been used as evidence for a distal axonopathy [42]. H reflexes can also be abnormal in plexopathies [43] and radiculopathies. H reflexes in the forearm flexor muscles may be abnormal with C6 or C7 root injury [32], and calf H reflexes may be abnormal with S1 radiculopathies [30,36,44,45]. H reflexes are affected by injury to both dorsal and ventral roots. H reflexes can therefore be important in the electrodiagnostic evaluation of radiculopathies by documenting injury to anterior rami, even when needle EMG is unrevealing due to sparing of the ventral roots.

H reflexes may be abnormally widespread in patients with CNS lesions and upper motor neuron (UMN) signs [46]. H reflexes in muscles where they are not normally present, such as in the tibialis anterior or small hand muscles, may be useful clinically for documenting central motor system dysfunction.

In patients with a hemiparesis, there is decreased potentiation of H reflexes with muscle contraction consistent with decreased background facilitation of motor neurons [47]. H/M ratios tend to be increased in patients with CNS lesions and UMN signs [48,49], and recruitment curves are altered [50] in a manner consistent with increased excitability of the central motor neuron pool. Conversely, H reflexes during cataplexy are depressed [51].

H reflexes are depressed acutely after spinal cord injury [52]. Increased H/M ratios develop during the weeks to months following a cerebrovascular lesion associated with the appearance of features of the UMN syndrome such as increased tone, brisk reflexes, and extensor plantar responses [49]. In patients with chronic UMN lesions, the vibratory inhibition of H reflexes is less than expected, possibly due to decreased presynaptic inhibition [17,53]. H reflex studies indicate that the abnormal modulation of stretch reflexes in the UMN syndrome is due to the abnormal regulation of dysynaptic reciprocal inhibition and presynaptic inhibition [54]. Vibratory inhibition of H reflexes has been reported to be enhanced in patients with acute cerebral lesions [55]. At a time when both Achilles’ reflexes and H reflex recovery curves are depressed with spinal shock, H reflexes are relatively well preserved [56–58]. Decreased vibratory inhibition of H reflexes has been associated with hypertonia, increased H/M ratios with increased reflexes, and late facilitation of the recruitment curve with clonus [59]. Within several months after a central injury, H-reflex excitability curves can show a pattern of abnormally rapid recovery, a pattern that differs from that in patients with parkinsonian rigidity or cerebellar hypotonia [19,60]. Recently, the enhanced recruitment curves in patients with UMN lesions have been attributed to the larger H reflexes generally present in these patients [61].

Studies of recovery curves and patterns of reciprocal inhibition of forearm flexor H reflexes have revealed abnormalities in patients with various types of dystonia, even in clinically normal body parts [27,62]. In patients with chronic UMN syndromes and pretibial H reflexes, depression of the
pretibial H reflex with weak stimulation of the tibial nerve accords with enhanced reciprocal inhibition of flexor muscles by extensors [63]. In patients with chronic long-tract motor dysfunction, H reflexes have been used to analyze altered patterns of reflex activity between flexor and extensor muscles [54,64–66].

In general, H reflexes have been found useful for investigating transmission changes in spinal pathways [20]. H-reflex analysis of recurrent inhibition in patients with UMN lesions has indicated altered patterns of Renshaw cell activation with postural or voluntary contractions consistent with supraspinal disruption of inhibitory control [67]. In patients with amyotrophic lateral sclerosis, recurrent inhibition appears decreased [68].

**F wave**

*Physiology and analysis*

F waves are low-amplitude, ubiquitous responses inherently variable in amplitude, latency, and configuration. They are produced by antidromic activation (“backfiring”) of motor neurons.

F waves are so named because they were originally recorded in small foot muscles [69]. The antidromic origin of F waves has been confirmed by the following: motor units are only present in F waves if they are also present in the direct motor response [70], F waves are present in deafferented animals and humans [71–73], and single-fiber EMG analysis has indicated that an F wave requires activation of the motor axon producing that particular response [74].

Although often 1 to 2 milliseconds shorter, the shortest F-wave latencies are comparable to H-reflex latencies. In contrast to H reflexes, F waves are most prominent with high-intensity stimulation [75]. Differences between H reflexes and F waves are outlined in Table 1.

Whether the stimulus is orthodromic or antidromic, motor neurons are activated by depolarization at the low-threshold initial segment and

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subsequent invasion of the soma [76]. In addition, impulses must pass orthodromically through an axonal initial segment that has been discharged by a preceding antidromic impulse. Because of this, the effect of altered motor neuron pool excitability on F waves is variable. If the motor neuron is at a high level of excitability, neuronal activation will occur rapidly and the resultant orthodromic axonal discharge may arrive at the initial segment at a time when it is still refractory. Increased excitability of the motor neuron pool could then result in decreased prominence of F waves [71,77]. As a result, the effects of agonist and antagonist contraction with F waves are less predictable than with H reflexes.

Individual motor neurons are activated infrequently with antidromic stimulation [77], and there are usually no more than several motor-unit action potentials in an F wave [75]. As a result, F waves may not appear after each stimulus, are variable in configuration, and are low in amplitude (Fig. 3). Whether the range of F-wave latencies reflects the full range of conductions in motor axons has been controversial. Studies that indicate a complete range of motor neuron activation in F waves have been reported [78–80]. The conclusion of these studies has been questioned, either because of the authors’ reasoning [81] or, because of these studies’ technical requirements, they were performed at submaximal stimulation. Therefore, the relevance of these findings to the usual situation in which F waves are recorded with supramaximal stimulation is uncertain. There is observational and direct evidence favoring selective activation of the largest, fastest conducting motor units in F waves [75,82,83]. Even with a relatively limited number of F waves, such as 10, the fastest F waves and maximal evoked response latencies have shown comparable changes with distance [83–86]. Given the large potential range of conductions in motor axons [87], this would seem unlikely without some selection of the fastest conducting motor units in F waves. They discharge more strongly as the stimulus intensity is increased [7] and least inhibit larger motor neurons [88,89].

The time between the start of antidromic activation and subsequent orthodromic discharge, that is, the central “turnaround” time, is uncertain. According to Eccles [76], this is commonly stated to be 1 millisecond, but this has never been demonstrated directly. In humans, identical F waves have been recorded from foot muscles with latency variations of 3 milliseconds [90]. Accurate measurement of individual F-wave latencies may be difficult because F waves frequently arise from an unstable baseline and there may be superimposed axon reflexes. For these reasons as well as because of the inherent variability of F waves, F-wave analysis requires evaluation of a series of F waves. This number has varied from 3 to 50 or greater but generally has been from 10 to 20 F waves. Recent studies of the abductor pollicis brevis muscle indicate that evaluation of 16 to 20 F waves (20 stimuli) is needed for accurate measurement of “true” latencies, based on an analysis of responses following up to 100 stimuli [91–93]. However, the normal variability of latencies in a series of F waves is about 10%, which is comparable to
Fig. 3. (A) F waves (right) with associated M waves (left) recorded from the abductor pollicis brevis muscle following supramaximal stimulation. (B) The inherent variability of F waves is emphasized in the superimposed recordings. The persistence in this series of 10 recordings is 90% because in one recording an F wave is absent. The two largest responses are repeater waves. Calibration per division: 5 mV for M waves, 500 μV; 5 ms. (From Fisher MA, Hoffen B, Hultman C. Normative F waves and the number of recorded F waves. Muscle Nerve 1994;17:1185–9; with permission.)
the range of error for measurements of other commonly used electrophyslogic responses. The clinical importance of defining F-wave parameter measurements with as much accuracy as possible ("true" values) varies. For F latencies, for example, this is important when the clinical question depends on small latency differences between sides, such as when evaluating radiculopathies (see later), but is less important when latency prolongations may be marked, such as in neuropathies.

Latencies are the most frequently reported parameters of F waves. F-wave latencies are directly related to height, limb length, and, to a lesser degree, age [94–97]. The accuracy of defining normal values is improved by considering these variables. F-wave latencies are reported most frequently as minimal latencies, but recording F-wave latencies as mean values minimizes the errors inherent in a single latency measurement and provides results that are more reproducible. This has been the recommendation of all studies that have addressed the question [91–94,99–101].

Proximal conduction is similar to distal conduction in comparing the latencies of F waves with M waves [102,103]. F-wave latencies have been used to estimate conduction in limited portions of proximal nerves [102], as have F-wave conduction velocities [84]. Conversion of F latencies to conduction has the advantage of allowing comparisons in subjects of different arm lengths [92]. However, F-wave conduction velocities are less accurate than latency values alone because additional errors of measurement may be introduced [105], and F-wave latencies can readily be normalized to a particular arm or leg length.

The analysis of F-wave parameters other than latency also has clinical utility. The difference between minimal and maximal latencies in a series of F waves (F chronodispersion) provides a measure of the range of conduction velocities in the axons in the recorded F waves [106]. F-wave duration and amplitude are related to both the size and number of motor units in a particular F wave [107]. F-wave persistence refers to the percentage of measurable F responses that follow a series of stimuli, and is related to the antidromic excitability of a particular motor neuron pool. The recurrence of individual motor units in a series of F waves measures the selectivity of F-wave discharge. The ratio of F-wave amplitudes to that of the associated M waves (i.e., F/M ratio) is a measure of the proportion of a motor neuron pool activated by the antidromic stimulation. Given the F-wave variability, mean F-wave rather than maximum F amplitudes are preferable for calculating F/M ratios.

F-wave recovery curves have been defined by measuring F-wave amplitudes or persistence following conditioning stimuli that precede the test stimulus at varying intervals. As with H reflexes, there is an early depression of the response, followed by a later facilitation from about 80 to 300 milliseconds [108].

F waves can be used as a "probe" for changes in spinal cord excitability [109]. F-wave studies, for example, have shown changes consistent with activation of group II afferents in leg muscles following stimulation of the
sural nerve [110]. In resting individuals, F-wave studies have shown a relatively increased central excitability of the antigravity calf muscle in comparison to the antagonist tibialis anterior muscles [111]. With isometric contraction, the central excitability of the tibialis anterior muscle increases relative to that of calf muscles [112], consistent with a more balanced central excitability state between flexor and extensor muscles with activity.

**Technique**

F waves are recorded in a manner similar to that used for direct motor responses, except that the stimulating cathode should be proximal to the anode to avoid the theoretical possibility of anodal block. In contrast to H reflexes, F waves are enhanced by high-intensity stimulation (ie, 25% above maximal for eliciting a direct response). A long stimulus duration is not required since there is no reason to preferentially activate large afferent fibers. Stimulus rates of less than 0.5 Hz are recommended in order to avoid the effects of an earlier stimulus on a subsequent response.

An adequate display of F waves usually requires an amplifier gain of 200 or 500 μV/div and a sweep of 5 or 10 milliseconds/div. As such, different recording parameters are usually required to evaluate fully the associated larger microvolts (M) wave. To be clearly identifiable, F waves should be at least 20 μV in peak-to-peak amplitude.

The number of F waves required to permit measurement of different F-wave parameters has been examined [91,93,97,100]. Data from 8 to 10 identifiable, sequential F waves (10 stimuli) can provide a reasonable estimate of persistence. Accurate F-wave latency measurements require 16 to 20 F waves (20 stimuli), with a statistical preference for mean rather than minimal values. The same number of F waves is adequate for measuring F/M ratios and the percentage of responses in a series of F waves that are the same (i.e., repeater waves). Even two F waves may define an abnormal chronodispersion if the two latencies are sufficiently dispersed, but determination of a truly representative value requires 45 to 55 F waves (50 to 60 stimuli). Accurate determination of the number of individual waves that repeat may require more than 90 F waves.

Muscle belly-tendon recordings are standard for hand and foot muscles, with the recording cathode placed over the motor point. For calf F responses, muscle belly recordings are preferable since this decreases the effects of extraneous muscle activity when recording the low-amplitude F waves. The active electrode is placed as for H-reflex measurement.

F waves are routinely recorded with the muscle relaxed. Slight voluntary contraction will enhance F waves, which is sometimes clinically helpful, but will alter F-wave parameters such as amplitude and increase the possibility of contamination by H reflexes [15,113].

F waves are ubiquitous in distribution. Recordings from proximal muscles are difficult because the low-amplitude F waves may then be superimposed
on the associated M wave. F waves, therefore, are routinely recorded only from muscles of the hand, foot, and leg with standard stimulation sites at the wrist, ankle, and knee, respectively. F waves can be recorded in hand muscles when stimulating in the axilla if collision techniques are used so that the orthodromic M wave from the axilla is blocked by colliding with antidromic impulses from the wrist [84].

F waves are usually recorded in a raster fashion such that individual responses and the associated maximum M waves are available for analysis (Fig. 3). A stable M wave is important to ensure stable conditions of stimulation and recording. Standard protocols include measurement of minimal and mean F-wave latency, F-wave chronodispersion, F-wave persistence, and the F/M amplitude ratio. The latter is calculated as the mean of the amplitudes of the F waves (in µV) divided by the M-wave amplitude (in mV), both measured peak to peak.

Clinical application

Reasonable upper limits of normal for minimal F latencies are 31, 36, and 61 milliseconds when recording from hand, calf, and foot muscles, respectively [114–118]. Mean latencies are about 2 to 3 milliseconds longer. Side-to-side differences exceeding 2 milliseconds are regarded as abnormal for both minimal and mean values when recording from the hand, 3 milliseconds are regarded as abnormal when recording from the calf, and 4 milliseconds when recording from the foot. Tables of normal latency values are readily available. F-wave latencies are best predicted using regression equations relating the latencies and age. Such regression equations are available for the abductor pollicis brevis, abductor digiti minimi, calf, and abductor hallucis muscles [94,96,97,119]. When recording from hand muscles, values of 3 milliseconds or more greater than the predicted value based on regression equations are abnormal, and those between 2 and 3 milliseconds are borderline; comparable values for the soleus are 4 and 3 milliseconds.

Published upper limits of normal for chronodispersion have varied [95,97,98,106,120–122] and may depend on the number of F waves recorded [91]. Based on the published reports, false-positive values are unlikely if the upper limits of normal are 6.2 milliseconds in the abductor pollicis brevis and adductor digiti minimi, 7 milliseconds for calf muscles, and 8 milliseconds for the extensor digitorum brevis. Normal mean values have been less than 5% except when recording from the abductor hallucis (8.8%) [95]. Mean values for F-wave persistences when recorded from the abductor pollicis brevis, abductor digiti minimi, soleus, and abductor hallucis are about 80% to 90%, whereas in the antigravity antagonist tibialis anterior, extensor digitorum brevis, and extensor digitorum communis muscles, these values are about 30% to 40%, but the range of normal is high for individual measurements [111,123]. Because of the low persistences in the antigravity muscles, recording adequate F-wave data from these muscles can be diffi-
The normal maximum frequency of an individual response in a series of F waves from hand muscles is about 10% [75,97]. The percentage of responses in which there are repeater waves may be higher because there may be more than one repeater wave in a series of F waves and each individual repeater wave may be present more than twice. A frequency of an individual repeater wave as high as 58% has been noted in recording from the extensor digitorum brevis of normal subjects (mean, 21.5%) [90].

Prolonged F-wave latencies are a sensitive abnormality in polyneuropathies and may be present even when more distal motor nerve conductions are unremarkable [41,95,96,122–124]. They may be more sensitive than standard motor conduction studies in axonal injury [71]. F waves are the most stable and reliable conduction study for observing patients with neuropathies [125]. Prominently prolonged F waves (>150% of the upper limit of normal) have been reported specific for demyelination, as has the absence of F waves in the presence of compound muscle action potential (CMAP) amplitudes [71]. F waves have provided evidence of focal proximal slowing in neuropathies [85,125].

Prominent slowing of proximal F-wave conduction in comparison to distal motor nerve conduction studies has been found in patients with the Guillain-Barré syndrome, confirming the importance of proximal nerve lesions in these patients [125]. Proximally predominant abnormalities have not been found in uremia [128,129], diabetes mellitus [130], or Charcot-Marie-Tooth disease [84,131].

F-wave parameters other than latency are important. F waves have been abnormal in greater than 90% of nerves in patients with acute and chronic demyelinating polyneuropathies [95,119]. F-wave latencies were abnormal in no more than 50% of these nerves, although in 50%, F waves were absent. Abnormal chronodispersion or persistence was present in about 25% to 50% of nerves and were frequently the only F-wave abnormality in that nerve [95]. F-wave abnormalities were at least as frequent as motor conduction study abnormalities [119]. F-wave chronodispersion may be prolonged in polyneuropathies [95,106,119,132]. The chronodispersion tends to be larger in nerves with demyelinating rather than axonal injury and to be relatively decreased with conduction block [119,132].

The percentage of repeater waves is increased in neurogenic injury, especially with atrophy [90]. The number of identical responses in a series of F waves may be greater in patients with neurogenic atrophy such as amyotrophic lateral sclerosis and cervical myeloradiculopathies [103]. This is consistent with a decreased number of motor neurons capable of responding to antidromic stimulation as well as an increased discharge of responding motor neurons in patients with UMN syndromes [77,90]. An increase in repeater waves has been reported to be a sensitive indicator of carpal tunnel syndrome [133]. This study was based on series of 100 F waves—an accurate but limiting approach in practice. Increased F-wave durations may be an early sign of diabetic neuropathies [134]. F/M amplitude ratios may be increased in
neuropathies. This is most characteristic of axonal injury [90], consistent with large amplitude motor units and decreased CMAP amplitudes.

F-wave latencies may be prolonged in proximal nerve or root injury [135,136]. The value of F-wave studies in detecting focal proximal injury, particularly radiculopathies, has, however, been controversial. Early studies [102,137] reported sensitivities of 50% to 80% for lumbosacral, especially S1, radiculopathies based on abnormal F-wave latencies or side-to-side latency differences. Subsequently, the clinical utility of F waves in radiculopathies has been questioned [138–140]. There have been a few concerns: latency delays may be “diluted” by the long course of the F waves; abnormalities may be masked by the presence of normal fibers, even if other fibers are injured; and there will be overlap between F-wave abnormalities and those of the needle EMG examination. F-wave latencies, however, can be prolonged, at times prominently, in other conditions with focal proximal injury, such as the Guillain-Barré syndrome. Concerning variable degrees of motor fiber injury, F-wave parameters, such as chronodispersion, could provide unique information about such findings. Studies that have questioned the utility of F waves in radiculopathies have not used 20 stimuli or mean, rather than minimal, latency values, even though these techniques may reveal small changes in F-wave latencies that may be important clinically. Similarly, these studies have failed to evaluate F-wave parameters other than latency, even though such parameters may reveal meaningful abnormalities. In recent studies of patients with L5/S1 radiculopathies that have evaluated not only latencies but also chronodispersion and persistence, F-wave sensitivities comparable to needle EMG studies have been reported [120,122,141,142]. In addition, there was enough discrepancy between the F-wave and needle EMG findings to indicate that these studies are complementary. There are no published reports evaluating the sensitivity of F waves in cervical radiculopathies. This may be true because about 90% of these radiculopathies involve the C5, C6, or C7 roots [143]. F-wave studies need not be considered a routine examination in patients with L5/S1 radiculopathies but should be performed thoughtfully where information from the F-wave studies may be useful for defining the patient’s condition.

In patients with spinal stenosis and multilevel root injury, 3 minutes of standing produced increased calf F-wave abnormalities, most noticeably in chronodispersion [144]. In some patients, this increase in chronodispersion was as much as 8 milliseconds. This study supports the idea that F waves may be useful for evaluating dynamic changes in nerve roots and may be helpful in those patients where the electrodiagnostic information may be most valuable—namely, in those patients with multilevel injury.

F-wave analysis to define increased central excitability states are more complicated than analysis with H reflexes. In patients with UMN syndromes, in comparison to normal subjects, F-wave latencies may be prolonged and durations and amplitudes are increased [145]. These data are consistent with the following: a greater number of smaller, more slowly—
conducting motor units discharge due to increased central excitability, while larger motor neurons are blocked because of too rapid activation. Single-fiber studies in patients with UMN syndromes indicate that antidromically activated motor neurons fire more frequently than do their normal counterparts [77]. At the same time, a frequently backfired motor neuron will discharge less frequently with activation by muscle contraction, although those motor neurons that discharge infrequently will increase their firing rate. These observations are consistent with F-wave studies in deafferented animals [71]. At times, therefore, increased central excitability can result in decreased discharge of larger motor neurons in an F wave due to blockage at the still refractory motor neuron initial segment. Despite this complexity, analyses of F waves have proven a valuable technique for monitoring central motor neuron excitability.

In patients with CNS lesions, the normal relative increased prominence of F waves in resting extensor muscles compared with flexor muscles may be disrupted [111]. After CNS lesions such as strokes, F-wave amplitudes and persistence are decreased acutely in clinically involved limbs when decreased tone and reflexes are common findings [111,147]. Similarly, F waves are absent acutely in patients with spinal shock [52]. F-wave amplitudes and persistence can be decreased by cerebellar stimulation consistent with increased cerebellar inhibitory outflow [148]. By contrast, F-wave persistence and average F amplitudes as well as F/M ratios are increased in patients with “spasticity” [149]. Huge F waves—as large as 75% of M-wave amplitudes—have been found in chronic tetanus [150]. These were associated with a shortened or absent silent period compatible with failure of Renshaw cell inhibition, thereby indirectly supporting a role for Renshaw cell activity in F-wave discharge.

Correlations between F-wave latencies, durations, and amplitudes are also disturbed in patients with motor disorders of central origin [151]. These data suggest that analyses of F waves could be used to define clinically different patterns of abnormal motor system states.

With H reflexes, a knowledgeable use of F waves requires the understanding that these responses originate at the interface between the central and peripheral nervous system. F-wave studies can provide physiologic insight into that interface. F/M amplitude ratios are increased in patients with polyneuropathy as well as spastic hyperreflexia [152]. Log F/M values are normally directly correlated with neuromuscular efficiency as defined by twitch tension/M-wave amplitudes. This relationship is disturbed most prominently in patients with CNS but also in patients with peripheral nerve dysfunction [153].

References


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Needle electromyography
Fundamentals, normal and abnormal patterns

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Nerve conduction studies and needle electromyography (EMG) are the most common electrophysiologic tests utilized to evaluate patients with suspected neuromuscular disorders. Both tests must be individualized, based on the clinical findings and differential diagnosis, and modified as the tests proceed. With needle EMG, almost every muscle in the body can be studied. However, this is neither practical for the electromyographer nor desirable for the patient. For each study, a balance must be reached between studying a sufficient number of muscles to reach or exclude a diagnosis and the patient’s ability to tolerate the exam; most patients tolerate the exam well, with minor discomfort, when performed skillfully.

The needle EMG is the more challenging part of the electrophysiologic exam. Knowledge of anatomy and physiology is required for a successful study, as are sound EMG technique and good patient rapport. Two competing influences make the needle EMG study especially demanding: First, many of the abnormalities on the needle study are subtle. At the same time, however, the range of normal findings is quite large and varies with age and the muscle being studied. Although the basics of the needle study, such as needle placement and recognition of certain types of abnormal spontaneous activity, can usually be learned in a short time, recognition of many of the uncommon and subtle needle EMG findings often take years to master. This
article focuses on the fundamentals of performing the routine needle EMG examination and interpreting the findings.

**Needle EMG examination**

**Needle electrode and equipment**

In addition to the EMG machine, an EMG needle and cable, ground electrode, and gloves are necessary to perform the needle EMG study. The ground electrode is applied to the limb being studied to ensure safety and to suppress noise. Disposable gloves must always be worn to prevent the transmission of blood-borne infections between the patient and the electromyographer. The EMG needle is connected to a cable and then plugged into the EMG machine. Either a concentric or monopolar EMG needle can be used (Fig. 1). When measuring an electrical potential, including the potentials measured during the needle EMG study, voltage is the difference

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Fig. 1. EMG Needle electrodes. Concentric needle (*left*) containing the active (G1) and reference (G2) electrodes. Monopolar needle (*right*) is teflon coated with the exposed tip serving as the active electrode (G1); an additional surface disk electrode is needed as a reference electrode containing the active electrode (G1) and the reference electrode (G2). (*From* Preston DC, Shapiro BE. Electromyography and neuromuscular disorders. Boston: Butterworth-Heinemann; 1998; with permission.)
between an active and reference-recording electrode. The concentric needle contains both the active and reference electrodes. The shaft of the needle serves as the reference electrode; the active electrode is a very small wire that runs through the center of the needle and is exposed at the needle tip. In the monopolar montage, the monopolar needle is Teflon-coated, with its exposed tip serving as the active recording electrode. An additional surface disk electrode is required as the reference electrode.

Both concentric and monopolar needles record electrical signals well from muscle. However, there are small differences between the two types of needle when recording motor-unit action potentials (MUAPs). With a concentric needle, MUAP amplitude is slightly smaller and the major spike rise time shorter than the potential obtained with a monopolar needle. Otherwise, there are no appreciable differences between the two in the recorded waveforms. The concentric needle is easier to use, as it does not require an additional reference electrode. However, the monopolar needle has the advantage of a smaller caliber and sharper point, and may be slightly less painful and easier for patients to tolerate. The major disadvantage of the monopolar needle is the need for an additional reference electrode. Because the reference electrode must be placed close to the active electrode, it must be moved from location to location with each muscle sampled. In addition, because the active electrode is an intramuscular needle and the reference is a surface disk, there is a much greater likelihood of electrode impedance mismatch and increased electrical noise.

Procedure

For each muscle studied, one must first identify the needle insertion point, and instruct the patient on how to properly activate the muscle. Once a muscle has been selected for study, the needle insertion point is located by identifying the proper anatomic landmarks. Second, while palpating for muscle movement, the patient is asked to activate and relax the muscle several times. Once muscle location is properly identified and palpated, the patient is asked to relax; this reduces the level of pain. Inserting a needle into a contracted muscle is much more painful than putting a needle into a relaxed one. Third, the needle is quickly inserted into the muscle, and the patient instructed to activate the muscle slightly, in order to confirm needle location. Sharp MUAPs with minimal contraction indicate a properly inserted needle. If sharp MUAPs are not indicated, the needle should be adjusted. The procedure should be repeated if sharp MUAPs are not indicated. One should not proceed until it is certain the needle has been inserted into the correct muscle.

Once correct needle placement is established, the first part of the examination is to assess insertional and spontaneous activity, with the muscle at rest. This is usually done with the sensitivity set at 50 microvolts (μV) per division, because spontaneous discharges are low amplitude. Five to ten brief insertions are performed looking for increased insertional activity and
spontaneous discharges at rest. Muscle is normally quiet at rest, with the exception of the potentials seen near the endplate zone. When the needle is quickly moved through muscle, there is a brief burst of muscle fiber potentials, known as insertional activity, which typically lasts no longer than 300 milliseconds after the needle has stopped moving. Increased insertional activity is defined as any activity, other than endplate potentials, that lasts longer than 300 milliseconds after brief needle movement. If the activity persists beyond 3 seconds, it is termed spontaneous activity, which can be normal or abnormal.

Once insertional and spontaneous activity has been characterized, the needle is left in place, and the analysis turns to the evaluation of MUAPs. The sensitivity is changed to 200 $\mu$V per division. MUAPs are typically much larger than most abnormal spontaneous activity and therefore require the change in sensitivity. To analyze MUAPs, the patient is asked to slowly and evenly contract the targeted muscle. MUAPs are difficult to interpret in patients with uneven muscle contraction, especially those with a tremor.

With the patient minimally activating the muscle, the needle is gently moved until the MUAPs become sharp, that is, louder and crisper. As the needle moves closer to the MUAP, there is less intervening tissue to attenuate and filter the potential. Thus, the closer the needle to the MUAP, the higher the amplitude and the shorter the major spike rise time. It is at this point that the MUAP can be properly evaluated. MUAPs are assessed for duration, amplitude, and number of phases (see later). In addition, the number of MUAPs and their relationship to the firing frequency (recruitment and activation pattern) are also determined. As the patient slowly increases force, both the firing frequency and the number of MUAPs normally increase. After MUAPs are assessed at one location, the needle is moved slightly within the muscle to a different site, and the process is repeated. Several different MUAPs are analyzed at each site.

**Insertional and spontaneous activity**

**Insertional activity**

The needle EMG examination of each muscle begins with the assessment of insertional activity. When a needle is quickly moved through muscle, muscle fibers depolarize in a normal brief burst for several hundred milliseconds (ms), known as *normal insertional activity*. At least four to six brief needle movements are made in four quadrants of each muscle to assess insertional activity. Needle movement resulting in any abnormal waveform that lasts longer than 300 ms indicates increased insertional activity. Increased insertional activity may be seen in both neuropathic and myopathic conditions. In rare conditions, where muscle has been replaced by fat and fibrous connective tissue, insertional activity may actually be decreased.
The role of spontaneous activity in the needle EMG examination

The ability to recognize and identify abnormal spontaneous activity is one of the most important parts of the needle EMG examination. The presence of abnormal spontaneous activity on an EMG can yield several key pieces of information. First, the distribution of abnormal spontaneous activity helps determine the neuroanatomic localization of the lesion. For example, in a radiculopathy, denervation potentials are restricted to muscles in the same myotome. Second, the type of spontaneous activity often provides specific diagnostic information. Certain types of spontaneous activity are associated with specific disorders. For example, myotonic discharges are seen only in a few conditions, such as myotonic dystrophy or myotonia congenita. Third, the degree or amount of spontaneous activity often helps to assess the severity of the lesion. Finally, the presence of abnormal spontaneous activity might yield information regarding the time course of the lesion. For example, in a radiculopathy, several weeks must pass before fibrillation potentials are seen in the limbs.

Analysis of spontaneous activity

The ability to recognize spontaneous activity improves with experience. However, careful analysis of any spontaneous waveform can usually lead to its correct identification. Each waveform should be analyzed for morphology, stability, and firing characteristics [1]. Practically, every spontaneous waveform can be properly identified through use of this information.

Morphology

The source of a spontaneous discharge can often be discerned by its morphology, including the size and shape of the potential and its initial deflection (Fig. 2) [1]. The source generators that must be differentiated include: neuromuscular junctions (NMJ), single muscle fibers, terminal axon twigs, motor neuron and axons, and linked multiple muscle fibers.

At the NMJ, miniature endplate potentials (mepps) occur spontaneously. They result from the normal spontaneous exocytosis of individual quanta of acetylcholine traveling across the neuromuscular junction, leading to a non-propagated, subthreshold endplate potential. If the EMG needle is near the endplate zone, mepps can often be recorded [2,3]. They have a distinctive small amplitude and monophasic negative morphology.

When a muscle fiber depolarizes to threshold, a muscle-fiber action potential (MFAP) is created. An MFAP can assume one of two basic morphologies, either a brief spike or a positive wave. The brief spike is typically from 1 to 5 milliseconds in duration, biphasic or triphasic, with low amplitude (typically, 10–100 μV). Brief spike morphology is commonly seen when muscle fibers depolarize spontaneously (eg, denervation), but can also occur through individual terminal axonal twig depolarizing followed by
propagation across the NMJ, which creates an MFAP. Attention to the initial deflection of the potential and whether the brief spike is biphasic or triphasic can often help distinguish between the two (Fig. 3). If depolarization begins under the recording needle electrode, a biphasic potential is seen, with an initial negative peak followed by a short positive phase. This signifies that the needle is at the endplate zone, where the depolarization begins, and is usually the result of the EMG needle irritating terminal nerve twigs near the endplate zone. Nerve twig action potential leads to an MFAP known as an endplate spike, which is a normal finding (see later). Otherwise, brief spikes occur from spontaneous depolarization of muscle fibers and are

Fig. 2. Spontaneous waveform generators and morphologies. (A) Neuromuscular junction (NMJ). Miniature endplate potential (monophasic negative). (B) Terminal axon. Brief spike (initial negative, diphasic). (C) Muscle fiber action potential—brief spike morphology (initial positive, triphasic). (D) Muscle fiber action potential—brief spike morphology (initial positive, slow negative). (E) Multiple muscle fibers (linked, multiple brief spikes). (F) Motor neuron/axon—motor-unit action potential. (Note the longer duration and higher amplitude compared to the muscle fiber potentials A–E.) (Adapted from Preston DC, Shapiro BE. Electromyography and neuromuscular disorders. Boston: Butterworth-Heinemann; 1998; with permission.)
associated with an initial positive, usually triphasic morphology, which is an abnormal finding. When a depolarization begins at a distance from the needle, there is an initial positive deflection as it moves toward the needle, followed by a negative phase as it moves beneath the needle, and then a final positive deflection as it moves away from the needle.

In addition to the brief spike, an MFAP can also assume a positive wave, biphasic morphology with an initial brief positive phase followed by a long negative phase. Both positive waves and initial positive, triphasic brief spikes are most often seen as denervating potentials, which are known as positive sharp waves and fibrillation potentials, respectively. However, myotonic discharges, which also originate in muscle fibers, have the same basic morphology as denervating potentials—either brief spikes or positive waves.
This emphasizes the important concept that morphology alone cannot be used to identify a potential. Although the morphology of a potential can usually be used to identify its source generator, additional information regarding stability and firing characteristics is needed to fully characterize and identify the potential (see later).

The next major category of spontaneous discharges arises from motor neurons or their axons. Any discharge that occurs as a result of the spontaneous depolarization of a motor neuron or its axon (prior to its terminal branches) leads to a potential with the morphology of a motor unit, known as a motor-unit action potential (MUAP). Spontaneous discharges generated by the motor neuron/axon include fasciculations, tetany, myokymic discharges, and neuromyotonic discharges and cramps, which all lie along the spectrum of abnormal spontaneous MUAPs. They can be differentiated from each other, however, by their stability and firing characteristics (see later). If the motor unit is normal, then the MUAP morphology will typically have two to four phases, duration of 5–15 milliseconds, and variable amplitude depending on the needle position. If the motor unit is pathologic, the number of phases, the duration, and the amplitude may change. Differentiating an MUAP from a single MFAP is usually straightforward and can typically be done quite simply by analyzing a waveform’s duration and amplitude.

The last distinctive waveform that must be recognized is that of time-linked individual muscle fibers, which occurs in complex repetitive discharges. Although a MUAP also contains many individual muscle fibers, the muscle fibers in a motor unit fire more or less synchronously, and in almost every situation summate to create a large potential, 5 to 15 milliseconds in duration. In contrast, multiple muscle fibers in a complex repetitive discharge fire consecutively, and are usually discernible as individual spikes that are time-linked together.

**Stability**

Assessment of the stability of any spontaneous waveform is essential. Most spontaneous potentials are relatively stable in their morphology. However, some waveforms may wax and wane, decrease, or change abruptly. MFAPs that wax and wane in amplitude are characteristically seen in myotonia. A marked decrement of a MUAP occurs in neuromyotonic discharges. Complex repetitive discharges are typically stable, but if additional loops or circuits drop in or out, the morphology may change in distinct or quantal jumps.

**Firing characteristics**

After assessing the potential’s morphology and stability, attention turns to its firing characteristics, including the discharge pattern and firing rate. One should note if the pattern is regular or irregular. Many types of irregular firing may be seen, including sputtering (endplate spikes), waxing/waning
(myotonic discharges), waxing (neuromyotonic discharges), and bursting (tetany and myokymic discharges). Equally important is the approximate firing rate. For instance, some potential typically fire slowly (eg, fasciculations), whereas others fire quickly (eg, 150–300 Hertz (Hz), in the case of neuromyotonic discharges.

Table 1 summarizes the morphology, stability, and firing characteristics of the common spontaneous potentials seen during the needle EMG.

**Spontaneous activity generated near the neuromuscular junction**

Muscle is normally electrically silent outside of the endplate zone. All spontaneous activity is abnormal with the important exception of potentials that occur in the endplate region (ie, the NMJ). Muscle endplate is usually found near the center of the muscle belly and is often encountered during routine EMG [4]. Patients frequently perceive a deep burning sensation when the needle is placed in the endplate region. Two types of spontaneous activity occur: endplate noise and endplate spikes. It is essential to properly identify these potentials (described in the following paragraphs), so as not to mistake them for abnormal spontaneous activity.

**Endplate noise (Fig. 4)** Endplate noise potentials are low-amplitude, monophasic, negative potentials that fire irregularly at 20 to 40 Hz, have a characteristic sea shell sound on EMG, physiologically represent mepps, and are recognized by their characteristic shape and sound and frequent association with endplate spikes.

**Endplate spikes (Fig. 4)** Endplate spikes are brief spikes that fire irregularly up to a frequency of 50 Hz. Endplate spikes are biphasic with an initial negative deflection, reflecting that the needle is at the site where the action potential is generated, and are usually seen along with endplate noise [5]. They are thought to occur as a result of needle-induced irritation of the terminal nerve twigs, which then causes nerve-twig action potentials and then MFAPs. They have a cracking, buzzing, or sputtering sound on EMG. The key features that differentiate endplate spikes from fibrillation potentials, which are also brief spikes, are their initial negative deflection and their highly irregular firing rate.

**Spontaneous activity generated from muscle fibers**

**Fibrillation potentials (Fig. 5)** Fibrillation potentials are electrophysiologic markers of denervation [6,7]. Although they are typically associated with neurogenic disorders, they may also be seen in muscle disorders (especially inflammatory myopathies and muscular dystrophies), and rarely in severe diseases of the NMJ (especially botulism). Fibrillation potentials are recognized as brief spikes with an
<table>
<thead>
<tr>
<th>Potential</th>
<th>Source generator/morphology</th>
<th>Sound on loudspeaker</th>
<th>Stability</th>
<th>Firing rate</th>
<th>Firing pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endplate noise</td>
<td>mepp (monophasic negative)</td>
<td>Sea shell</td>
<td>—</td>
<td>20–40 Hz</td>
<td>Irregular (hissing)</td>
</tr>
<tr>
<td>Endplate spike</td>
<td>Muscle fiber initiated by terminal axonal twig (brief spike, diphasic, initial negative)</td>
<td>Sputtering fat in a frying pan</td>
<td>—</td>
<td>5–50 Hz</td>
<td>Irregular (sputtering)</td>
</tr>
<tr>
<td>Fibrillation</td>
<td>Muscle fiber (brief spike, diphasic or triphasic, initial positive)</td>
<td>Rain on a tin roof or tick-tock of a clock</td>
<td>Stable</td>
<td>0.5–10 Hz (occasionally up to 30 Hz)</td>
<td>Regular</td>
</tr>
<tr>
<td>Positive sharp wave</td>
<td>Muscle fiber (diphasic, initial positive, slow negative)</td>
<td>Dull pops, rain on a tin roof, or tick-tock of a clock</td>
<td>Stable</td>
<td>0.5–10 Hz (occasionally up to 30 Hz)</td>
<td>Regular</td>
</tr>
<tr>
<td>Myotonia</td>
<td>Muscle fiber (brief spike, initial positive, or positive wave)</td>
<td>Revving engine</td>
<td>Waxing/waning</td>
<td>20–150 Hz</td>
<td>Waxing/waning</td>
</tr>
<tr>
<td>CRD</td>
<td>Multiple muscle fibers time-linked together</td>
<td>Machine</td>
<td>Usually stable, may change in discrete jumps</td>
<td>5–100 Hz</td>
<td>Perfectly regular (unless overdriven)</td>
</tr>
<tr>
<td>Fasciculation</td>
<td>Motor unit (motor neuron/axon)</td>
<td>Corn popping</td>
<td>—</td>
<td>Low (0.1–10 Hz)</td>
<td>Irregular</td>
</tr>
<tr>
<td>Myokymia</td>
<td>Motor unit (motor neuron/axon)</td>
<td>Marching soldiers</td>
<td>—</td>
<td>1–5 Hz (interburst) 5–60 Hz (intraburst)</td>
<td>Bursting</td>
</tr>
<tr>
<td>Cramp</td>
<td>Motor unit (motor neuron/axon)</td>
<td>—</td>
<td>—</td>
<td>High (20–150 Hz)</td>
<td>Interference pattern or several individual units</td>
</tr>
<tr>
<td>Neuromyotonia</td>
<td>Motor unit (motor neuron/axon)</td>
<td>Pinging</td>
<td>Decrementing</td>
<td>Very high (150–250 Hz)</td>
<td>Waning</td>
</tr>
</tbody>
</table>

Abbreviations: CRD, complex repetitive discharge; mepp, miniature endplate potential.

(Adapted from: Preston DC, Shapiro BE. Electromyography and neuromuscular disorders. Boston: Butterworth-Heinemann; 1998; with permission.)
initial positive deflection, duration of 1 to 5 milliseconds, and low amplitude (typically, 10–100 μV). Their firing pattern is regular, with a rate usually of 0.5 to 10 Hz. In the most chronic conditions (> 6–12 mo), fibrillation potentials may become very small (<10 μV in amplitude). On EMG, single fibrillation potentials often sound like rain on the roof. Although fibrillation potentials fire at a regular rate, they may slow down gradually over several seconds before stopping.

**Positive sharp waves (Fig. 5)**

Positive sharp waves have the same significance as fibrillation potentials: they occur in denervation and represent spontaneous depolarizations of

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Fig. 4. Endplate noise (*top traces*) and endplate spikes (*bottom traces*). (*Adapted from* Preston DC, Shapiro BE. Electromyography and neuromuscular disorders. Boston: Butterworth-Heinemann; 1998; with permission.)
single muscle fibers. Positive sharp waves have a brief initial positivity followed by a long negative phase, and sound like a dull pop. The amplitude is variable (usually 10–100 μV, occasionally up to 3 mV). Like fibrillation potentials, their firing pattern is regular. This is a key point, because voluntary MUAPs at a distance occasionally have positive wave morphology but can be differentiated by their lack of a regular firing pattern. Positive sharp waves are usually accompanied by fibrillation potentials but may be seen alone, sometimes early in denervation. The mechanism by which MFAPs take on two distinctive morphologies, either a brief spike or a positive wave, involves the actual EMG needle (Fig. 6)[8]. Probably, the needle mechanically
deforms an irritable muscle fiber, thereby rendering part of the membrane electrically inexcitable. When an action potential arises at a distance down the fiber, it can propagate toward the area deformed by the needle but not beyond it, resulting in the positive wave morphology. Supporting this hypothesis is that fibrillation potentials can change to positive sharp waves with needle movement.

Positive sharp waves and fibrillation potentials conventionally are graded from 0 to 4 (0, none present; +1, persistent single trains of potentials [>2–3 s] in at least two areas; +2, moderate numbers of potentials in three or more areas; +3, many potentials in all areas; +4, full interference pattern of potentials).

**Complex repetitive discharges**

Complex repetitive discharges (CRDs) result from the depolarization of a single muscle fiber followed by ephaptic spread to adjacent denervated fibers (Fig. 7) [9–11]. If a circus movement is created whereby the original pacemaker muscle fiber is reactivated, a recurrent discharge develops. These
discharges usually occur spontaneously or after needle movement. CRDs are recognized on EMG as high frequency (typically 20–150 Hz), multiserated, repetitive discharges with an abrupt onset and termination (Fig. 8). Occasionally, individual phases or additional loops drop in and out, creating an abrupt change in frequency and sound. In rare cases, if the pacemaker is overdriven by another discharge, the CRD may be irregular. As soon as the overdriving pacemaker frequency falls below the inherent frequency of the CRD, the CRD again becomes regular.

CRDs are identical in morphology from one discharge to the next, creating a machine-like sound on EMG. They occur in both chronic neuropathic and myopathic disorders and may arise in any setting where denervated fibers lie adjacent to one another. In neuropathic diseases, this occurs where denervation is followed by reinnervation and subsequent denervation (ie, the pathologic equivalent of grouped atrophy). This situation may also occur in myopathic disorders associated with denervation/reinnervation (eg, inflammatory myopathies) or with muscle fiber splitting.

**Myotonic discharges**

A myotonic discharge is the spontaneous discharge of a muscle fiber, similar to fibrillation potentials and positive sharp waves. However, it is differentiated from fibrillation potentials and positive sharp waves by the waxing and waning of both amplitude and frequency (Fig. 9) [12]. The firing rate
is generally between 20 to 150 Hz. An individual myotonic potential may have either a positive wave or brief spike morphology (identifying the source generator as a muscle fiber) and the repetitive nature. CRD triggered on a delay line. The bottom trace shows all traces superimposed. Note the repetitive nature of a CRD. When superimposed, there is little or no jitter between successive potentials. (From Preston DC, Shapiro BE. Electromyography and neuromuscular disorders. Boston: Butterworth-Heinemann; 1998; with permission.)
Spontaneous activity generated from motor neurons

Fasciculation potentials (Fig. 10)

A fasciculation is a single, spontaneous, involuntary discharge of an individual motor unit [7]. Unlike a voluntary motor unit, fasciculations generally fire slowly and irregularly, usually between 0.1 to 10 Hz, whereas voluntary MUAPs fire initially at 4 to 5 Hz. The source generator is the motor neuron or its axon, prior to its terminal branches. On EMG, fasciculations usually have the morphology of simple MUAPs, or can be complex and large if they represent pathologic motor units. Despite the association of fasciculations with diseases of the anterior horn cell, the actual site of origin of most fasciculations is distal in the axon [13].

Clinically, fasciculations are recognized as individual brief twitches that seldom result in significant movement of a joint. Fasciculations are associated with numerous disease processes affecting the lower motor neuron, which amyotrophic lateral sclerosis is the most well known. However, fasciculations can be seen in many other disorders, including radiculopathies, polyneuropathies, and entrapment neuropathies. In addition, most normal individuals have occasional fasciculations, so-called benign fasciculations.

Differentiating benign from malignant fasciculations on a clinical basis is difficult. Benign fasciculations are not associated with muscle weakness, wasting, or any abnormality of reflexes. In general, benign fasciculations tend to fire faster and affect the same site repetitively (eg, eyelid twitching), as opposed to fasciculations in pathologic conditions that tend to be more random.

Doublets, triplets, multiplets (Fig. 10)

Spontaneous MUAPs that fire in groups of two, three, or multiple potentials are known as doublets, triplets, and multiplets, respectively. These potentials fundamentally have the same significance as fasciculation potentials: they represent the spontaneous depolarization of a motor unit or its axon. Doublets, triplets, and multiplets can be seen in any situation where fasciculation potentials occur (ie, neuropathic conditions), but are also characteristically seen in hypocalcemia. If hypocalcemia results in tetany, the distal muscles are predominantly affected, with involuntary spasms affecting the hands and feet (carpopedal spasms). In hands, a characteristic posture
Fig. 10. Fasciculations (top trace) and doubles (bottom trace).
develops: adduction of the thumb and fingers, extension of the interphalangeal joints, and flexion of the metacarpal-phalangeal joints and wrist. On needle EMG, doublets, triplets, and multiplets are characteristically seen during tetany.

**Myokymic discharges**

Myokymic discharges are bursting, repetitive discharges of the same MUAP (Fig. 11). The firing frequency within the burst is typically 5 to 60 Hz, with the number of potentials within a burst varying and sometimes changing from burst to burst. The firing frequency between bursts is much slower, typically less than 2 Hz, and produces a marching sound on EMG. The bursting pattern of a myokymic discharge is more easily recognized if the sweep is changed to a longer sweep speed. Myokymic discharges are thought to arise from spontaneous depolarization or ephaptic transmission along demyelinated segments of nerve.

Clinically, myokymia is recognized as continuous involuntary quivering, rippling, or undulating movement of muscle. The finding of myokymia on EMG narrows the differential diagnosis to a limited set of disorders [1,14] (Display Box 1).

**Cramp discharges**

Clinically, cramps are painful, involuntary contractions of muscle, which tend to occur when a muscle is in the shortened position and contracting. Electrically, cramps are high-frequency discharges of MUAPs, thus marking them as a nerve rather than as a primary muscle phenomenon [1,15,16]. EMG shows either a full interference pattern of MUAPs with a normal morphology, or several MUAPs firing repetitively and sometimes irregularly at

![Fig. 11. Myokymic discharges (rastered traces). Note the high-frequency pattern within the burst and the slow frequency between the bursts.](image-url)
high frequencies (usually 40–60 Hz; Fig. 12). Cramps may be benign (eg, nocturnal calf cramps, postexercise cramps) or can be associated with a wide number of neuropathic, endocrinologic, and metabolic conditions. Clinically, cramps may resemble the contractures that occur in several of the metabolic muscle diseases. However, whereas the needle EMG of a cramp consists of rapidly firing MUAPs, a contracture is typically electrically silent.

Display Box 1
Disorders commonly associated with myokymic discharges

Radiation injury (usually brachial plexopathy)
Guillain-Barré syndrome (facial)
Multiple sclerosis (facial)
Pontine tumors (facial)
Hypocalcemia
Timber rattlesnake envenomation

Occasionally seen in
Guillain-Barré syndrome (limbs)
Chronic inflammatory demyelinating polyneuropathy
Nerve entrapments
Radiculopathy


Voluntary Contraction

![Cramp discharge](image)

---

Fig. 12. Cramp discharge. *(Top trace)* The subject is voluntarily contracting strongly, which is followed by a cramp discharge. *(Bottom trace)* During the subject’s cramp, EMG shows one or several motor units firing repetitively and sometimes irregularly at high frequencies (usually 40–60 Hz). *(From* Preston DC, Shapiro BE. EMG waveforms—video companion to electromyography and neuromuscular disorders. Boston: Butterworth-Heinemann; 1999; with permission.*)
Neuromyotonic discharges

Neuromyotonic discharges are high-frequency (150–250 Hz) repetitive discharges of a single MUAP [17], which marks them as a neuropathic phenomenon. They characteristically wane in amplitude and frequency, which results in a pinging sound on EMG (Fig. 13). These discharges are rare and are seen either in chronic motor neuron diseases (e.g., poliomyelitis and adult spinal muscular atrophy) or in syndromes of continuous motor-unit activity (CMUA). The nomenclature of the syndromes of CMUA is complicated. These disorders have been described as Isaac’s syndrome, neuromyotonia, pseudomyotonia, neurotonia, normocalcemic tetany, and continuous muscle-fiber or motor-unit activity [18]. They share clinical features of generalized stiffness, hyperhidrosis, delayed muscle relaxation, fasciculations, and myokymia [19–21]. Some cases are familial. However, there is increasing evidence that many cases of acquired neuromyotonia or CMUA may have an autoimmune etiology, with the target antigen being peripheral nerve potassium channels [22].

The delay in relaxation and improvement with repetitive use seen in neuromyotonia may be difficult to distinguish clinically from myotonia, which originates in muscle. Electrically, however, the neuromyotonic syndromes are easily differentiated from the muscle myotonias. Whereas the myotonic syndromes are associated with the spontaneous discharges of muscle fibers, the neuromyotonic disorders are associated with involuntary spontaneous discharges of motor units. Other motor neuron/axon discharges often

![Fig. 13. Neuromyotonic discharges. Enlarged section of top trace shows change in sweep speed which identifies each potential as the same motor unit. (From Preston DC, Shapiro BE. Electromyography and neuromuscular disorders. Boston: Butterworth-Heinemann; 1998; with permission.)](image-url)
accompany neuromyotonic discharges, especially fasciculations and myokymic discharges.

Voluntary MUAPs

Following the assessment of insertional and spontaneous activity, the needle EMG examination moves on to the evaluation of voluntary MUAPs. Similar to the analysis of spontaneous activity, MUAPs are assessed for morphology, stability, and firing characteristics. The pattern of MUAP abnormalities usually allows a determination of whether a disorder is primarily neuropathic or myopathic, and often helps determine the time course (acute versus chronic) and severity of the lesion.

Physiology

The basic component of the peripheral nervous system is the motor unit, defined as an individual motor neuron, its axon, and associated neuromuscular junctions and muscle fibers [23]. The extracellular needle EMG recording of a motor unit is the MUAP [5,24–26]. The number of muscle fibers per motor unit varies greatly, from 5 to 10 in laryngeal muscles to hundreds in the soleus. The territory of a motor unit usually ranges from 5 to 10 mm in adults, with many motor-unit territories overlapping with one another. Because of this overlap, two muscle fibers from the same motor unit rarely lie adjacent to each other. Transverse motor-unit territory increases greatly with age, doubling from birth to adulthood, mostly due to the increase in individual muscle fiber size.

When a motor neuron depolarizes to threshold, a nerve action potential is generated and propagates down the axon [27]. Under normal circumstances, this results in all muscle fibers of the motor unit being activated and depolarizing more or less simultaneously. Any variability between muscle fiber depolarization times is due to differences in the length of the terminal axons and NMJ transmission times.

The size principle governs many of the properties of motor units [28]. The size of the motor neuron is directly related to the following: (1) the size of the axon, (2) the thickness of the myelin sheath, (3) the conduction velocity of the axon, (4) the threshold to depolarization, and (5) the metabolic type of muscle fibers that are innervated. The larger motor neurons have larger axons, with the thickest myelin sheath (ie, fastest conduction velocity), and the highest threshold to depolarization and connections to type II, fast-twitch muscle fibers. Conversely, the smaller motor units have smaller axons, less myelin sheath, slower conduction velocity, a lower threshold to depolarization, and, in general, connections to type I, slow-twitch muscle fibers. Thus, with voluntary contraction, the smallest motor units with the lower thresholds fire first. As contraction increases, progressively larger
motor units begin to fire. The largest type II motor units fire with maximum contraction. During routine needle EMG, most MUAPs analyzed are the smaller, low-threshold motor units that innervate type I muscle fibers. (Note: this explains the lack of EMG findings in steroid myopathy, which characteristically affects type II fibers.)

During the needle EMG examination, each MUAP recorded represents the extracellular compound potential of the muscle fibers of a motor unit, weighted heavily toward the fibers nearest to the needle [29]. A MUAP amplitude recorded just outside a muscle membrane is 1/10th to 1/100th of the actual transmembrane potential, and decreases rapidly as the distance between the needle and the membrane increases [30]. The classification of a MUAP as normal, neuropathic, or myopathic rests on no single finding. MUAPs must be assessed for morphology (duration, polyphasia, amplitude), stability, and firing characteristics before any conclusions can be reached.

Normal findings

Morphology

For every muscle, MUAP morphology is assessed for duration, amplitude, and number of phases (Fig. 14). However, there is a wide range of normal motor-unit morphology, with large, medium, and small motor units present within each muscle (Fig. 15). Therefore, to determine normal versus abnormal, the mean duration, amplitude, and number of phases are compared with a set of normal values for that particular muscle and age group [16,27]. MUAP morphology also varies depending on the muscle being studied and the patient’s age (Table 2). This is found most consistently for MUAP duration. In general, MUAPs in proximal muscles tend to be shorter in duration than those in more distal muscles. MUAP size in adults is larger than in children, primarily due to an increase in the size of muscle fibers during development. In addition, MUAP size is generally larger in older individuals, probably because of drop-out of motor units from the normal effects of aging [24].

Duration. MUAP duration reflects the number of muscle fibers within a motor unit. Typical MUAP duration is 5 to 15 milliseconds [5,25]. Duration is defined as the time from the initial deflection from baseline to the final return of the MUAP to baseline (see Fig. 14). It depends primarily on the number of muscle fibers within the motor unit and the dispersion of their depolarizations over time. Duration lengthens as the number of fibers and the territory of a motor unit increases; it varies directly with age, inversely with temperature, and depends on the individual muscle being studied. Proximal and cranial muscles have shorter duration MUAPs. When performing EMG, it is often more rewarding to listen to the potential than to see it. This is especially true when evaluating MUAP duration, as duration correlates well with pitch. Long-duration MUAPs (low frequencies)
sound dull and thuddy, and short-duration MUAPs (higher frequencies) sound crisp and sharp.

**Amplitude.** MUAP amplitude varies widely among normals. Most MUAPs have an amplitude greater than 100 μV and less than 2 mV. Amplitude is generally measured from peak to peak of the MUAP (see Fig. 14). Unlike duration, most muscle fibers of a motor unit contribute little to the amplitude [26,30,31]. MUAP amplitude reflects only those few fibers nearest to the needle [29]. Several factors are associated with increased amplitude, including the following: (1) the proximity of the needle to the motor unit, (2) increased number of muscle fibers in a motor unit, (3) increased diameter of muscle fibers (i.e., muscle fiber hypertrophy), and (4) more synchronized firing of the muscle fibers. The amplitude of MUAPs is correlated not with pitch but with the volume, when listening to the EMG.

*Polyphasia/serrations/satellite potentials.* Polyphasia is a measure of synchrony (i.e., how well muscle fibers within a motor unit fire at the same time) [24]. This is a nonspecific measure and may be abnormal in myopathic and
neuropathic disorders. The number of phases can easily be calculated by adding 1 to the number of baseline crossings of the MUAP (see Fig. 14). Normally, MUAPs have two, three, or four phases. However, up to 10% of the MUAPs in a muscle may have increased polyphasia, which is considered normal. Note that in the deltoid, up to 25% polyphasia may be normal. Increased polyphasia beyond 10% in most muscles and 25% in the deltoid is abnormal. Polyphasic MUAPs have a high-frequency clicking sound on EMG. Serrations (or turns) are defined as a change in the direction of the potential that does not subsequently cross the baseline. Increased polyphasia and serrations have similar implications, indicating less synchronous firing of muscle fibers within a motor unit. Often, a serration can be changed into an additional phase with needle movement. Satellite potentials (or linked potentials, parasite potentials) are seen in early reinnervation. Following denervation, collateral sprouts from adjacent intact motor units often reinnervate muscle fibers. The newly formed sprout is often small, thinly myelinated, and, therefore, slowly conducting. Because of the slow conduction time and increased distance, reinnervated muscle fibers are seen as time-locked potentials that trail the main MUAP. These satellite potentials are extremely unstable (see later) and may vary slightly in their firing rate, or may block and not fire at all. Over time, the sprout matures and the thickness of the myelin, and consequently the conduction velocity, increases. The satellite

Fig. 15. Range of normal motor-unit action potential (MUAP) duration and amplitude. Histogram of MUAP duration and amplitude in the biceps brachii of a normal subject. Note: both MUAP duration and amplitude vary markedly in normal muscles with small, medium, and large units in the same muscle. MUAP duration or amplitude should not be classified as abnormal based on one or two MUAPs, but requires a mean of many units. (From Buchthal F, Guld C, Rosenfalck P. Acta Physiol Scand 1954; with permission.)
<table>
<thead>
<tr>
<th>Age, yrs</th>
<th>Deltoid</th>
<th>Biceps</th>
<th>Triceps</th>
<th>Thenar</th>
<th>ADM</th>
<th>Quad, BF</th>
<th>Gastroc</th>
<th>Tib ant</th>
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<tr>
<td>0–4</td>
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<td>6.4–8.2</td>
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<td>8.3–10.6</td>
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<td>5–9</td>
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<td>6.5–8.8</td>
<td>7.3–9.9</td>
<td>7.2–9.8</td>
<td>8.4–11.4</td>
<td>7.3–9.9</td>
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<td>9.4–12.2</td>
<td>10.3–13.5</td>
<td>6.0–7.9</td>
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</table>

**Abbreviations:** ADM, abductor digiti minimi; BF, biceps femoris; EDB, Extensor digitorum brevis; MUAP, motor-unit action potential; Quad, quadriceps; Tib ant, tibialis anterior.

(From Buchthal F, Rosenfalck P. Action potential parameters in different human muscles. Acta Psych Neurol Scand, copyright 1955, Munskaard International Publishers, Copenhagen, Denmark; with permission.)
potential then fires more closely to the main potential and will ultimately become an additional phase or serration within the main complex.

**Stability**

MUAPs are usually stable in morphology from potential to potential. This stability is because each time a nerve action potential is generated, there is normally effective transmission across the NMJ, and all muscle fibers of the motor unit fire. If there is impaired NMJ transmission, unstable MUAPs may result. Unstable MUAPs occur when individual muscle fibers are either blocked or come to action potential at varying intervals, leading to an MUAP that changes in configuration from impulse to impulse. Either the amplitude and/or number of phases or serrations changes between potentials. Although unstable MUAPs always indicate unstable NMJs, they may occur not only in primary disorders of the NMJ (eg, myasthenia gravis), but are often seen as a secondary phenomenon in neuropathic and myopathic disorders. Any disorder associated with denervation may demonstrate unstable MUAPs.

**Firing pattern**

One of the most difficult tasks for the electromyographer is the assessment of firing pattern and its relationship to the number of MUAPs. MUAPs normally fire in a semi-rhythmic pattern—that is, there is slight variation in the time interval between the same consecutive MUAP (Fig. 16). This unique firing pattern helps identify the potential as an MUAP under voluntary control. When an individual is asked to slowly activate a muscle, a single motor unit begins firing semi-rhythmically at 4 to 5 Hz [32,33]. As force is increased, the first motor unit increases its firing rate followed by a second motor unit firing, and so forth. This process continues, with the firing rate increasing and additional motor units being recruited, as force is increased. Normally, the ratio of firing frequency to the number of different MUAPs firing is approximately 5 to 1 [2]. Thus, when the firing frequency of the first MUAP reaches 10 Hz, a second MUAP should begin to fire; by 15 Hz, a third unit should fire, and so forth. During maximal contraction, multiple MUAPs normally overlap and create an interference pattern in which it is difficult to discern individual MUAPs. For most muscles, the maximal firing frequency is 30 to 50 Hz. Important exceptions include quick ballistic contractions, in which the firing frequency may transiently reach 100 Hz, and muscles that are predominantly slow twitch (eg, soleus), in which the maximal firing frequency is approximately 15 Hz.

When assessing MUAP firing pattern, two key parameters must be determined: activation and recruitment. **Activation** refers to firing rate and represents a central process. Poor activation (ie, low firing rate) may be seen in diseases of the central nervous system (CNS) or as a manifestation of pain, poor cooperation, or functional disorders. **Recruitment** refers to the ability to add motor units as the firing rate increases (Fig. 17). Recruitment is
reduced primarily in neurogenic diseases, and rarely, in severe endstage myopathy. The key question to answer in assessing recruitment is: Are the number of different MUAPs firing appropriate for the firing rate? Or, is the ratio of firing rate to number of MUAPs approximately 5 to 1? It is essential to appreciate that an incomplete interference pattern may be due to either poor activation or poor recruitment (Fig. 18). Many electromyographers judge recruitment only during maximum contraction, by examining the interference pattern. However, recruitment is more easily evaluated during

Fig. 16. Motor-unit action potential (MUAP) firing pattern. (Top trace) Single voluntary MUAP firing at ≈6 Hz. Note variation in interpotential intervals. (Bottom traces) Single voluntary MUAP placed on a delay line and rastered. First potential of each trace triggers the sweep. Note the variation between firing time of the next consecutive MUAP. The pattern is not quite regular (ie, semi-rhythmic). This firing pattern is only seen with voluntarily activated MUAPs. (From Preston DC, Shapiro BE. Electromyography and neuromuscular disorders. Boston: Butterworth-Heinemann; 1998; with permission.)
moderate levels of contraction. For instance, if only one MUAP is firing at 15 to 20 Hz (medium level of activation), then recruitment is decreased, regardless of the interference pattern. There is no need to increase the firing rate using maximal contraction, in order to assess recruitment. Furthermore, maximal contraction with the EMG needle in the muscle is often perceived as more painful and is best avoided or minimized.

The final concept to understand when assessing MUAP firing pattern is that of early recruitment. In diseases where individual muscle fibers drop out from a motor unit (eg, myopathies, periodic paralysis or NMJ diseases with block), the motor unit becomes smaller and subsequently can generate less force. Because each motor unit generates less force, many motor units must fire to generate even a small amount of force. This is known as early recruitment, which refers to the inappropriate firing of many motor units to generate a small amount of force. On the screen, many MUAPs appear to fire almost simultaneously when the patient is asked to contract the muscle.
minimally. Usually, only the electromyographer who is performing the study can assess early recruitment, since this judgement requires knowledge of how much force is being generated.

**Patterns of MUAP abnormalities**

The morphology and firing pattern of the MUAP can usually discriminate among the various disorders affecting the motor unit. No single parameter identifies an MUAP as myopathic, neuropathic, or associated with an NMJ disorder. Rather, specific patterns of abnormalities in MUAP morphology and firing pattern reflect whether the underlying disorder is (1) acute, chronic, or end stage; (2) neuropathic, myopathic, or associated with an NMJ transmission defect; or (3) if neuropathic, whether the primary pathophysiology is axonal loss or demyelination (Table 3).

**Acute neuropathic disorders—axonal loss**

Following an acute axonal injury, Wallerian degeneration occurs within the first week, followed by denervation of muscle fibers of the involved motor units [34]. Reinnervation normally occurs as surviving nearby axons...
form sprouts, which grow and eventually reinnervate denervated fibers. When this occurs, the number of muscle fibers in the reinnervated MUAP is larger than normal, leading to an MUAP with increased duration, amplitude, and number of phases. However, this process takes time, usually many weeks to months. In the acute setting, MUAP morphology remains normal. The only abnormality seen on EMG in an acute neuropathic lesion is a decreased recruitment pattern in weak muscles, due to loss of motor units. The acute neuropathic pattern associated with axonal loss characteristically occurs in the first several weeks following trauma, compression, or nerve infarction. The only other situation in which a similar needle EMG pattern occurs is with a relatively pure demyelinating lesion with conduction block (see later).

Chronic neuropathic disorders—axonal loss

Following axonal loss and denervation, the process of reinnervation occurs by one of two mechanisms. If there has been complete denervation, then the only possible mechanism for reinnervation is through axonal regrowth from the point of injury (see later discussion on early reinnervation following severe or complete denervation). In contrast, if there is partial or gradual denervation, which is the more common scenario, reinnervation usually occurs through collateral sprouting by adjacent surviving motor

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### Table 3

MUAP patterns and pathophysiology

<table>
<thead>
<tr>
<th>MUAP morphology</th>
<th>MUAP firing pattern</th>
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<tbody>
<tr>
<td>Duration</td>
<td>Amplitude</td>
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<tr>
<td>Acute neuropathic—axonal</td>
<td>Normal</td>
</tr>
<tr>
<td>Chronic neuropathic—axonal</td>
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</tr>
<tr>
<td>Neuropathic—demyelinating (CV slowing)</td>
<td>Normal</td>
</tr>
<tr>
<td>Neuropathic—demyelinating (conduction block)</td>
<td>Normal</td>
</tr>
<tr>
<td>Early reinnervation after severe denervation (nascent units)</td>
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</tr>
<tr>
<td>Acute myopathic</td>
<td>↓↑</td>
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<tr>
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</tr>
<tr>
<td>Myopathic—end stage</td>
<td>↓↑</td>
</tr>
<tr>
<td>NMJ disorders—mild</td>
<td>Normal</td>
</tr>
<tr>
<td>NMJ disorders—intermittent block</td>
<td>Normal/↑*</td>
</tr>
<tr>
<td>NMJ disorders—severe block</td>
<td>↓</td>
</tr>
<tr>
<td>CNS disorders</td>
<td>Normal</td>
</tr>
</tbody>
</table>

**Abbreviations:** CNS, central nervous system; MUAP, motor-unit action potential; NMJ, neuromuscular junction; ↑, increased; ↓, decreased; ↓/↑, may be decreased and/or increased; ↓↓, usually markedly decreased; *, may vary from potential to potential (unstable MUAPs).

(From Preston DC, Shapiro BE. Electromyography and neuromuscular disorders. Boston: Butterworth-Heinemann; 1998; with permission.)
units. As the number of muscle fibers per motor unit increases, MUAPs become prolonged in duration, with a high amplitude, and increased polyphasia (Fig. 19). These changes in MUAP configuration, in conjunction with decreased recruitment of MUAPs, are the hallmarks of reinnervated motor units, and nearly always imply chronic neuropathic disease. Long-duration, high-amplitude, polyphasic MUAPs are never seen acutely. When present, they always imply that the process has been present for at least several weeks, and more often months or years.

**Neuropathic disorders—demyelinating lesions**

Loss of axons results in denervation and ultimately reinnervation with resultant changes in MUAP morphology. If, however, the pathology is purely or predominantly demyelinating, the underlying axon remains intact. Thus, there is neither denervation nor subsequent reinnervation. Consequently, in pure demyelinating lesions, MUAP morphology remains normal. If demyelination results in conduction velocity slowing alone, the number of functioning motor units remains normal. In this case, there will be no change in either MUAP morphology or recruitment pattern. How-

![Image of motor-unit action potential morphologies]

**Fig. 19.** Motor-unit action potential morphologies. (From Preston DC, Shapiro BE. Electromyography and neuromuscular disorders. Boston: Butterworth-Heinemann; 1998; with permission.)
ever, if demyelination results in conduction block, then the number of available MUAPs effectively decreases. In this situation, the firing pattern shows decreased recruitment, although MUAP morphology remains normal. This pattern of reduced recruitment with normal MUAP morphology is seen only in demyelinating lesions with conduction block or in cases of acute axonal loss before enough time has passed for reinnervation to occur.

**Acute myopathic disorders**

In myopathies, the number of functioning muscle fibers in a motor unit decreases. Because there are fewer muscle fibers per motor unit, this results in shorter-duration and smaller-amplitude MUAPs [35–37] (see Fig. 19). In addition, there is less synchronous firing, and consequently polyphasia, of MUAPs, due to dysfunction of the remaining muscle fibers. However, the actual number of functioning motor units remains normal. Thus, the recruitment pattern remains normal for the level of activation. However, because each motor unit contains fewer muscle fibers, it cannot generate as much force as a normal motor unit. To compensate, more MUAPs will fire than normally needed for a certain level of force, resulting in early recruitment. Consequently, the pattern associated with an acute myopathy is short-duration, small-amplitude, polyphasic MUAPs, with normal or early recruitment.

**Chronic myopathic disorders**

In chronic myopathies, especially those with inflammatory or necrotic features (e.g., polymyositis, muscular dystrophies), some denervation and subsequent reinnervation commonly occurs. Consequently, long-duration, high-amplitude, polyphasic MUAPs can develop, although such MUAPs are most commonly seen in chronic neuropathic disorders. In many chronic myopathies, two populations of MUAPs are seen, often in the same muscle: long-duration, high-amplitude, polyphasic MUAPs in combination with short-duration, small-amplitude, polyphasic MUAPs. Rarely, only long, large, polyphasic MUAPs are seen. The key to differentiating chronic myopathic from neuropathic MUAPs is the assessment of recruitment pattern. In chronic myopathies, recruitment is usually normal or early. If an early recruitment pattern is not seen, then, at the least, the recruitment pattern appears better than what would be expected from the chronic MUAP changes. In some cases of the most chronic myopathy (especially inclusion body myositis), the EMG pattern may resemble that of active motor neuron disease (fibrillation potentials; long-duration, high-amplitude, polyphasic MUAPs), with the exception of recruitment.

**Myopathic disorders—end stage**

In the latest stages of some muscular dystrophies, in periodic paralysis, and in unusual, very chronic focal myopathies (eg, inclusion body myositis),
end-stage muscle may occur. In these situations, if every muscle fiber of some motor units is damaged, the actual number of motor units may effectively decrease. This results in an unusual pattern of reduced recruitment of short-duration, small-amplitude, polyphasic MUAPs, either alone or in combination with long-duration, high-amplitude, polyphasic MUAPs. Although decreased recruitment nearly always signifies neuropathic disease, the rare exception arises in end-stage muscle from myopathy.

**Reinnervation following severe denervation**

Reinnervation occurs most frequently from collateral sprouting by adjacent surviving motor units. If there is severe or complete denervation, with no nearby surviving axons, the only possible mechanism for reinnervation is regrowth of the axon from the site of injury. As the axon regrows, it will eventually reinnervate some, but not all of the original muscle fibers. At that point, the MUAP will be short-duration, small-amplitude, and polyphasic, similar in morphology to an acute myopathic motor unit (Fig. 20). Early reinnervated motor units following severe denervation are known as nascent motor units. The key factor that differentiates nascent motor units from myopathic motor units is the recruitment pattern. Nascent MUAPs are always seen in the context of markedly reduced recruitment, whereas myopathic MUAPs are seen in the context of normal or early recruitment.

![Fig. 20. Nascent motor units. (Left) Normal trace. (Middle) Following a severe axonal lesion, Wallerian degeneration occurs distal to the injury resulting in denervation. (Right) Trace shows that if there are no surviving nearby axons, reinnervation can occur only from axonal regrowth from the terminal stump.](image-url)
Neuromuscular junction disorders

MUAP morphology and firing patterns in neuromuscular junction disorders depend on the severity of the disorder. If the NMJ disorder is mild, both the morphology and recruitment of the MUAP will be normal. If the disorder is more severe, resulting in the intermittent blocking of some muscle fibers within the motor unit, the MUAP will become unstable. In this situation, the morphology (amplitude and/or the number of phases) will vary from potential to potential. With greater and more persistent block, individual muscle fibers within a motor unit are effectively lost. In this case, the MUAP becomes short, small, and polyphasic, similar to a myopathic MUAP. Similarly, recruitment remains normal, or may become early as each motor unit can generate less force. Finally, in cases of severe NMJ block, such as botulism, all the fibers in some motor units may be blocked, effectively resulting in the loss of motor units. In these cases, the remaining MUAPs are of short duration, small amplitude and polyphasic, but with decreased recruitment, which reflects the reduced number of available motor units. This uncommon pattern can also be seen in end-stage myopathy and in nascent motor units.

CNS disorders

In CNS disorders, there is normally no loss of anterior horn cells, and accordingly, no denervation or reinnervation. MUAP morphology and recruitment remain normal. On needle EMG, weakness is demonstrated as the inability to fire motor units rapidly (i.e., reduced activation). Thus, although the interference pattern is incomplete, with a reduced number of motor units firing, the actual number of motor units firing (i.e., recruitment) is appropriate for the reduced level of activation.

Occasionally, other patterns may be seen with CNS disorders. In spinal cord lesions, motor units may be lost at the level of the lesion, due to segmental loss of anterior horn cells. For example, in a C6 spinal cord lesion, denervation, reinnervation, and decreased recruitment may be seen in the biceps, deltoid, and other C6 innervated muscles. In the lower extremities, however, only decreased activation will be seen, and recruitment remains normal. Muscles partially supplied by the C6 root (e.g., the pronator teres with C6-7 innervation) may show both decreased recruitment and activation. Only rarely are other EMG abnormalities seen in CNS disorders. In some patients with multiple sclerosis, signs of denervation and reinnervation may be seen, presumably from involvement of motor fibers leaving the anterior horn cell in the spinal cord prior to exiting and becoming motor roots. Whether EMG abnormalities can be seen in other CNS disorders, especially stroke, remains controversial. Stroke patients are susceptible to entrapment and compression palsies because of poor mobility, which more often explains any EMG abnormalities.

Last, tremor may occur in some CNS disorders, which can complicate the interpretation of both spontaneous activity and MUAP morphology. Tre-
mor is recognized as a bursting pattern of voluntary MUAPs separated by relative silence. As multiple MUAPs fire simultaneously, the morphology of individual MUAPs may be difficult to assess, and polyphasia appears increased. When tremor occurs at rest (eg, Parkinson’s disease), the spontaneous burst discharge may be mistaken for myokymia. Although both myokymia and tremor result in a bursting pattern of MUAPs, the major difference is that in myokymia the same MUAP fires repetitively in a burst, whereas in tremor, the burst is composed of many different MUAPs. In addition, most patients can voluntarily alter their tremor by changing their limb position or action, as opposed to myokymia, which cannot be voluntarily influenced by the patient.

References

Electrodiagnostic approach to the patient with suspected radiculopathy

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Radiculopathy is one of the most common causes for referral to the electromyography (EMG) laboratory. However, the value of electrodiagnosis in the assessment of possible radiculopathy is extremely variable. Depending on issues of patient selection, segmental level of involvement, and the electrodiagnostic (EDX) modalities used, reports have suggested both high and low correlation between EDX testing and either neuroimaging or surgical localization [1–3]. Many patients referred to the laboratory have nonspecific symptoms that represent nonneurologic disorders caused by musculoskeletal disease. Among patients with true radiculopathy, most have only radicular pain and sensory symptoms, which do not have electrophysiologic correlates measurable with standard nerve conduction studies and needle electrode examination (NEE).

EDX testing is most valuable in patients with motor or other focal neurologic deficits, such as muscle stretch reflex asymmetry. In this setting, EDX testing can aid in the segmental localization of the lesion and can provide information regarding the physiology (axon loss or conduction block), age, activity, and severity of the process. EDX testing can aid in the exclusion of other disorders masquerading as radiculopathy and may be of value in the assessment of patients with post surgical deficits, multi-segmental neurologic deficits, or multilevel intraspinal structural changes.

The approach to the patient with suspected radiculopathy should incorporate data from various sources: clinical history, general and neurologic examination, and imaging studies. In the patient with classic localizable symptoms of radiculopathy, focal neurologic deficits, and appropriately positioned structural abnormalities on neuroimaging studies, clinical decisions can be made without the confirmatory findings provided by the EMG examination. Unfortunately, the medical picture is usually not completely...
clear, especially when pain hampers the reliability of muscle strength testing at the bedside. This chapter explores the principles of electrodiagnosis in radiculopathy and discusses various testing procedures and their relative value.

**Anatomy and pathophysiology**

There are 31 pairs of spinal nerve roots: eight cervical, twelve thoracic, five lumbar, five sacral, and one coccygeal. Each spinal nerve root is composed of a dorsal (somatic-sensory) root and a ventral (somatic-motor) root, which join in the intraspinal region, just proximal to the neural (intervertebral) foramen (Fig. 1). In the extraspinal region, just distal to the neural foramen, the nerve root divides in two parts: a small posterior primary ramus, which innervates the paraspinal muscles and skin of the neck and trunk; and a large anterior primary ramus, which innervates the limbs and trunk, including intercostal and abdominal wall muscles. Neural foramina are formed between each pair of vertebral bodies and are bounded superiorly and inferiorly by pedicles, anteriorly by intervertebral disks and vertebral bodies, and posteriorly by facet joints (Fig. 1). The spinal nerve roots, recurrent meningeal nerves, and radicular blood vessels pass through the neural foramina. Cervical roots C1–7 enter the neural foramen above the vertebral body of the same number, such that the C3 root exits the spinal canal via the C2–3 neural foramen. Because there are only seven cervical vertebrae, the C8 root exits through the C7–T1 neural foramen. As a result,
all thoracic, lumbar, and sacral roots exit below the vertebral body of the same number.

A capillary network derived from the radicular arteries provides the blood supply to spinal nerve roots. In the transitional region between the peripheral and central nervous system (the root entry zone) of the rat, blood vessels are positioned on the surface of rootlets and in inter-radicular spaces, but not in rootlets themselves. The density of capillaries is very high in the ventral nerve root entry zone [4]. Distal to the rootlets in rats, at the proximal and distal root levels, ventral root capillary density is higher than at the dorsal roots [5].

Cell bodies of the motor nerve fibers reside in the anterior horns of the spinal cord, whereas those of the sensory nerve fibers reside in the dorsal root ganglia (DRG). DRG are, in general, located in a protected position within the neural foramina and are therefore not intraspinal. However, at the lumbar and sacral levels, there is a tendency for DRG to reside proximal to the neural foramina, in intraspinal locations. About 3% of L3 and L4 DRG are intraspinal, about 11% to 38% of L5 DRG are intraspinal, and about 71% of S1 DRG are intraspinal, according to recent cadaver, radiographic, and magnetic resonance imaging studies [6,7]. In the cervical region, the C5 and C6 DRG also have a tendency to reside in relative intraspinal locations [8]. When DRG are in intraspinal positions, they are more exposed and therefore vulnerable to injury. With disk or bony compression of DRG, or with disruption of sensory axons distal to DRG, sensory axons degenerate and sensory nerve action potential (SNAP) amplitude loss is seen during nerve conduction studies.

Nerve root fibers are vulnerable to the same types of injury as other peripheral nerves: entrapment, compression, infiltration, ischemia, and transection. The likelihood of nerve root compression by disk rupture at lumbosacral levels may be increased by the presence of extrathecal dural and foraminal ligaments, which anchor nerve roots and reduce their plasticity [9]. Mild injury may result in focal demyelination, leading to conduction block or conduction velocity slowing along nerve root fibers. Axon loss at the root level results in Wallerian degeneration along the whole course of affected nerve fibers. Conduction block and axon loss produce symptoms and neurologic deficits if a sufficient number of nerve fibers are affected. Conduction velocity slowing alone is insufficient to produce weakness or significant sensory loss, although sensory modalities that require timed volleys of impulse transmission along their pathways, such as vibration and proprioception, can be altered.

Nerve conduction studies

Many factors reduce the sensitivity of nerve conduction studies in the diagnosis of radiculopathy. First, most radiculopathies are caused by compression from disk protrusion or spondylosis, and result in damage to only a
fraction of nerve root fibers, producing limited motor and sensory deficits. Second, in the acute setting, radiculopathy manifests itself most commonly by symptoms of pain and alteration of sensory perception. Sensory radiculopathy can only rarely be reliably localized segmentally by EDX techniques for the following reasons: symptoms of pain and paresthesia are primarily mediated through C-type sensory fibers, which are too small to be studied by routine EDX techniques; the peripheral processes of sensory root fibers remain intact with intraspinal lesions, so SNAPs remain normal; and the intraspinal location of most lesions makes it impossible to perform direct nerve conduction studies on the nerve root proximal to the damaged segment, preventing the diagnosis of conduction block or focal conduction velocity slowing along the damaged segment of the root.

NCS are an important part of the routine EDX work-up for radiculopathy as a means to exclude other disorders that may coexist with radiculopathy or may clinically masquerade as radiculopathy. Such disorders include focal mononeuropathies and polyneuropathy. The tibial H-reflex is one nerve conduction study that is useful in supporting the diagnosis of S1 radiculopathy [53].

**Routine studies**

Sensory NCS performed along peripheral nerve trunks are characteristically normal in radiculopathy. The SNAP amplitude, distal latency, and nerve conduction velocity should not be affected in radiculopathy. The SNAP amplitude may be abnormal if DRG are affected in the pathologic process. In pathologic processes that infiltrate or extend from the intraspinal space into the neural foramen, such as malignancy, infection, or meningioma, DRG are damaged and Wallerian degeneration along sensory axons occurs, resulting in SNAP amplitude loss. When DRG reside in an intraspinal location, as mentioned previously, they become vulnerable to compression by disk protrusion and spondylolysis. Therefore, L5 radiculopathy can uncommonly be associated with loss of the superficial peroneal SNAP [10]. However, S1 radiculopathy is almost never associated with sural SNAP amplitude loss. Although S1 DRG are even more commonly intraspinal than L5 DRG, intraspinal location is caudal to the L5-S1 disk space where most compressive S1 radiculopathies occur. When nerve root damage occurs distal to the neural foramen, SNAP amplitude will be affected [10,11].

Motor nerve conduction studies are relatively insensitive in the diagnosis of motor radiculopathy for several reasons. First, most radiculopathies interrupt only a fraction of the total number of motor root fibers, whereas loss of close to 50% of motor axons in a nerve trunk is required to reliably establish a significant reduction in the compound muscle action potential (CMAP) amplitude, compared with the same response on the uninvolved side [12]. Second, to identify an abnormality of CMAP amplitude in a motor radiculopathy, the muscle belly from which the CMAP is generated must be in the myotome of the injured root. For example, a severe C8 radiculopathy
would be expected to produce some change in the ulnar CMAP amplitude, recording from either the abductor digiti minimi or the first dorsal interosseous. In the C5 myotome, the musculocutaneous and axillary nerve trunks can be stimulated to assess CMAPs from the biceps and deltoid muscles, respectively. However, muscles in the C6 and C7 myotomes are not spatially isolated from muscles of other myotomes, and therefore CMAPs derived from them are unreliable. Table 1 outlines the screening nerve conduction studies for nonspecific arm and leg symptoms.

**Late responses**

Late responses are electrical stimulus evoked motor potentials that can be used to measure the travel time of propagated nerve action potentials from a distal point of electrical stimulation along a peripheral nerve trunk, proximally to the spinal cord, and then back down the limb to a muscle belly innervated by the same peripheral nerve trunk. Theoretically, they make possible the assessment of conduction through the damaged segment of a nerve root, but there are a number of limitations. First, the sensitivity is low because even severe slowing over a short segment will not usually prolong the total latency enough to be significant. Second, as long as a few nerve fibers conduct normally through a damaged segment, a normal shortest latency will be recorded, even in the presence of severe nerve root damage. Finally, late responses such as F-waves are of limited value in the diagnosis of radiculopathy because they are not recorded along sensory nerve fibers and are therefore useless in the assessment of sensory symptoms.

The F-wave was first described by McDougal and Magladery in 1950, so named because it was originally recorded from foot muscles. The F-wave is a motor response often recorded from a muscle belly after stimulation of the peripheral nerve trunk innervating the muscle. It is thought to arise from

<table>
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<tr>
<th>Table 1</th>
<th>Screening nerve conduction studies for arm and leg pain</th>
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<tr>
<td><strong>Arm pain</strong></td>
<td><strong>Leg pain</strong></td>
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<tr>
<td>Sensory</td>
<td>Motor</td>
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<tr>
<td>Distal amplitude and latency</td>
<td>Distal latency, distal and proximal amplitudes, conduction velocity, and F latency</td>
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<tr>
<td>Median</td>
<td>Median (recording from thenar eminence)</td>
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<tr>
<td>Ulnar</td>
<td>Ulnar (recording from hypothenar eminence)</td>
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<td>Radial</td>
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the backfiring of motor neurons as impulses arrive antidromically from a peripheral site of nerve trunk stimulation. The F-wave occurs after the CMAP, but as the point of nerve trunk stimulation is moved more proximally, the CMAP latency lengthens and the F-wave latency shortens, indicating that the impulse eliciting the F-wave travels away from the recording electrodes toward the spinal cord before returning to activate distal muscles. Traditionally, minimal latency of at least eight consecutive discharges is measured. The absence of an F-wave response from stimulation of the median, ulnar, or tibial nerve in the presence of normal evoked CMAPs from the same muscle suggests conduction block or very recent (<5–8 d) axon loss somewhere along the nerve trunk proximal to the point of nerve stimulation. This is most often encountered in the setting of acute demyelinating polyneuropathy, but could conceivably be a feature of isolated radiculopathy when occurring in a single myotomal distribution. Peroneal F-responses are not reliably recorded in healthy individuals.

Some studies have suggested that other F-wave measurements may be more sensitive than minimal latency, including F-wave duration, mean F-latenecy, and chronodispersion (the interval between the shortest and longest F-latenecy in a consecutive series of stimuli) [13]. Several studies suggested that using these methods increases the sensitivity of F-wave analysis in L5/S1 radiculopathy to a level close to the sensitivity of the NEE [14,15]. One study reported that F-wave chronodispersion increased in patients with lumbar canal stenosis and L5/S1 root lesions after 3 minutes of standing [16]. However, F-wave changes can be seen in a number different peripheral neuropathic disorders, and therefore cannot themselves support radiculopathy.

Hoffmann first described the H-reflex in 1918. Traditionally, this response has been considered the electrophysiologic equivalent of the Achilles’ tendon muscle stretch reflex. Although the contention that the H-reflex represents conduction through a monosynaptic pathway is likely to be overly simplistic, it is clear that the electrical stimulus travels orthodromically along Ia afferents to the spinal cord, where the motor neuron in the same segment is activated, producing a motor response peripherally [17,18]. When elicited from the tibial nerve with stimulation at the popliteal fossa, a motor response in the soleus-gastrocnemius muscle complex occurs. In some healthy individuals, there is discordance between the ability to elicit the H-reflex and the presence of the ankle muscle stretch reflex [19].

The H-reflex can be elicited from other nerve trunks. With corticospinal tract disease, H-reflexes can be elicited from many nerve trunks, as a result of loss of the normal central inhibitory influences on motor neuron pools. Under normal circumstances, aside from the tibial H-reflex, the H-reflex can be elicited reliably only from the median nerve, recording over the flexor carpi radialis. Abnormalities of the median H-reflex have been found in patients with C6-7 radiculopathy. One study identified 11 of 25 patients with an absence of the median H-reflex, whereas 6 of the remaining 14 patients had prolonged H-reflex latency [20]. The upper limit for the median H-reflex
has been reported as 20 milliseconds, but nomograms taking into account the effect of arm length allow more precision in diagnosis [20]. Only the tibial H-reflex is routinely used in clinical practice, where it is an extremely sensitive test for the assessment of the integrity of the tibial/S1 sensory pathway, including the intraspinal course of the S1 root. In one study, the H-reflex was absent or low in amplitude in over 80% of surgically proven cases of S1 radiculopathy [21]. It is markedly reduced in amplitude or absent in axon loss lesions affecting the S1 root and the tibial nerve at or proximal to the popliteal fossa. Reports have explored the sensitivity of the H-reflex latency compared with the H-reflex amplitude [22]. The upper limit of normal for the tibial H-reflex latency is often 34 to 35 milliseconds, but normal latency values vary depending on age, limb length, and height. Use of nomograms can narrow the normal range and potentially improve diagnostic precision [23]. Still, the most direct and reliable measurement appears to be the assessment of the side-to-side difference in H-amplitude. A report of side-to-side differences in healthy individuals suggested that an H-amplitude ratio (abnormal H-amplitude divided by the contralateral H-amplitude) of less than 0.4 is likely to be abnormal, although 1 of 47 individuals had a ratio of 0.33 [24]. In our laboratory, an additional criterion for abnormality is amplitude of less than 1 mV in individuals aged younger than 60 years.

The H-reflex is likely to show an abnormality with any disturbance of conduction through the tibial/S1 pathway. Although sensitive, the H-reflex has reduced specificity, resulting in a number of clinical limitations. First, the response is not reliably present in healthy individuals over the age of 60, although normal responses have been identified at all ages. Second, although unilateral absence of the H-reflex is abnormal at any age, bilateral absence of H-responses is often of uncertain clinical significance. Technical factors and generalized neuropathic processes can affect the H-reflex. Possible causes include obesity and inadequate penetration of the stimulus in the popliteal fossa, prior lumbar spine surgery, and peripheral polyneuropathy, especially in individuals with diabetes. Bilateral absence of the H-reflex may be the earliest EDX feature of acute demyelinating peripheral polyneuropathy (Guillain-Barré syndrome). Abnormalities along the tibial/S1 sensory or motor pathway will alter the H-response, including posterior tibial mononeuropathies proximal to the branch point of the nerve to the soleus and gastrocnemius muscles. Thus, an H-reflex abnormality is insufficient by itself to confirm the presence of an S1 radiculopathy.

Somatosensory evoked responses

Theoretically, somatosensory evoked potentials (SEPs) should be a valuable tool in the assessment of conduction abnormalities along sensory fibers at the root level. Electrical stimuli are delivered on the skin surface to a mixed sensory and motor nerve trunk, a sensory nerve trunk, or the skin...
in a specific dermatomal distribution. Responses are recorded over the spine and scalp, and latencies are measured to assess the conduction time along large diameter sensory fibers across various segments of the peripheral and central conduction pathways primarily subserving proprioception and vibratory sense.

Unfortunately, several limitations diminish the value of this technique. First, amplitude measurements are too variable in healthy individuals to have clinical significance, thus the assessment of partial axon loss lesions and partial conduction block is not reliable. Second, focal slowing in the root segment is diluted by normal conduction along the rest of the sensory pathway. Third, nerve trunk stimulation often simultaneously activates nerve fibers belonging to more than one root segment, masking the abnormality in the abnormal root in question [25]. SEPs assess conduction along primarily large fiber sensory pathways that subserve proprioceptive and vibratory perception functions, not the pain and cutaneous sensation pathways that are more likely to be affected in radiculopathy. Fourth, the procedure is time consuming and subject to technical artifacts.

Given the previously mentioned limitations, SEPs obtained from nerve trunk stimulation have been shown to add little diagnostic value [26,27]. Likewise, SEPs derived from L5/S1 dermatomal stimulation have not been found to be as useful as standard EDX techniques [26,28].

Cutaneous sensory nerves have more specific and isolated root innervations, and thus SEPs derived from cutaneous nerve stimulation have a potential diagnostic advantage. Studies have been performed on the saphenous, sural, and superficial peroneal sensory nerves. Scalp-recorded cutaneous SEPs were abnormal in 57% of 28 cases of cervical and lumbosacral radiculopathy in one report, based on findings of abnormal amplitude and waveform configuration [29]. Using the same technique, Seyal, Sandhu, and Mack [30] found 20% of patients had abnormal scalp-recorded recordings; however, abnormal cases increased to approximately 50% when spine-recorded SEP latency, or response size was measured. In spite of these results, the overall correlation has not been optimal between the SEP abnormality and the clinical localization of the sensory radicular symptoms [31].

In summary, SEPs do not have either the specificity or sensitivity of other EDX techniques, such as the NEE, to recommend them for routine radiculopathy diagnosis.

Other conduction studies

A few studies have explored the value of spinal nerve root stimulation, performed at the level of the vertebral lamina. Studies assessed latency and amplitude asymmetry, and appeared to have greater reliability at the cervical levels than at the lumbosacral levels [32,33]. Two factors decrease the potential value of this technique. First, it is not clear at what site the root is being stimulated. Stimulation of the root at or distal to the neural fora-
men would not include the likely site of nerve compression for most cases of radiculopathy. Second, the procedure is uncomfortable, because it produces contraction of paraspinal muscles and proximal muscles in the shoulder or hip girdles.

Studies have also explored the value of magnetic stimulation at the spinal root level. Opinions differ regarding whether the exact site of root stimulation occurs at or distal to the neural foramen [34,35]. For measuring latency and conduction times at cortical and spinal stimulation sites, reports have suggested a correlation with clinical patterns of weakness and the ability to discriminate medially versus laterally located disc herniations that produce nerve root compression [36,37].

Needle electrode examination

General concepts

Although the needle electrode examination (NEE) assesses the motor component of radiculopathy, it is the most specific and sensitive of the EDX tests for the identification of axon loss radiculopathy. In many cases, the NEE provides information about the root level of involvement, the degree of axon loss present, the degree of ongoing motor axon loss, and the chronicity of the process. In most laboratories, patients with arm or leg pain receive a general NEE survey that samples all major root and nerve trunk distributions in the limb. If abnormalities are identified, the examination is modified to focus on the cause for the abnormality. If a symptom is in a specific region of the limb (eg, the shoulder girdle or posterior thigh), muscles in that region are examined. Tables 2 and 3 outline the screening NEE for nonspecific arm and leg symptoms, respectively.

The localization of a nerve root lesion requires the identification of neurogenic abnormalities in a distribution of muscles that shares the same root innervation but involves more than one peripheral nerve distribution. The abnormalities may include one or more of the following abnormalities: increased insertional activity in the form of positive waves or sharp spikes;

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<thead>
<tr>
<th>Muscle</th>
<th>Root level</th>
<th>Nerve trunk</th>
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<tbody>
<tr>
<td>First dorsal interosseus</td>
<td>C8</td>
<td>Ulnar</td>
</tr>
<tr>
<td>Flexor pollicis longus</td>
<td>C8</td>
<td>Anterior interosseus (median)</td>
</tr>
<tr>
<td>Extensor indicis proprius</td>
<td>C8</td>
<td>Posterior interosseus (radial)</td>
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<tr>
<td>Pronator teres</td>
<td>C6–7</td>
<td>Median</td>
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<tr>
<td>Triceps</td>
<td>C6–7</td>
<td>Radial</td>
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<tr>
<td>Biceps</td>
<td>C5–6</td>
<td>Musculocutaneous</td>
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<tr>
<td>Deltoid</td>
<td>C5–6</td>
<td>Axillary</td>
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<tr>
<td>C7 paraspinal</td>
<td>Overlap</td>
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abnormal spontaneous activity in the form of fibrillation potentials; reduced (neurogenic) recruitment of motor-unit firing; and features of chronic motor unit action potential (MUAP) reinnervation, such as increased duration, increased amplitude, and polyphasia.

The timing of the NEE is important. In acute radiculopathy, fibrillation potentials are the abnormality most likely to confirm the presence of a motor radiculopathy. Fibrillation potentials seldom develop before 2 weeks have elapsed from the onset of weakness and, in some patients, may not appear for 4 to 6 weeks. The most efficient use of the EMG is to delay the performance of the NEE for at least 3 weeks after the onset of motor symptoms.

**Root localization by NEE**

The choice of muscles for the NEE must be tailored to the specific clinical questions and symptoms, but must be comprehensive enough to maximize diagnostic certainty. The particular muscles showing neurogenic changes in the myotome in question will vary from case to case because most root lesions are partial, and not all muscles in the myotome will be affected equally. During the NEE, the more muscles identified as abnormal in the myotome, the more secure the electrodiagnosis. To make a reliable diagnosis of a single-root lesion, at least two muscles in that myotome should be found with neurogenic changes, and they should not share the same peripheral nerve innervation. In myotomes where it is possible, involvement of proximal and distal muscles should be sought to increase the certainty of the diagnosis and exclude peripheral mononeuropathy as the cause for the abnormalities. To complete the NEE in an individual with an identified single-root lesion, muscles in the myotomes framing the involved root level should be examined to verify that those myotomes are normal. For example, the biceps and first dorsal interosseus muscles should be normal in a patient with a C7 radiculopathy.

Paraspinal muscle involvement should always be sought, as it adds important support for the diagnosis of an intraspinal lesion, and rules out plexopathy and peripheral mononeuropathy as the cause of extremity mus-

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<tr>
<th>Muscle</th>
<th>Root level</th>
<th>Nerve trunk</th>
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<tbody>
<tr>
<td>Abductor hallucis</td>
<td>S1</td>
<td>Posterior tibial</td>
</tr>
<tr>
<td>Medial gastrocnemius</td>
<td>S1</td>
<td>Posterior tibial</td>
</tr>
<tr>
<td>Biceps femoris (short head)</td>
<td>S1</td>
<td>Peroneal</td>
</tr>
<tr>
<td>Extensor digitorum brevis</td>
<td>L5 (S1)</td>
<td>Peroneal</td>
</tr>
<tr>
<td>Tibialis anterior</td>
<td>L5 (L4)</td>
<td>Peroneal</td>
</tr>
<tr>
<td>Tibialis posterior</td>
<td>L5</td>
<td>Posterior tibial</td>
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<td>Gluteus medius</td>
<td>L5</td>
<td>Superior gluteal</td>
</tr>
<tr>
<td>Rectus femoris</td>
<td>L2,3,4</td>
<td>Femoral</td>
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<td>S1 paraspinal</td>
<td>Overlap</td>
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### Table 3
Screening needle electrode survey for leg pain
cle involvement. However, the following factors reduce their value. First, paraspinal muscle fibrillation can be seen in disorders of the root, processes affecting anterior horn cells, and muscle disorders such as necrotizing myopathy. Second, paraspinal muscle involvement cannot precisely localize the segmental level of root damage because segmental innervation of paraspinal muscles can overlap as much as four to six segments [38]. Third, clear evidence of paraspinal denervation with cervical and lumbosacral radiculopathies is seen only in approximately 50% of cases [21,39]. Causes include overlapping segmental innervation of paraspinal muscles and the tendency of muscles in close proximity to the nerve lesion site to reinnervate sooner and more completely than muscles further from the point where nerve regeneration must begin. Fourth, in paraspinal muscles that are close to a prior laminectomy site, fibrillation might persist indefinitely because of iatrogenic denervation. In routine practice, we do not examine paraspinal muscles in areas of prior surgery.

Anatomic, clinical, and EMG myotomal charts are used to correlate the pattern of EMG abnormalities in a limb with a specific root level. Tracing root and peripheral nerve innervations of muscles from cadaver studies has been used to create anatomic charts. Clinical charts have been derived by correlating the distribution of clinical muscle weakness in patients with specific traumatic lesions. Although these charts are useful, they are not entirely applicable to the NEE. Muscles are chosen for the NEE because of specific attributes of root innervation and accessibility. Some muscles, such as the anconeus, pronator teres, and brachioradialis, are not easily isolated in the clinical examination, but are easily isolated by the NEE, and are important in root localization. Thus, EMG-derived myotomal charts are useful in the electrodiagnosis of radiculopathy [21,39]. Figs. 2 and 3 are EMG-derived myotomal charts.

**Defining an acute radiculopathy**

In axon loss radiculopathy, determining the age of the lesion requires combining information about the duration of the symptoms with NEE attributes of both active and chronic motor axon loss. When MUAPs are of normal configuration and size, the presence of abnormal insertional or spontaneous activity in the form of trains of brief sharp spikes or positive waves indicates recent motor axon loss. Abnormal insertional activity alone suggests that the process may be only several weeks old. The presence of spontaneous activity in the form of fibrillation potentials indicates a process of at least 3 weeks duration.

Although EDX testing for radiculopathy is most valuable when significant axon loss has occurred, testing may also uncover evidence of a prominent conduction block lesion at the root level as the cause for weakness. When examining a muscle whose CMAP is of normal amplitude, the presence of a reduced recruitment pattern of MUAP activation in the absence of
## Needle Electrode Examination Results

Grouped by the Surgically Defined Root Level of Involvement

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fibrillation potentials suggests conduction block. If this pattern is seen in multiple muscles of a specific myotome, a diagnosis of radiculopathy can be made. This strategy is not reliable for the diagnosis of conduction block if the onset of weakness occurs less than 4 weeks prior to the EDX study, since an acute axon loss lesion may not clearly manifest fibrillation potentials for 3 or more weeks after onset of symptoms.

Defining a chronic radiculopathy

The diagnosis of a chronic/active or a chronic/remote root lesion is based on the observation of neurogenic MUAP changes, in the presence or absence of evidence of fibrillation potentials, respectively. In the early stages of reinnervation of denervated muscle fibers, between 6 to 26 weeks after nerve root injury, collateral sprouting from surviving nerve fiber terminals gives rise to MUAPs of increased serration or polyphasis. These MUAPs may also demonstrate instability (moment-to-moment variation in configuration). As more time elapses and reinnervation becomes more complete, MUAPs lose their instability and develop the characteristic features of a chronic lesion; increased duration and amplitude. An NEE demonstrating these chronic neurogenic MUAP changes without fibrillation potentials indicates the residuals of a remote lesion. These MUAP changes are permanent, reflecting the histopathologic changes in the reinnervated muscle, and will remain unchanged unless the motor unit is injured again. After a significant motor axon loss process has occurred, MUAPs never return to their preinjury morphology.

Chronic lesions can be classified into a chronic/active category if there are both fibrillation potentials and chronic neurogenic MUAPs. In root distributions where the myotome includes muscles in both distal and proximal regions of a limb (especially the L5 and S1, and perhaps the C5-6, root distributions), the presence of a chronic and ongoing axon loss process can be more clearly defined when fibrillation potentials are seen in both distal and proximal muscles in the root distribution. In lesions where fibrillation potentials are seen in distal muscles only, the diagnosis of an ongoing axon loss process is less certain. Some inactive but severe axon loss processes never fully reinnervate, especially in muscles farthest from the injury site, leaving some muscle fibers denervated indefinitely. The NEE findings at progressive stages of axon loss radiculopathy are summarized in Table 4.

Fig. 2. Needle electrode examination results in 50 patients with cervical radiculopathies. Closed circle: positive waves or fibrillation potentials, with or without neurogenic recruitment and motor unit changes; half-closed circle: neurogenic recruitment changes only; open circle: normal examination. Abbreviations: SUP, supraspinatus; INF, infraspinatus; DEL, deltoid; BRAC, brachioradialis; BIC, biceps; PT, pronator teres; FCR, flexor carpi radialis; TRIC, triceps; ANC, anconeus; EDC, extensor digitorum communis; EIP, extensor indicis proprius; FPL, flexor pollicis longus; APB, abductor pollicis brevis; FDI, first dorsal interosseus; ADM, abductor digitii minimi; PSP, paraspinal muscle. (From Levin KH, MaggianoHJ, Wilbourn AJ. Cervical radiculopathies: comparison of surgical and EMG localization of single–foot lesions. Neurology 1996; 46:1022-25; with permission.)
Defining the severity of a radiculopathy

The severity of an axon loss process can be graded during the NEE by assessing the degree of motor unit loss in the root distribution. This is determined by a subjective measurement of the degree of reduced recruitment of motor units. Fig. 3. Needle electrode examination results grouped by the surgically defined root level of involvement in 43 patients with lumbrosacral radiculopathies. Abbreviations: AL, adductor longus; IL, iliacus; VL, vastus lateralis; RF, rectus femoris; VM, vastus medialis; FDL, Flexor digitorum longus; PT, posterior tibialis; TA, tibialis anterior; EDB, extensor digitorum brevis; PL, peroneus longus; EHL, extensor hallucis longus; GMED, gluteus medius; ST, semitendinosus; TFL, tensor fascia lata; MG, medial gastrocnemius; LG, lateral gastrocnemius; ADQ, abductor digiti quinti; BFSH, biceps femoris (short head); GMX, gluteus maximus; AH, abductor hallucis; PSP, paraspinal; H, H-reflex.

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motor-unit potential activation. Although there is a correlation between the degree of reduced recruitment of motor units in a neurogenic process and the degree of weakness, reduced recruitment is not necessarily due to axon loss unless the CMAP elicited from the same muscle is also reduced in amplitude. Thus, defining the severity of an axon loss radiculopathy requires evaluation of both the CMAPs in the myotome in question (when possible) and the degree of reduced recruitment of MUAP activation. Measuring the number of fibrillation potentials in a muscle is highly subjective and does not correlate as well with the degree of axon loss.

**Cervical radiculopathies**

The most complete clinical study of specific cervical root lesions was carried out by Yoss, Corbin, MacCarty, and Love [40]. In that study, clinical and radiographic evidence of radiculopathy was found to occur at the C7, C6, C8, and C5 levels in 70%, 19%–25%, 4%–10%, and 2% of the time, respectively. The following NEE data on individual cervical radiculopathies come from a study of isolated single-root lesions based on confirmed surgical localization [39] (Fig. 2):

- **C5 radiculopathy** produces a rather stereotyped pattern of muscle involvement, affecting the spinati, biceps, deltoid, and brachioradialis with about equal frequency, but not all of them together in any one patient. The pronator teres is never involved in C5 radiculopathy. Because the rhomboid major muscle is said to have prominent C5 innervation, it should be examined in unclear cases. The upper trapezius, with its prominent C4 innervation, is spared in C5 radiculopathy. Nerve conduction studies are not likely to be helpful, although severe lesions may be associated with axillary and musculocutaneous CMAP amplitude loss.
• **C7 radiculopathy** produces a rather stereotyped pattern of muscle involvement, affecting particularly the triceps, but also the anconeus, flexor carpi radialis, and pronator teres. The triceps muscle is affected in essentially all cases of C7 radiculopathy. Because the extensor carpi radialis is not reliably affected in most C7 radiculopathies, it is not usually part of the routine NEE survey for radiculopathy. An important part of the clinical diagnosis of C7 radiculopathy rests upon the finding of a diminished triceps deep tendon reflex, but several studies have shown that the reflex is abnormal in less than 70% of patients. [39,40] There are no reliably performed motor nerve conduction studies that can be used to generate CMAPs from C7 innervated muscles.

• **With C6 radiculopathy**, there is no single characteristic pattern of muscle involvement. Rather, two patterns are discernible: the first is very similar to the C5 pattern, with additional involvement of triceps and pronator teres in some; and the second is similar to the C7 pattern. The pronator teres is abnormal in 80% of patients with C6 radiculopathy, but is also abnormal in 60% of the cases of C7 radiculopathy. The triceps is abnormal in over half the cases of C6 radiculopathy. Thus, significant EMG overlap occurs between C5 and C6 radiculopathy, and between C6 and C7 radiculopathy. There are no reliably performed motor nerve conduction studies that can be used to generate CMAPs from C6 innervated muscles.

• **C8 radiculopathy** produces a stereotyped pattern of muscle involvement, including the ulnar innervated muscles, extensor indicis proprius, and flexor pollicis longus. Abductor pollicis brevis is involved less often, and to a lesser degree than other muscles. Of all the root lesions, C8 radiculopathy is the most clearly identified by NEE because of the limited myotomal overlap. Nerve conduction studies are not likely to be helpful, although severe lesions may be associated with ulnar (recording from the abductor digiti minimi or first dorsal interosseus) CMAP amplitude loss.

• **T1 radiculopathy** is the least common isolated root lesion affecting the arm. Although all C8 muscles of the hand are said to have T1 contributions, the abductor pollicis brevis muscle appears to be the only muscle with predominately T1 innervation [41,42]. In a single case of T1 radiculopathy with neuroimaging and intraoperative confirmation, the EMG showed chronic and active denervation limited to the abductor pollicis brevis [42].

**Lumbosacral radiculopathies**

According to one large study, lumbar disk herniations leading to EMG-determined motor radiculopathy occurs at the L4–5, L5–S1, and L3–4 levels in 55%, 43%, and 2% of the time, respectively [43]. At lumbosacral levels, the anatomic localization of the site of root injury, the identification of single-root
lesions, and the accuracy of electrodiagnosis are all less successful than at the cervical levels.

First, there is the issue of the longer intraspinal course of most lumbosacral roots. All lumbar and sacral spinal nerve roots are constituted at the T12–L1 vertebral level, where the spinal cord ends as the conus medullaris. The roots then course down the canal as the cauda equina, until they exit at their respective neural foramina. Depending upon the nature and location of intraspinal compression, roots may be injured at any disk level, from the L1–L2 level to the level of their exit into the neural foramen. For example, the L5 root can be compressed by a central disk protrusion at the L2–3 or L3–L4 levels, a lateral disk protrusion at the L4–L5 level, or foraminal stenosis at the L5–S1 level. Thus, the EDX localization of a specific root lesion does not specify the vertebral level of damage. Second, because of the presence of multiple spinal nerve roots in the cauda equina, the likelihood of multiple, bilateral radiculopathies increases. This occurrence reduces EDX accuracy and introduces possible confusion with other disorders, such as peripheral polyneuropathy and motor neuron disease. Thus, the identification of a lumbosacral radiculopathy requires at least a limited evaluation of the contralateral side for evidence of concurrent lesions. The following NEE data on individual lumbosacral radiculopathies come from a study of isolated single-root lesions with active axon loss, confirmed by surgical localization [21] (Fig. 3):

- **With S1 radiculopathy**, there was a stereotyped pattern of muscle involvement, including the gastrocnemius muscles, the short and long heads of the biceps femoris, and the abductor hallucis. The biceps femoris short head, biceps femoris long head, and medial gastrocnemius were found exclusively innervated by the S1 root, although other studies have described significant L5 root innervation of these muscles [44–46]. Muscles involved in over 80% of these patients included the gastrocnemius (both medial and lateral heads) and the biceps femoris (both short and long heads). Paraspinal denervation was seen in only 25% of patients, because of the significant overlap of paraspinal segmental innervation. The gastrocnemius muscles are often difficult to voluntarily activate, making the assessment of MUAP recruitment and morphologic changes incomplete. Therefore, the identification of abnormalities in proximal muscles, such as the biceps femoris short head and long head and the gluteus maximus, is crucial for the confirmation of an S1 radiculopathy, eliminating the possibility of more distal peripheral mononeuropathies. The biceps femoris short head (BFSH) was never involved in any L5 root lesion, although some reports have described significant L5 innervation of that muscle [44].

- **With L5 radiculopathy** the NEE showed involvement of the peroneus longus and tensor fascia lata in essentially all patients, and in the flexor digitorum longus/tibialis posterior, and tibialis anterior muscles in over
75% of the patients. In this study, the L5 root exclusively innervated the tibialis anterior, although other studies have described significant L4 root innervation of that muscle [45,47,48]. About 50% of patients with L5 radiculopathy demonstrated paraspinal fibrillation potentials. NEE of the posterior tibialis or flexor digitorum longus is critical, as these are the only L5 innervated muscles below the knee not innervated by the peroneal nerve. Abnormalities in either of these muscles exclude the diagnosis of peroneal mononeuropathy. To verify the presence of an L5 radiculopathy, abnormalities should be sought in proximal L5 muscles, such as the tensor fascia lata and gluteus medius, in order to eliminate the diagnoses of sciatic and peroneal mononeuropathies. This is especially true in elderly individuals whose superficial peroneal sensory responses may be absent because of age, and in whom peroneal and sciatic mononeuropathy may not be as easily excluded.

• L2–L4 radiculopathies are not reliably distinguished from each other because of the overlap of innervation of the anterior thigh muscles. The problem in reliable localization is compounded by the absence of proximal and distal muscles to examine, and the low incidence of L2–L4 radiculopathies, which has prevented definitive analysis. We routinely examine the rectus femoris, vastus lateralis, iliacus, and adductor longus in patients with a question of upper lumbar radiculopathy. All these muscles appear to be equally likely to be involved at these levels, but they are seldom all involved in any single root lesion. As the adductor longus is the only muscle not innervated by the femoral nerve, its evaluation is critical for the differentiation of femoral mononeuropathy and L2–L4 radiculopathy. Paraspinal fibrillation potentials are commonly seen in patients with active axon loss radiculopathies at these segmental levels, but the paraspinal fibrillation potentials are often seen at the L5, S1, or S2 vertebral levels.

Other radicular disorders

Extraspinal radiculopathies

Extraspinal radiculopathy (focal damage to anterior primary rami) constitutes an unusual group of disorders that is difficult to diagnose. In the cervical region, two such disorders have traditionally been categorized as types of brachial plexopathy, but EDX evidence suggests that they are more likely to represent damage to extraspinal root fibers traveling in the anterior primary rami. First, neurogenic thoracic outlet syndrome, long considered a type of lower trunk brachial plexopathy, produces most severe axon loss in the abductor pollicis brevis muscle and the medial antebrachial cutaneous SNAP distribution, both sharing principally T1 root innervation [41]. In most cases, lower trunk/C8 structures are affected to a much lesser extent. Second, median sternotomy brachial plexopathy, an iatrogenic disorder that
can result from rib cage retraction during open heart surgery, is manifested by most severe axon loss in the ulnar SNAP and C8 root distribution, with little involvement of T1 innervated structures.

These two lesions show distributions of involvement that, in their purest forms, may be mutually exclusive: the abductor pollicis brevis and the medial antebrachial cutaneous response with neurogenic thoracic outlet syndrome, and C8 muscles and the ulnar sensory response with median sternotomy brachial plexopathy. However, the nerve fibers innervating all these structures travel together in the lower trunk of the brachial plexus. Therefore, neurogenic thoracic outlet syndrome and median sternotomy brachial plexopathy more likely represent, respectively, extraspinal T1 and C8 root lesions proximal to the formation of the lower trunk (Figs. 4 and 5).

**Polyradiculopathies**

The term polyradiculopathy indicates damage to multiple root segments simultaneously or in progressive order, occurring in a single limb or, more frequently, bilaterally, and sometimes diffusely. Its causes are diverse and not always clear. Some neurologic disorders, such as polyradiculopathy, coexist with lesions in distal peripheral nerves or lesions in the central nervous system. Following is a brief description of the most prominent causes of polyradiculopathy, and Table 5 lists causes of polyradiculopathy and their differential diagnosis.

**Compressive polyradiculopathies**

Spondylosis of the spine is often multifocal, and multiple roots may suffer compressive damage concurrently. This is especially true at the lumbosacral level, where spondylosis causes lumbar canal stenosis and multilevel neural foraminal stenosis. In our laboratory, we see few elderly patients with single lumbosacral root lesions, but many more with multiple simultaneous radiculopathies, often show a combination of active and more chronic features. Lumbar canal stenosis exerts compressive effects on the cauda equina, resulting in the potential for multiple root involvement. It may present clinically with weakness in a single root distribution, in several distributions, or as chronic progressive weakness of the legs in a diffuse distribution. Alternatively, lumbar canal stenosis may present as intermittent progressive fatigability and aching of the legs elicited by walking or exercise, a symptom complex known as intermittent neurogenic claudication. The EDX picture of lumbar canal stenosis is extremely variable; some patients demonstrate no changes, while others show bilateral, multilevel motor axon loss.

Regardless of the cause of lumbosacral polyradiculopathy, EDX specificity is hampered when NEE abnormalities are bilateral and confluent. In the chronic state, the NEE changes are usually most prominent in distal muscles of the myotome, shading to normal in more proximal muscles. When chronic motor axon loss spans the L5 and S1 distributions symmetrically, the
electrical picture resembles the confluent changes seen in peripheral polyneuropathy. This is especially true in elderly individuals, when physiologic loss of sural and superficial peroneal sensory responses can prevent the clear distinction between axon loss peripheral polyneuropathy and a chronic or active pattern of bilateral L5 and S1 radiculopathies.

When the process is chronic and active, the EMG pattern may be difficult to distinguish from early to midstage progressive motor neuron disease.

Fig. 4. Diagram depicts the likely anatomic relationship between the T1 and C8 nerve roots and the offending ligamentous band in neurogenic thoracic outlet syndrome, and shows entrapment of the T1 and C8 nerve trunks. Roman numerals indicate vertebral body levels; circled numbers indicate root levels. FTR = first thoracic rib.
(ALS) or progressive necrotizing myelopathy. In ALS, contiguous muscles of the same root or adjoining roots are more likely to show a similar degree neurogenic damage. Early to midstage ALS is also more likely to show a significant distal to proximal gradient of muscle involvement in a limb.

**Diabetic polyradiculopathies**

Radiculopathies caused by diabetes can occur at the thoracic, lumbar, and sacral levels, but have been rarely reported at cervical levels [50]. Approximately

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Fig. 5. Diagram depicts the anatomic relationship between the C8 nerve root and fracture of the first rib near the costotransverse articulation in a patient who has undergone median sternotomy. FTR = first thoracic rib.
25% of diabetic polyradiculopathies occur in the absence of underlying peripheral polyneuropathy [51].

Thoracic radiculopathies occur either unilaterally or bilaterally. They are clinically characterized by cutaneous pain and dysesthesia in the posterior and anterior aspects of the torso in the distributions of the involved roots, and there may be weakness and bulging of the abdominal wall from denervation of rectus abdominus muscles. Thoracic radiculopathies can be confused clinically with intra-abdominal disorders. The NEE shows evidence of denervation in thoracic paraspinal muscles as well as in associated rectus abdominis muscles.

Diabetic lumbosacral radiculopathies may occur at any segmental level, but the L3–L4 levels are especially vulnerable. In one study, 15 of 16 cases...
of diabetic lumbosacral radiculopathy included the L3–L4 level, and 5 of the 15 were limited to that distribution [52]. L5 root involvement occurred in 10 cases. S1 root involvement occurred in seven of these cases and all but one exhibited L5 root involvement. In only one case did L5 and S1 root involvement occur in the absence of L3–L4 root involvement. Bilateral involvement occurred in 11 cases. These data support the clinical observation that diabetic lumbosacral radiculopathy usually begins at the L3–L4 level, often increases over weeks and months to involve contiguous root levels, and eventually may involve the contralateral side.

References

Electrodiagnostic approach to the patient with suspected brachial plexopathy

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Most neurologists encounter with some frequency patients with disorders of the brachial plexus, a reflection of the susceptibility of that structure to injury by trauma and other diseases. Its vulnerability to trauma is related principally to its position between two highly mobile structures—the neck and the shoulder (eg, closed traction injuries). It also is at risk because of the diseases that affect the structures to which it is adjacent (eg, lymph nodes, lung, major blood vessels) \cite{1}. These susceptibilities combine to make disorders of the brachial plexus more than a rare occurrence and mean that it is necessary for electrodiagnosticians to be able to recognize brachial plexus lesions, determine the brachial plexus elements involved, characterize the lesions pathophysiologically, and ascertain the prognosis for recovery, as well as properly plan follow-up electrodiagnostic (EDX) studies based on the EDX abnormalities present. This necessitates an understanding of brachial plexus anatomy, the various pathophysiologies associated with nerve fiber injury, and the EDX manifestations of these pathophysiologies \cite{2}.

Because the brachial plexus is one of the largest and most complex structures of the peripheral nervous system (PNS), there is no single nerve conduction study (NCS) that can be performed or muscle assessed on needle electrode examination (NEE) that can adequately evaluate it. Nonroutine NCS, especially sensory NCS, and extensive NEE assessments typically are required for its adequate evaluation. In addition, the contralateral asymptomatic limb often must also be studied. This permits relative NCS...
and NEE abnormalities of the symptomatic limb to be detected. Therefore, the EDX evaluation of the brachial plexus is typically quite time-consuming. Ironically, the very complexity of this structure is of diagnostic utility because it permits lesions affecting its individual elements (eg, trunks; cords) to be recognized; that is, the pattern of sensory and motor NCS and NEE abnormalities can localize the damage to individual brachial plexus elements. When studies are properly performed, information can be provided to the referring physician that can aid in subsequent management.

In this article, the following are reviewed: (1) brachial plexus anatomy, (2) the classification of brachial plexus lesions, (3) the pathophysiology associated with brachial plexopathies and their EDX manifestations, (4) the courses through the brachial plexus of the sensory and motor nerve fibers composing the major nerves of the upper extremity and shoulder girdle, and (5) the particular nerve fibers assessed by the sensory and motor NCS and by the NEE. The terms myotome and dermatome refer to spinal cord segments and, therefore, can only be applied to the root elements of the PNS. For example, the term C5 myotome refers to all of the muscles innervated by motor nerve fibers emanating from the C5 spinal cord segment. Because this group of muscles is identical to those innervated by the primary C5 ventral nerve root, the term C5 myotome also is used to refer to those muscles innervated by this structure. Likewise, the term C5 dermatome refers to the cutaneous area supplied by the sensory nerve fibers emanating from the C5 spinal cord segment or contained within the primary C5 dorsal nerve root. Because a significant amount of intermingling occurs among these elements as they extend peripherally, the terms myotome and dermatome cannot be applied to them. Thus, the terms upper trunk myotome and median nerve dermatome are improper. Consequently, alternate terms are required when discussing the motor and sensory nerve fibers contained within these elements. We prefer the term muscle domain for the muscles innervated by the motor nerve fibers contained within an individual PNS element, and the term sensory domain for the cutaneous territory subserved by that same PNS element. Consequently, the muscle domain of the upper trunk refers to all of the muscles innervated by motor nerve fibers contained within the upper trunk, whereas the sensory domain of the median nerve indicates the cutaneous territory subserved by the sensory nerve fibers contained within this nerve.

Anatomy of the brachial plexus

The brachial plexus contains approximately 100,000 to 160,000 individual nerve fibers that run inferolaterally from the neck toward the axilla (Fig. 1) [1]. Along their courses they intermingle and give rise to the various brachial plexus elements. The latter can be grouped into five components: roots, trunks, divisions, cords, and terminal nerves. Together, there are five
“roots” (C5 through T1); three trunks (upper, middle, and lower); six divisions (three anterior and three posterior); three cords (lateral, posterior, and medial); and several terminal nerve branches (the latter represent the very proximal aspects of some of the major nerve trunks arising from the brachial plexus).

**Roots**

Anatomically, the dorsal and ventral rootlets exiting from each spinal cord segment fuse to form the primary dorsal and ventral roots, respectively. These traverse the intraspinal canal and enter the intervertebral foramen, where they fuse to form a mixed spinal nerve. The mixed spinal nerve, almost immediately after exiting the foramen, gives off a posteriorly directed branch—the posterior primary ramus—and then continues as the anterior primary ramus (APR). Anatomists consider the roots of the brachial plexus and the APR to be synonymous, whereas surgeons who deal extensively with brachial plexus injuries typically define the roots as consisting of the APR, the posterior primary rami, the mixed spinal nerves, the dorsal and ventral primary roots, and the dorsal and ventral rootlets. Throughout this article, the surgeons’ definition of the term “root” will be utilized. With the surgeons’, but not the anatomists’, approach, avulsion injuries are brachial

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**Fig. 1. The brachial plexus. n = nerve.**

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plexus lesions. Although the brachial plexus typically originates from the C5 through T1 roots, not infrequently the C4 and T2 roots contribute nerve fibers to it. Whenever the C4 contribution is large and the T1 contribution is small, the brachial plexus is termed prefixed; the label postfixixed is used when the C5 contribution is small and the T2 contribution is large [3]. Branches arising from the APR include the unnamed nerves to the scalene and longus colli muscles (via the C5 through C8 APR); the long thoracic nerve (via the C5 through C7 APR), which innervates the serratus anterior; a portion of the phrenic nerve (via the C5 APR), which innervates the diaphragm; and a portion of the dorsal scapular nerve (via the C5 APR), which innervates the levator scapulae and rhomboideus major and minor muscles. Because of their proximal location, these elements cannot be studied using percutaneous stimulation [4,5].

**Trunks**

These brachial plexus elements are named for their relationship to each other: the upper, middle, and lower trunks. The upper trunk is formed by the fusion of the C5 and C6 APR, the middle trunk is a continuation of the C7 APR, and the lower trunk results from the joining of the C8 and T1 APR. The trunk elements give off two motor branches, both from the proximal aspect of the upper trunk: the nerve to the subclavius muscle and the suprascapular nerve. The mid and distal portions of the trunk elements can be studied by percutaneous stimulation applied to the supraclavicular fossa. The proximal aspects of the trunks are not accessible and therefore not accessible by this technique [4,5].

**Divisions**

Two division elements (one anterior and one posterior) are derived from each trunk element. When the body is in the anatomic position, the divisions lie behind the clavicle. This fact is the basis for the most important clinical division—into supraclavicular (roots, trunks) and infraclavicular (cords, terminal nerves) portions—of the brachial plexus. In general, nerve branches do not arise from the divisions [4,5].

**Cords**

These brachial plexus elements are named for their relationship to the second portion of the axillary artery. The lateral cord is formed by the fusion of the anterior divisions of the upper and middle trunks; it contains nerve fibers derived from the C5 through C7 roots. The posterior cord is formed by the joining of all three posterior divisions and contains axons from the C5 through C8 roots. The medial cord is simply a continuation of the anterior division of the lower trunk, and contains nerve fibers derived...
from the C8 and T1 roots. The lateral and medial pectoral nerves arise from the lateral and medial cords, respectively, just after the cords are formed. The lateral cord next gives off the musculocutaneous nerve and then terminates as the lateral head of the median nerve. The posterior cord gives off the subscapular, thoracodorsal, and axillary nerves and continues as the radial nerve. The medial cord gives off the medial brachial cutaneous, medial antebrachial cutaneous, and ulnar nerves and then terminates as the medial head of the median nerve. The cord elements can be studied by percutaneous stimulation [4,5].

**Terminal branches**

Depending on the author, the number of terminal branches derived from the brachial plexus varies from three (median, radial, and ulnar) to five (the latter three nerves plus the musculocutaneous and axillary nerves). The joining of the lateral and medial heads of the median nerve forms the median nerve. Consequently, the median nerve is unique in that it arises from two cord elements. The terminal branches can be studied by percutaneous stimulation [4,5].

**Commentary**

From the above discussion, three clinically relevant points are derived—all of which are important for localizing brachial plexus lesions. First, despite the fact that percutaneous stimulation can only be used to assess the brachial plexus distal to the midportion of the trunks, it is nonetheless possible to identify axon loss lesions lying proximal to this portion of the brachial plexus because the rhomboids and serratus anterior muscles are innervated by branches derived from the C5 through C7 APR. Thus, whenever NEE abnormalities are noted in these muscles, the responsible lesion must lie at or proximal to the APR level of the brachial plexus (i.e., proximal to the upper and middle trunks). Although no branches arise from the C8 and T1 APR elements, the C8 and T1 mixed spinal nerves contain preganglionic sympathetic fibers that when interrupted, produce a Horner’s syndrome. For that reason, whenever a Horner’s syndrome is identified, the lesion often lies at or proximal to the C8 and T1 mixed spinal nerves and, therefore, proximal to the lower trunk. Second, because the pectoral nerves are derived from the most proximal aspects of the cord elements, their involvement or lack thereof can be used to differentiate diffuse supraclavicular lesions from diffuse infraclavicular ones. Third, in general, the motor fibers contained in the supraclavicular brachial plexus elements ultimately innervate both flexor and extensor muscles, whereas the motor fibers contained within the infraclavicular brachial plexus elements innervate either flexor or extensor muscles, but not both. This difference reflects motor fiber rearrangements at the division level. Consequently, APR and trunk lesions are
more similar in appearance to each other than they are to cord or terminal nerve lesions, just as cord and terminal nerve lesions are more similar in appearance to each other than they are to APR or trunk lesions. When one considers that the trunk elements are simply extensions of the root elements minus any fibers exiting at the APR level, and that the terminal nerve branches all derive from the cord elements, these similarities and differences are anatomically quite logical. Whenever a mixed lesion is encountered (i.e., a lesion affecting more than one brachial plexus element), localization is much more challenging, especially when both supraclavicular and infraclavicular elements are involved simultaneously.

**The classification of brachial plexus lesions**

Brachial plexus lesions are divided into supraclavicular and infraclavicular plexopathies because injuries at the division level are infrequent in isolation and, as already stated, lesions affecting the supraclavicular elements resemble each other, as do those involving the infraclavicular elements. More importantly, because these two categories differ in their incidence, severity, and prognosis, this classification system has clinical relevance. Lesions of the supraclavicular plexus are more common and, due to their nature, frequently are more severe; for this reason, they tend to have a worse prognosis [6,7]. Supraclavicular plexus lesions are further divided into upper plexus (the upper trunk and the C5 and C6 roots), middle plexus (the middle trunk and the C7 root), and lower plexus (the lower trunk and the C8 and T1 roots) lesions (see Fig. 1). These categories also have clinical relevance. Upper plexus lesions often have a better prognosis than lower plexus lesions because (1) their pathophysiology is more commonly demyelinating conduction block (ie, recovery tends to be much more complete than with axon regeneration); (2) their location is more proximate to the muscles they innervate (ie, reinnervation by proximo-distal axon regeneration is more likely); and (3) they are more frequently extraforaminal (ie, they are more amenable to surgical repair). Unlike upper plexus lesions, lower plexus lesions are (1) less frequently due to demyelinating conduction block (more commonly axon loss); (2) typically much further from the muscles they innervate (and therefore the latter are less likely to undergo reinnervation by proximo-distal axon regrowth from the lesion site); and (3) more frequently intraforaminal (less amenable or not amenable to surgical repair); thus, they tend to be more severe and, therefore, their prognosis is worse. For these reasons, upper trunk lesions have more complete resolution than lower trunk lesions, despite initially equal severity [8]. Consequently, an axon loss supraclavicular plexus lesion that initially involves all three trunk elements equally may appear as a remote lower trunk lesion when it is studied years after the inciting event. The individual disorders associated with supra- and infraclavicular plexus lesions also differ. *Supraclavicular plexopathies* are primarily
related to closed-traction injuries (eg, obstetric paralysis, motor vehicle accidents, burn syndrome); malpositioning on the operating table (eg, classic postoperative paralysis); rucksack palsy; neoplastic processes (especially lung or breast cancer); true neurogenic thoracic outlet syndrome; disputed thoracic outlet syndrome surgery; and plexopathies related to median sternotomy (eg, open heart surgery), whereas infraclavicular plexopathies are more frequently related to trauma (eg, radiation, gun shot and stab wounds, humeral head fractures, midshaft clavicular fractures, shoulder dislocations); medial brachial fascial compartment syndrome; crutch use; and iatrogenic causes (shoulder operations, shoulder arthroscopy, axillary arteriogram, axillary regional anesthetic blocks) [9,10].

EDX manifestations of the various pathophysiologic subtypes

Although the individual nerve fibers composing the brachial plexus can be injured by a multitude of mechanisms, their pathologic and pathophysiologic responses are limited. When lesions produce maximal nerve fiber damage, axon continuity is lost and results in Wallerian degeneration (ie, axon loss) pathologically, and conduction failure pathophysiologically. Until Wallerian degeneration occurs (usually first apparent on NCS 2–3 days after nerve damage), however, the distal stump remains quite capable of conducting nerve impulses. The latter phenomenon has profound consequences on the timing of the EDX study and on its interpretation (discussed later). Lesions of lesser severity may result in solely or predominantly demyelination. The pathophysiologic response of the demyelinated fibers then depends upon whether they have lost their ability to conduct impulses (ie, demyelinating conduction block) or continue to do so, but at a slower rate (ie, demyelinating conduction slowing). Each of these pathophysiologies has unique EDX and clinical manifestations (now discussed).

Axon loss lesions

Most brachial plexus lesions are axon loss in nature and, among these, most are solely of this type (ie, they are not accompanied by a component of focal demyelination). Examples are avulsions and neoplastic processes. Therefore, axon loss plexopathies are the most commonly studied type of brachial plexus lesion in the electromyography laboratory. Infrequently, concomitant demyelination is present (early traumatic lesions, radiation-induced plexopathies). As previously stated, axon loss produces conduction failure. Because the amplitude reflects the total number of conducting fibers, conduction failure reduces the amplitude of the sensory nerve action potential (SNAP) and of the compound muscle action potential (CMAP). In contrast, the latencies and conduction velocities reflect the conduction rates along only the fastest conducting fibers. Thus lesion can be quite severe and yet spare some of the faster conducting fibers. In this setting, the calculated
latencies and conduction velocities are normal, despite the fact that the recorded amplitude is quite low. When Wallerian degeneration occurs and the distal stump becomes incapable of propagating impulses, the recorded amplitude is the same regardless of where the nerve is stimulated (ie, proximal to, at, or distal to the lesion) because the affected nerve fibers cannot generate or propagate action potentials. Consequently, whether the lesion affects the cell body of origin of the axon (the motor neuron located in the spinal cord for the motor fiber or the sensory neuron located in the dorsal root ganglion (DRG) for the sensory fiber) or the axon itself, the effect that it has on the recorded SNAP or CMAP is the same: the amplitude is reduced. Whenever the amplitude of the recorded response is less than the age-based laboratory control value for that NCS, the response is considered absolutely abnormal. Whenever it is less than half the amplitude of the homologous response recorded from the contralateral side, in most EDX laboratories it is termed relatively abnormal. On NEE, fibrillation potentials and motor unit action potential (MUAP) dropout may be observed in the setting of axon loss. Although MUAP dropout is present from the time the nerve fiber becomes disrupted, usually it cannot be appreciated when the assessed muscle is only mild-to-moderately denervated. Because most limb muscles have an innervation ratio (ie, the average number of muscle fibers innervated per motor nerve fiber) of a few hundred to several hundred or more, hundreds of fibrillation potentials are produced per disrupted motor nerve fiber. In general, fibrillation potentials appear about 3 weeks after the motor nerve fiber is injured and, because of the innervation ratio, can be quite prominent even when the lesion is only minimal in degree. Because axon loss lesions of the brachial plexus are on a continuum from minimal to extremely severe, their EDX manifestations vary. With minimal lesions affecting both the sensory and motor fibers, only fibrillation potentials may be observed; the SNAPs and CMAPs are spared. With more severe lesions, the appropriate SNAP amplitudes decrease. Greater severity next produces a decrease in CMAP amplitude and concomitant MUAP loss. At this point, the SNAP responses typically are quite low in amplitude or unelicitable. With even more severe lesions, the appropriate CMAP amplitudes decline further and MUAP dropout becomes more obvious. Of the various components of the EDX examination (ie, sensory NCS; motor NCS; NEE), the CMAP amplitudes are the most useful for quantifying the amount of axon loss suffered by a nerve [8]. The other EDX study components are less helpful: SNAP amplitudes frequently are absent when far less than all of the axons contained within the element under study have undergone degeneration, whereas fibrillation potentials typically are widespread even with minimal degrees of axon loss (a reflection of the high innervation ratio of most limb muscles). Also, the MUAP dropout apparent on NEE is challenging to quantify. Thus, prior to reinnervation, the CMAP amplitudes are the most reliable indicator of the amount of axon loss present, and the relationship is roughly one to one. For example, if the value...
of the CMAP amplitude from the symptomatic side is 5 mV, whereas that of the homologous response recorded from the asymptomatic side is 10 mV, then approximately 50% of the motor axons contained within the affected element are affected (discussed further later).

The timing of the EDX study also is extremely important. Failure to consider the temporal relationship between the inciting event and the EDX study often results in significant misinterpretations of the acquired data, with resulting misleading conclusions. In general, the CMAP amplitudes begin to decrease on day 2 or 3 and reach their nadir at day 7, whereas the SNAP amplitudes begin to drop on day 6 and reach their nadir around day 10 or 11. As already mentioned, fibrillation potentials often do not fully appear until the beginning of the fourth week (i.e., after day 21) after the inciting event. Although MUAP loss occurs immediately, it may not be appreciated unless the lesion is at least moderate in degree. Thus, when a patient with a severe upper trunk lesion is studied on day 6, the pattern of normal SNAPs and abnormal CMAPs may be mistakenly localized to the intraspinal canal (eg, C5,C6 root avulsion injury, severe C5 or C6 radiculopathy).

After enough time has passed for some of the affected muscle fibers to become reinnervated—via either progressive advancement of affected motor fibers from their injury site to the denervated muscle fibers (proximodistal regeneration) or the collateral sprouting from unaffected motor fibers—EDX features of reinnervation may become apparent in the appearance of the MUAPs. These include prolonged duration, increased polyphasia and, occasionally, heightened amplitude.

Prognostication is another important EDX function. For axon loss lesions, this usually is dictated by the potential for reinnervation, which can be determined by considering the grade of the injury, the distance between the injury site and the denervated muscle fibers, and the completeness of the lesion. The grade of the injury reflects the damage sustained by the supporting structures of the affected nerve (ie, the endoneurium, perineurium, and epineurium). When all of the supporting structures are affected, axon advancement cannot occur. In this setting, any reinnervation must occur either by collateral sprouting or following surgical treatment of the injured segment. When all of the supporting structures are spared, there is no impediment to proximodistal regeneration other than the distance between the lesion site and the denervated muscle fibers (discussed later). In this setting, both collateral sprouting and proximodistal regeneration can occur. The length of nerve between the lesion site and the denervated muscle fibers determines the distance that the motor fibers must advance. In general, advancement occurs at a rate of about 1 in/mo and denervated muscle fibers survive for approximately 18 to 24 months. After this period of time has elapsed, the muscle fibers undergo degeneration and, from that point onward, can no longer be reinnervated. Consequently, whenever the denervated muscle fibers lie more than 2 ft from the injury site,
reinnervation generally cannot occur by proximodistal regeneration. Rather, it must do so by collateral sprouting. When the lesion is complete (ie, when all of the nerve fibers are affected), there are no nerve fibers from which collateral sprouts may arise. Thus, collateral sprouting requires that the lesion be incomplete. Hence, the more incomplete the lesion, the better the potential for reinnervation by this mechanism. In summary, the best prognosis for motor recovery exists when (1) the supporting structures are spared, (2) the distance between the lesion and the denervated muscle fibers is short, and (3) the lesion is incomplete. Because the end organs of the sensory nerve fibers do not undergo degeneration, there is no time limit on sensory nerve fiber regeneration. Consequently, if it requires more than 2 years for the sensory fibers to reach their end organs, reinnervation of the latter can still be successful. Clinically, the degree of SNAP amplitude decrement correlates rather well with the amount of large fiber sensory modality loss (vibratory and proprioceptive perceptions). This also is true for the CMAP amplitude reductions and clinical weakness. Thus, when the CMAP recorded from an affected muscle is 50% less than the contralateral side, that muscle usually has lost about half of its strength. Paralyzed muscles typically are associated with absent CMAPs. During motor NCS, the negative area under the curve parameter is even more accurate than is the amplitude for making these determinations.

When a significant axon loss lesion lies within the intraspinal canal (ie, proximal to the DRG), it may affect the motor and sensory fibers located there. Because the motor fibers project distally and contribute to the PNS elements studied by the motor NCS and NEE components of the EDX examination, their involvement is recognizable. Because the affected sensory fibers are preganglionic and enter the central nervous system, they are not identified by sensory NCS because the Wallerian degeneration that they induce does not involve the ganglionic or postganglionic PNS elements assessed by the sensory NCS. Therefore, intraspinal canal lesions may affect the motor NCS and NEE components of the electromyography examination, but not the sensory NCS; an exception exists when the DRG lies within the intraspinal canal [11]. This pattern of motor NCS and NEE involvement with sensory NCS sparing is also observed with muscle fiber (eg, myopathies), neuromuscular junction (eg, Lambert-Eaton myasthenic syndrome), and terminal motor branch (eg, early Guillain-Barre syndrome) disorders, as well as with nerve element axon loss lesions studied at a time (eg, days 5–7 after injury) when the amplitudes of the motor NCS have been recognizably affected by Wallerian degeneration but those of the sensory NCS have not as yet. Although isolated CMAP abnormalities strongly suggest that the lesion lies at a site other than where the sensory and motor nerve fibers are contiguous, this statement does not apply to isolated SNAP abnormalities because sensory fibers are more sensitive to axon loss lesions than motor fibers. Consequently, isolated SNAP abnormalities cannot be used to exclude motor axon involvement. Mild
motor axon loss does not register on motor NCS and, after the fibrillation potentials associated with the denervated muscle fibers disappear (ie, after reinnervation), it is typically too subtle to be recognized by MUAP inspection during NEE. When enough time has elapsed to allow for reinnervation by collateral sprouting, even previously severe motor nerve fiber loss may no longer be evident on motor NCS because enough muscle fibers have been reinnervated to normalize the recorded CMAP. Fortunately, however, such severe motor nerve fiber loss with subsequent reinnervation is permanently reflected on the NEE as increased duration MUAPs and reduced MUAP recruitment (ie, MUAPs firing in decreased numbers with a firing rate that is more rapid than that normally observable). Because the sensory NCS are so sensitive to axon loss processes, it is important to perform extensive sensory NCS whenever an axon loss brachial plexopathy is suspected. As will be discussed later, the pattern of sensory NCS abnormalities often localizes the lesion to a particular brachial plexus element before the motor NCS and NEE are even performed. Prior to reinnervation, motor axon loss is most readily identified, but not well quantified, by the presence of fibrillation potentials on NEE. In addition, the pattern of fibrillation potentials often can be used to localize a lesion to a particular brachial plexus element. After reinnervation has occurred, however, MUAP parameters (eg, duration, number firing, and firing rate) are more sensitive to motor fiber loss than are CMAP changes. In general, roughly 50% of the motor fibers must be lost before the CMAP becomes significantly reduced in amplitude.

Demyelinating lesions

Demyelinating lesions may be focal (eg, carpal tunnel syndrome), multifocal (multifocal motor neuropathy; radiation injury), or generalized (eg, hereditary motor-sensory polyneuropathy) in distribution; only focal lesions are pertinent to a discussion of brachial plexus lesions. Unlike axon loss lesions, which induce pathologic changes distal to the disrupted axon and affect the NCS regardless of stimulation site, demyelinating lesions do not induce nerve fiber changes proximal or distal to the focal lesion. Therefore, their direct recognition is stimulation site-dependent; they are readily identified only when the lesion lies between the stimulating and recording electrodes.

There are two types of pathophysiology associated with demyelination: conduction slowing and conduction block. With demyelinating conduction slowing, all of the impulses traverse the lesion site, albeit at a slower-than-normal rate. Because they all ultimately reach their respective end organs, weakness and sensory loss typically are absent. For that reason, patients with brachial plexus lesions related to this pathophysiology are asymptomatic with regard to negative phenomena (ie, numbness, weakness) and, thus, seldom referred to EDX laboratories. Therefore, this type of pathophysiology will not be discussed further. Unlike demyelinating conduction
slowing, demyelinating conduction block, as the term implies, stops the propagation of impulses at the lesion site, thereby preventing them from reaching their end organs. As a result, this pathophysiology, when it affects a sufficient number of axons, is symptomatic, and the symptoms are identical to those produced by axon loss lesions (except that the sensory deficits involve only large fiber modalities). Unlike axon loss, however, demyelinating conduction block is seldom observed in isolation. Instead, some accompanying axon loss usually is present. The rationale behind this finding is straightforward: any lesion severe enough to produce demyelinating conduction block along most of the affected nerve fibers generally is severe enough to produce axon loss in at least some of them [5]. When weakness has been present for 7 days (the time required for axon loss-related motor NCS changes to be evident on stimulation along the distal stump), significant demyelinating conduction block lesions are identified when the CMAP amplitude obtained on distal stimulation is significantly higher than the one obtained on stimulating proximal to the lesion site. Whenever both the stimulating and recording electrodes lie either proximal or distal to the demyelinating conduction block lesion, this amplitude discrepancy is not noted. Thus, whenever a significant demyelinating conduction block is located proximal to both the stimulating and recording electrodes, the distal and proximal CMAP amplitudes appear normal. Clinically, however, the CMAP amplitudes are too preserved for the degree of clinical weakness reported or observable and, for that reason, a demyelinating conduction block lesion should be suspected. The presence of such a lesion proximally can be recognized by the discordance between the normal/near normal CMAP amplitude recorded from the weak muscle and the degree of MUAP dropout (ie, reduced MUAP recruitment) noted on NEE of it. In this setting, an attempt to localize the proximal lesion, by stimulating at progressively more proximal nerve sites (ie, axilla; supraclavicular) must be made. Whenever the lesion lies proximal to the upper midtrunk level (ie, the most proximal stimulation site available for surface stimulation of the brachial plexus), a CMAP amplitude decrement will not be observed with surface stimulation. Nonetheless, its presence can be inferred, based on the CMAP/NEE discordance just described. With demyelinating conduction block lesions, the degree of MUAP dropout should match the degree of CMAP amplitude decrement seen on stimulation proximal to the injury site. Clinically, one should be aware that although most demyelinating conduction block lesions reflect acute trauma and are associated with a good prognosis, there are at least two chronic brachial plexus conditions in which demyelinating conduction block is the predominant pathophysiology and the prognosis is not good: the early and middle stages of radiation-induced plexopathy (these lesions later convert to axon loss and never resolve) and multifocal motor neuropathy and its variants (these lesions tend to be slowly progressive in nature and may not respond well to treatment).
EDX assessment of the brachial plexus

Each brachial plexus element, in addition to having its own muscle domain (ie, the muscles innervated by the motor nerve fibers composing that element), also has its own SNAP domain (ie, the sensory nerve fibers traversing it that subserve sensory NCS) and CMAP domain (ie, the motor nerve fibers traversing it that subserve motor NCS). Consequently, whenever it sustains an axon loss injury, a particular pattern of EDX abnormalities (ie, SNAP, CMAP, and NEE changes) often results, recognition of which permits localization of the lesion to that element. As expected for a structure of its size, an adequate EDX assessment of the brachial plexus requires the performance of a large number of sensory and motor NCS and an extensive NEE. Consequently, there are no shortcuts to its proper EDX evaluation. All components of the EDX examination (ie, sensory and motor NCS and NEE) must be performed, as each one complements the information obtained by the other two. Omitting any one of these examinations often renders the assessment incomplete and, frequently, misleading. The sensory NCS are extremely useful for identifying and localizing lesions affecting the various brachial plexus elements [12] because they are the only portion of the EDX examination that assesses the ganglionic sensory neurons because they and their postganglionic nerve fibers (ie, the sensory nerve fibers traversing the brachial plexus), are extremely sensitive to axon loss. Moreover, based on the pattern of abnormalities observed, they are often capable of precisely localizing the lesion to an individual brachial plexus element even before the motor NCS and NEE are performed [13]. This reflects the fact that the sensory nerve fibers subserving each sensory NCS traverse the brachial plexus along known pathways [12]. The latter are illustrated in Figs. 2 through 6 (the pathways taken by the sensory nerve fibers subserving the ulnar NCS recording from fifth digit (Uln-D5) and medial antebrachial cutaneous (MABC) NCS are not shown because they are anatomically defined and, therefore, not debated; they traverse the medial cord and the lower trunk to enter the C8 DRG and T1 DRG, respectively). Even when the sensory NCS localize an axon loss lesion, performance of the motor NCS and NEE are still required. The motor NCS document the severity of the axon loss lesion, whereas the NEE helps to localize its proximal extent. The motor NCS are less sensitive to axon loss than are the other two components of the EDX study. Thus, low amplitude CMAPs usually indicate that the axon loss is at least moderate to severe in degree. One of the most beneficial attributes of motor NCS is their ability to quantify axon loss. In the setting of an axon loss lesion—before reinnervation has begun to occur—the amplitude and negative area under the curve values, when compared to the contralateral values, are the most useful parameters by which to estimate the percentage of motor axon loss, assuming that the contralateral responses are normal. The NEE is the most sensitive component regarding motor axon loss. One
negative attribute of this portion of the EDX study is its tendency to mis-localize lesions more distally than they actually are, which is a reflection of two facts: (1) partial proximal lesions mimic distal lesions and (2) recovery is more complete proximally than distally. For example, when a lower trunk lesion spares the C8/radial nerve-innervated muscles (eg, extensor indicis proprius; extensor pollicis brevis), it mimics a medial cord lesion. In addition, in the setting of mild motor axon loss, when the denervated muscle fibers in the affected muscles are reinnervated, they frequently are no longer recognized as being abnormal. Because recovery tends to proceed in a proximal-to-distal direction, only the muscles located more distally appear abnormal. Thus, the lesion appears to lie distal to its actual position.

Assessment of individual brachial plexus elements

Knowing which sensory and motor nerve fibers are contained within an individual brachial plexus element allows one to determine its CMAP and SNAP domains. The muscle domain of an individual brachial plexus element is ascertained from the standard myotomal charts. Thus, because the biceps muscle belongs to both the C5 and C6 myotomes, it receives its innervation from motor axons derived from the C5 and C6 anterior horn cells. Based on known anatomy, these motor axons must traverse the C5 and C6 roots, the C5 and C6 mixed spinal nerves, the C5 and C6 APR, the upper trunk, the lateral cord, and the musculocutaneous nerve to reach the biceps muscle. Consequently, each of these PNS elements includes the biceps muscle in its muscle domain, and their CMAP domains include the musculocutaneous CMAP, recording biceps. The derivation of the SNAP domain for a given brachial plexus element is more complicated. Fortunately, however, these domains are known [12].

At this point, the SNAP, CMAP, and muscle domains of the individual brachial plexus elements will be discussed. For ease of understanding, the term NEE domain will be taken to be synonymous with the term muscle domain. The median and ulnar palmar NCS and the dorsal ulnar cutaneous NCS are omitted from this discussion because, with regard to brachial plexus lesions, they do not provide additional information not already realized by the standard sensory NCS. The SNAP domains of the trunk and cord elements are provided in Box 1, respectively. The NEE domains of the individual brachial plexus elements can be readily derived through anatomic reasoning. Thus, the NEE domain of any brachial plexus element is equivalent to the sum of the NEE domains of the elements forming it, minus the NEE domains of the elements departing prior to its formation. For example, the NEE domain of the upper trunk is equivalent to the sum of the NEE domains of the C5 and C6 roots (ie, the proximal elements forming the upper trunk) minus the sum of the NEE domains of the long thoracic (serratus anterior) and dorsal scapular (levator scapulae, rhomboideus major and minor)
Box 1
The SNAP domains of the trunk and cord elements

<table>
<thead>
<tr>
<th>Upper trunk</th>
<th>Lateral cord</th>
</tr>
</thead>
<tbody>
<tr>
<td>LABC (100%)</td>
<td>LABC (100%)</td>
</tr>
<tr>
<td>Med-D1 (100%)</td>
<td>Med-D1 (100%)</td>
</tr>
<tr>
<td>S-Radial (60%)</td>
<td>Med-D2 (100%)</td>
</tr>
<tr>
<td>Med-D2 (20%)</td>
<td>Med-D3 (80%)</td>
</tr>
<tr>
<td>Med-D3 (10%)</td>
<td>Posterior cord</td>
</tr>
<tr>
<td>Middle trunk</td>
<td>S-Radial</td>
</tr>
<tr>
<td>Med-D2 (80%)</td>
<td>Medial cord</td>
</tr>
<tr>
<td>Med-D3 (70%)</td>
<td>Uln-D5 (100%)</td>
</tr>
<tr>
<td>S-Radial (40%)</td>
<td>MABC (100%)</td>
</tr>
<tr>
<td>Lower trunk</td>
<td>Med-D3 (20%)</td>
</tr>
<tr>
<td>Uln-D5 (100%)</td>
<td></td>
</tr>
<tr>
<td>MABC (100%)</td>
<td></td>
</tr>
<tr>
<td>Med-D3 (20%)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: LABC, lateral antebrachial cutaneous NCS; Med-D1, median NCS recording from first digit; Med-D2, median NCS recording from second digit; Med-D3, median NCS recording from third digit; MABC, medial antebrachial cutaneous NCS; S-Radial, superficial radial NCS; Uln-D5, ulnar NCS recording from fifth digit.

nerves (ie, the nerve branches exiting the C5 and C6 roots). The myotome charts differ slightly by author. We have included those muscles that we consider most useful from the standpoint of the EDX examination. The NEE domains of individual nerves are not provided, as these are well known. The CMAP domains of the trunk and cord elements of the brachial plexus can be derived from the NEE domains of these elements; they are provided in Box 2. Those NEE domains of the trunk and cord elements most useful for NEE are provided in Box 3.

C5 APR

There are no sensory nerve fibers traversing this element that can be assessed with a sensory NCS. Thus, there is no SNAP domain for this element. Its CMAP domain includes the musculocutaneous NCS, recording biceps (Musc-biceps) and the axillary NCS, recording deltoid (Ax-deltoid). Its NEE domain includes those muscles contained within the C5 myotome.

C6 APR

The sensory nerve fibers traversing this element subserve the lateral antebrachial cutaneous NCS (LABC; 100%), the median NCS recording from
first digit (Med-D1; 100%), the superficial radial NCS (S-Radial; 60%), the
median NCS recording from second digit (Med-D2; 20%), and the median
NCS recording from third digit (Med-D3; 10%) sensory NCS. For this rea-
son, these sensory NCS are included in its SNAP domain [12]. Because the
biceps and deltoid muscles belong to the C6 myotome, the CMAP domain
of the C6 APR includes the Musc-biceps and the Ax-deltoid motor NCS. Its
NEE domain includes muscles belonging to the C6 myotome.

C7 APR

The sensory nerve fibers traversing this element subserve the Med-D2
(80%), the Med-D3 (70%), and the S-Radial (40%) sensory NCS and, con-
sequently, these sensory NCS are included in its SNAP domain [12]. Al-
though the radial NCS, recording extensor digitorum communis (Radial-
EDC) response is contained within its CMAP domain, the heavy C6 input
to this muscle makes it a less-than-adequate assessor of this element. Its
NEE domain includes muscles belonging to the C7 myotome.

C8 APR

The sensory nerve fibers traversing this element subserve the Uln-D5 sen-
sory NCS and, hence, this sensory NCS is contained in its SNAP domain.
The sensory nerve fibers composing the MABC nerve predominantly traverse the T1 APR and, therefore, this response is not included in the SNAP domain of the C8 APR [5,8]. The CMAP domain of the C8 APR includes the ulnar NCS, recording abductor digiti minimi (Ulnar-ADM); the ulnar NCS, recording first dorsal interosseous (Uln-FDI); and the radial NCS, recording extensor indicis proprius (Radial-EIP) motor NCS; and to a lesser extent, the median NCS, recording abductor pollicis brevis (Median-APB) motor NCS. Its NEE domain consists of those muscles belonging to the C8 myotome.

**T1 APR**

The sensory nerve fibers traversing this element subserve the MABC sensory NCS and, for that reason, this sensory NCS is included in its SNAP domain [11,12]. Its CMAP domain is the same as that of the C8 APR. Because the abductor pollicis brevis muscle receives innervation mostly from T1 anterior horn cells [5,8], the Median-APB NCS is a more reliable assessor of this element than are the ulnar motor NCS. Its NEE domain consists of those muscles belonging to the T1 myotome. Of these, the abductor pollicis brevis and flexor pollicis longus muscles are the most helpful in its assessment.

**Upper trunk**

After the dorsal scapular and long thoracic nerve branches exit from the APR level of the brachial plexus, the C5 and C6 APR join to form the upper trunk. Because there are no reliable sensory NCS available for the exiting nerves or for the C5 APR, the SNAP domain of the upper trunk element is the same as that for the C6 APR. Because the CMAP domain of the C5 and C6 APR are identical, the CMAP domain of the upper trunk also is the same. The NEE domain of the upper trunk is equivalent to the NEE domains of the C5 and C6 APR minus the NEE domains of the dorsal scapular and long thoracic nerves. The most useful muscles for NEE of this element are provided in Box 3.

**Middle trunk**

The middle trunk is a continuation of the C7 APR minus the nerve branch to the long thoracic nerve. Thus, its SNAP and CMAP domains are the same as those of the C7 APR. Its NEE domain is equivalent to the C7 NEE domain minus the serratus anterior muscle. The most useful muscles for NEE of this element are listed in Box 3.

**Lower trunk**

The lower trunk is formed by the fusion of the C8 and T1 APR. Consequently, its SNAP, CMAP, and NEE domains are equivalent to the sum of
those of the C8 and T1 APR. The most useful muscles for NEE of this element are provided in Box 3.

**Lateral cord**

Anatomically, the lateral cord consists of the anterior divisions of the upper and middle trunks minus the suprascapular nerve. For that reason, the SNAP domain of the lateral cord includes the LABC, Med-D1, Med-D2, and Med-D3 sensory NCS; and its CMAP domain includes the Musc-biceps motor NCS. The NEE domain of the lateral cord is equivalent to the sum of the NEE domains of the upper and middle trunks minus those muscles innervated by the suprascapular, subscapular, thoracodorsal, radial, and axillary nerves whose motor nerve fibers traverse the upper or middle trunks. The most useful muscles for NEE of this element are shown in Box 3.

**Posterior cord**

Anatomically, the posterior cord consists of the sum of the posterior divisions of all three trunks (ie, the subscapular thoracodorsal, axillary, and radial nerves). Consequently, its SNAP, CMAP, and muscle domains are equivalent to the sum of those of these nerves. The most useful muscles for NEE of this element are listed in Box 3.

**Medial cord**

Anatomically, the medial cord represents the continuation of the anterior division of the lower trunk. Thus, its SNAP, CMAP, and muscle domains are equivalent to those of the lower trunk minus the SNAP, CMAP, and NEE domains of its posterior division. The most useful muscles for NEE of this element are shown in Box 3.

**Axillary nerve**

There are no sensory NCS that assess this nerve and, therefore, there is no SNAP domain for this nerve. Its CMAP domain is the Ax-deltoid CMAP. Its NEE domain consists of the axillary nerve-innervated muscles.

**Musculocutaneous nerve**

The sensory nerve fibers composing the musculocutaneous nerve are assessed by the LABC response, the only sensory NCS in its SNAP domain. Its CMAP domain consists of the Musc-biceps response and its NEE domain includes the musculocutaneous nerve-innervated muscles.

**Radial nerve**

The S-Radial sensory NCS constitutes its SNAP domain, whereas the Radial-EDC and Radial-EIP motor NCS compose its CMAP domain. Its
Box 3
Useful muscles for NEE of the trunk and cord elements

<table>
<thead>
<tr>
<th>Upper trunk</th>
<th>Lateral cord</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supraspinatus</td>
<td>Biceps</td>
</tr>
<tr>
<td>Infraspinatus</td>
<td>Brachialis</td>
</tr>
<tr>
<td>Teres minor</td>
<td>Pronator teres</td>
</tr>
<tr>
<td>Deltoid</td>
<td>Flexor carpi radialis</td>
</tr>
<tr>
<td>Biceps</td>
<td>Posterior cord</td>
</tr>
<tr>
<td>Brachioradialis</td>
<td>Latissimus dorsi</td>
</tr>
<tr>
<td>Pronator teres</td>
<td>Teres minor</td>
</tr>
<tr>
<td>Extensor carpi radialis</td>
<td>Deltoid</td>
</tr>
<tr>
<td>Pectoralis major</td>
<td>Triceps</td>
</tr>
<tr>
<td>(Triceps)</td>
<td>Anconeus</td>
</tr>
<tr>
<td>Middle trunk</td>
<td>Brachioradialis</td>
</tr>
<tr>
<td>Triceps</td>
<td>Extensor carpi radialis</td>
</tr>
<tr>
<td>Anconeus</td>
<td>Extensor digitorum</td>
</tr>
<tr>
<td>Pronator teres</td>
<td>communis</td>
</tr>
<tr>
<td>Flexor carpi radialis</td>
<td>Extensor carpi ulnaris</td>
</tr>
<tr>
<td>Extensor carpi radialis</td>
<td>Extensor pollicis brevis</td>
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<tr>
<td>Extensor digitorum</td>
<td>Extensor indicis proprius</td>
</tr>
<tr>
<td>communis</td>
<td>Medial cord</td>
</tr>
<tr>
<td>Lower trunk</td>
<td>Flexor carpi ulnaris</td>
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<tr>
<td>Flexor carpi ulnaris</td>
<td>Flexor digitorum</td>
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<tr>
<td>Flexor digitorum profundus–4/5</td>
<td>profundus–4/5</td>
</tr>
<tr>
<td>Extensor digitorum communis</td>
<td>Flexor pollicis longus</td>
</tr>
<tr>
<td>Extensor carpi ulnaris</td>
<td>Abductor digiti minimi</td>
</tr>
<tr>
<td>Extensor pollicis brevis</td>
<td>First dorsal interosseous</td>
</tr>
<tr>
<td>Extensor indicis proprius</td>
<td>Abductor pollicis brevis</td>
</tr>
<tr>
<td>Abductor digiti minimi</td>
<td>Opponens pollicis</td>
</tr>
<tr>
<td>First dorsal interosseous</td>
<td></td>
</tr>
<tr>
<td>Abductor pollicis brevis</td>
<td></td>
</tr>
</tbody>
</table>

NEE domain consists of those muscles innervated by the radial and posterior interosseous nerves.

**Median nerve**

The Med-D1, Med-D2, and Med-D3 sensory NCS make up its SNAP domain, whereas the Median-APB motor NCS constitutes its CMAP domain. Its NEE domain consists of those muscles innervated by the median nerve.
Ulnar nerve

The Uln-D5 sensory NCS constitutes its SNAP domain, the Ulnar-ADM and Ulnar-FDI motor NCS constitute its CMAP domain, and the muscles innervated by the ulnar nerve make up its NEE domain.

MABC nerve

The MABC sensory NCS constitutes the SNAP domain of this element. There is no CMAP or NEE domain because this nerve contains only sensory nerve fibers.

Commentary

Based on the SNAP domains of the brachial plexus elements outlined above, the pathways through the brachial plexus that are traversed by the sensory nerve fibers subserving the various sensory NCS are easily determined (see Figs. 2–6). As shown in these figures, each sensory NCS assesses more than one brachial plexus element. Knowing which brachial plexus elements are assessed by the various sensory NCS permits one to localize lesions to the particular brachial plexus element(s) involved. The pathways taken by the sensory nerve fibers subserving each of the seven sensory NCS utilized in brachial plexus assessment and their variations are discussed next. The frequency that axon loss lesions of individual brachial plexus elements produce sensory NCS abnormalities is shown in Table 1, and is the basis for the following commentary [12].

- The LABC response assesses the LABC nerve, the musculocutaneous nerve, the lateral cord, the upper trunk, and the C6 APR 100% of the time.

![Fig. 2. The brachial plexus elements assessed by the LABC sensory NCS. antebrach. = antebra- chial; cut. = cutaneous; lat. = lateral; med. = medial; n. = nerve; post. = posterior.](image-url)
• The Med-D1 response assesses the median nerve, the lateral cord, the upper trunk, and the C6 APR 100% of the time (Fig. 3).
• The Med-D2 response assesses the median nerve and lateral cord 100% of the time, the upper trunk and C6 APR 20% of the time, and the middle trunk and C7 APR 80% of the time (Fig. 4).
• The Med-D3 response assesses the median nerve 100% of the time, the lateral cord 80% of the time, the medial cord 20% of the time, the upper trunk and C6 APR 10% of the time, the middle trunk and C7 APR 70% of the time, and the lower trunk and C8 APR 20% of the time (Fig. 5).
- The S-Radial response assesses the superficial radial nerve, the radial nerve, and the posterior cord 100% of the time, the upper trunk and C6 APR 60% of the time, and the middle trunk and C7 APR 40% of the time (Fig. 6).
- The Uln-D5 response assesses the ulnar nerve, the medial cord, the lower trunk, and the C8 APR 100% of the time.
- The MABC response assesses the MABC nerve, the medial cord, the lower trunk, and the T1 APR 100% of the time.

Fig. 5. The brachial plexus elements assessed by the Med- D3 sensory NCS. antebrach. = antebrachial; cut. = cutaneous; lat. = lateral; med. = medial; n. = nerve; post. = posterior.

Fig. 6. The brachial plexus elements assessed by the S-Radial sensory NCS. antebrach. = antebrachial; cut. = cutaneous; lat. = lateral; med. = medial; n. = nerve; post. = posterior.
An approach to the EDX assessment of the brachial plexus

Rather frequently, patients determined to have brachial plexopathies in the EDX laboratory were referred with some other diagnostic consideration, and the brachial plexus lesion became apparent during the EDX assessment. If only the diagnostic considerations put forth by the referring physician were sought, many of these brachial plexus lesions would be missed. For example, when a patient with a lower trunk lesion is referred for EDX evaluation of a suspected ulnar neuropathy, if only ulnar sensory and motor NCS are performed and only ulnar nerve-innervated muscles are sampled on NEE, then an incorrect confirmation will result. To avoid this pitfall, a detailed EDX approach is required. The ideal one would equally assess all of the PNS elements contained within the upper extremity. Our approach toward any patient referred with upper extremity symptoms begins with a “general survey” (Box 4). Although this assesses every PNS element in the upper extremity including all elements of the brachial plexus, it does not evaluate all of the brachial plexus elements equally. Rather, it assesses the medial cord and lower trunk elements most extensively, the lateral cord, posterior cord, and middle trunk elements to a lesser extent, and the upper trunk element the least. Consequently, whenever an individual is referred for assessment of the brachial plexus, or whenever the EDX findings suggest the presence of a brachial plexus lesion—especially an upper trunk lesion—additional NCS are required. Typically, the appropriate sensory NCS are added first and, when abnormal, are followed by the pertinent motor NCS. The NEE also is expanded.

Trunks

Regarding the trunk elements, the general survey best assesses the lower trunk and least assesses the upper trunk. Consequently, whenever upper
trunk lesions are suspected, the general survey must be expanded. We typically add contralateral Med-D2 and radial sensory NCS (the ipsilateral Med-D2 and radial sensory NCS are included in the general survey) and bilateral LABC, Med-D1, and Med-D3 sensory NCS. If indicated, on the motor NCS portion of the EDX study, bilateral Musc-biceps and Ax-deltoid responses are added. These motor NCS also are added whenever the patient is noted to have forearm flexion or upper extremity abduction weakness, or whenever reduced MUAP recruitment is seen on NEE in either the biceps or deltoid muscles. On NEE, in addition to the general survey muscles, several muscles from the upper trunk NEE domain are added. Because the suprascapular nerve exits the upper trunk at its proximal aspect, whenever NEE abnormalities are detected in one of the spinati muscles (infraspinatus, supraspinatus), a more proximal lesion is suggested. For that reason, NEE of the rhomboids (dorsal scapular nerve off C5 APR) and serratus anterior (long thoracic off C5 through C7 APR) muscles is added. Unfortunately, brachial plexus lesions affect the upper trunk more than any other brachial plexus element. Consequently, additional studies typically are required. In addition, it is necessary to distinguish an upper trunk lesion from a lateral cord lesion. The sensory NCS are most helpful for this
purpose. With upper trunk lesions, the Med-D1 and LABC responses are abnormal 100% of the time, the Med-D2 response is abnormal 20% (one fifth) of the time, and the Med-D3 response is abnormal 10% (one tenth) of the time (see Table 1). Thus, with an upper trunk lesion, all four responses are abnormal only 2% of the time \( (1 \times 1 \times 1/5 \times 1/10 = 1/50) \). With lateral cord lesions, however, all four responses tend to be abnormal, and usually to essentially the same degree. The motor NCS may also help with this differentiation. Whereas upper trunk lesions may affect both the Musc-biceps and the Ax-deltoid responses, lateral cord lesions can only affect the Musc-biceps response. Consequently, if both responses are affected, or solely the Ax-deltoid response is affected, an isolated lateral cord lesion is excluded. Differentiation by NEE utilizes the C5,6-radial and axillary nerve-innervated muscles (eg, brachioradialis, deltoid, teres minor). The latter muscles can be affected with upper trunk lesions but are spared with lateral cord lesions.

Evaluation of the middle trunk also requires expansion. We usually add the Med-D3 sensory NCS bilaterally and the Med-D2 and radial sensory NCS contralaterally. Because the middle trunk is sandwiched between the upper and lower trunks, all of the NCS and NEE studies that assess the middle trunk also assess one of the adjacent trunks. Thus, there are no NCS or NEE studies available that solely assess this brachial plexus element. With isolated middle trunk lesions, the LABC, Med-D1, Uln-D5, and MABC responses are spared, whereas the Med-D2 and Med-D3 tend to be affected. The S-Radial response is not useful for differentiating a middle trunk lesion (affected about 40% of the time) from an upper trunk lesion (affected about 60% of the time). On motor NCS, bilateral Radial-EDC responses are added. On NEE, many muscles must be studied before one can conclude a lesion is localized solely to the middle trunk (fortunately, a very rare event). Again, there are no muscles contained solely in the muscle domain of the middle trunk (ie, private muscles) that are not also contained in the muscle domain of one of the adjacent trunks (ie, shared muscles). Nonetheless, isolated middle trunk lesions can be differentiated. Thus, whenever shared middle trunk muscles (ie, muscles that belong to the muscle domains of both the upper and middle trunks or to the muscle domains of both the middle and lower trunks) are affected, and private upper and lower trunk muscles are spared, the lesion is located within the middle trunk. In our review of the EDX abnormalities associated with over 400 brachial plexus lesions, we encountered this pattern only once (an intraoperatively verified case caused by an idiopathic fibrotic process) [12].

Because the routine survey assesses the lower trunk element to a greater degree than the other trunk elements, few additional studies are required in its EDX assessment. We typically add a contralateral Uln-D5 sensory NCS and bilateral MABC sensory NCS. Additional motor NCS are not needed, although bilateral Radial-EIP responses may be helpful. We usually expand the NEE with radial (eg, extensor pollicis brevis), ulnar (eg, abductor digiti
minimi, flexor carpi ulnaris), and median (eg, abductor pollicis brevis) nerve-innervated muscles. Differentiating a lower trunk lesion from a medial cord lesion can be challenging because most of the available studies assess both elements. There is no sensory NCS that distinguishes between these two sites, although conceivably, a distal medial cord lesion could spare the MABC response because its axons would have arisen from the medial cord more proximally. On motor NCS, an abnormal Radial-EIP response identifies a lower trunk lesion, but a normal one does not identify a medial cord lesion because a partial lower trunk lesion could produce an identical picture. For differentiating lower trunk lesions from medial cord lesions, the most helpful component of the EDX study is NEE of C8/radial nerve-innervated muscles (ie, extensor indicis proprius; extensor pollicis brevis). When affected, the lesion is accurately localized proximal to the medial cord (eg, lower trunk). As with the motor NCS, however, sparing of the C8/radial nerve-innervated muscles does not identify a medial cord lesion because a partial lower trunk lesion could also spare these muscles. This differentiation has profound clinical pertinence. For example, among individuals with ulnar sensory and motor nerve symptoms following open heart surgery, the question arises as to whether the symptoms reflect an ulnar neuropathy at the elbow or a C8 APR lesion. If only a focused ulnar nerve evaluation is performed, all of the C8 APR lesions will be falsely localized to the ulnar nerve.

Cords

Regarding the cord elements, as previously stated, the general survey is biased toward assessment of the medial cord. Consequently, whenever lateral cord lesions are suspected, the general survey is expanded. We usually add contralateral Med-D2 and S-Radial NCS and bilateral LABC, Med-D1, and Med-D3 sensory NCS. With lateral cord lesions, the LABC, Med-D1, Med-D2, and Med-D3 responses are usually abnormal, whereas with upper trunk lesions, only the LABC and Med-D1 responses typically are affected (discussed previously). Bilateral Musc-biceps motor NCS may be helpful, especially if forearm flexion weakness has been recognized or if NEE abnormalities were noted in the biceps muscle. Unlike upper trunk lesions, which tend to affect both the Musc-biceps and the Ax-deltoid responses, lateral cord lesions can only alter the Musc-biceps response. Thus, the Ax-deltoid response is added and is expected to be normal with lateral cord lesions. On NEE, muscles from the upper trunk, lateral cord, and posterior cord are added to the general survey to demonstrate that only those muscles belonging to the NEE domain of the lateral cord are affected (ie, C5,6 radial and axillary nerve-innervated muscles are spared).

With suspected posterior cord lesions, we generally add a contralateral S-Radial sensory NCS, bilateral Ax-deltoid motor NCS, and one of the radial motor NCS (ie, Radial-EDC or Radial-EIP) bilaterally. On NEE,
additional radial and axillary nerve-innervated muscles are incorporated. Differentiation of a posterior cord lesion from a middle trunk lesion is important. On sensory NCS, the Med-D2 and Med-D3 sensory NCS are helpful: they are always spared by posterior cord lesions but commonly affected when the underlying lesion involves the middle trunk. On motor NCS, the Ax-deltoid and Radial-EIP responses are affected by posterior cord lesions but spared by middle trunk lesions. On NEE, the C7/median nerve-innervated muscles (ie, pronator teres, flexor carpi radialis) are spared with posterior cord lesions but may be affected by middle trunk lesions.

With suspected medial cord lesions, we typically add a contralateral Uln-D5 sensory NCS and bilateral MABC sensory NCS. Bilateral Radial-EIP motor NCS are added to help differentiate a lower trunk process from a lesion affecting the medial cord. We usually expand the NEE with C8/radial (eg, extensor pollicis brevis), C8/ulnar (eg, flexor carpi ulnaris), and C8/median (eg, abductor pollicis brevis) nerve-innervated muscles. The NEE of the C8/radial nerve-innervated muscles (ie, extensor indicis proprius; extensor pollicis brevis) is mandatory for differentiating a medial cord lesion from a lower trunk lesion and is the best way to differentiate a postoperative ulnar neuropathy from a median sternotomy-related C8 APR lesion. The triceps muscle, contrary to popular belief, is not very helpful in this regard because it receives little C8-derived innervation; this explains why it is infrequently affected with both true neurogenic thoracic outlet syndrome (this syndrome affects the T1 > C8 APR) and with median sternotomy-induced brachial plexopathies (this disorder primarily affects the C8 APR).

Summary

Of the four major PNS plexuses, disorders of the brachial plexus are encountered far more frequently than those of the others. The EDX examination is probably the best procedure available by which to evaluate brachial plexus lesions. It provides localizing, pathologic, pathophysiologic, severity, and prognostic information. By localizing the lesion and identifying the underlying pathophysiology, it often predicts the underlying etiologic process; for example, (1) major T1 APR involvement with true neurogenic thoracic outlet syndrome; (2) C8 APR involvement with postmedian sternotomy brachial plexopathies; (3) supraclavicular demyelinating conduction block with classic postoperative paralysis (often confined to the upper plexus); (4) widespread infraclavicular demyelinating conduction blocks with radiation plexopathy; (5) severe progressive axon loss with neoplastic processes; (6) motor NCS abnormalities exceeding sensory NCS abnormalities for the same peripheral nervous system segment with intraspinal canal lesions (eg, avulsions); (7) demyelinating conduction block with sparing of the pertinent sensory NCS study with multifocal motor neuropathy; and (8) lack of EDX abnormalities with hysteria, conversion reactions, and
malingering, as well as with disputed neurogenic thoracic outlet syndrome. In addition, incorrect clinical considerations may be excluded (eg, when abnormal SNAPs are identified, an isolated radiculopathy is excluded). Among the various EDX study components, the sensory NCS are the most useful for brachial plexus element localization. One drawback of the sensory NCS for localization occurs in the setting of concomitant carpal tunnel syndrome; the latter negates the utility of the median sensory NCS for brachial plexus localization. The motor NCS and NEE often overcome this drawback and, regardless of sensory NCS findings, are always performed.

References

Electrodiagnostic approach to the patient with suspected mononeuropathy of the upper extremity

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Upper extremity mononeuropathies are common. Their diagnosis depends on a working knowledge of neuroanatomy, a detailed history and clinical examination, and electrodiagnostic studies. The electrodiagnostic examination, being an extension of the clinical evaluation, confirms the clinical diagnostic hypothesis, excludes competing diagnoses, and assesses severity, chronicity, and activity of the mononeuropathy. Electrodiagnostic studies are of most value when they are focused by a comprehensive clinical evaluation.

This article considers an electrodiagnostic approach to upper extremity mononeuropathies, according to the presenting complaint as follows:

• “Weak or painful shoulder”
• “Weakness about the elbow”
• “Wrist or finger drop”
• “Pain and weakness/numbness in the forearm or wrist and hand”
• “A numb or weak hand”

A working knowledge of upper extremity neuroanatomy and of the clinical features of upper extremity entrapment syndromes is assumed. For each neuropathy, the authors provide their opinion on the most effective electrodiagnostic strategy. The terms entrapment and compression are used interchangeably, although it should be recognized that a true “entrapment neuropathy” implies compression of neural structures in a fibro-osseous canal.
General principles

The electrodiagnostic consultant should address a number of questions that ultimately guide management decisions (see Box 1). The authors believe the electromyographer is best served by a conservative approach. Conclusions based on a single measure of nerve function or on equivocal data are prone to error and may lead to inappropriate care [1,2]. Timing of electrodiagnostic studies is critical. In the setting of acute focal peripheral nerve lesions, the authors generally recommend that electrodiagnostic studies be performed 2 to 3 weeks after onset of symptoms to maximize information gained regarding the degree of axon loss.

“Weak or painful shoulder”

Long thoracic neuropathies

Long thoracic neuropathies are traumatic or nontraumatic in origin. Traumatic causes include acute direct injury (eg, radical mastectomies), repetitive stretch or traction injury (eg, weight training), or external compression (eg, “rucksack palsy”). Most nontraumatic cases form a subgroup of neuralgic amyotrophy with selective involvement of the long thoracic nerve [3]. Patients complain of shoulder pain, weakness, and reduced range of motion at the shoulder. Occasionally, scapula winging is reported. Physical examination discloses winging of the scapula that is accentuated by protraction of the arm against resistance.

Electrodiagnostic approach

Needle examination is the mainstay of electrodiagnosis (see Box 2 on next page). The long thoracic nerve has a purely motor supply to the serratus

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**Box 1**

*Goals of the electrodiagnostic examination*

- What is the localization of the lesion?
- Are motor or sensory fibers involved or both?
- What is the physiologic basis of the lesion (eg, axon loss, demyelination)?
- What is the severity of the lesion?
  - Degree of axon loss?
  - Is axonal continuity present?
- What is the chronicity of the lesion?
  - Is there evidence of reinnervation of evidence or ongoing axon loss?
- What is the prognosis?
anterior. Electrodiagnosis focuses on the demonstration of isolated involvement of the serratus anterior muscle. Other C5–7-innervated muscles are sampled to exclude a cervical radiculopathy, brachial plexopathy, or a myopathy (eg, facioscapulohumeral dystrophy). Nerve conduction studies (NCS) should be performed in the upper extremity to exclude coexistent compression neuropathies (eg, hereditary neuropathy with liability to pressure palsies (HNPP) and to evaluate for evidence of a brachial plexopathy. The authors do not routinely perform long thoracic NCS [4–6]; their opinion is that these studies are technically unreliable and add little to the needle examination findings in what is typically an axon loss lesion [7].

**Suprascapular neuropathies**

The suprascapular nerve innervates the supraspinatus and infraspinatus muscles, and provides sensation to the glenohumeral and acromioclavicular joints. It originates from the proximal upper trunk of the brachial plexus, with predominantly C5 nerve root innervation. Suprascapular nerve entrapment occurs primarily at two sites: the suprascapular notch and the spinoglenoid notch [8]. Proximal entrapment of the suprascapular nerve at the suprascapular notch results in shoulder pain and weakness of the supraspinatus and infraspinatus muscles. More distal entrapment at the spinoglenoid notch produces isolated, usually painless weakness and atrophy of the infraspinatus muscle. The suprascapular nerve is also prone to trauma at other sites along its course including in the posterior triangle of the neck.

**Electrodiagnostic approach**

Evaluation of putative suprascapular nerve palsy relies largely on needle electromyography (see Box 3 on next page). The supraspinatus and infraspinatus muscles are sampled to determine the presence of suprascapular nerve involvement, the likely site of suprascapular nerve injury, and the severity and acuity thereof.

At a minimum, other C5/6-innervated limb muscles (deltoid, biceps, ±Rhomboideus) and C5/6 cervical paraspinal muscles should be sampled
to exclude a C5/6 radiculopathy or an upper trunk brachial plexopathy. If the diagnosis of brachial neuritis is a possibility (suprascapular palsies can be a dominant feature of brachial neuritis), then it may be necessary to sample other muscles (eg, serratus anterior and flexor pollicis longus (FPL)).

The authors obtain upper extremity NCS to exclude a coexistent brachial plexopathy or evidence of HNPP (slowed distal sensory and motor conduction velocities). NCS techniques are available for the suprascapular nerves. The suprascapular nerves may be studied bilaterally by stimulating over Erb’s point, with monopolar needle recordings from the infraspinatus and the supraspinatus muscles. A side-to-side delay, or segmental prolongation of latency, may be of localizing value (eg, a prolonged latency with recording from the infraspinatus muscle, but not the supraspinatus, suggests entrapment at the spinoglenoid notch) [8]. The authors do not routinely perform suprascapular NCS, as they add little to a careful needle electromyography (EMG) examination and, in their opinion, should not be relied on for localization of a suprascapular neuropathy.

**Pitfalls**

Care needs to be taken to avoid pneumothorax when performing needle EMG of the supraspinatus and serratus anterior muscles [9]. Also, because infraspinatus lies deep to the lower trapezius muscle, needle examination generally requires deep insertion of the electrode down to the periosteum of the scapula bone to ensure that EMG activity arises from the infraspinatus muscle [9].

**Axillary neuropathies**

The axillary nerve consists of sensory and motor fibers that derive from C5 and C6 roots. It is one of the terminal branches of the posterior cord of

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**Box 3**

*Suggested electrodiagnostic approach to suprascapular neuropathies*

**Nerve conduction studies (ipsilateral)**
- Antidromic median and ulnar sensory responses (digits 2 and 5)
- Ulnar and median motor responses, forearm conduction velocities and F responses

**Needle examination**
- Supraspinatus, infraspinatus, deltoid, biceps, C5/6 paraspinal muscles

**Optional**
- Rhomboids, serratus anterior, triceps, flexor carpi radialis, flexor pollicis longus, first dorsal interosseous

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the brachial plexus and provides innervation to the deltoid and teres minor muscles [10]. The axillary nerve supplies cutaneous sensation to a patch of skin over the upper lateral arm. Axillary mononeuropathies are characterized by weakness of shoulder abduction, typically with localized sensory loss over the upper lateral arm. Axillary mononeuropathies may result from shoulder trauma (eg, dislocations of the glenohumeral joint) or occasionally as a manifestation of brachial neuritis [3,11].

Electrodiagnostic approach

Needle examination forms the basis of the electrodiagnostic assessment (see Box 4 on next page). The objective is to demonstrate selective denervation or reinnervation of the deltoid and teres minor muscles. The authors study all three components of the deltoid muscle (posterior, middle, and anterior) and teres minor because selective patterns of reinnervation may be seen. Other causes of shoulder abduction weakness (eg, a C5/6 radiculopathy, upper trunk brachial plexopathy, and suprascapular nerve palsy) should be excluded. The authors study the triceps muscle to exclude a posterior cord lesion. Axillary motor NCS are easily and reliably performed, stimulating percutaneously at Erb’s point and recording over the mid-deltoid with surface electrodes [12]. Side-to-side comparison of deltoid compound muscle action potential (CMAP) amplitudes is helpful in estimating the degree of axon loss. There are no nerve conduction techniques to directly assess the sensory branch of the axillary nerve.

“Weakness about the elbow”

Musculocutaneous neuropathies

The musculocutaneous nerve originates from the lateral cord and is composed of sensory and motor fibers that traverse C5–7 nerve roots and the upper trunk of the brachial plexus [10]. It innervates the coracobrachialis, brachialis, and biceps brachii muscles. It also provides sensation to the lateral arm and forearm through the lateral cutaneous nerves of the arm and forearm; the latter nerve represents the terminal extension of the musculocutaneous nerve [10]. The musculocutaneous nerve is prone to injury at the level of the coracobrachialis, and the distal sensory branch is vulnerable as it pierces fascia to enter the forearm because its position is relatively fixed at both sites [7]. Proximal injury results in weakness of elbow flexion and shoulder adduction, an absent or reduced biceps reflex, and reduced sensation over the lateral aspect of the volar forearm. Distal injury at the elbow produces a pure sensory syndrome with pain and tenderness in the cubital fossa, and sensory loss over the lateral volar forearm to the level of the wrist [7,10].

Electrodiagnostic approach

The goal of electrodiagnostic testing is to demonstrate selective involvement of musculocutaneous-innervated muscles on needle EMG and selective
abnormalities of the lateral cutaneous nerve of the forearm on sensory NCS (see Box 5). A C5/6 radiculopathy or a predominantly upper trunk brachial plexopathy should be excluded as they may mimic the pattern seen with musculocutaneous nerve lesions.

The authors perform lateral antebrachial cutaneous (LAC) sensory NCS, with side-to-side comparison of amplitudes [13]. The authors also obtain radial and median sensory responses (recording over the thumb with side-to-side comparison) to exclude involvement of other sensory fibers that traverse the upper trunk or lateral cords of the brachial plexus.

Bilateral musculocutaneous motor NCS can be performed by stimulating at Erb’s point and at the axilla, and recording the biceps CMAPs with surface electrodes. Side-to-side comparison of amplitudes is essential. Latency comparisons are unreliable [14]. The authors do not routinely obtain musculocutaneous motor conduction studies because similar information can generally be obtained on needle examination. However, in cases where conduction block (eg, multifocal motor neuropathy) is suspected, musculocutaneous motor NCS may be helpful.

Needle examination is essential. The authors study the biceps brachii muscle to assess for active denervation, axonal continuity, and the degree of reinnervation. Although the brachialis muscle is easily studied, it provides little additional information and may receive dual innervation from the radial nerve [7,15]. The authors do not routinely examine the coracobrachialis muscle because it is more difficult to access and is typically spared in proximal musculocutaneous nerve palsies [7].

The authors do study other C5–7-innervated muscles (infraspinatus, deltoid, triceps, and cervical paraspinals) to exclude a cervical radiculopathy or a predominantly upper trunk brachial plexopathy.

Distal musculocutaneous nerve lesions at the elbow manifest as isolated abnormalities on LAC nerve testing in the distal forearm. A >50% reduction in the LAC sensory nerve action potential (SNAP) amplitude on the affected

---

**Box 4**

*Suggested electrodiagnostic approach to axillary neuropathies*

**Nerve conduction studies**
- Median or radial sensory responses (record from the thumb with side-to-side comparison)
- Median motor responses and F waves
- Axillary motor responses (stimulate at Erb’s point)—perform bilaterally

**Needle examination**
- Deltoid (anterior, middle, posterior), teres minor, infraspinatus, biceps, triceps, C5/6 paraspinals
side is considered abnormal [16]. LAC nerve responses may be difficult to elicit (even on the “normal side”) in obese or older patients.

“Wrist or finger drop”

Radial neuropathies

The radial nerve is composed of motor fibers from C5–8 (infrequently T1) nerve roots and sensory fibers that arise in the C5–8 dorsal root ganglia. Nerve fibers destined to form the radial nerve traverse all three trunks of the brachial plexus and the posterior cord. From an electrodiagnostic standpoint, it is useful to consider radial neuropathies as occurring at four anatomic levels: (1) axilla/upper arm above the spiral groove, (2) at or just distal to the spiral groove, (3) posterior interosseous neuropathies, and (4) superficial radial neuropathies [17–19].

The radial nerve—a terminal branch of the posterior cord—innervates the long and medial heads of the triceps in the axilla. It supplies the lateral head of the triceps—the anconeus muscle—and gives off the posterior cutaneous nerves of the arm and forearm in the upper arm above the spiral groove. Between the spiral groove and the elbow, it innervates brachialis (partial), brachioradialis, extensor carpi radialis longus and, in some individuals, extensor carpi radialis brevis. At the elbow, the radial nerve divides into its two terminal branches: the posterior interosseous nerve (PIN) and the superficial radial nerve (SRN). The PIN passes under the fibrous arcade of Frohse and enters the supinator. It contains purely motor fibers and innervates extensor carpi radialis brevis, extensor digitorum communis, extensor digiti minimi, extensor carpi ulnaris, abductor pollicis longus, and extensor pollicis longus and brevis. Finally it innervates extensor indicis proprius (EIP) [20].
The SRN travels deep to the brachioradialis in the anterolateral forearm. In the distal third of the forearm, it passes to the posterior aspect of the radial forearm and then over the tendons of the anatomic snuffbox where it can be easily palpated. It supplies cutaneous sensation to the posterolateral hand and the proximal portions of the dorsum of the thumb and digits 2 to 4 [15].

High radial neuropathies (“above spiral groove”) present with weakness of elbow extension (triceps), mild weakness of elbow flexion (brachioradialis, weakness that may be difficult to elicit, but by inspection is easily seen not to contract), and wrist and finger extension. If the lesion is as proximal as the posterior cord, then there is weakness of the deltoid and latissimus muscles as well. There may be variable loss of sensation over the posterior arm, forearm, and hand. The triceps and brachioradialis reflexes are lost or reduced. The more common spiral groove lesion is similar but, importantly, spares the triceps. PIN neuropathies are purely motor, and manifest as finger drop, with variable weakness of wrist extension and radial deviation of the extended wrist. Elbow extension, and flexion are normal [17]. SRN neuropathies (cheiralgia paresthetica) manifest with isolated pain, numbness, and paresthesias over the dorsolateral aspect of the hand and the dorsum of the proximal thumb and digits 2 to 4 [19].

Electrodiagnostic approach

Electrodiagnostic testing demonstrates abnormalities confined to the radial nerve territory (see Box 6 on page 460). The electromyographer localizes the level, severity, and chronicity of the radial nerve lesion, and assesses whether the neuropathy is primarily demyelinative (conduction block) or axon loss in nature [21]. It is necessary to exclude other lesions that may mimic a radial neuropathy, including a C7 radiculopathy, posterior cord lesion, multifocal motor neuropathy, or lead neuropathy, and a central nervous system process (eg, stroke) [20].

The authors obtain radial sensory responses (forearm) recording over the superficial radial nerve at the anatomic snuffbox. If responses are in the low-normal range or abnormal, the authors test the contralateral side, accepting a >50% amplitude difference side-to-side as being abnormal (on the side of the lower amplitude) [16]. In young adults, it is particularly important to obtain side-to-side superficial radial studies because a response amplitude on the affected side that is in the low-normal range may, in fact, be low for someone who otherwise has responses in the upper-normal range at baseline.

The authors obtain radial motor NCS bilaterally. The authors use surface recording over the EIP muscles, and stimulate the radial nerve in the mid-posterolateral forearm, antecubital fossa (lateral to the biceps tendon) and in the lateral arm above and below the spiral groove (Fig. 1). In cases where radial nerve compression is suspected in the axilla, the authors may also stimulate more proximally at the level of Erb’s point to demonstrate conduction block across the axilla. Side-to-side comparison of the radial motor distal CMAP amplitude provides a useful index of the degree of axon loss,
as early as 1 week following the onset of the neuropathy. Motor conduction studies may be helpful in localizing the lesion, as in the commonly encountered conduction block at the level of the spiral groove (see Fig. 1) or, uncommonly, the conduction block seen (between the forearm and elbow) with PIN lesions. Measurement of segmental conduction velocity is usually not helpful due to problems with distance measurement.

Needle examination is important in the evaluation of radial neuropathies. It serves to localize the level of the lesion, exclude C6/7 radiculopathies and posterior cord plexopathies, and provides information regarding the severity, activity, and chronicity of the lesion.

The authors study the triceps brachii, brachioradialis, extensor digitorum communis, and EIP muscles to confirm involvement of radial-innervated muscles, and to localize the level of the lesion to above the spiral groove, at or below the spiral groove, or to the PIN. The authors also assess nonradial-innervated C6/7 muscles (eg, flexor carpi radialis) to exclude a radiculopathy, and the deltoid to evaluate the posterior cord.

In the case of radial nerve lesions above the spiral groove, abnormality is expected on needle examination within the triceps muscle and in more distal

![Fig. 1. (A) A normal radial motor NCS (surface recording from the EIP), with stimulation in the forearm (A1), elbow (A2), below the spiral groove (A3), and above the spiral groove (A4). (B) A radial neuropathy with motor conduction block across the spiral groove. The distal radial CMAP amplitude (A1) is similar to the unaffected side (A), suggesting a primarily demyelinative lesion, and a good prognosis.](image)
radial-innervated muscles. The superficial radial response is usually reduced in amplitude, except in very acute lesions (within the first 10 days) or, in purely demyelinating lesions, where conduction block may be present in sensory fibers, producing radial sensory loss, yet a normal distally recorded superficial radial response. Lesions at the spiral groove spare the triceps, but involve more distal radial-innervated muscles including brachioradialis, which receives its innervation from the radial nerve just distal to the spiral groove. The SRN is affected, as in high radial neuropathies. Radial neuropathies at the spiral groove are frequently demyelinating (neuropraxic), thus, with the distal CMAP amplitude on the symptomatic side being comparable to the asymptomatic side. Radial neuropathies below the level of the spiral groove, but above the elbow, spare the brachioradialis muscle but affect distal radial and PIN-innervated muscles and the SRN.

PIN neuropathy with entrapment at the arcade of Frohse is usually an axon loss lesion, and spares the triceps and brachioradialis muscles, with variable involvement of wrist extensors (eg, extensor carpi ulnaris). Extensor digitorum communis and EIP should show abnormality with acute denervation and/or reduced recruitment and, in more chronic lesions, signs of reinnervation. The superficial radial response is normal. This lesion is infrequently demyelinating.

**Box 6**

**Suggested electrodiagnostic approach to radial neuropathies**

**Sensory nerve conduction studies (NCS)**
- Superficial radial nerve (bilaterally) (stimulate forearm, record snuffbox)
- Posterior cutaneous nerve of forearm (rarely required)

**Motor NCS**
- Radial motor NCS bilaterally (record from extensor indicis proprius EIP, stimulate forearm, antecubital fossa, and arm above and below spiral groove)
- Ulnar and other motor NCS (if a brachial plexopathy, lead neuropathy, multifocal motor neuropathy, multifocal acquired demyelinating sensory and motor neuropathy, etc. suspected)

**Needle examination**
- Triceps, brachioradialis, extensor digitorum communis, EIP (to localize radial nerve/posterior interosseous nerve involvement)

**Flexor carpi radialis, first dorsal interosseous, cervical paraspinals to exclude a C7,8 radiculopathy; deltoid to exclude a posterior cord lesion**
“Pain and weakness/numbness in the forearm/wrist/hand”

Median neuropathy in the arm/forearm

Median nerve fibers derive from C6–T1 nerve roots, and traverse all three trunks and the medial and lateral cords of the brachial plexus. Median sensory fibers (C6/7 dorsal root ganglia, upper and middle trunks, lateral cord) that provide cutaneous innervation in most individuals to the thumb, digits 2 and 3, and the lateral half of digit 4, pass through the carpal tunnel. The palmar cutaneous branch arises from the median nerve just proximal to the wrist, and travels anterior to the carpal tunnel to provide sensation to the thenar eminence [15].

Median motor fibers originate from nerve roots C6–T1, all three trunks, and the medial and lateral cords of the brachial plexus. The first major motor branches supply pronator teres. Subsequent branches innervate flexor digitorum superficialis and flexor carpi radialis and, finally, the large purely motor branch, the anterior interosseous nerve (AION) in the proximal forearm. The AION innervates flexor pollicis longus, flexor digitorum profundus (FDP) subserving digits 2 and 3, and pronator quadratus. The median nerve then passes through the carpal tunnel, and innervates abductor pollicis brevis (APB), opponens pollicis, the superficial head of flexor pollicis brevis, and the first and second lumbricals [15].

Anatomic variants (eg, median to ulnar crossovers in the forearm: Martin–Gruber anastomoses) and median-to-ulnar crossovers in the hand (Riche Cannieu anastomoses) occasionally complicate the clinical and electrodiagnostic picture in median neuropathies (Fig. 2) [22].

![Stimulus Site Table](image)

<table>
<thead>
<tr>
<th>Stimulus Site</th>
<th>Lat ms</th>
<th>Amp mV</th>
<th>CV m/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1: Wrist</td>
<td>6.0</td>
<td>5.325</td>
<td></td>
</tr>
<tr>
<td>A2: Elbow</td>
<td>8.3</td>
<td>5.534</td>
<td>87</td>
</tr>
</tbody>
</table>

Fig. 2. A Martin–Gruber anastomosis in a patient with a MNW. The higher median CMAP amplitude at the elbow (A2) compared with the wrist (A1) stimulation site suggests a crossover of median-to-ulnar nerve fibers in the forearm. The initial positive dip seen with median stimulation at the elbow (but not at the wrist) results from innervation of thenar muscles by crossover fibers that are not slowed in the carpal tunnel. The crossover fibers and initial positive dip in median CMAP (elbow stimulation) cause a spuriously fast median motor conduction velocity in the forearm.
In the proximal arm, the median nerve may be subject to external compression (eg, crutch palsy in the axilla/upper arm) or to trauma from humeral fractures [15]. Proximal entrapments occur at four sites [23,24]: (1) the Ligament of Struthers in the distal arm (rarest); (2) the Lacertum fibrosis (fibrous entrapment of the median nerve in the antecubital fossa); (3) between the hypertrophied heads of pronator teres (the most common entrapment site for proximal median neuropathies); and (4) at the level of the flexor digitorum superficialis. The AION may be entrapped at tendinous origins of the deep head of the pronator teres or of the flexor digitorum superficialis. The AION may also be entrapped at an accessory head of the flexor pollicis longus. Distal median nerve entrapment invariably occurs within the carpal tunnel (described later).

Proximal median neuropathies are variable in their manifestations. In the mildest cases, pain and paresthesias predominate [25]. Median neuropathies in the arm present with pain in the distal arm and forearm, a sensory disturbance involving median-innervated digits and the thenar eminence, and weakness of both AION and median nerve-innervated muscles including pronator teres. Median nerve entrapment in the forearm, either at the level pronator teres or flexor digitorum superficialis, presents similarly, although the pronator teres muscle is always spared in flexor digitorum superficialis syndromes and classically, but not always, spared in the pronator syndrome [27,28]. AION neuropathy, a purely motor disorder, manifests with volar forearm discomfort and flexor weakness of the terminal phalanx of the thumb [27].

Electrodiagnostic approach

NCS techniques have been described for selective evaluation of the AION and for the pronator syndrome [28–30]. The authors do not generally employ these techniques in their laboratory because the techniques add little to the clinical evaluation and are subject to significant technical limitations. The authors initially perform standard ulnar and median motor and sensory conduction studies (see Box 7). The results are frequently normal in proximal median neuropathies, but serve to exclude entrapment at more distal sites (eg, the carpal tunnel) or the presence of Martin–Gruber anastomoses [31]. The needle examination is most helpful in confirming and localizing proximal median neuropathies and assessing the degree of axon loss [26,32]. The authors study the pronator teres, flexor carpi radialis, flexor pollicis longus, and APB muscles to confirm involvement of median-innervated muscles, and to assess the likely site of the lesion. If an AION syndrome is suspected, the authors also assess pronator quadratus. The authors study nonmedian nerve-innervated C6–T1 muscles (first dorsal interosseous [FDI], triceps, biceps, and cervical paraspinal) to exclude cervical radiculopathy or brachial plexopathy. Because brachial neuritis may present with relatively selective involvement of the AION, the authors typically evaluate
muscles commonly involved in brachial neuritis (eg, spinatii and serratus anterior) in patients with AION syndromes [33].

**Median neuropathy at the wrist (MNW)**

MNW is the most common entrapment neuropathy. A suggested algorithm for the evaluation of MNW is detailed later in this section. Several points deserve special consideration:

- In studies from the Mayo Clinic, median motor distal latencies were prolonged in just 51% and median sensory peak latencies were abnormal in only 64% of subjects with carpal tunnel syndrome [34]. The authors thus perform one or more additional internal comparison studies between the median and ulnar/radial sensory nerves when carpal tunnel syndrome is suspected.
- For each individual NCS, 2.5% of the normal population will be misclassified as abnormal when using commonly employed mean ±2 SD reference ranges [2]. Studies designed to increase diagnostic sensitivity (eg, use of short nerve segments and comparison of more than one nerve) increase the likelihood of technical errors. The authors thus require abnormalities on two separate tests of median nerve function that localize to the carpal tunnel to make a diagnosis of MNW.
- The fascicular arrangement of the median nerve within the carpal tunnel is such that individual fascicles may be variably affected. It is important to individualize testing according to the patient’s symptoms. It is appro-

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**Box 7**

**Suggested electrodiagnostic approach to proximal median neuropathies**

**Sensory nerve conduction studies (NCS)**
- Median and ulnar antidromic sensory responses (digits 2 and 5)

**Motor NCS**
- Median motor NCS (record from abductor pollicis brevis (APB)), ulnar motor NCS (record from abductor digiti quinti (ADQ))

**Needle examination**
- Pronator teres, flexor carpi radialis, flexor pollicis longus, APB, and pronator quadratus (if anterior interosseous nerve syndrome suspected)

**Study:** triceps, biceps, first dorsal interosseous, lower cervical paraspinal muscles to evaluate for C6–8 radiculopathy or brachial plexopathy
priate, for instance, to assess sensory responses from digit 3 (rather than digit 2) if this is the most symptomatic digit.

- The concept of “double crush” as it applies to median neuropathy and the risk of coexistent cervical radiculopathy is controversial [35]. Nonetheless, when median nerve abnormalities across the wrist are minimal, when symptoms are atypical of carpal tunnel syndrome, or when clinical features suggest a coexistent cervical radiculopathy, the authors perform additional needle studies to examine this possibility.

- “Motor only” carpal tunnel syndrome is uncommon (incidence of 3.5% in the Mayo Clinic series) [34]. In this situation, C8/T1 radiculopathy or focal onset motor neuron disease deserve consideration.

- Martin–Gruber anastomoses and carpal tunnel syndrome may co-exist (see Fig. 2). The finding of an initial positive “dip” in the median CMAP (APB), present with stimulation at the elbow (but not with stimulation at the wrist) implies a MNW, in the setting of a Martin–Gruber anastomosis. The initial positive dip reflects median-to-ulnar crossover fibers that pass through the ulnar rather than the carpal tunnel. They reach their target thenar muscle fibers (e.g., adductor pollicis, flexor pollicis brevis) before median fibers—locally slowed in the carpal tunnel—reach their APB target. The presence of an initial positive dip gives rise to a spuriously fast “median” forearm conduction velocity [22].

- MNW and polyneuropathy frequently coexist [36]. Thus, depending on the clinical circumstances, electrodiagnostic screening for underlying polyneuropathy may be warranted (see later discussion). Conversely, the identification of MNW may be difficult in subjects with polyneuropathies (in particular, diabetes) [34]. In instances of severe sensory polyneuropathy, where sensory responses are absent in the upper extremities, a comparison between median and ulnar motor distal latencies and between the lumbrical–interosseous distal latencies may be helpful to demonstrate segmental slowing across the carpal tunnel (see later discussion) [37].

- The severity of the MNW, as determined by electrodiagnostic studies, is often used to guide therapy. Various empiric severity grading scales have been suggested [34]. Sensory and motor latencies are reported to correlate poorly with the degree of clinical symptomatology [34]. Historically, sensory and motor axon loss (reduced SNAP and CMAP amplitudes, and signs of denervation on needle examination) and clinical evidence of median nerve sensory or motor deficits suggested the need for surgical intervention [34]. The authors empirically grade MNW as mild when median sensory or motor slowing occurs without evidence of sensory or motor axon loss; as mild-to-moderate when median sensory or motor slowing is accompanied by mildly reduced median SNAP amplitudes or mild chronic reinnervation; as moderate when median sensory or motor slowing occurs with moderate sensory or motor axon loss (eg, moderate reductions in median SNAP or CMAP amplitudes, or
moderate chronic partial denervation/reinnervation); and severe when
the median SNAP (at wrist or palm) is unobtainable or when a severe
reduction of median CMAP amplitude is present with active denerva-
tion or severe chronic denervation/reinnervation.

- Electrodiagnostic studies are often requested on subjects who have un-
dergone carpal tunnel release surgery and in subjects whose symptoms
have persisted, become worse, incompletely resolved, or recurred. Med-
ian NCS results generally improve after surgery and relate to a decrease
in symptoms. This improvement in NCS results usually occurs within 6
weeks after surgery [34]. However, because nerve conduction abnormal-
ities may not fully resolve after surgery (despite relief of symptoms), the
electromyographer should be conservative in interpreting residual post-
surgical abnormalities. In this situation, the authors try to obtain the
preoperative NCS for comparison. If the MNW has shown interval de-
terioration both clinically and electrodiagnostically, then recurrent car-
pal tunnel syndrome is likely. If NCS results are normal or improved
from the preoperative study, the authors consider other possible causes
for the symptoms (e.g., cervical radiculopathy). In cases where NCS re-
sults are unchanged or preoperative conduction studies are not available
and the median nerve abnormalities are of a mild nature, follow-up stu-
dies may be of value if symptoms progress [34].

Specific techniques in the evaluation of MNW
NCS performed in all patients. The authors obtain median and ulnar
CMAPs, conduction velocities, and F responses in the symptomatic limb
or limbs (see Box 8 on page 468). The authors perform antidromic median
sensory studies (recording from digit 2 or the most symptomatic digit), with
stimulation of the median nerve at the wrist (proximal to the carpal tunnel)
and in the palm distal to the carpal tunnel. The authors also obtain ulnar
sensory responses, recording from digit 5, with stimulation at the wrist. Cri-
teria for abnormality of the median sensory onset or peak latency should be
established by each electrodiagnostic laboratory, controlling for tempera-
ture, age, body mass index, and distance [38–40]. Stimulation of median sen-
sory fibers at the wrist and in the palm permits localization of slowing of
median sensory conduction velocities to the carpal tunnel segment. In our
laboratory, slowing of conduction velocities in the wrist to palm, relative
to the palm-to-digit segment, of 13 m/s or more is considered abnormal
[37,41]. This technique requires digital averaging of responses, uniform
warming of digits and the hand, careful measurement of stimulation dis-
tances, and an even baseline without significant shock artifact. It is not
uncommon for symptomatic subjects with “normal” wrist-to-digit sensory
latencies to have significant slowing across the wrist segment. In addition,
carpal tunnel syndrome patients with presumptive axon loss based on a
low amplitude wrist-to-digit sensory response are often found to have a
demyelinating lesion when the palm-to-digit potential shows a normal
amplitude response (Fig. 3). Conversely, segmental stimulation may demonstrate that a prolonged median sensory peak latency is due to diffuse slowing, as in an axonopathy.

The authors perform one or more of the following internal comparison studies if criteria for MNW are not met on two of the previously mentioned studies:

**Comparison of median sensory latencies to ulnar or radial sensory latencies.** Comparisons of antidromic median and ulnar sensory latencies to digit 4 permit use of a single placement of recording electrodes [42]. The median and ulnar nerves each are stimulated separately at the wrist using the same stimulation distance. A median sensory latency that exceeds the ulnar latency to digit 4 by \(\geq 0.5\) milliseconds is considered abnormal. The median latency to digit 2 can similarly be compared with the ulnar response recorded from digit 5 if the same stimulation distances are used for each nerve. If an ulnar neuropathy is present, the median sensory latency recorded from the thumb can be compared with the superficial radial sensory latency recorded from the thumb [43].

**Comparison of median and ulnar mixed nerve (midpalmar) latencies.** Comparison of the latency difference (peak or onset) between the mixed median

![Wrist and Palm Stimulus](image)

<table>
<thead>
<tr>
<th>Stimulus Site</th>
<th>Latency (ms)</th>
<th>Amplitude (uV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist</td>
<td>4.5</td>
<td>5.25</td>
</tr>
<tr>
<td>Palm</td>
<td>1.7</td>
<td>34.97</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Segment</th>
<th>Distance (mm)</th>
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<tr>
<td>Digit 2 - Wrist</td>
<td>160</td>
<td>36</td>
</tr>
<tr>
<td>Digit 2 - Palm</td>
<td>80</td>
<td>47</td>
</tr>
<tr>
<td>Wrist - Palm</td>
<td>80</td>
<td>29</td>
</tr>
</tbody>
</table>

Fig. 3. Antidromic stimulation of median sensory fibers at the wrist and in the palm (recording from digit 2) shows a dramatically reduced median SNAP amplitude with wrist stimulation, relative to a normal median SNAP amplitude with palm stimulation, in a patient with carpal tunnel syndrome. This finding suggests focal demyelination of median sensory fibers across the carpal tunnel without significant axon loss. Note also that there is a segmental drop of median conduction velocity in the palm-to-wrist versus palm-to-digit nerve segments.
and ulnar nerves across the carpal tunnel increases the diagnostic yield of standard median motor and sensory studies by about 21% [34]. Focal slowing of the median nerve within the carpal tunnel is more evident using this technique because of the shorter stimulation distance (8 cm). The median and ulnar nerves are stimulated separately, in the midpalm, and bar recording electrodes are placed over the respective nerves 8 cm proximal to the site of stimulation (just proximal to the distal wrist crease). In their laboratory, the authors consider a ≥0.4-millisecond latency difference (ie, longer for the median nerve) as abnormal. This is somewhat controversial because various laboratories accept anywhere between a 0.3- and 0.5-millisecond difference as significant [34].

Comparison of lumbrical (median) and interosseous latencies (ulnar) (Fig. 4). Through placement of surface electrodes (active just radial to the middle of the third metacarpal, and reference over the proximal interphalangeal joint), one may record an interosseous CMAP if the ulnar nerve is stimulated at the wrist and a lumbrical CMAP if the median nerve is stimulated at the wrist. If a standard stimulation distance of 8 to 10 cm is used for separate stimulation of the median and ulnar nerves, a lumbrical distal latency exceeds the interosseous (ulnar) distal latency by 1 millisecond. (C) UNW: the interosseous (ulnar) distal latency is 0.9 milliseconds longer than the lumbrical distal latency.

<table>
<thead>
<tr>
<th>Stimulus Site</th>
<th>Lat (ms)</th>
<th>Amp (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Wrist</td>
<td>3.1</td>
<td>2.22</td>
</tr>
<tr>
<td>Ulnar Wrist</td>
<td>3.0</td>
<td>7.02</td>
</tr>
</tbody>
</table>

Fig. 4. (A) A normal lumbrical–interosseous study. The median (A1) and ulnar nerves (A2) are stimulated at the wrist using identical stimulation distances (8–10 cm), with the active recording electrode just radial to the middle of the third metacarpal. The lumbrical and interosseous distal latencies are comparable. (B) CTS: the lumbrical (median) distal latency exceeds the interosseous (ulnar) distal latency by 1 millisecond. (C) UNW: the interosseous (ulnar) distal latency is 0.9 milliseconds longer than the lumbrical distal latency.
latency of ≥0.6 milliseconds longer than the interosseous latency is indicative of a MNW. It is important that the recording electrode be adjusted such that the lumbral potential has a short rise time. This technique is particularly useful in severe median neuropathies at the wrist, where median and ulnar sensory responses and the median motor response recording from APB may be absent [37,44,45].

Studies with low sensitivity or specificity. The terminal latency index and residual latency has a low sensitivity, and the authors do not calculate this in

<table>
<thead>
<tr>
<th>Box 8</th>
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<tr>
<td><strong>Suggested electrodiagnostic approach to median neuropathy at the wrist (MNW)</strong></td>
</tr>
</tbody>
</table>

**Routine**
- Antidromic median sensory responses (digit 2 or 3): stimulate wrist and palm, compute amplitude, onset, and peak latency, and conduction velocity across wrist segment. A >10 m/s drop in conduction velocity across the wrist is abnormal.
- Median motor nerve conduction studies (NCS) and F response (record abductor pollicis brevis (APB), stimulate wrist and elbow): distal latency >4.4 milliseconds is abnormal under age 60 (stimulation distance 7 cm)
- Ulnar motor (record abductor digiti quinti) and sensory NCS (record digit 5)

If above studies are normal or if only one piece of data supports MNW, the authors perform one or more internal comparison studies:
- Median-to-ulnar palmar comparison (abnormal if median latency ≥0.4 milliseconds longer)
- Comparison of median-to-ulnar antidromic sensory responses recorded from digit 4 using the same stimulation distance (11–14 cm) for each nerve (abnormal if median latency ≥0.5 milliseconds longer)

**Needle examination**
- APB, if abnormal assess first dorsal interosseous; the authors also examine flexor carpi radialis (FCR) and triceps. If coexistent radiculopathy is suspected, a more detailed examination is done including cervical paraspinals. If FCR abnormal, triceps normal, more detailed examination of other proximal median-innervated muscles is done to exclude median neuropathy at the elbow.
their laboratory [2]. The authors perform F responses to exclude a more proximal lesion or underlying demyelinating polyneuropathy. Minimal F wave latencies may be prolonged in proportion to the prolongation in median motor distal latencies, however they are of no localizing value. Median motor conduction velocities may be mildly slowed in a minority of subjects with MNW, presumably due to conduction block or axon loss of the fastest median motor fibers at the wrist. This finding does not imply a proximal median neuropathy.

Needle examination. The authors routinely perform a needle examination in the evaluation of possible MNW. Needle examination of APB serves to assess the severity, activity, and chronicity of the median neuropathy. A C6–C8 radiculopathy, proximal median neuropathy, or brachial plexopathy should be excluded in subjects with hand numbness, tingling, or weakness when MNW is not evident on NCS results or when the finding of mild MNW is insufficient to explain the clinical presentation.

Ulnar neuropathy at the elbow (UNE)

UNE is the second most common focal mononeuropathy [46]. The ulnar nerve consists of motor and sensory fibers that arise in C8–T1 roots and associated dorsal root ganglia, and travels in the lower trunk and medial cord of the brachial plexus [15]. The ulnar nerve provides sensation to digit 5, the medial half of digit 4, the hypothenar eminence (superficial and palmar cutaneous branches that arise just proximal to Guyon’s canal), and the dorsomedial aspect of the hand (dorsal cutaneous nerve that arises above the wrist). The motor branch to flexor carpi ulnaris arises at or above the level of the cubital tunnel (humeroulnar arcade) and the flexor digitorum profundus (digits 4/5) arises in the humeroulnar arcade. In the hand, it innervates the hypothenar muscle group (e.g., abductor digiti quinti; ADQ), and a deep motor branch that arises in Guyon’s canal, innervates lumbricals 3/4, palmar and dorsal interossei, flexor pollicis brevis (deep head), and adductor pollicis brevis.

Manifestations of UNE range from elbow pain and intermittent paresthesias of the medial hand to marked sensory loss, wasting and weakness, and a claw hand. Sensory loss over the dorsum of the hand and weakness of FDP 4/5 localize the ulnar neuropathy to above the wrist. In UNE, compression typically occurs at either the retroepicondylar groove (located 0–2 cm above the medial epicondyle), or the humeroulnar arcade, typically located 0 to 3 cm below the medial epicondyle [47,48]. Entrapment just above the elbow at the arcade of Struthers or more distally at the deep flexor-pronator aponeurosis is less common [1]. Compression at each of these sites produces an indistinguishable clinical syndrome.

Most cases of UNE are chronic, and manifest electrophysiologically as a primarily demyelinating lesion (segmental conduction slowing across the
elbow), an axon loss lesion, or a combination of the two. About 6% of patients with UNE have acute motor conduction block across the elbow [48]. Such cases usually have an acute or subacute presentation [49]. The differential diagnosis of UNE includes ulnar neuropathy at the wrist (UNW), a lower trunk or medial cord brachial plexopathy, C8/T1 radiculopathy, or early motor neuron disease. UNE may be a clue to an underlying polyneuropathy (e.g., diabetes mellitus, Hereditary neuropathy with liability to pressure palsy).

**Electrodiagnostic approach**

**Routine NCS.** The authors study antidromic ulnar (digit 5) and median (digit 2) sensory responses in all subjects (see Box 9). The authors obtain ulnar motor NCS, recording from the ADQ, with stimulation at the wrist below elbow and above elbow. The authors perform ulnar motor NCS with the elbow flexed 70 to 90°, and with a 10-cm stimulation distance between above and below elbow sites. In this position, measured distances between the recording and stimulating electrodes better approximate the length of the ulnar nerve by reducing slack in the nerve that occurs with elbow in the extended position. Consequently, in the extended position, underestimation of the length of the ulnar nerve may result in spuriously low conduction velocities across the elbow [50].

Ulnar SNAP amplitudes reduced below 10 µV, CMAPs reduced to below 7 mV, or absolute ulnar motor conduction velocities in the above-to-below elbow segment of <50 m/s suggest ulnar nerve involvement, but do not localize the site of the lesion [51].

Ulnar motor NCS is the most important study for localization of UNE. With the elbow in the flexed position, ≥11 m/s slowing in conduction velocities across the elbow relative to the forearm is considered significant [50]. If recording from the ADQ is nonlocalizing, the authors record from the FDI because selective fascicular involvement may occur [52]. In one study [52], slowing of ulnar motor conduction velocities across the elbow relative to the forearm (elbow flexed 70–90°) has been found in 71% of UNE patients when recording from the ADQ, and in 83% of cases when recording from the FDI.

Secondary criteria on routine ulnar motor NCS that localize UNE include a >20% drop in ulnar CMAP amplitude from the below elbow to the above stimulation sites (assumes a 10-cm stimulation distance) [51]. This finding likely indicates focal demyelination [51]. A drop in ulnar CMAP amplitude across the elbow of >50% (or area reduction of >40%, with <30% increase in duration) is unequivocal evidence of conduction block [53,54].

Routine motor NCS more often fail to localize UNE that is purely sensory or axon loss in type and where substantial axonal degeneration (loss of large myelinated fibers) leads to slowing in the wrist-to-elbow segment of the ulnar motor nerve [1]. In these circumstances, several alternative studies may localize UNE:
• Short-segment incremental stimulation studies (1-cm segments; across the elbow) allow precise localization of the UNE to the retroepicondylar groove or to the Humeroulnar arcade (Fig. 5) [47]. Focal slowing on short-segment incremental stimulation may be evident when routine ulnar motor NCS results are normal.

• In predominantly sensory UNE, mixed nerve stimulation studies may be helpful [52,55]. With stimulation of the ulnar nerve orthodromically at the wrist, mixed nerve responses can be recorded from the ulnar nerve above and below the elbow, and the mixed nerve conduction velocity across the elbow compared with the conduction velocity below the elbow. The authors perform this study in their laboratory with elbow in the straight position, and accept as abnormal >22 m/s slowing across the

Fig. 5. UNE. (A) Standard ulnar motor NCS (recording from ADQ), with stimulation at the wrist, below elbow, and above the elbow reveal a borderline abnormal (10 m/s) drop in ulnar motor conduction velocity in the below–above elbow segment relative to the forearm. (B) Short-segment incremental stimulation of the ulnar nerve across the elbow confirms UNE with focal slowing, localized 0–1 cm above the medial epicondyle. In this segment, there is a latency shift of 1.1 millisecond, much larger than the 0.2- to 0.5-millisecond shifts seen across the other 1-cm segments.
elbow segment [52]. Mixed nerve responses are usually not obtainable when the ulnar SNAP is absent.

- The authors evaluate the dorsal ulnar cutaneous nerve bilaterally in cases where distinction between UNW and elbow remain unclear after

**Box 9**

_Suggested electrodiagnostic approach to ulnar neuropathy at the elbow_

**Routine**

Antidromic ulnar and median sensory nerve conduction studies (NCS)

Ulnar motor NCS and F responses (record from abductor digiti quinti, stimulate at the wrist, below elbow and above the elbow). A $\geq 11$ m/s drop in conduction velocity (elbow flexed $90^\circ$), in the below-to-above elbow segment relative to the forearm is abnormal.

Median motor NCS and F responses

If the ulnar NCS results are nonlocalizing (with normal median NCS), and the index of suspicion is high, the authors perform one or more of the following studies to localize suspected ulnar neuropathy elbow:

- Ulnar motor NCS recording from first dorsal interosseous (FDI; stimulate at the wrist, below elbow and above the elbow)
- Short-segment incremental stimulation of the ulnar motor nerve across the elbow (see Fig. 5)
- Mixed ulnar nerve stimulation (stimulate at the wrist, double channel recording below and above the elbow)
- Dorsal ulnar cutaneous sensory responses (optional)

**Needle examination**

FDI, flexor digitorum profundus 4, abductor pollicis brevis (APB), extensor indicis proprius (EIP) to localize ulnar involvement, and exclude a C8/T1 radiculopathy or lower trunk brachial plexopathy

If the ulnar sensory nerve action potential is normal (with side-to-side comparison), and the median compound muscle action potential low, or needle electromyography abnormalities are present in the APB or EIP, the authors perform the following:

- Medial antebrachial cutaneous nerve studies bilaterally, and assess low cervical/upper thoracic paraspinal muscles to distinguish a lower trunk or medial cord brachial plexopathy from a C8/T1 radiculopathy
- Median motor NCS are performed to exclude a lower trunk plexopathy or more diffuse process.
routine evaluation. An asymmetrically absent or low (<50% the amplitude of the asymptomatic side) dorsal ulnar cutaneous response localizes the lesion to the ulnar nerve above the wrist (or the medial cord or lower trunk of the brachial plexus). However, a normal dorsal cutaneous response does not exclude UNE because it is unaffected in 25% of cases of UNE due to selective fascicular involvement [56].

There are several caveats: first, as in the case of MNW, the authors require two pieces of concordant data to confirm UNE [1]. Second, short-segment incremental stimulation and mixed ulnar nerves studies have more technical limitations than routine ulnar NCS, and should only be performed by electromyographers who have an appreciation of the technical pitfalls of these studies [50]. In our opinion, they should not be used as the sole piece of data supporting UNE.

Needle examination. Needle examination aids in localization of UNE, and helps exclude lower trunk brachial plexopathy or C8/T1 radiculopathy. It provides an important measure of the severity, chronicity, and degree of axon loss. The authors routinely study FDI and FDP subserving digits 4 or 5 (FDP4 or FDP5). The finding of fibrillation potentials or reinnervation in the FDP4 muscle, in the setting of an ulnar mononeuropathy, localizes the lesion to at or above the elbow. The FDP4/FDP5 is spared in about 50% of cases of UNE. The authors rarely study the flexor carpi ulnaris; it is less often involved in UNE because the branches supplying this muscle are frequently given off above the elbow. The FDI is the most commonly involved muscle in UNE; however, abnormality in this muscle has no localizing value. The authors also study the APB and EIP muscles to exclude a lower trunk brachial plexopathy or C8/T1 radiculopathy.

“Weakness and/or numbness in the hand”

Ulnar Neuropathy at the Wrist (UNW)

UNW is suspected in the patient with isolated focal hand weakness involving ulnar-innervated muscles. Compression usually occurs at one of 5 sites [56,57]:

1. Proximal portion of Guyon’s canal: involving deep (motor) and the superficial (sensory) branches of the ulnar nerve. All ulnar-innervated hand muscles are affected. There is a sensory disturbance involving the medial half of the fourth finger and the fifth finger.
2. Lesion of the superficial branch in Guyon’s canal: a purely sensory disturbance involving the fifth digit and medial half of the fourth digit, sparing the dorsal ulnar cutaneous distribution.
3. A proximal lesion of the deep motor branch in Guyon’s canal: pure motor disturbance with weakness of all ulnar nerve-innervated hand muscles.
4. A more distal lesion of the deep motor branch (in the region of the Hamate): weakness of the interossei, with sparing of the hypothenar muscles and superficial sensory branch.

5. A very distal lesion of the deep motor branch: isolated weakness of the FDI and adductor pollicis muscles.

**Electrodiagnostic approach**

Precise localization of UNW can be difficult because of the various possible sites of compression. Diagnosis and localization requires a combination of NCS and a detailed needle examination (see Box 10). UNW should be distinguished from UNE, lower trunk brachial plexopathy, a C8 radiculopathy and, in the case of a purely motor presentation, focal onset motor neuron disease. The authors obtain routine ulnar sensory and motor (recording from both ADQ and FDI) NCS. The authors also perform median motor and sensory NCS to confirm that findings are limited to the ulnar nerve territory. In UNW types 1 and 2, the ulnar SNAP (recorded from digit 5) is of low amplitude or of prolonged distal latency [58]. In UNW types 3 to 5, the ulnar SNAP is normal. Ulnar motor studies may demonstrate reduced- or normal-amplitude CMAP, with a prolonged distal latency. In UNW types 1 and 3, these abnormalities are present both with recording from the ADQ and the FDI. There should be no focal slowing of ulnar motor conduction velocity across the elbow. In UNW types 4

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**Box 10**

**Suggested electrodiagnostic approach to ulnar neuropathy at the wrist**

**Routine**

- Ulnar and median sensory nerve conduction studies (NCS)
- Ulnar motor NCS and F responses (record from both first dorsal interosseous (FDI) and abductor digiti quinti (ADQ), stimulate at the wrist, below elbow and above elbow)
- Lumbrical-interosseous study
- Median motor NCS and F responses

**Needle examination**

- FDI, ADQ, flexor digitorum profundus 4, abductor pollicis brevis, extensor indicis proprius

**Optional**

- Dorsal ulnar cutaneous sensory responses
- Median-to-ulnar midpalmar comparison studies
- Short-segment incremental stimulation recording from FDI (useful if conduction block is suspected)
and 5, ulnar motor responses recorded from ADQ are normal, but those from FDI are often reduced in amplitude and prolonged in latency. A side-to-side ulnar motor distal latency (recording from FDI) difference of 1.3 milliseconds or a 2-millisecond difference between the FDI and ADQ ulnar motor distal latencies is supportive of distal UNW (types 4 or 5) [60].

In addition to ulnar sensory and motor latency criteria, the authors find the lumbral-interosseous study described above for the evaluation of MNW also to be quite useful for UNW [61]. In normal subjects, the lumbral distal latency (median nerve stimulation at the wrist) is equal to the interosseous distal latency (ulnar nerve stimulation at the wrist). An interosseous latency >0.4 milliseconds longer than the lumbral recording suggests UNW (see Fig. 4) [61].

The needle EMG examination is very helpful in the evaluation of possible UNW. It aids in localization of the lesion to the ulnar nerve, and in the separation of UNW types 1 and 3 from 4 and 5. The authors use the needle examination to exclude a coexistent lower trunk brachial plexopathy, a C8 radiculopathy, and focal onset motor neuron disease.

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**Fig. 6.** (A) Normal ulnar motor NCS (surface recording from FDI), with stimulation in the palm (A1) and at the wrist (A2). (B) Ulnar neuropathy at the wrist (UNW). Ulnar motor NCS (recording from FDI) demonstrates a 73% drop in ulnar CMAP amplitude at the wrist (A1) relative to the palmar stimulation site (A2), indicative of partial conduction block and focal demyelination. The distal ulnar CMAP amplitude is approximately 50% lower than the unaffected side (A), suggesting associated axon loss.
The authors study the FDI, ADQ, and FDP4. In UNW, the FDP 4 is normal. The FDI is affected in UNW types 1, 3, 4, and 5, whereas the ADQ is abnormal in types 1 and 3 but spared in types 4 and 5. The authors also examine APB and EIP to exclude a C8 radiculopathy or a lower trunk brachial plexopathy.

Finally, in patients in whom the ulnar motor CMAP amplitudes to the FDI or ADQ are reduced and the needle examination is suggestive of partial conduction block (decreased recruitment with little active denervation or reinnervation), the authors perform short-segment incremental stimulation studies (recording from FDI) across the wrist to confirm conduction block and localize the site of the lesion (Fig. 6) [62].

References


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Electrodiagnostic approach to the patient with suspected mononeuropathy of the lower extremity

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The electrodiagnostic (EDX) studies of patients with suspected mononeuropathies of the lower extremity are often challenging and more complex than those of the upper limb. This complexity is related to several factors: (1) technical difficulties in obtaining sensory nerve action potentials (SNAPs) such as the sural or the superficial SNAPs, often due to age, limb swelling, or obesity; (2) lack of available SNAPs (or extreme difficulty in obtaining them) for many sensory nerves, particularly those located proximally, such as the ilioinguinal or genitofemoral nerves; and (3) neurogenic changes occurring in asymptomatic subjects (usually elderly), such as large motor unit action potentials (MUAPs) in foot muscles and fibrillation potentials in lumbar paraspinal muscles. These disadvantages may cause difficulty distinguishing lumbosacral radiculopathies, peripheral polyneuropathies or, less often, lumbosacral plexopathies from mononeuropathies, and lead to unwarranted diagnostic or surgical procedures such as lumbar spine surgery.

This article discusses the EDX aspects of lower extremity mononeuropathies, following a brief review of anatomic and clinical features. These mononeuropathies are listed in groups, based on their main clinical manifestations. The terms *entrapment* and *compression* are used interchangeably, although strictly speaking, in entrapment the nerve is compressed within a fibro-osseous tunnel.

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Foot weakness

Common and deep peroneal mononeuropathy

The common peroneal nerve shares a common sheath with the tibial nerve to form the sciatic nerve. The only branch of the common peroneal nerve in the thigh is a motor branch that innervates the short head of biceps femoris, whereas all other hamstrings are supplied by the tibial nerve. In the popliteal fossa, the common peroneal nerve gives off the lateral cutaneous nerve of the calf, which innervates the skin over the upper third of the lateral aspect of the leg. Then, the common peroneal nerve winds around the fibular neck and divides into its terminal branches: the deep and superficial peroneal nerves. The deep peroneal nerve innervates the tibialis anterior, extensor hallucis longus, peroneus tertius and extensor digitorum longus, and the skin of the web space between the first and second toes. The superficial peroneal nerve gives motor branches to the peroneus longus and brevis, and innervates the skin of the lower two thirds of the lateral aspect of the leg and the dorsum of the foot (except for the first web space).

Common peroneal mononeuropathies occur often at the fibular neck and are usually caused by nerve compression or by knee trauma [1–4]. Intraoperative compression is the most common cause of acute peroneal mononeuropathies at the fibular neck. It usually occurs during anesthesia for surgical procedures in which the peroneal nerve is distant from the surgical field. Weight loss often causes a subacute onset peroneal nerve compression at the fibular neck. Similarly, prolonged hospitalization, bed rest, or coma, particularly when associated with weight loss, are common causes of peroneal nerve compression at the fibular neck. Prolonged squatting and devices placed on the leg (such as casts, orthoses, pneumatic compression devices, and antithrombotic stockings, bandages, and straps) may also compress the peroneal nerve at the fibular neck. Finally, blunt or open trauma and nerve injury during surgical procedures in which the peroneal nerve is in or near the operative field (such as knee surgery) are other common causes of peroneal nerve injuries.

Most peroneal nerve lesions are unilateral, whereas bilateral lesions constitute about 10% of all the cases [1,5]. Acute or subacute foot drop, which may be complete or partial, is the most common presenting symptom. Weakness of ankle and toe dorsiflexion is the most prominent neurologic finding, whereas ankle eversion is relatively stronger because the superficial peroneal nerve often is less damaged than the deep peroneal nerve [6]. Ankle inversion, toe flexion and plantar flexion are normal. Sensory loss is limited to the lower two thirds of the lateral leg and dorsum of foot, and Tinel’s sign may be elicited by percussion of the common peroneal nerve at the fibular neck.

Common peroneal nerve lesions may be confused with sciatic mononeuropathy (especially when affecting the common peroneal nerve predominantly), lumbosacral plexopathy (particularly when involving the lumbosacral trunk lesion), or lumbar radiculopathy (particularly an L5 radiculopathy).
Electrodiagnostic (EDX) studies

The EDX examination of patients with foot drop and suspected peroneal mononeuropathy is one of the most fulfilling investigations done in the electromyography (EMG) laboratory. The EDX study helps in localizing the cause of the foot drop to the common peroneal nerve at the fibular neck or upper thigh, to the deep peroneal nerve, to the sciatic nerve, or to the L5 root or plexus (Table 1). The EDX examination is also extremely useful in defining the primary pathology of the peroneal nerve lesion (demyelinating versus axonal versus mixed). Hence, it often can predict the prognosis and expected course of recovery. Sequential needle EMG studies are important in axon-loss lesions because they assess the presence and extent of spontaneous or postoperative (post nerve repair) reinnervation.

In addition to the sural sensory, peroneal motor, recording extensor digitorum brevis (EDB), and tibial motor nerve conduction studies (NCS), which are common routine studies done in most EMG laboratories, the peroneal motor NCS, recording tibialis anterior, and superficial peroneal sensory NCS should be performed. Performing the peroneal motor study, recording EDB only (and omitting the peroneal motor study recording tibialis anterior) has two disadvantages: (1) the motor fibers destined to the tibialis anterior are far more pertinent than the EDB fibers in predicting the outcome of foot drop in patients with peroneal nerve lesions; and (2) the EDB is not uncommonly atrophic and denervated in isolation (probably due to local trauma), and a low-amplitude compound muscle action potential (CMAP), recording EDB, may erroneously suggest that the peroneal lesion is axonal and severe.

The peroneal nerve should be stimulated below and above fibular neck with particular attention to CMAP amplitudes and areas. Also, the peroneal motor and sensory NCS should be obtained in both legs in order to compare the distal CMAP amplitudes and areas and SNAP amplitudes, looking for signs of significant axonal loss (see later discussion). In addition, the sural sensory and tibial motor NCS and the tibial H-reflexes should be studied bilaterally when there is a suspicion of a sciatic nerve lesion or a proximal (high) common peroneal mononeuropathy.

During the needle EMG, at least two deep peroneal-innervated muscles (such as tibialis anterior, extensor hallucis longus, or EDB) should be sampled. One superficial peroneal-innervated muscle (such as peroneus longus) should also be examined. This muscle is affected in common peroneal mononeuropathy but spared in deep peroneal nerve lesions. In axon-loss common peroneal mononeuropathies, which are unlocalizable by NCS, sampling the short head of biceps femoris is mandatory to exclude a proximal common peroneal lesion, that is, a sciatic neuropathy affecting the peroneal nerve predominantly or exclusively. Sampling nonperoneal L5-innervated muscles is important, particularly in deep peroneal lesions because their NCS pattern is identical to that of moderate or severe L5 radiculopathy (see later discussion). This should include muscles innervated by
the L5 root located distally, such as the tibialis posterior or flexor digitorum longus, and proximally, such as the tensor fascia lata or gluteus medius. These muscles are also abnormal in lumbosacral plexopathy affecting the lumbosacral trunk predominantly (such as occurring after childbirth) (see Table 1). Finally, tibial-innervated muscles not innervated predominantly by L5 fibers, such as the medial gastrocnemius, and long head biceps femoris, are also useful, particularly in suspected sciatic nerve lesion.

The findings from EDX studies in patients with peroneal nerve lesions follow certain predictable patterns, with rare deviations (Table 2 and Fig. 1) [1,2,4,6,7]. One of the following patterns is often encountered:

Conduction block across the fibular neck. Conduction block across the fibular neck may be complete or partial. With partial block, there is a significant (>20%, often more than 50%) drop in CMAP amplitude, area, or both across the fibular neck. The primary pathology is segmental demyelination of some or all of the peroneal fibers, the extent of which may be determined by comparing the distal and proximal CMAP amplitudes and areas. The time required for Wallerian degeneration should be taken into account because motor “axon conduction block” may occur when NCS are performed less than 5–6 days following the onset of acute axonal lesions. In contrast to conduction block, focal slowing across the fibular neck is rarely seen in isolation; when present, it is often associated with the localizing conduction block but may also be encountered in patients recovering from peroneal nerve lesions across the fibular neck. Because the primary pathology of these lesions is segmental demyelination, prognosis is excellent, with expected recovery in 2 to 3 months, provided the cause of compression is eliminated.

Axon loss. Axon loss may also be complete or partial involving the common peroneal nerve at the fibular neck, common peroneal nerve in the thigh, or deep peroneal nerve. The NCSs, when done after 10 days from symptom onset, reveal low-amplitude or absent distal and proximal peroneal CMAPs, recording EDB and tibialis anterior. The peroneal motor conduction velocities are normal or slightly reduced diffusely, without focal slowing. The superficial peroneal sensory study is absent, except in selective deep peroneal nerve lesions. On needle EMG, there is often fibrillation potentials and decreased number of MUAPs, which fire rapidly, in all deep peroneal-innervated muscles, but also in the peroneus longus (in common peroneal lesions) and the short head of biceps femoris (in high common peroneal nerve lesions). The EDX testing cannot confirm the exact location of these axon-loss lesions because they are not accompanied by conduction block or focal slowing. They may be classified, based on needle EMG, to be (1) between fibular neck and midthigh (origin of the branch to the short head of biceps femoris); (2) above midthigh (above of the origin of the branch to the short head of biceps
<table>
<thead>
<tr>
<th>Nerve lesion</th>
<th>Peroneal neuropathy at the fibular neck</th>
<th>L5 radiculopathy</th>
<th>Lumbosacral plexopathy (lumbosacral trunk)</th>
<th>Sciatic neuropathy (mainly peroneal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peroneal motor study</td>
<td>Low in amplitude or conduction block across fibular head or both</td>
<td>Usually normal but can be low in amplitude</td>
<td>Low in amplitude</td>
<td>Low in amplitude</td>
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<tr>
<td>Superficial peroneal sensory study</td>
<td>Low or absent&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Normal</td>
<td>Low or absent</td>
<td>Low or absent</td>
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<tr>
<td>Sural sensory study</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal or low amplitude</td>
<td>Normal or low amplitude</td>
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<tr>
<td>Peroneal muscles&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Abnormal</td>
<td>Abnormal</td>
<td>Abnormal</td>
<td>Abnormal</td>
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<tr>
<td>Tibial L5 muscles&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Normal</td>
<td>Usually abnormal</td>
<td>Usually abnormal</td>
<td>Normal or abnormal</td>
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<tr>
<td>Other L5 muscles&lt;sup&gt;d&lt;/sup&gt;</td>
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<td>Normal or abnormal</td>
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<td>Normal</td>
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<tr>
<td>Biceps femoris (short head)</td>
<td>Normal</td>
<td>Usually normal</td>
<td>Usually normal</td>
<td>Abnormal</td>
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<td>Paraspinal muscles fibrillations</td>
<td>Absent</td>
<td>May be absent</td>
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<td>Absent</td>
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</tbody>
</table>

<sup>a</sup> Can be normal in purely demyelinating lesions or lesion of the deep peroneal nerve only.
<sup>b</sup> Below knee (Tib ant, extensor digitorum longus, EDB, extensor hallucis, +/- peroneus longus).
<sup>c</sup> Tibialis posterior and flexor digitorum longus.
<sup>d</sup> Gluteus medius and tensor fascia lata.

Abbreviations: EDB, extensor digitorum brevis; Tib ant, tibialis anterior.

Adapted from Katirji B. Electromyography in clinical practice. St. Louis, MO: Mosby; 1998; with permission.
<table>
<thead>
<tr>
<th>Pattern</th>
<th>Site of lesion</th>
<th>Frequency</th>
<th>Superficial peroneal SNAP</th>
<th>Distal peroneal CMAP&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Conduction block at fibular head</th>
<th>Focal slowing across the fibular head</th>
<th>Needle EMG of peroneus longus</th>
<th>Needle EMG of biceps femoris (short head)</th>
<th>Prognosis for recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conduction block</td>
<td>Fibular head</td>
<td>20–30%</td>
<td>Normal</td>
<td>Normal</td>
<td>Present</td>
<td>Rare</td>
<td>Abnormal</td>
<td>Normal</td>
<td>Excellent</td>
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<td>Axonal loss</td>
<td>Mid thigh and fibular head&lt;sup&gt;b&lt;/sup&gt;</td>
<td>45–50%</td>
<td>Usually absent</td>
<td>Low amplitude or absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Abnormal</td>
<td>Normal</td>
<td>Protracted</td>
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<tr>
<td></td>
<td>Deep peroneal</td>
<td>5%</td>
<td>Normal</td>
<td>Low amplitude or absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Normal</td>
<td>Normal</td>
<td>Fair</td>
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<tr>
<td></td>
<td>Proximal&lt;sup&gt;c&lt;/sup&gt;</td>
<td>&lt;5%</td>
<td>Usually absent</td>
<td>Low amplitude or absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Abnormal</td>
<td>Abnormal</td>
<td>Very poor</td>
</tr>
<tr>
<td>Mixed</td>
<td>Fibular head</td>
<td>25–30%</td>
<td>Low amplitude or absent</td>
<td>Low amplitude or absent</td>
<td>Present</td>
<td>Rare</td>
<td>Abnormal</td>
<td>Normal</td>
<td>Biphasic</td>
</tr>
</tbody>
</table>

<sup>a</sup> Recoding tibialis anterior and EDB.<br>
<sup>b</sup> Usually around the fibular head.<br>
<sup>c</sup> High, proximal to the gluteal fold.

Abbreviations: CMAP, compound muscle action potential; EDB, extensor digitorum brevis; EMG, electromyography; SNAP, sensory nerve action potential.

femoris); or (3) involving the deep peroneal nerve selectively. Axon-loss peroneal nerve lesions have worse prognosis than those with demyelination because recovery is dependent on sprouting and proximodistal reinnervation. The prognosis is worst in high lesions because the distance to the target muscles (anterior compartment muscles) is long, whereas lesions around the fibular neck reinnervate faster because the nerve damage is near the denervated muscles.

**Mixed (conduction block and axon loss).** These common peroneal nerve lesions are characterized by a low amplitude or area (or both) of the distal peroneal CMAPs, recording EDB, tibialis anterior, or both muscles, with partial or complete conduction block across the fibular neck. The superficial peroneal SNAP is low in amplitude or absent. Peroneal motor conduction
velocities are usually normal and, rarely, there is an accompanying focal slowing. The findings may also show a fascicular nerve injury with different pathophysiologic processes involving fibers directed to the EDB versus tibialis anterior [1,6]. For example, it is not uncommon to find conduction block across the fibular neck (consistent with segmental demyelination) while recording the tibialis anterior, and low amplitude distal and proximal peroneal CMAPS (consistent with axonal loss) while recording the EDB. Recovery of the neurologic deficit in mixed lesions is usually biphasic; the first phase is due to remyelination and is relatively rapid, occurring over 6 to 8 weeks, whereas the second phase is due to reinnervation and sprouting and is more protracted, extending into months or years.

**Sciatic mononeuropathy**

The sciatic nerve fibers originate from the L4, L5, S1, and S2 roots. The sciatic nerve is composed of two nerves that are separate from the outset and do not exchange any fascicles: the common peroneal nerve placed laterally, and the tibial nerve placed medially. The sciatic nerve leaves the pelvis via the sciatic notch where the nerve usually passes underneath the piriformis muscle. At times, the peroneal division only may pass through or above the piriformis muscle, or the entire sciatic nerve pierces the piriformis muscle. In the thigh, the tibial nerve innervates most hamstring muscles (semitendinosus, semimembranosus, and long head of biceps femoris), and supplies a branch to the adductor magnus, whereas the common peroneal nerve innervates the short head of biceps femoris only.

In sciatic nerve lesions around the hip, the peroneal division is often more vulnerable to physical injury than the tibial division [8,9]. This vulnerability is related to two reasons:

- The difference in the fascicular pattern of the perineurium among these two nerves in the upper thigh: the peroneal nerve has fewer and larger fascicles with limited supportive tissue, whereas the tibial nerve is composed of many cushioning fascicles, well placed between the elastic epineurial tissue. This difference renders the peroneal division of the sciatic nerve more susceptible to external pressure.
- The anatomic course of the common peroneal and tibial nerves: the peroneal nerve is taut and secured at the sciatic notch and fibular neck, whereas the tibial nerve is loosely fixed posteriorly. Hence, traction of the sciatic nerve in the upper thigh (such as during total hip replacement) results in more extensive stretch injury to the peroneal nerve than the tibial nerve.

Causes of sciatic mononeuropathies include total hip replacement, hip fracture or dislocation, femoral fracture, gluteal injection, gluteal compartment syndrome, gunshot or knife wound, and acute compression during coma, drug overdose, prolonged sitting, or intensive care unit hospitalization [10,11].
Sciatic mononeuropathy at the hip presents with weakness, pain, and sensory loss. Severe sciatic nerve lesions are associated with a flail foot (i.e., weak foot and ankle in all directions), hamstring weakness, and sensory loss of the dorsum and plantar surfaces of the foot. In moderate lesions, the foot weakness commonly manifests as a foot drop because the peroneal component is usually more affected than the tibial. In addition to weakness of ankle dorsiflexion and eversion, there is often mild weakness of knee flexion, plantar flexion, and ankle inversion. The ankle jerk is usually asymmetrically depressed or absent, a useful clinical clue in patients with mild sciatic lesions. Occasionally, sciatic nerve lesions at the hip are essentially pure high common peroneal lesions, manifesting very similarly to common peroneal lesions at the fibular neck.

Severe or complete sciatic nerve lesions pose little difficulty in diagnosis because the weakness involves all muscles below the knee, often with the hamstrings. Also, the sensory loss below the knee spans both the peroneal and tibial distributions while sparing the medial leg (saphenous nerve distribution). In contrast, partial sciatic nerve lesions, which usually present with foot drop, may be difficult to differentiate from peroneal mononeuropathy, lumbosacral radiculopathy, and lumbosacral plexopathy.

Electrodiagnostic (EDX) studies

The EDX examination often confirms the presence of axon-loss sciatic mononeuropathy and helps to exclude a common peroneal nerve lesion around the fibular neck, a lumbosacral radiculopathy, or plexopathy (see Table 1). In severe lesions, all the peroneal and tibial motor studies and the superficial peroneal and sural sensory studies are absent or low in amplitude. The needle EMG reveals that all common peroneal-innervated muscles and all the tibial-innervated muscles including the hamstring muscles have fibrillation potentials, decreased recruitment, and large MUAPs [12]. The short head of biceps femoris, innervated by the common peroneal nerve, frequently is much more affected than the other hamstrings. Occasionally, neurogenic changes in the thigh adductors may be detected because the adductor magnus receives dual innervation from the sciatic and the obturator nerves. However, the glutei, tensor fascia lata, and lumbar paraspinal muscles are normal, which helps to exclude a lumbosacral plexopathy or radiculopathy.

In mild or moderately severe lesions, the NCS may suggest that the lesion is an axon-loss common peroneal mononeuropathy because the peroneal nerve is often affected more severely than the tibial nerve [8,9]. Although the peroneal motor and sensory studies may be absent or low in amplitude, helpful clues for the presence of a sciatic nerve lesion include an asymmetrically low-amplitude sural SNAP, H-reflex, or tibial CMAP. Therefore, it is highly recommended that the contralateral H-reflex, and sural sensory and tibial motor NCS are performed for comparison purposes in all patients with foot drop, especially when a sciatic nerve lesion is considered. It is important to recall that an abnormally low-amplitude sural SNAP does not automatically
indicate involvement of the tibial nerve. The sural nerve, which originates from the tibial nerve in the popliteal fossa, often receives a branch from the common peroneal nerve in the popliteal fossa. This may contribute to the antidromic sural SNAP, stimulating at the calf and recording at the ankle.

On rare occasions, the common peroneal component of the sciatic nerve is selectively injured in the hip or thigh [2,13]. On these occasions, the H-reflex, tibial motor conduction studies, and all tibial-innervated muscles above and below the knee are normal. These lesions are purely axonal and mimic a common peroneal mononeuropathy at the fibular neck (see Table 2). Thus, sampling the short head of biceps femoris is mandatory in all patients with peroneal mononeuropathy, especially those axonal ones that could not be localized by NCS due to the lack of conduction block or focal slowing.

Foot pain/numbness

Tarsal tunnel syndrome (TTS)

The tibial nerve separates completely from the common peroneal nerve in the upper popliteal fossa. Soon, it gives off its first branch, the sural nerve, a purely sensory nerve that innervates the skin over lateral aspect of the lower leg and foot, including the little toe. The tibial nerve innervates all the posterior leg compartment muscles including the gastrocnemius, soleus, tibialis posterior, flexor digitorum longus, and flexor hallucis longus. At the ankle, the tibial nerve passes posterior to the medial malleolus and through the tarsal tunnel (also called medial tarsal tunnel) to enter the foot. The tarsal tunnel is roofed by the lancinate ligament (flexor retinaculum) that extends between the medial malleolus and the calcaneus. It contains, in addition to the tibial nerve, the posterior tibial artery and the tibialis posterior, flexor digitorum longus, and flexor hallucis longus tendons. There, or slightly distal to that point, the tibial nerve divides into its three terminal branches: (1) the calcaneal branch, a purely sensory nerve that innervates the skin of the sole of the heel; (2) the medial plantar nerve that innervates the abductor hallucis, flexor digitorum brevis, and flexor hallucis brevis in addition to the skin of the medial sole and, at least, the medial three toes; and (3) the lateral plantar nerve that innervates the abductor digiti quinti pedis, flexor digiti quinti pedis, adductor hallucis, and the interossei in addition to the skin of the lateral sole and two lateral toes.

TTS is caused by compression of the tibial nerve or any of its three terminal branches under the flexor retinaculum [14–16]. The disorder is insidious in onset, more common in women, and is usually unilateral. Most cases of TTS are idiopathic, whereas others are due to remote ankle trauma, arthritis and tenosynovitis, ill-fitting foot wear, heel varus or valgus deformity, or mass lesions (ganglion, lipoma, schwannoma).

The most common symptoms of TTS are burning pain and numbness in the sole of the foot and heel. The pain may worsen (or occur only) after
prolonged standing, walking, jogging, or running. The neurologic examination reveals sensory impairment in the sole in the distribution of the medial plantar or lateral plantar branches or both. Sensation in the calcaneal distribution is often spared. Tinel’s sign, induced by percussion of the tibial nerve behind the medial malleolus, is present in most patients with TTS.

TTS may be difficult to distinguish from more common orthopedic, rheumatologic, and neurologic conditions, particularly in patients with a prior history of foot or ankle trauma. Proximal tibial mononeuropathy often presents with indolent symptoms that may mimic TTS. Although such lesions often cause foot pain and numbness, there is often associated calf weakness or atrophy or absent or depressed ankle jerk, findings not consistent with TTS. An S1 or S2 radiculopathy may result in foot numbness or pain that is often worse with walking or standing. However, there is usually low back and posterior thigh pain, depressed or absent ankle jerk, or weakness of gastrocnemius or glutei muscles. A particularly difficult task is distinguishing patients with TTS from those with early sensory peripheral polyneuropathy, particularly in the elderly. A useful feature is that TTS is rarely bilateral, whereas peripheral polyneuropathy often affects both feet. Also, the sensory loss in polyneuropathy usually involves both the sole and dorsum of foot, and rarely is associated with Tinel’s sign at the flexor retinaculum.

**Electrodiagnostic (EDX) studies**

Several EDX techniques are used to assess for TTS. Most of these involve assessing sensory, motor, or mixed nerve fibers of the medial or the lateral plantar nerves [14,16–18]. The tibial motor NCS recording from the abductor hallucis and the abductor digiti quinti pedis is easy to perform but not sensitive because they only assess plantar motor fibers. A prolonged medial or lateral (or both) plantar motor distal latency, using absolute values or by comparison to the contralateral asymptomatic limb, is diagnostic. It is estimated that only about half of symptomatic limbs have abnormal motor latencies. The mixed medial and lateral plantar NCS are more sensitive than the tibial motor distal latencies (abnormal in about two thirds of symptomatic limbs). Hence, they are the most widely employed studies for the evaluation of TTS. They are obtained by percutaneous (surface) stimulation of the medial and lateral plantar nerves on the sole of the foot while recording with surface electrodes over the tibial nerve posterior to the medial malleolus. These studies are the counterparts of the median and ulnar palmar mixed studies performed in the hand for the evaluation of carpal tunnel syndrome. Asymmetric slowing of latency of the medial or lateral (or both) mixed nerve action potentials is abnormal. Another likely significant (although poorly localizing) abnormality is absent mixed plantar responses on the symptomatic side. Despite their high sensitivities, the mixed plantar studies are technically difficult to elicit in subjects with foot calluses on the plantar surface of the foot, ankle edema, foot deformities, or even in normal adults over 45 years of age.
The medial and lateral plantar SNAPs that assess solely the sensory fibers of the medial and lateral plantar nerves are technically difficult and have not gained wide popularity [16,17]. The orthodromic techniques consist of stimulating the first or fifth toes while recording from the tibial nerve proximal to the flexor retinaculum. Antidromic studies stimulating the ankle and recording the toes are also possible. A variation of the orthodromic sensory NCS technique includes recording via a needle electrode placed closely to the tibial nerve and proximally to the flexor retinaculum [18]. Unfortunately, with any of these NCS procedures, the elicited SNAPs are extremely low in amplitude in normal subjects and require signal averaging. As with the other plantar NCS techniques, prolonged latencies are sought. A possibly significant finding is absent SNAPs on the symptomatic side. These sensory studies are sensitive and reported to be abnormal in up to 90% of symptomatic limbs.

Needle EMG of the abductor hallucis and abductor digiti quinti pedis may be abnormal with TTS if axon loss has occurred. MUAP loss, chronic neurogenic MUAP changes, and fibrillation potentials in various combinations may be found. Unfortunately, these muscles are painful, difficult to activate, and may show denervation changes in asymptomatic patients, especially in the older age group [19].

An important task of the EDX studies is to differentiate TTS from peripheral polyneuropathy or S1/S2 radiculopathy because all these entities result in abnormal tibial motor conduction studies and denervation of intrinsic muscles (Table 3). Distinguishing these three disorders is difficult, particularly in the elderly patients in whom lower extremity SNAPs and H-reflexes may be absent.

**Anterior tarsal tunnel syndrome (ATTS)**

Lesions of the distal segment of the deep peroneal nerve on the dorsum of the ankle are sometimes referred to as ATTS. However, the anterior tarsal tunnel is not a true anatomic tunnel, in contrast to the carpal tunnel or medial tarsal tunnel. Its floor is the fascia overlying the talus and navicular, and its roof is the inferior extensor retinaculum.

Causes of ATTS include direct contusion to the dorsum of the ankle, chronic pressure from shoe rims or straps, ganglion cyst, pes cavus, talonavicular osteophyte, or fractures, dislocations, or sprains of the ankle [15,20]. Unusual positioning of the foot such as with marked foot plantar flexion accompanied by dorsiflexion of the toes (eg, with wearing high-heeled shoes), or extreme inversion of the foot (eg, with spasticity or dystonia) are also associated with this syndrome.

The syndrome is slightly more common in women, probably related to the use of high-heeled shoes. There is often numbness and paresthesiae limited to the web space between the first and second toes. Ankle and foot pain that is worse at night is common, whereas foot weakness is not part of the syndrome. On examination, there is diminished sensation in the web space
<table>
<thead>
<tr>
<th></th>
<th>Tarsal tunnel syndrome</th>
<th>Chronic S1/S2 radiculopathy</th>
<th>Peripheral polyneuropathy</th>
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<tr>
<td><strong>Nerve conduction studies</strong></td>
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<tr>
<td>Paraspinal muscles</td>
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<td>Normal or fibrils</td>
<td>Normal or fibrils</td>
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<tr>
<td>Symmetry of findings</td>
<td>Asymmetrical&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Asymmetrical&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Symmetrical</td>
</tr>
</tbody>
</table>

<sup>a</sup> When bilateral.

*Abbreviations*: AH, abductor hallucis; ADQP, abductor digiti quinti pedis; EDB, extensor digitorum brevis; fibrils, fibrillations.

*Adapted from* Katirji B. Electromyography in clinical practice. St. Louis, MO: Mosby; 1998; with permission.
between the first and second toes (ie, in the region innervated by the terminal portion of the deep peroneal nerve) and wasting of the EDB muscle. Tinel’s sign over the deep peroneal nerve at the ankle may be elicited. ATTS may be asymptomatic, being detected only incidentally during EDX testing of the lower limb for other symptoms such as lumbosacral radiculopathies. This finding has raised many questions as to the true existence of this entity.

Electrodiagnostic (EDX) studies

The EDX findings in ATTS are limited to (1) prolongation of peroneal motor distal latency, recording EDB, with a normal peroneal proximal conduction velocity; and (2) chronic neurogenic MUAP changes, usually with fibrillation potentials, in the EDB muscle. The peroneal CMAP, recording EDB, is normal or low in amplitude, whereas the CMAP, recording tibialis anterior, and the superficial peroneal SNAP are always normal. Similarly, needle EMG of common peroneal and L5- or S1-innervated muscles are normal. The findings may be unilateral or bilateral. In asymptomatic patients, it may difficult to separate the above findings from the common occurrence of denervation of the EDB, with or without slowing of peroneal motor distal latency. It is advised that the diagnosis of ATTS be reserved to patients with typical manifestations and EDX findings.

Distal superficial peroneal mononeuropathy

Isolated superficial peroneal mononeuropathies are usually due to nerve entrapment in the leg or ankle and are purely sensory because they affect the nerve distal to the motor branches to the peroneus longus and brevis. A common site of entrapment is at the facial defect, 10 cm above the lateral malleolus, where the nerve becomes superficial; this occurs mostly in athletes. Another site is more distal near the ankle, where superficial peroneal nerve injuries may be iatrogenic (such as during ankle arthroscopy or needle insertion) or due to tight foot wear (shoes or boots), neuromas, or acute contusions [21].

Lesions to the superficial peroneal nerve at the facial defect manifest with sensory loss in the lower lateral third of the leg and dorsum of foot, excluding the first web space. Pain in the distal anterolateral leg is common. Both numbness and pain may be worse with walking or running. Tinel’s sign may be induced there. Ankle pain with or without numbness over the dorsum of the foot is the only manifestation of superficial peroneal lesions at the ankle. The pain is variable, and may be present at rest or with exercise. Symptoms may worsen with foot plantar flexion or ankle inversion.

Electrodiagnostic (EDX) studies

The EDX studies in patients with superficial peroneal mononeuropathy in the distal leg often reveal an absent or low-amplitude superficial peroneal SNAP, with or without a delay in its distal latency. In contrast, peroneal motor NCS and needle EMG of all peroneal-innervated muscles including
the peroneus longus and brevis is normal. With ankle lesions, the SNAP abnormalities are less consistent, partially because most superficial peroneal sensory nerve techniques are performed proximal to these lesions [22,23].

**Proximal leg weakness**

*Femoral mononeuropathy*

The femoral nerve is formed by the combination of the posterior divisions of the ventral rami of L2, L3, and L4 spinal roots (the anterior divisions of the same roots form the obturator nerve). Soon after its formation in the pelvis, the femoral nerve innervates the psoas muscle that receives additional separate branches from the L3 and L4 roots directly. The femoral nerve passes between the psoas and iliacus muscles and is covered by the tight iliacus fascia, which forms the roof of the iliacus compartment. The femoral nerve emerges from the iliacus compartment after passing underneath the rigid inguinal ligament in the groin. About 4 to 5 cm before crossing the inguinal ligament, it innervates the iliacus muscle. Soon after passing underneath the ligament, the femoral nerve branches widely into (1) terminal motor branches to all four heads of the quadriceps (rectus femoris, vastus lateralis, vastus intermedius, and vastus lateralis) and sartorius muscles; and (2) three terminal sensory branches, the medial and intermediate cutaneous nerves of the thigh that innervate the skin of the anterior thigh, and the saphenous sensory nerve that innervates the medial leg.

Because of its short course, the main trunk of the femoral nerve is usually injured at one of two sites: the retroperitoneal pelvic space or the inguinal ligament [24,25]. Most femoral mononeuropathies in the pelvis are iatrogenic, occurring during intra-abdominal, intrapelvic, inguinal, or hip surgical or diagnostic procedures. Most cases occur following the use of self-retracting blades compared with hand-held blades. Acute hemorrhage in the iliacus compartment may lead to a compartmental syndrome that results in iliopsoas muscle or femoral nerve ischemia, or both. Occasionally, the hematoma is large and extends into the psoas muscle or retroperitoneal space leading to a more extensive injury of the lumbar plexus or entire lumbosacral plexus. These hematomas may be a complication of anticoagulant therapy (heparin or warfarin), hemophilia or other blood dyscrasias, ruptured abdominal aortic aneurysm, pelvic operations, or femoral vessel catheterization for coronary, cerebral, and aortic angiography. Compression of the femoral nerve at the inguinal ligament occurs during lithotomy positioning (for vaginal delivery, vaginal hysterectomy, prostatectomy, and laparoscopy), occurs particularly with extreme hip flexion and external rotation [24,26].

Most cases of femoral mononeuropathies are unilateral, although bilateral lesions may occur, particularly after lithotomy positioning. The clinical presentation of femoral nerve lesions is often acute, with thigh weakness and anterior thigh and leg numbness. Patients frequently complain that their leg
buckles underneath them, which may lead to falls. Acutely, groin or thigh pain is usually mild; however, it may be very painful with retroperitoneal hematomas. A deep delayed pain and hyperesthesia are not uncommon. The neurologic examination reveals weakness of knee extension with absent or depressed knee jerk. Thigh adduction and ankle dorsiflexion are, however, normal. Hip flexion is usually weak when the lesion is intrapelvic (such as during pelvic surgery), but is spared when the lesion is at the inguinal region (such as during lithotomy positioning). Hypesthesia over the anterior thigh and medial calf is common. A positive reversed straight leg test (pain in anterior thigh with extension of hip) may occur in femoral nerve lesion.

Quadriiceps weakness with absent or depressed knee jerk and sensory manifestations in anterior thigh are manifestations shared not only by femoral neuropathy but also by an upper lumbar (L2, L3, and L4) radiculopathy and lumbar plexopathy. Careful examination of the thigh adductors, innervated by the L2, L3, and L4 roots via the obturator nerve, is extremely important because weakness of these muscles is inconsistent with a femoral neuropathy and point to a lesion proximal to the femoral nerve. Also, weakness of ankle dorsiflexion (tibialis anterior), innervated by the L4 and L5 roots via the common peroneal nerve, is highly suggestive of an L4 radiculopathy or lumbar plexopathy. Sensory loss in the anterior thigh due to femoral neuropathy may occasionally be confused with meralgia paresthetica (lesion of the lateral femoral cutaneous nerve). The sensory loss in meralgia paresthetica is lateral, does not extend beyond the knee, and rarely crosses the anterior midline of the thigh. In contrast, the sensory loss in femoral nerve lesions is anterior and often extends beyond the knee to include the medial leg (saphenous distribution).

Electrodiagnostic (EDX) studies

The EDX studies in a patient with suspected femoral neuropathy are extremely useful in (1) confirming the presence of a selective femoral mononeuropathy, (2) excluding a lumbar plexopathy and radiculopathy, (3) localizing the site of femoral nerve injury, and (4) predicting the prognosis by assessing the primarily pathophysiologic process (segmental demyelination or axonal loss).

The saphenous SNAP evaluates the L4 dorsal root ganglion and postganglionic sensory fibers and plays an important role in the differential diagnosis of femoral nerve lesions. It is often absent in axon-loss femoral neuropathy and lumbar plexopathy but normal in L4 radiculopathy because the root lesion is intraspinal (i.e., proximal to the dorsal root ganglion; Table 4). Rarely, the saphenous SNAP is normal in “purely” demyelinating femoral mononeuropathies where there is no Wallerian degeneration, which is usually complete in 10 to 11 days in sensory fibers. The saphenous SNAPs should be studied bilaterally for comparison because these potentials may be difficult to obtain in elderly and obese patients and in patients with leg edema.

Femoral motor conduction studies are important in the assessment of the primary pathophysiologic process and prognostication of femoral
mononeuropathy [24,25]. In contrast to other peripheral nerves, the femoral nerve may be stimulated only in the groin, allowing evaluation of a distal CMAP only. A femoral CMAP amplitude or area (or both) obtained after 5 to 6 days from injury (the time needed for completion of Wallerian degeneration of motor axons) reflects the primary pathophysiologic process and predicts the prognosis. If the femoral CMAP amplitude or area (or both) is low or absent in the presence of moderate or severe impairment of recruitment of quadriceps MUAPs, the lesion is primarily axonal. The prognosis is relatively protracted because it will depend on sprouting and reinnervation. Patients with CMAP amplitude more than 50% of the contralateral side improve within 1 year, whereas fewer than half the patients with a CMAP less than 50% of the contralateral side improve [25]. In contrast, when the femoral CMAP amplitude or area (or both) is normal despite reduction of MUAP recruitment, the lesion is primarily demyelinating, and the prognosis is excellent because it is dependent on remyelination. All patients with such findings recover in 6 to 8 weeks. In general, compressive femoral mononeuropathies at the inguinal ligament following childbirth or laparoscopy are demyelinating and recover rapidly [24], whereas lesions caused by iliacus hematomas are axonal with a more protracted recovery.

Needle EMG is essential in all patients with femoral mononeuropathy in order to localize the site of femoral nerve lesion and exclude a lumbar radiculopathy or plexopathy. Fibrillation potentials and decreased recruitment of MUAPs of quadriceps is common in all three entities. However, these changes are also present in the thigh adductors in patients with upper lumbar radiculopathy or plexopathy only (see Table 4). Also, in L4 radiculopathy, similar neurogenic changes may be present in the tibialis anterior. Because the branch to the iliacus muscle originates 4 to 5 cm above the inguinal ligament, sampling this muscle determines whether the femoral nerve lesion is distal (ie, around the inguinal ligament) or proximal (ie, intrapelvic). Fibrillation potentials are a poor quantitative measure of the extent of this axonal loss because they are identified whenever any axonal loss

<table>
<thead>
<tr>
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<th>Lumbar plexopathy</th>
<th>Lumbar radiculopathy</th>
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<tr>
<td>Thigh adductors</td>
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<td>Denervation</td>
<td>Denervation</td>
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<tr>
<td>Tibialis anterior</td>
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<tr>
<td>Saphenous SNAP(^b)</td>
<td>Low or absent(^c)</td>
<td>Low or absent(^c)</td>
<td>Normal</td>
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<tr>
<td>Paraspinal fibrillations</td>
<td>Absent</td>
<td>Absent</td>
<td>Usually present</td>
</tr>
</tbody>
</table>

\(^a\) Abnormal in L4 radiculopathy/plexopathy only.

\(^b\) May be technically difficult, particularly in the elderly patients or if there is leg edema.

\(^c\) Normal in purely demyelinating lesions.

*Abbreviations:* SNAP, sensory nerve action potential.

*Adapted from* Katirji B. Electromyography in clinical practice. St. Louis, MO: Mosby; 1998; with permission

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Table 4
The electrodiagnostic differential diagnosis of femoral mononeuropathy

<table>
<thead>
<tr>
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\(^c\) Normal in purely demyelinating lesions.

*Abbreviations:* SNAP, sensory nerve action potential.

*Adapted from* Katirji B. Electromyography in clinical practice. St. Louis, MO: Mosby; 1998; with permission
occurs, even if minimal. The amplitude and area of the femoral CMAP are the best quantitative measures of motor axonal loss [25].

**Obturator mononeuropathy**

The obturator nerve derives its fibers from the ventral divisions of L2, L3, and L4 spinal roots (the femoral nerve originates from the dorsal divisions of the same roots). The obturator nerve passes along the medial edge of the psoas muscle and over the sacroiliac joint before it reaches the obturator canal. At that point, the obturator nerve divides into anterior and posterior branches to innervate the thigh adductors: the adductor longus, adductor brevis, and adductor magnus (the latter receives additional innervation from the sciatic nerve). The obturator nerve also innervates a small area of skin in the inner thigh.

Obturator nerve lesion often accompanies femoral mononeuropathy as a component of a lumbar plexopathy. Isolated obturator mononeuropathy may be a manifestation of obturator hernia, endometriosis, or a new or recurrent pelvic malignancy. Patients with obturator mononeuropathy and no history pelvic or hip surgery or pelvic trauma should undergo pelvic computed tomography or magnetic resonance imaging to exclude pelvic malignancy [27]. Pelvic trauma, particularly when associated with pelvic fractures, may injure the obturator nerve. Iatrogenic lesions occur during hip surgery, genitourinary procedures, and abdominal operations or vaginal deliveries (particularly when using a forceps). The clinical presentations of obturator mononeuropathies are variable. Neuralgic pain in the medial thigh, sometimes referred to as obturator neuralgia, is worse with exercise and affects athletes or patients with obturator hernia. Numbness in the medial thigh is common, whereas subjective weakness or gait impairment are rare. In few patients, obturator nerve injury is detected only on clinical or EDX examination. The neurologic findings are limited to weakness of thigh adduction sometimes associated with sensory loss in the medial thigh. Circumduction of the weak leg, due to abnormal hip abduction, may result in a wide-based gait.

Obturator mononeuropathy may be mistaken as a lumbar radiculopathy such as an L4 or L3 radiculopathy, or a lumbar plexopathy such as a diabetic amyotrophy. A radiculopathy or plexopathy is distinguished by the presence of quadriceps weakness, iliopsoas weakness, or depressed/absent knee jerk. Disorders of the symphysis or pubis may have referred pain in the medial thigh mimicking an obturator nerve lesion.

**Electrodiagnostic (EDX) studies**

The needle EMG component of EDX studies is the most useful EDX testing because there are no motor or sensory conduction study techniques available for the obturator nerve. Needle EMG reveals fibrillation potentials, large MUAPs recruited rapidly, or both, in the thigh adductors only. In contrast, needle EMG of the quadriceps, iliacus, and lumbar paraspinal muscles are normal.
Gluteal mononeuropathies

The superior gluteal nerve originates from the L4, L5, and S1 spinal roots and exits the pelvis through the suprapiriform foramen. It then passes through the gluteus medius and minimus, and innervates both muscles before ending in the tensor fascia lata muscle. The inferior gluteal nerve originates from the L5, S1, and S2 spinal roots and exits the pelvis underneath the piriformis in close association with the sciatic nerve and the posterior femoral cutaneous nerve (PFCN). The inferior gluteal nerve innervates the gluteus maximus only.

Lesions of the gluteal nerves are usually iatrogenic. Superior gluteal nerve injuries may occur with intramuscular injections. This may result in lesions before or after the nerve supplies the gluteus medius and minimus muscles. The inferior gluteal nerve and the accompanying PFCN may result from intrapelvic masses such as colorectal malignancy, or large iliac artery aneurysm. Both gluteal nerves may be injured after total hip replacement. The superior gluteal nerve may be entrapped by the anterior-superior tendinous fibers of the piriformis muscle, whereas the inferior gluteal nerve may be compressed, with the sciatic nerve, as it passes under the piriformis muscle.

Weakness of abduction of the affected hip with a waddling gait is the main manifestation of a superior gluteal mononeuropathy. When the patient is asked to stand on one leg, there is a pelvic tilt towards the healthy side (Trendelenburg sign). Atrophy of buttock and weakness of hip extension are the common features of inferior gluteal nerve lesions.

Electrodiagnostic (EDX) studies

EDX studies are limited to needle EMG because the gluteal nerves are not accessible to NCS. Fibrillations and loss of MUAPs in the tensor fascia lata and gluteus medius are features of superior gluteal nerve lesions. At times, the gluteus medius is spared when the lesion is distal, such as with intramuscular injections. Isolated denervation of the gluteus maximus is the only finding in inferior gluteal mononeuropathy, although abnormal posterior femoral cutaneous SNAP or findings of sciatic nerve involvement may coexist. The EDX findings in gluteal mononeuropathies should be distinguished from L5 and S1 radiculopathy, where denervational changes tend to be prominent in distal L5- and S1-innervated muscles such as the tibialis anterior or medial gastrocnemius, respectively.

Groin and thigh numbness

Lateral femoral cutaneous mononeuropathy (meralgia paresthetica)

The lateral femoral cutaneous nerve (LFCN) is formed from sensory fibers originating from the ventral rami of L2 and L3 spinal roots. The nerve travels within the lower abdominal muscles and crosses the iliacus muscle. The LFCN leaves the pelvis by passing underneath or within the inguinal
ligament anterior or medial to its lateral insertion at the anterior superior iliac spine. The LFCN then changes its direction from a horizontal to a vertical course and pierces the fascia lata a short distance below the inguinal ligament. Soon after, the LFCN divides into its terminal branches in the leg to innervate the skin of the lateral thigh.

Meralgia paresthetica is often due to entrapment of the LFCN under or through the inguinal ligament where it is engulfed by multiple layers of fascia. It is often idiopathic, although it may be precipitated by diabetes mellitus, pregnancy, and obesity [28]. Compression of the nerve at the inguinal ligament may occur during occupational activities such as wearing large tool belts, leaning against a tool bench or gymnastic bars, or simply by wearing tight clothing or large pagers. Iatrogenic lesions are described following iliac bone graft, misplaced injection, or pelvic surgery such as renal transplantation, gastric bypass, and laparoscopic herniorrhaphy. A pelvic or bone mass such as abdominal aortic aneurysm or metastatic tumor to the iliac crest may present with manifestations of a mononeuropathy of the LFCN [28].

Patients present with numbness and pain in the lateral thigh, hence the name meralgia paresthetica. The symptoms may worsen with standing, walking, or turning in bed, or improve with hip flexion. The neurologic examination often detects a well-circumscribed area of sensory loss to touch and pin prick in the distribution of the LFCN or one of its terminal branches. Meralgia paresthetica may be confused with a lumbar radiculopathy, a femoral mononeuropathy, or lumbar plexopathy.

EDX testing in meralgia paresthetica may be useful but is technically difficult, particularly in women and obese individuals [29,30]. SNAP of the LFCN may be recorded antidromically or orthodromically but may be absent in healthy subjects or on the asymptomatic side in symptomatic individuals. Asymmetrically low-amplitude or absent SNAPs on the symptomatic side are the most useful EDX findings. The EDX studies are most useful in excluding other disorders such as femoral mononeuropathy and lumbar radiculopathy.

**Posterior femoral cutaneous mononeuropathy**

The posterior femoral cutaneous nerve (PFCN) arises from the S1 to S3 spinal roots. It exits the pelvis with the inferior gluteal nerve through the greater sciatic notch under the piriformis muscle, and enters the thigh near the sciatic nerve at the lower border of the gluteus maximus. The PFCN innervates the skin of the lower buttock, posterior thigh, popliteal fossa, and proximal third of the calf. It also gives off branches to the perineum and scrotum in men or labium majus in women.

Intramuscular injections, or lacerations or gunshot wounds may selectively injure the PFCN, but often there is a concomitant lesion of the inferior gluteal nerve, sciatic nerve, or both. Compression of the nerve by prolonged pressure on the buttock may occur during gymnastic exercises or long bicycle
riding. Pelvic mass lesions, such as colorectal tumors or venous malformations, may cause mononeuropathy of the PFCN.

Paresthesiae in the lower buttock and posterior thigh are the predominant features. Burning or throbbing pain may accompany the sensory symptoms and often radiates to the perineum, scrotum, or labium majus. The pain may be worse in the sitting or lying positions. A lumbosacral radiculopathy, particularly S1 or S2 radiculopathy, or a sacral plexopathy may mimic a lesion of the PFCN. Depressed or absent ankle jerk and calf or hamstring muscle weakness, atrophy or denervation help to exclude a PFCN lesion from a lumbosacral radiculopathy or plexopathy. SNAP of the PFCN is useful but may be difficult to evoke. The SNAP should be done bilaterally and compared with the asymptomatic side [31,32].

Ilioinguinal, iliohypogastric, and genitofemoral mononeuropathies

The ilioinguinal nerve originates from L1 spinal root and innervates the lower abdominal muscles and a strip of skin along the inguinal ligament to the base of penis and scrotum in men or labia majora in women. The iliohypogastric nerve originates from the L1 spinal root, with occasional contribution from the T12 root, and divides into two cutaneous terminal branches: a lateral branch that innervates a small strip of skin in the upper lateral buttock, and an anterior branch that innervates a small area of skin above the pubis symphysis. The genitofemoral nerve is formed from the L1 and L2 spinal roots and divides into femoral and genital branches. The femoral branch passes under the inguinal ligament and innervates a small area of skin on the anterior aspect of the thigh. The genital branch travels medially with the ilioinguinal nerve to supply the cremasteric muscle and the skin of the scrotum or labium majus.

Lesions of the ilioinguinal nerve are usually caused by iatrogenic nerve damage (such as during laparoscopic or traditional hernia repair), trauma, or entrapment [33]. The iliohypogastric nerve is often damaged with the ilioinguinal nerve due to proximity. The genitofemoral nerve may be injured mostly during appendectomy, but also following inguinal herniorrhaphy, nephrectomy, cesarean section, or blunt abdominal trauma. Because of proximity, damage of the genital branch often occurs with injuries of the ilioinguinal nerve at the inguinal ligament [33].

Patients with ilioinguinal mononeuropathy often complain of burning pain in the lower abdomen radiating to the upper thigh and into the scrotum or labium majus. Sensory loss in the ilioinguinal nerve distribution is also common. The pain or sensory symptoms may worsen with extension of the hip, and the patients may be only comfortable in the flexed position. Bulging of the lower abdominal wall due to weakness of transverse and internal oblique muscles may occur in severe lesions. When the iliohypogastric nerve is also involved, there is sensory loss in a small area above the symphysis. Genitofemoral mononeuropathy presents with pain and paresthesiae in the
medial inguinal area and scrotum or labia majora. The symptoms overlap significantly with ilioinguinal mononeuropathy such that some authors combine these injuries into a common term, *ilioinguinal neuralgia*. On examination, there may be sensory loss in the genitofemoral distribution, often overlapping with the ilioinguinal distribution. Absent or diminished cremasteric reflex may occur on the affected side. These sensory neuropathies may difficult to distinguish from each other or from an L1 or L2 radiculopathy, based on clinical grounds. Diagnostic nerve blocks may be useful.

Sensory NCS are not available because these proximal sensory nerves are small, inaccessible, and often lie underneath thick adipose tissue. Hence, the role of EDX studies in these sensory mononeuropathies is mainly to exclude other disorders such as an upper lumbar radiculopathy or plexopathy. Occasionally, needle EMG of lower abdominal muscles may reveal denervation in patients with ilioinguinal mononeuropathies [34].

References


The true prevalence of peripheral neuropathy remains unknown; however some have speculated, based on limited epidemiological studies, that the prevalence might be as high as 8% [1,2]. Peripheral neuropathy is a common manifestation of many systemic diseases, with diabetes and alcohol abuse (plus its associated nutritional factors) being the most common etiologies in the developed world, and leprosy being the primary cause of treatable neuropathy in the world [3]. The myriad of etiologies of peripheral neuropathy seems to pose a daunting task for the clinician. Despite the increasing number of diagnostic tests (namely antibody panels and genetic testing), up to 22% of neuropathies will be of an idiopathic etiology, although approximately 42% of undiagnosed neuropathies may be attributed to a familial neuropathy if a meticulous family history is taken and relatives are carefully examined [4,5].

To many clinicians, the evaluation of peripheral neuropathy invokes much pessimism and skepticism at the likelihood of discovering a cause or a treatment for the underlying neuropathy. Investigating peripheral neuropathy may be costly, because physicians frequently use a “shotgun” approach by ordering a standard battery of tests, including serology evaluations [6,7]. This approach is common and frequently results in an incorrect diagnosis secondary to incidental abnormalities found on serology testing, such as an insignificantly elevated antibody titer or an incomplete history (medical, family, social, or occupational). Recently Dyck et al. described a methodology they identified as the “Gestalt” approach [6]. This methodol-
ogy is used by many clinicians and is based on recognition of the clinical pattern of neuropathy to help guide investigations. It is based on a standard series of questions that can help hone in on the cause of the neuropathy by limiting the number of disorders included in the differential diagnosis [8]. By focusing on symptoms, signs, and electrodiagnostic (EDX) features, the most likely causes of the neuropathy are identified. These features include inquiry about the presence or absence of weakness, sensory complaints including pain, autonomic dysfunction, plus clinical examination to identify the magnitude and distribution of neurologic impairments. When combined with the characteristics of the EDX testing, this information allows the clinician to identify the cause of the neuropathy in a cost-effective way by using a systematic rational approach that tailors laboratory investigations based on the more limited differential diagnosis [9]. This approach is limited, at least in part, by the experience of the clinician and the ability to recognize patterns of abnormality.

Several individuals have suggested the use of a series of algorithms to establish the etiology of a neuropathy. Dyck et al described the “10 P’s for characterizing peripheral neuropathy” (Box 1) [6]. These are a series of 10 questions designed to lead the clinician in a logical and sequential manner to help establish a correct diagnosis. Questions asked range from inquiry about the distribution of symptoms and signs to the results of serologic testing. Barohn (Box 2) proposed a slightly different set of questions that are used to identify the evolution of symptoms and to establish the presence or absence of symmetry, sensory or motor involvement, pain, autonomic dysfunction, a positive family history, and the opportunity for neurotoxic exposure, to mention a few [10]. Others have developed diagrammatic algorithms to guide the clinician through the differential diagnosis of peripheral neuropathies [11,12].

**Box 1**

The 10 P’s for characterizing peripheral neuropathy [6]

1. Pattern: anatomic and temporal
2. Population of neurons
3. Part of neuron assumed to be the primary site of pathologic abnormality
4. Physiology
5. Pathology
6. Prickling
7. Phenomena: toxic exposures, diseases, or signs
8. Pedigree
9. Plasma: laboratory abnormalities
10. Pharmacology: response to therapies
The following approach is a combination of the above algorithms that should provide clinicians with an efficient and logical approach to the evaluation of peripheral neuropathy. Although there are few cardinal or diagnostic features that are specific for any particular form of neuropathy, there are features useful in limiting the number of diagnostic considerations. In the material that follows, individual characteristics of the patient’s neuropathy are used to identify disorders that share those characteristics. For example, features related to symptom localization, the presence of pain, temporal progression, EDX evidence of demyelination, exclusive or predominant motor or sensory involvement, and the presence of asymmetry all suggest a limited number of known possible causes for the neuropathy. Those causes are identified in the tables and briefly discussed. For neuropathies that are

---

**Box 2**

**Peripheral neuropathy patterns [10]**

1. Symmetric sensory loss without motor involvement
   - Cryptogenic
   - Metabolic
   - Toxic
2. Symmetric distal motor with sensory loss
   - Metabolic
   - Hereditary
   - Toxic
3. Symmetric distal and proximal motor with sensory loss
   - AIDP
   - CIDP
4. Asymmetric distal motor with sensory loss
   - Metabolic
   - Infectious
   - Vasculitis
5. Asymmetric distal motor without sensory loss
   - Motor neuron disease
   - Multifocal motor neuropathy with conduction block
6. Asymmetric proximal and distal motor with sensory loss
   - Plexopathy
   - Radiculopathy/polyradiculopathy
7. Asymmetric sensory loss without motor involvement
   - Sensory neuropathy (neuronopathy)
8. Autonomic

---

**Abbreviations:** AIDP = acute inflammatory demyelinating polyneuropathy; CIDP = chronic inflammatory demyelinating polyneuropathy; HNPP = hereditary neuropathy with liability to pressure palsy.
characterized by several uncommon features, a small number of explanations may be common to the lists of possible cause for each feature. At the very least, by identifying the most likely explanations, the need for additional diagnostic testing is greatly reduced.

Localization, anatomic, and pathology considerations

Patients may present with several sensory or motor complaints, not all of which are necessarily caused by peripheral nerve disease, and accurate localization within the nervous system is critical in establishing a correct diagnosis. Sensory symptoms and signs should either follow a dermatomal distribution, a stocking-and-glove distribution, or a distribution of complaints that make anatomic sense. These findings should be associated with hyporeflexia. The patient’s presenting clinical syndrome may include symptoms and signs of autonomic dysfunction. In addition, the clinical features of the neuropathy should follow one of the eight patterns of peripheral neuropathy (Box 2). Individuals not fulfilling any of these descriptions should be evaluated for a possible central nervous system or somatic etiology to their disorder. Subjects with corresponding cervical or lumbosacral pain should be evaluated for a potential radiculopathy. Polyneuropathies are generally symmetric in distribution and nerves are affected in a length-dependent manner, whereas polyradiculopathies or polyradiculoneuropathies typically involve proximal and distal nerves.

Confirmation of a peripheral nerve disorder may be achieved by way of EDX testing. The results of electromyography (EMG) (ie, nerve conduction studies and the needle EMG examination) may yield vital information regarding nerve pathology. These results can be used to characterize the disorder as either axonal or demyelinating (hereditary or acquired), or a mixture of axonal degeneration and demyelination (Box 3a & Box 3b). Axonal neuropathies generally display a distal-to-proximal gradient as longer nerves tend to be affected first. Primary demyelinating neuropathies affect the nerve at multiple segments and thus produce distal and proximal symptoms and signs [13].

Clinical history

Pain

Frequently patients present for evaluation of allodynia (pain following nonpainful stimulation), dysesthesias (unpleasant sensation following a nonpainful stimulus), hyperalgesia (increased pain sensation, greater than normal), or paresthesias (irritating spontaneous sensations). The presence of a painful neuropathy raises the possibility of several etiologies (Tables 1a, 1b, and Box 4). Most neuropathies are not particularly painful, however,
and the presence of severe pain is an important feature. In Table 1, distinction is made between those neuropathies in which pain is a predominant feature (Table 1a), and those neuropathies that may be associated with pain, although typically not as a characteristic feature (Table 1b). The association of severe pain and dysautonomia raises the possibility of amyloidosis,

<table>
<thead>
<tr>
<th>Box 3a</th>
<th>Electrodiagnostic criteria for demyelinating polyneuropathy [30]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Nerve conduction studies must have three of the following four criteria:</td>
<td></td>
</tr>
<tr>
<td>A. Decreased conduction velocity (CV) in 2 or more motor nerves</td>
<td></td>
</tr>
<tr>
<td>i. &lt;80% lower limit of normal (LLN) if CMAP amplitude &gt;80% LLN</td>
<td></td>
</tr>
<tr>
<td>ii. &lt;70% LLN if CMAP amplitude &lt;80% LLN</td>
<td></td>
</tr>
<tr>
<td>B. Partial conduction block or abnormal temporal dispersion in at least one motor nerve</td>
<td></td>
</tr>
<tr>
<td>C. Prolonged distal latencies in greater than two nerves</td>
<td></td>
</tr>
<tr>
<td>i. &gt;125% of upper limit of normal (ULN) if amplitude &gt;80% LLN</td>
<td></td>
</tr>
<tr>
<td>ii. &gt;150% of ULN if amplitude &lt;80% LLN</td>
<td></td>
</tr>
<tr>
<td>D. Absent F waves or prolonged minimum F-wave latencies in two or more nerves</td>
<td></td>
</tr>
<tr>
<td>i. &gt;120% of ULN if amplitude &gt;80% of LLN</td>
<td></td>
</tr>
<tr>
<td>ii. &gt;150% of ULN if amplitude &lt;80% of LLN</td>
<td></td>
</tr>
<tr>
<td>2. Additional supportive findings:</td>
<td></td>
</tr>
<tr>
<td>A. Sensory conduction velocity &lt;80% LLN</td>
<td></td>
</tr>
<tr>
<td>B. Absent H reflex</td>
<td></td>
</tr>
</tbody>
</table>

and the presence of severe pain is an important feature. In Table 1, distinction is made between those neuropathies in which pain is a predominant feature (Table 1a), and those neuropathies that may be associated with pain, although typically not as a characteristic feature (Table 1b). The association of severe pain and dysautonomia raises the possibility of amyloidosis,

<table>
<thead>
<tr>
<th>Box 3b</th>
<th>Dutch Guillain-Barre Study Group criteria for acute inflammatory demyelinating polyneuropathy [31]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Distal motor latency of &gt;150% upper limit normal (ULN)</td>
<td></td>
</tr>
<tr>
<td>2. F-wave latency &gt;150% ULN</td>
<td></td>
</tr>
<tr>
<td>3. Conduction velocities &lt;70% lower limit normal</td>
<td></td>
</tr>
<tr>
<td>4. Abnormal proximal-to-distal CMAP drop</td>
<td></td>
</tr>
<tr>
<td>5. Distal CMAP duration &gt;300% ULN</td>
<td></td>
</tr>
<tr>
<td>6. Temporal dispersion &gt;150% ULN</td>
<td></td>
</tr>
</tbody>
</table>
although other disorders, including diabetes mellitus, produce similar problems. Physical examination may demonstrate angiookeratomas suggestive of Fabry disease in a patient with painful neuropathy. A neuropathy with episodes of lancinating pain associated with enlarged, yellow/orange tonsils and hypocholesterolemia suggests a diagnosis of Tangier disease. This genetic disease is characterized by a deficiency in high density lipoproteins, which leads to abnormal fatty deposits in the tonsils giving them their classic appearance. This disorder is distinct from most of the other forms of small fiber neuropathy as there are additional findings on neurological examination. Some of these patients develop a progressive, symmetric polyneuropathy with dissociative loss of pain and temperature in the upper trunk and extremities, with combined faciobrachial muscle wasting in a pattern similar to that associated with syringomyelia. Painful HIV neuropathy generally presents in the late stages of the disease, making the diagnosis apparent because the systemic diagnosis is typically established by the time neuropathy develops [14]. A list of painful mononeuropathies is found in Box 4.

Altered sensation to pain and temperature sensation associated with painful dysesthesias and on occasion autonomic dysfunction is characteristic of small fiber neuropathies, most of which are characterized by pain. Small fiber neuropathies have few objective signs on neurological examination. Deep tendon reflexes are usually preserved, as is the balance and the motor examination, compared with the large fiber neuropathies in which they are typically abnormal. Nerve conduction studies that evaluate large nerve fibers are often normal, although there may be some minor abnormalities because most small fiber-predominant neuropathies also have some compo-

### Table 1a

<table>
<thead>
<tr>
<th>Primary painful polyneuropathies [32,33]</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic</td>
<td></td>
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<tr>
<td>Idiopathic distal small fiber neuropathy</td>
<td></td>
</tr>
<tr>
<td>Inflammatory</td>
<td></td>
</tr>
<tr>
<td>Vasculitic neuropathy</td>
<td>Vasculitic workup/biopsy</td>
</tr>
<tr>
<td>Perineuritis</td>
<td>Biopsy</td>
</tr>
<tr>
<td>Hereditary</td>
<td></td>
</tr>
<tr>
<td>Fabry&quot; disease</td>
<td>Alpha-galactosidase A</td>
</tr>
<tr>
<td>HSAN type V</td>
<td></td>
</tr>
<tr>
<td>Tangier disease&quot;</td>
<td>Hypocholesterolemia, low serum alpha-lipoprotein</td>
</tr>
<tr>
<td>Metabolic</td>
<td></td>
</tr>
<tr>
<td>Amyloidosis&quot;</td>
<td>Biopsy/genetic testing</td>
</tr>
<tr>
<td>Diabetes&quot;</td>
<td>AM glucose/2 hour GTT</td>
</tr>
<tr>
<td>Painful symmetrical polyneuropathy</td>
<td></td>
</tr>
<tr>
<td>Asymmetric polyradiculoneuropathy</td>
<td></td>
</tr>
<tr>
<td>Truncal mononeuropathy</td>
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</tbody>
</table>

" Denotes small fiber neuropathy.
Table 1b
Polyneuropathies associated with pain [30,31]

<table>
<thead>
<tr>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic</td>
</tr>
<tr>
<td>Cryptogenic sensory neuropathy</td>
</tr>
<tr>
<td>Skin biopsy PGP 9.5 stain</td>
</tr>
<tr>
<td>Infectious</td>
</tr>
<tr>
<td>HIV</td>
</tr>
<tr>
<td>HIV serology</td>
</tr>
<tr>
<td>Inflammatory</td>
</tr>
<tr>
<td>AIDP</td>
</tr>
<tr>
<td>EMG/lumbar puncture</td>
</tr>
<tr>
<td>Malignancies</td>
</tr>
<tr>
<td>Paraneoplastic</td>
</tr>
<tr>
<td>Small cell carcinoma</td>
</tr>
<tr>
<td>CT chest</td>
</tr>
<tr>
<td>Lymphoma</td>
</tr>
<tr>
<td>Bone marrow</td>
</tr>
<tr>
<td>Other carcinomas</td>
</tr>
<tr>
<td>Malignancy workup</td>
</tr>
<tr>
<td>Paraproteinemia</td>
</tr>
<tr>
<td>Protein electrophoresis</td>
</tr>
<tr>
<td>Multiple myeloma</td>
</tr>
<tr>
<td>Bence-Jones proteins</td>
</tr>
<tr>
<td>Waldenstrom</td>
</tr>
<tr>
<td>Bone marrow</td>
</tr>
<tr>
<td>Metabolic</td>
</tr>
<tr>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>TSH</td>
</tr>
<tr>
<td>Uremia</td>
</tr>
<tr>
<td>BUN, creatinine</td>
</tr>
<tr>
<td>Nutritional</td>
</tr>
<tr>
<td>Alcohol</td>
</tr>
<tr>
<td>History</td>
</tr>
<tr>
<td>B12/thiamine deficiency</td>
</tr>
<tr>
<td>B12/folate</td>
</tr>
<tr>
<td>Toxic</td>
</tr>
<tr>
<td>Arsenic/thallium</td>
</tr>
<tr>
<td>Mees lines</td>
</tr>
<tr>
<td>Dideoxynosine</td>
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<tr>
<td>EMG/history</td>
</tr>
<tr>
<td>Dideoxycytosine</td>
</tr>
<tr>
<td>EMG/history</td>
</tr>
<tr>
<td>Isoniazid/pyridoxine deficiency</td>
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<tr>
<td>EMG/history</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
</tr>
<tr>
<td>EMG/history</td>
</tr>
<tr>
<td>n-Hexane</td>
</tr>
<tr>
<td>EMG/history/biopsy</td>
</tr>
<tr>
<td>Vincristine</td>
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<tr>
<td>EMG/history</td>
</tr>
</tbody>
</table>

nent of large fiber involvement. Abnormalities may be found on sympathetic skin response testing. Quantitative thermal sensory threshold testing and qualitative and quantitative evaluation of skin sweating (distribution and amount) are sometimes helpful adjunctive tests to evaluate small nerve fiber function. The short list of potential etiologies is found in Table 1a.

History is of crucial importance as it helps eliminate or identify potential nutritional disorders, toxic exposures, or hereditary disorders. For example, a history of substantial weight loss or anemia and fatigue may suggest an underlying malignancy. A history of possible toxic exposure does not indicate that the exposure produced the neuropathy, but the opportunity for exposure is one of several important aspects of establishing causation. Conversely, a careful history may eliminate the many potential etiologies, and investigations may focus on appropriate laboratory investigations that may include evaluation of fasting blood sugar, thyroid and renal function studies (TSH, BUN, creatinine) and serum protein electrophoresis (SPEP) to help establish a diagnosis in a cost-effective manner.
Time course of symptoms

The history also helps establish the tempo of the neuropathy (i.e., whether it is subacute or chronic). Subacute neuropathies tend to progress over days to several weeks, whereas chronic neuropathies progress over many months to years, usually with insidious onset. Insidious onset of a chronic neuropathy should raise a red flag, as this type of presentation is frequently associated with the hereditary neuropathies.

A history of subacute onset is suggestive of acute inflammatory demyelinating polyneuropathy (AIDP) and a limited number of disorders that mimic AIDP, including porphyric neuropathy, Tick paralysis, and acute arsenic intoxication. The list of neuropathies with a subacute onset is short (Table 2).

**Box 4**

**Painful mononeuropathies [30,31]**

<table>
<thead>
<tr>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Axonal</strong></td>
</tr>
<tr>
<td>Porphyria</td>
</tr>
<tr>
<td>Tick paralysis</td>
</tr>
<tr>
<td>Toxins (arsenic)</td>
</tr>
<tr>
<td><strong>Demyelinating</strong></td>
</tr>
<tr>
<td>Arsenic (acute exposure)</td>
</tr>
<tr>
<td>AIDP</td>
</tr>
<tr>
<td>Diphtheria</td>
</tr>
<tr>
<td><strong>Other</strong></td>
</tr>
<tr>
<td>Mononeuritis multiplex</td>
</tr>
<tr>
<td>Paraneoplastic sensory neuronopathy</td>
</tr>
<tr>
<td>Parsonnage-Turner</td>
</tr>
<tr>
<td>(Idiopathic brachial plexopathy)</td>
</tr>
<tr>
<td>Proximal diabetic neuropathy</td>
</tr>
</tbody>
</table>
Nerve conduction studies and history help further tailor the diagnosis by establishing whether the neuropathy is axonal or demyelinating or if a plexopathy or polyradiculopathy is involved. An AIDP-like presentation picture may be seen with diphtheria where there is associated ophthalmoparesis. Among patients with diphtheria, examination of the oropharynx may reveal a green exudate or history may reveal a concurrent upper respiratory infection, a non-specific association in isolation. Demyelinating features are seen on the EMG, and like AIDP, albumino-cytologic dissociation may be seen in the spinal fluid. The presence of associated abdominal pain, nausea, vomiting, dysautonomia, and neuropathy is characteristic of acute porphyric neuropathy. Tick paralysis should be suspected in individuals with recent travel to endemic areas. The development of acute arm pain in a radicular or polyradicular pattern may suggest an idiopathic brachial plexopathy (Parsonnage-Turner syndrome), whereas the acute onset of a painful lower extremity in association with diabetes mellitus suggests diabetic amyotrophy. Finally, mononeuritis multiplex should always be considered in an individual who experiences an acute or subacute onset of an asymmetric and progressive neuropathy. Physical examination and investigations should always focus on ruling out an underlying systemic vasculitic disorder. Chronic neuropathies should be assessed by symptoms, history, and physical examination in conjunction with the pattern of distribution.

Chronic demyelinating polyneuropathies have a restrictive differential diagnosis in which nerve conduction studies can help group these disorders in two categories based on uniform versus nonuniform slowing (Table 3). Nonuniform slowing is seen in acquired demyelinating polyneuropathies such as chronic inflammatory demyelination polyneuropathy (CIDP),

<table>
<thead>
<tr>
<th>Uniform slowing</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebrotendinous xanthomatosis</td>
<td>Cholestanol</td>
</tr>
<tr>
<td>Congenital hypomyelinating neuropathy</td>
<td>Nerve biopsy, PO point mutation</td>
</tr>
<tr>
<td>EGR2 point mutation</td>
<td>EGR2 point mutation</td>
</tr>
<tr>
<td>HMSN I,III</td>
<td>PMP-22 Dupl/Del</td>
</tr>
<tr>
<td>Leukodystrophies</td>
<td></td>
</tr>
<tr>
<td>Adrenomyeloneuropathy</td>
<td>VLCFA</td>
</tr>
<tr>
<td>Metochromatic</td>
<td>Arylsulfatase A</td>
</tr>
<tr>
<td>Krabbes</td>
<td>Galactosykeramidase</td>
</tr>
<tr>
<td>Cockaynes</td>
<td>Sudanophilic material</td>
</tr>
<tr>
<td>Refsum disease</td>
<td>Phytic acid</td>
</tr>
<tr>
<td>Tangier disease</td>
<td>Orange tonsils, HDL and total cholesterol level</td>
</tr>
<tr>
<td>Nonuniform slowing</td>
<td></td>
</tr>
<tr>
<td>CIDP</td>
<td>See Box 3a, Box 3b</td>
</tr>
<tr>
<td>Dysproteinemias</td>
<td>SPEP, immunoglobulins, bone marrow</td>
</tr>
<tr>
<td>Osteosclerotic myeloma</td>
<td>Skeletal survey, SPEP</td>
</tr>
</tbody>
</table>
including those forms of CIDP associated with paraproteinemias and osteosclerotic myeloma. Lumbar puncture, quantitative immunoglobulins, and a skeletal survey may distinguish these disorders. Uniform conduction slowing is seen in hereditary demyelinating neuropathies such as hereditary motor sensory neuropathy (HMSN) type I or III. The presence of central nervous system findings on clinical examination should raise the possibility of an inherited white matter disease as described in Table 3.

Prominent motor symptoms

The number of neuropathies that present with pure motor symptoms or primarily motor symptoms is limited, and analysis of the pattern of weakness may help establish the diagnosis (Table 4). Hereditary motor and sensory neuropathy (HMSN) presents as a distal motor greater than sensory neuropathy generally associated with pes cavus deformities. Examination of family members or a history of relatives with similar problems may support the diagnosis. Nerve conduction studies further classify these disorders as either demyelinating or axonal. Genetic testing is currently available for HMSN I (PMP-22 duplication/deletion, PO and EGR2 point mutations), HMSN II (Myelin Protein Zero, Neurofilament Light). An acquired demyelinating neuropathy with symmetric distal weakness identified in association with a monoclonal gammopathy may suggest the need for additional evaluation. This evaluation should begin with a skeletal survey, looking for the presence of an underlying lymphoproliferative disorder such as osteosclerotic myeloma.

Asymmetry associated with pure motor symptoms is a worrisome sign for possible motor neuron disease (MND), but such asymmetry is also frequently seen in multifocal motor neuropathy with conduction block. Clinically, MND usually has preserved (early in the disorder) or increased

Table 4
Etiologies of exclusively motor/predominantly motor neuropathies

<table>
<thead>
<tr>
<th>Diagnosis</th>
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<tbody>
<tr>
<td>Predominantly Distal</td>
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<tr>
<td>HMSN</td>
</tr>
<tr>
<td>Lead</td>
</tr>
<tr>
<td>Monoclonal gammopathy with demyelinating neuropathy</td>
</tr>
<tr>
<td>Motor neuron disease</td>
</tr>
<tr>
<td>Multifocal motor neuropathy with conduction block</td>
</tr>
<tr>
<td>Proximal and Distal</td>
</tr>
<tr>
<td>AIDP/CIDP</td>
</tr>
<tr>
<td>Lymphoma motor neuronopathy</td>
</tr>
<tr>
<td>Plexopathy</td>
</tr>
<tr>
<td>Porphyria</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>EMG/genetic testing</td>
</tr>
<tr>
<td>EMG/lead level/skeletal x-ray</td>
</tr>
<tr>
<td>EMG</td>
</tr>
<tr>
<td>Immunoglobulins</td>
</tr>
<tr>
<td>EMG</td>
</tr>
<tr>
<td>EMG/anti GM1</td>
</tr>
<tr>
<td>See Box 3a, Box 3b, EMG/CSF</td>
</tr>
<tr>
<td>Bone marrow</td>
</tr>
<tr>
<td>EMG</td>
</tr>
<tr>
<td>EMG, urine porphyrin excretion, enzyme levels</td>
</tr>
</tbody>
</table>

reflexes associated with fasciculations and atrophy. Multifocal motor neuropathy generally causes asymmetric weakness in the upper extremities without significant atrophy but with associated hyporeflexia or areflexia. EDX studies demonstrate a motor neuropathy associated with conduction block, helping differentiate multifocal motor neuropathy with conduction block from MND. The presence of anti-ganglioside M-1(GM1) antibodies supports the diagnosis of multifocal motor neuropathy with conduction block but are found in only 20–80% of patients [15,16].

Predominant or exclusive proximal weakness or proximal and distal weakness of comparable magnitude generally are associated with either a plexopathy or radiculopathy. Either AIDP (predominantly the axonal form) or CIDP have also been associated with proximal weakness. Other rare disorders presenting with this pattern of weakness are porphyria and a motor neuronopathy secondary to lymphoma.

Prominent sensory symptoms

Pure sensory neuropathies/neuronopathies are uncommon and, like pure motor neuropathies, carry a limited differential diagnosis (Box 5) [17]. The

<table>
<thead>
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<td>Sensory neuropathies (neuronopathies)</td>
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</tbody>
</table>

**Symmetric Distal**
- Amyloidosis
- Hereditary
- Friedrich ataxia
- HSAN
- HIV
- Toxic
- Cisplatin
- Ethyl alcohol
- Metronidazole
- Pyridoxine
- Styrene
- Thalidomide
- Thallium
- Vitamin E deficiency

**Asymmetric**
- Idiopathic sensory ganglionitis
- Fisher variant of GBS
- Leprosy
- Praneoplastic (ANNA-1/anti-Hu syndrome)
- Sjogren syndrome
presence of keratoconjunctivitis sicca and xerostomia associated with a predominantly sensory neuropathy with or without multifocal features or cranial neuropathies are considered classical findings of Sjogren syndrome. The most common neuropathy in the third world is leprosy, which may present as an asymmetric predominantly sensory neuropathy. The Fisher variant of AIDP may be distinguished from AIDP based on its acute onset, prominent or exclusive sensory involvement with sensory ataxia, and ophthalmoparesis. Most challenging is the anti-Hu/ANNA-1 paraneoplastic syndrome generally associated with small cell lung cancer. Individuals with risk factors for carcinoma of the lung and a sensory neuronopathy should be screened routinely, as the antibody and the sensory neuropathy frequently are detected before the diagnosis of the cancer.

Symmetric, distal, pure sensory neuropathies may be seen with amyloidosis. Amyloid neuropathy is generally painful and associated with prominent autonomic dysfunction. Hereditary sensory autonomic neuropathy (HSAN) types I–V present at either birth or up to the second decade with concomitant mutilation and autonomic dysfunction. History may also be helpful in identifying HSAN I, because this is the only autosomal dominant HSAN. A careful history of potential exposures, including use of vitamins or other substances not considered neurotoxic, may identify a possible cause for a sensory neuropathy. A list of potential offending agents that cause a sensory neuropathy are found in Box 5. Of note, pyridoxine intoxication and cisplatin toxicity, when severe, may have proximal (in addition to distal) involvement, as opposed to the distal-predominant sensory loss characteristic of most sensory neuropathies.

**Proximal and distal sensorimotor neuropathies**

Identification of proximal involvement in any sensorimotor neuropathy should herald an additional element of anticipation from the clinician, as frequently these neuropathies are treatable. Again, history and physical examination in conjunction with EDX studies narrows the differential diagnosis. Proximal and distal sensorimotor neuropathies may be further subcategorized as symmetric or asymmetric. AIDP and CIDP generally present symmetrically. The duration of symptoms, the temporal profile, and the EDX findings (Box 3a and Box 3b) differentiate these two entities. Both disorders are responsive to plasmapheresis or intravenous immunoglobulin.

**Etiologies of proximal and distal sensorimotor neuropathies:**
- Asymmetric
  - Diabetic amyotrophy
  - Infiltrative of inflammatory plexopathies
  - Infectious or infiltrative polyradiculopathies
  - Vasculitis
- Symmetric
  - AIDP
  - CIDP
Asymmetry in a neuropathy should always raise the possibility of an underlying vasculitis. A careful history may suggest the presence of an initial mononeuropathy, possible with proximal symptoms, with subsequent progression to a confluent mononeuritis multiplex that may appear as a symmetric, distal predominant sensorimotor neuropathy by the time the patient presents for evaluation. Infiltration of nerve roots or of the plexus by a carcinomatous process may also present with proximal sensorimotor symptoms and signs. The presence of pain, supraclavicular masses, a Horner syndrome, or even chronic headache may suggest the possibility of carcinomatous meningitis. Hereditary neuropathy with liability to pressure palsies (HNPP) may occasionally cause a proximal neuropathy. One of the more common proximal asymmetric neuropathies (or more specifically polyradiculoneuropathy) is diabetic amyotrophy. Fairly abrupt in onset, it most commonly involves predominantly the L2 to L4 nerve roots (iliopsoas, quadriceps femoris, and hip adductors) associated with mild sensory loss over the anterior thigh [18]. With time, symptoms spread from proximal to distal. Finally, idiopathic brachial plexitis is a diagnosis by exclusion.

**Autonomic nervous system dysfunction**

Autonomic nervous system dysfunction may be manifest by labile blood pressure, orthostatic intolerance, erectile dysfunction, syncope, postprandial fatigue, gastroparesis, bladder dysfunction, and absent sweating. Neuropathies associated with autonomic system involvement may be divided into acute or chronic neuropathies (Box 6). Vacor or vincristine exposure may cause acute autonomic dysfunction, with vincristine also causing an associated motor greater than sensory or sensorimotor polyneuropathy without

<table>
<thead>
<tr>
<th>Box 6</th>
<th>Neuropathies associated with autonomic nervous system dysfunction</th>
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<tbody>
<tr>
<td>Acute</td>
<td>Idiopathic pandysautonomic neuropathy</td>
</tr>
<tr>
<td></td>
<td>Guillain-Barre syndrome</td>
</tr>
<tr>
<td>Toxic</td>
<td>Vincristine</td>
</tr>
<tr>
<td></td>
<td>Vacor</td>
</tr>
<tr>
<td>Chronic</td>
<td>Amyloid</td>
</tr>
<tr>
<td></td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td></td>
<td>HIV</td>
</tr>
<tr>
<td></td>
<td>HSAN</td>
</tr>
<tr>
<td></td>
<td>Paraneoplastic sensory neuropathy</td>
</tr>
</tbody>
</table>
substantial conduction slowing. The presence of acute areflexia associated with EDX evidence of a demyelinating polyradiculoneuropathy, albuminocytologic dissociation, and autonomic dysfunction frequently occurs in AIDP. A rapid onset pandysautonomia is sometimes associated with this syndrome, and patients may develop severe orthostatic hypotension, anhidrosis, dry mouth and eyes, a fixed heart rate and fixed pupils with bowel and bladder dysfunction before onset of areflexia.

Chronic autonomic dysfunction is most commonly seen with diabetes mellitus and may involve the sympathetic, parasympathetic, or both autonomic nervous systems. The presence of pain associated with chronic autonomic dysfunction is frequently seen in amyloidosis and in HIV neuropathy (which presents late in the course of the illness). A paraneoplastic sensory neuronopathy associated with autonomic dysfunction presents with an accompanied sensory ataxia, global areflexia, and evidence of sensory neuronopathy on EDX testing. HSAN is generally found at infancy or in the early second decade and frequently it is associated with mutilation or a history of multiple painless fractures. Diabetes mellitus, however, is the most likely culprit of autonomic dysfunction in the western world.

Facial nerve involvement

Bell palsy is a benign condition, however on rare occasion, facial neuropathy may be found in conjunction with either an acute or chronic polyneuropathy.

Neuropathies associated with facial nerve involvement:
AIDP
Amyloid (Gelsolin familial)
CIDP
Lyme disease
Sarcoid
Tangier disease

In the acute setting of AIDP, bifacial weakness is present in up to 50% of patients. Less frequently, facial weakness occurs in association with CIDP [17]. Tangier disease (see small fiber neuropathies) may present with facio-brachial weakness. There is usually, however, an associated small fiber neuropathy and the presence of orange tonsils helps clarify the diagnosis. Lyme disease should be considered in patients with recurrent facial palsy or bilateral facial mononeuropathy, particularly if they are from endemic areas. Early in the course of the illness, there may be an accompanying painful (poly)radiculopathy. In the later stages of Lyme disease, a reversible polyradiculoneuropathy may be present. Sarcoidosis may be distinguished from other forms of neuropathy by its association with several atypical features: multiple cranial neuropathies, multiple mononeuropathies, truncal sensory neuropathy, a cauda equina syndrome, and a chronic symmetric sensorimotor
neuropathy accompanied by wrist extensor and foot dorsiflexion weakness. The diagnosis of sarcoidosis may be made by nerve, muscle, or lymph node biopsy and supported by abnormal angiotensin converting enzyme (ACE) levels or systemic evidence of sarcoidosis.

**Neurocutaneous manifestations**

In addition to the neurological evaluation, the general physical examination may provide clues helpful in identifying the cause of the underlying peripheral neuropathy (Table 5). The presence of alopecia is suggestive of thallium poisoning, whereas evidence of Mees lines in the fingernails suggests an acute intoxication such as that from arsenic or thallium. Skin hypopigmentation is seen in leprosy and the POEMS (polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes) syndrome, a lymphoproliferative disorder associated with an acquired demyelinating neuropathy. Raised skin lesions suggestive of angiokeratomas are found in Fabry disease. The presence of purpura and neuropathy should suggest the possibility of cryoglobulinemia, whereas purpura associated with livido reticularis is frequently seen in individuals with an underlying vasculitis. In Tangier disease, orange tonsils may be seen in association with a small fiber neuropathy, with sensory and motor symptoms similar to those associated with syringomyelia. The presence of unhealed foot ulcers in conjunction with neuropathic symptoms should alert the physician to possible undiagnosed diabetes mellitus.

**Family history**

Increasingly, hereditary neuropathies are being implicated in and are believed to make up a large percentage of those patients diagnosed with “idiopathic” chronic neuropathy [18]. A detailed family history can be rewarding for the physician, particularly when faced with a patient referred

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Neurocutaneous findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsenic intoxication</td>
<td>Mees lines</td>
</tr>
<tr>
<td>Cryoglobulinemia</td>
<td>Purpura</td>
</tr>
<tr>
<td>Fabry disease</td>
<td>Angiokeratomas</td>
</tr>
<tr>
<td>Giant axonal neuropathy</td>
<td>Curly hair</td>
</tr>
<tr>
<td>Leprosy</td>
<td>Hypopigmented skin</td>
</tr>
<tr>
<td>POEMS</td>
<td>Hypopigmented skin</td>
</tr>
<tr>
<td>Tangier</td>
<td>Orange tonsils</td>
</tr>
<tr>
<td>Thallium poisoning</td>
<td>Mees lines, alopecia</td>
</tr>
<tr>
<td>Variegate porphyria</td>
<td>Bullous lesions</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>Livedo reticularis, purpura</td>
</tr>
</tbody>
</table>
for an idiopathic neuropathy for which no cause is apparent. Detailed questioning regarding other family members who may have a history of poor athletic performance, difficulty running, gait difficulties requiring orthotics or braces, inability to walk on the heels or toes, difficulty getting up from a seated position, high arched feet, hammer toes or claw hands, frequent foot ulcers, or atrophic hand or foot muscles. The answers to these questions may help elucidate a history of a familial neuropathy. It is frequently helpful to have the patient contact other family members to inquire about the presence of the above symptoms. It is reported that only 20% of individuals with hereditary neuropathy seek medical attention. Thus, obtaining a thorough family history may limit an otherwise potentially expensive investigation [19].

Electrodiagnostic studies

EDX testing is an essential tool in the diagnostic approach to peripheral nerve disease and can be thought of as a direct extension of the neurological examination. In the EMG laboratory, one can identify the predominant pathophysiology: axonal loss, uniform or segmental demyelination or conduction block. Occasionally, history may be inadequate and EDX studies may add further information regarding the duration of the symptoms (acute, chronic, and actively ongoing). Individuals with a primarily motor neuropathy may be unaware of concomitant involvement of peripheral sensory nerves or vice versa. Demonstration of unanticipated involvement therefore completely alters the differential diagnosis. In addition, EDX results not only quantify the severity of the disorder but also allow the clinician to confirm which aspects of the peripheral nervous system are involved and confirm the distribution of involvement. Individuals with an underlying neuropathy may be predisposed (secondary to pre-existing nerve injury) to developing a superimposed mononeuropathy. All individuals with a mononeuropathy should be screened for an underlying polyneuropathy. More importantly, it is essential that in the evaluation of a peripheral neuropathy several nerves be compared bilaterally to establish if there is substantial asymmetry. Some investigators have even proposed classifying neuropathies by their EDX studies [8]. The value of this approach is seen in the evaluation of toxic neuropathies (Table 6). Frequently, one is left with a history of a possible toxic exposure, and the EDX profile not only confirms the presence of a polyneuropathy but also identifies a particular pattern of the neuropathy on nerve conduction studies (motor or motor > sensory with conduction slowing, motor or motor > sensory without conduction slowing, pure sensory, sensorimotor without conduction slowing). Recognition of these patterns helps develop a rational approach to find the cause of the neuropathy.

Axonal and demyelinating neuropathies have distinct electrophysiologic pictures. Axonal neuropathies are characterized by decreased distal amplitudes with relative preservation of conduction velocities, whereas demyeli-
nating neuropathies result in significant slowing of conduction velocities with preservation of distal amplitudes. In *axonal neuropathies*, the loss of axons leads to atrophy of the target muscle and results in a decreased compound muscle action potential (CMAP) or sensory nerve action potential (SNAP) (Fig. 1A). The loss of amplitude reflects the degree of axonal loss (Fig. 1B). In severe axonal neuropathies, more large, fast conducting fibers may be affected. In addition to a severely decreased CMAP or SNAP amplitude, there is also some resultant slowing of conduction velocity. The degree of slowing reflects the conduction velocity of the remaining nerve fibers. In general, conduction velocities are normal or mildly slowed in axonal neuropathies, which also results in normal or prolonged distal latencies; the degree of prolongation is proportionate to conduction velocity slowing. Most axonal neuropathies are length-dependent (dying back neuropathies), and the most distal nerve terminals are affected first.

EDX information derived from the results of nerve transection is helpful in understanding the abnormalities associated with axonal neuropathy. Following complete nerve transection, evoked responses disappear in 3 to 7 days, and increased insertional activity on needle examination may be noted as early as 7 to 10 days or as late as 3 weeks, depending on the distance of the target muscle or sensory fiber from the site of transection. With partial motor axon loss, a decreased recruitment pattern is seen on needle EMG. At onset, Motor Unit Action Potentials (MUAPs) are of normal amplitude and duration. Within 10 to 14 days, however, polyphasic MUAPs are seen

<table>
<thead>
<tr>
<th>Motor or motor-sensory neuropathies with conduction slowing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsine</td>
</tr>
<tr>
<td>Cytosine arabinoside (ara-C)</td>
</tr>
<tr>
<td>n-Hexane</td>
</tr>
<tr>
<td>Suramin</td>
</tr>
<tr>
<td>Motor or motor-sensory involvement, without conduction slowing</td>
</tr>
<tr>
<td>Cimetidine</td>
</tr>
<tr>
<td>Disulfiram</td>
</tr>
<tr>
<td>Hyperinsulin/hypoglycemia</td>
</tr>
<tr>
<td>Organophosphate esters</td>
</tr>
<tr>
<td>Sensorimotor involvement without conduction slowing</td>
</tr>
<tr>
<td>Acrylamide</td>
</tr>
<tr>
<td>Arsenic</td>
</tr>
<tr>
<td>Colchicine</td>
</tr>
<tr>
<td>Ethyl alcohol</td>
</tr>
<tr>
<td>Elemental mercury</td>
</tr>
<tr>
<td>Hydralazine</td>
</tr>
<tr>
<td>Lithium</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
</tr>
<tr>
<td>Paclitaxil</td>
</tr>
<tr>
<td>Phenytoin</td>
</tr>
<tr>
<td>Vincristine</td>
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</table>

Table 6
Toxic agents associated with neuropathy [29]

<table>
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<tr>
<td>Arsine</td>
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EDX information derived from the results of nerve transection is helpful in understanding the abnormalities associated with axonal neuropathy. Following complete nerve transection, evoked responses disappear in 3 to 7 days, and increased insertional activity on needle examination may be noted as early as 7 to 10 days or as late as 3 weeks, depending on the distance of the target muscle or sensory fiber from the site of transection. With partial motor axon loss, a decreased recruitment pattern is seen on needle EMG. At onset, Motor Unit Action Potentials (MUAPs) are of normal amplitude and duration. Within 10 to 14 days, however, polyphasic MUAPs are seen
Fig. 1. Computerized model of peripheral motor nerve. Muscle fibers are denoted by solid bars to the right of each axon. The arrows represent the stimulation sites. The compound muscle action potentials (CMAP) are shown below each nerve in the schematic screen. Upper trace recording: resultant CMAP following distal nerve stimulation. Lower recording: resultant CMAP following proximal nerve stimulation. (A) Normal nerve demonstrating summation of eight individual muscle fiber action potentials to produce the CMAP. Individual axons are of slightly different sizes and, therefore, conduct at different rates.
because of axonal sprouting and reinnervation of some denervated muscle fibers. Within months of an acute lesion, large amplitude, long duration, polyphasic MUAPs develop [20,21]. Axonal neuropathies develop similar patterns of abnormality, depending in part on the duration and severity of axonal loss.

Demyelinating neuropathies are hallmarked by decreased conduction velocities secondary to impaired saltatory conduction. Criteria for demyelina-

Fig. 1. (B) Nerve with axonal degeneration following random loss of 75% of axons.
In pure demyelinating neuropathies, the axon is intact and there is no loss of contact with the motor or sensory target. As a result, there is no associated muscle atrophy, nor is there evidence of fibrillation potentials or positive sharp waves in affected muscles. When demyelination are described in Box 3a and Box 3b. In pure demyelinating neuropathies, the axon is intact and there is no loss of contact with the motor or sensory target. As a result, there is no associated muscle atrophy, nor is there evidence of fibrillation potentials or positive sharp waves in affected muscles. When demyelination are described in Box 3a and Box 3b. In pure demyelinating neuropathies, the axon is intact and there is no loss of contact with the motor or sensory target. As a result, there is no associated muscle atrophy, nor is there evidence of fibrillation potentials or positive sharp waves in affected muscles. When demyelination are described in Box 3a and Box 3b. In pure demyelinating neuropathies, the axon is intact and there is no loss of contact with the motor or sensory target. As a result, there is no associated muscle atrophy, nor is there evidence of fibrillation potentials or positive sharp waves in affected muscles. When demyelination are described in Box 3a and Box 3b. In pure demyelinating neuropathies, the axon is intact and there is no loss of contact with the motor or sensory target. As a result, there is no associated muscle atrophy, nor is there evidence of fibrillation potentials or positive sharp waves in affected muscles. When
present, these abnormalities are modest and commensurate with a mild degree of axonal loss. In focal demyelination with conduction block, motor and sensory responses cannot be obtained or are of low amplitudes when stimulating proximal to the lesion, but these responses are normal when the nerve is stimulated distal to the lesion (Fig. 1B). In focal demyelination without conduction block, EDX findings reveal a substantial reduction of conduction velocity across the lesion, findings also displayed with chronic nerve compression. In uniform demyelinating disorders (Table 3), there is homogenous involvement of all fibers and therefore a normal evoked response with distal and proximal stimulation, despite a markedly decreased conduction velocity. Multifocal demyelination will also show decreased conduction velocities with preserved evoked response amplitudes with distal stimulation. Proximal stimulation results in abnormal temporal dispersion of the CMAP, however, with the proximal response being of smaller amplitude and longer duration than the response obtained with distal stimulation. Distal demyelination may also produce prolonged distal latencies [8].

AIDP is a prototype of an acquired demyelinating neuropathy. In AIDP, EDX findings are variable depending on when they are performed relative to disease onset. Given the acute onset of this disorder, establishing a diagnosis entirely on EDX findings may be difficult. In the first 1 to 2 weeks of illness, when establishing a diagnosis is most important, the only finding may be absent or prolonged F wave latencies. Other abnormalities, such as reduced CMAP amplitudes, are more common than is conduction slowing [22]. Motor conduction abnormalities peak at about the third week. In AIDP, motor abnormalities are generally diffuse and homogenous when compared with the patchy nature of sensory nerve abnormalities. Another characteristic of AIDP seen in approximately 50% of patients in the first 4 weeks of illness is a pattern of a normal sural but an abnormal median sensory response, a finding unusual for most forms of polyneuropathy. On needle examination, abnormally increased insertional activity appears in distal and proximal muscles between weeks 2 and 4 of illness, whereas changes in MUAP morphology typically develop shortly thereafter (weeks 4 to 5). EDX findings in CIDP are similar to those seen in AIDP, differing primarily in association with the temporal profile of the illness.

Hereditary demyelinating neuropathies may also be identified on EDX studies by several pertinent features. HMSN I and III are characterized by conduction velocity slowing to less than 85% of the lower limit of normal. As this disorder is representative of uniform demyelination of all fibers, abnormal temporal dispersion is not usually present. Among HMSN type III patients with markedly reduced conduction velocity, the possibility of phase cancellation may lead to abnormal temporal dispersion and diagnostic confusion [23–25]. In general, however, the absence of abnormal temporal dispersion is helpful in distinguishing acquired from hereditary demyelinating neuropathies. In HMSN type I or III, F wave latencies, when obtainable, are prolonged, as are distal latencies, and SNAPs are generally
absent. There may be decrease in CMAP amplitudes, reflecting the degree of superimposed axonal degeneration. Needle examination reveals increased MUAP amplitude and duration with mild to moderate distal denervation proportionate to the amount of loss of axon.

HMSN II is an autosomal dominant sensorimotor polyneuropathy of the axonal type with an onset in the third to fifth decades. Nerve conduction studies are manifest by normal to decreased CMAP amplitudes and essentially normal conduction velocities. Approximately 50% of HMSN type II patients have absent SNAPs, and most of the remaining patients have abnormally low SNAP amplitudes. Needle EMG examination reveals chronic neurogenic changes that are most prominent distally. The magnitude of abnormal insertional activity in this disorder reflects the degree of partial denervation and the rate of progression.

Hereditary neuropathy with liability to pressure palsies (HNPP), also termed tomaculous neuropathy, is caused by a deletion of the PMP-22 gene on chromosome 17. HNPP most commonly affects the ulnar nerves at the elbow and the peroneal nerves at the fibular head. Other nerves commonly affected are those associated with localized focal compression, such as the radial nerve at the spiral groove of the humerus and the median nerve at the wrist. The mononeuropathies associated with HNPP are often precipitated by minor trauma and are usually painless. Complete recovery generally occurs in days to weeks [26–28]. The predominant abnormality on EDX testing is evidence of focal or multifocal demyelinating lesions at common pressure sites. Nerve conduction studies also may show prolonged distal latencies, often out of proportion to the mild slowing of conduction velocities, perhaps in association with a confluent mononeuropathy multiplex. Nerve conduction studies may demonstrate mild conduction slowing among asymptomatic but affected relatives. Thus, unexpected EDX findings of slowed conduction velocities or evidence of multifocal demyelination on evaluation of a patient with a “routine entrapment” neuropathy should raise a suspicion for HNPP.

**Conclusion**

There are a multitude of potential etiologies for peripheral neuropathy. For this and other reasons, the evaluation of patients with neuropathy may at times seem overwhelming and frustrating to the clinician. By combining information derived from a thorough history and clinical examination with the results of the EDX examination, however, it is possible to substantially reduce the number of disorders included in the differential diagnosis. Important features include information about the temporal course of symptoms, characterization of symptoms as predominantly sensory, motor, sensorimotor, or autonomic, and determining whether pain is a primary feature. The clinical examination is used to confirm the clinical impression based on the patient’s symptoms, and also includes careful evaluation for autonomic
dysfunction, facial nerve involvement, and neurocutaneous manifestations. The EDX study results confirm the peripheral localization and characterize the neuropathy by the primary physiologic abnormality. This characterization includes documentation of the patterns and types of abnormality as symmetric or asymmetric, proximal or distal, and demyelinating or axonal. This process permits generation of a limited, more focused differential diagnosis that sometimes suggests the etiology or pathogenesis of the neuropathy. This process also results in an evaluation plan that is based on logical and cost-effective investigations that ultimately help to establish a final diagnosis.

References


Electrodiagnostic approach to the patient with suspected motor neuron disease

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Amyotrophic lateral sclerosis (ALS) is a relentlessly progressive, neurodegenerative disorder involving motor neurons in the cerebral cortex, brainstem, and spinal cord. Specifically targeted are the giant Betz cells of the motor cortex and the motor neurons of the brainstem and spinal cord with the exception of the oculomotor nuclei and the nucleus of the sacral spinal cord (nucleus of Onuf) that controls the external urethral and anal sphincters [1]. The clinical findings that develop over time comprise a combination of upper motor neuron (UMN) signs (loss of dexterity, spasticity, hyperreflexia, and pathological reflexes), and lower motor neuron (LMN) signs (muscle weakness, atrophy, and fasciculations) in a widespread distribution. The annual incidence is 1 to 2 per 100,000 population and the prevalence is about 6 per 100,000 [2,3]. There is a slight male predominance of approximately 1.5 men to 1 woman. The disease occurs throughout adult life with the peak occurring between 55 and 70 years of age. Age is the most significant risk factor for ALS. Most cases are sporadic but approximately 5% to 10% are familial and the majority is inherited in an autosomal dominant fashion. About 10% to 20% of these cases have been attributed to mutations in the gene coding for Cu/Zn-superoxide dismutase (SOD1). The average survival after onset of ALS symptoms is approximately 3 years but about 25% of patients survive (without intervention for respiratory support) for at least 5 years and more than 10% have a survival in excess of 10 years [2]. Patients with longer survival display a poorly understood “resistance” to ALS [4] and may have a more benign form of the disease.

The diagnosis of ALS per se may be challenging because there is no single diagnostic test for ALS (with the exception of finding a mutation in the
SOD1 gene). Additionally, the disease may begin focally and resemble a variety of other neurologic disorders that share clinical features with ALS. This latter point emphasizes an important imperative for the clinician—the need to consider a broad range of peripheral and central nervous system disorders in the process of differential diagnosis of ALS, especially when the disease is in its early stages. We review the diagnostic criteria for ALS and discuss which features to consider in determining the degree of certainty or level of confidence in the diagnosis. We then enumerate the important differential diagnostic possibilities that emerge from a careful consideration of the clinical features and comment on neuroimaging studies and laboratory tests employed in the diagnostic process. Next, we turn our attention to the important role played by electrophysiologic studies in the diagnostic evaluation of the patient with suspected ALS. We then return to a focused consideration of selected disorders in the differential diagnosis of ALS, and conclude with a summary of our diagnostic approach for this disease.

Diagnosis of ALS

ALS is almost always a pure motor disorder without clinically significant sensory impairment, ocular palsy, or bladder and bowel dysfunction [5]. In fact, the presence of these latter features would argue against the diagnosis of ALS. Dementia occurs rarely, in about 1% to 2% of cases.

To make the diagnosis of ALS, a combination of upper and lower motor neuron signs with evidence of spread within a region or to other CNS regions is required (Table 1) [6]. Additionally, there must be no electrophysiologic, or neuropathologic evidence of other disease processes that might explain the clinical signs of neuronal degeneration, and in turn, no neuroimaging evidence of other disease processes to explain the clinical or electrophysiologic signs of lower motor neuron or upper motor degeneration or both.

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<th>Features present</th>
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<td>Evidence of lower motor neuron degeneration by clinical, electrophysiological or neuropathological examination</td>
<td>Electrophysiological or pathological evidence of other disease processes that might explain signs of lower motor neuron or upper motor degeneration or both</td>
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<tr>
<td>Evidence of upper motor neuron degeneration by clinical examination</td>
<td>Neuroimaging evidence of other disease processes that might explain the observed clinical and electrophysiological signs</td>
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<td>Progressive spread of signs within a region, or to other regions as determined by history or examination</td>
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physiologic signs. According to the revised El Escorial criteria the clinical diagnosis of ALS (without pathological confirmation) may be made with varying degrees or levels of certainty by clinical assessment alone. These levels of certainty (Table 2) are determined by the extent to which upper and lower motor neuron signs are distributed in four cardinal topographical anatomic regions of the central nervous system—the brainstem, and three spinal cord regions, cervical, thoracic, and lumbosacral.

Clinically definite ALS is defined on clinical evidence alone by the presence of UMN as well as LMN signs, in the bulbar region and at least two spinal regions, or the presence of UMN and LMN signs in three spinal regions. *Clinically probable ALS* is defined on clinical evidence alone by UMN and LMN signs in at least two regions with some UMN signs necessarily rostral to the LMN signs. *Clinically probable ALS–laboratory supported,* is defined when clinical signs of UMN and LMN dysfunction are in only one region, or when UMN signs alone are present in one region and LMN signs defined by electrophysiologic criteria are present in at least two regions. Additionally, there must be proper application of neuroimaging and clinical laboratory protocols to exclude other causes. The addition of the category, “clinically probable ALS–laboratory supported,” marks a key difference from the first set of El Escorial criteria [7] because the combination of EMG and clinical findings is used in the diagnostic assessment. The rationale for this criterion is discussed in detail later. Finally, *clinically possible ALS* is defined when clinical signs of UMN and LMN dysfunction are found together in only one region, or UMN signs are found in two or more regions, or LMN signs are found rostral to UMN signs. The diagnosis of clinically possible ALS

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<td>Definite ALS</td>
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<td>UMN and LMN signs in three spinal regions</td>
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<tr>
<td>Probable ALS</td>
<td>UMN and LMN signs in at least two regions with some</td>
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<td>UMN signs necessarily rostral to the LMN signs</td>
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<tr>
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<td>UMN signs alone are present in one region; and</td>
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<td>LMN signs defined by electrophysiologic criteria are present in at least two regions</td>
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infers that EMG criteria for LMN involvement as established for clinically probable ALS—laboratory supported have not yet been met, but that other conditions that could mimic ALS have been excluded.

**Differential diagnosis**

A variety of neurological disorders may mimic some aspect of ALS and a major goal of the diagnostic process is to exclude them systematically. Stated another way, the clinician’s responsibility is to entertain the diagnosis of any possible ALS “look alike,” however superficial the resemblance may be, so as not to overlook a potentially treatable disorder, or at least one more manageable than ALS. For example, ALS may present with differing patterns of weakness: a focal onset (restricted to bulbar muscles or to a single limb), a bibrachial paresis, hemiparesis, or paraparesis. Moreover, the weakness seen in ALS may be exclusively LMN in type at the outset. In this instance the disease might simulate a disorder of anterior horn cells other than ALS, or an abnormality of nerve roots, plexuses or multiple peripheral nerves, even neuromuscular junction and muscle [8]. Alternatively, the initial presentation of ALS might be predominantly upper motor neuron in type, suggesting a lesion in the cerebrum, brainstem, or spinal cord. Accordingly, the differential diagnosis by anatomic site is presented in Table 3; further comment is presented later in this article.

**Diagnostic testing**

The four components of diagnostic testing are clinical laboratory studies, neuroimaging, neuropathology, and electrophysiology [6]. Except for an elevated CK of mild-to-moderate degree found in many ALS patients, clinical laboratory testing is expected to be normal. In general, in the context of suspected ALS, we look for evidence of treatable or reversible metabolic, autoimmune, neoplastic, infectious, or vasculitic disorders [9]. For example, a multiple motor mononeuropathic presentation would prompt us to look for anti-ganglioside (GM1) autoantibodies seeking supporting evidence of multifocal motor neuropathy. A bulbar-onset presentation might lead us to test for the acetylcholine receptor antibody for evidence of myasthenia gravis, or to a search for the DNA abnormality of Kennedy’s syndrome (see later discussion)

Neuroimaging of the brain and spinal cord are critically important to exclude structural pathology of the brain, brainstem, cervicomedullary junction, spinal cord, and nerve roots that might explain UMN findings or LMN findings or both. For example, before the diagnosis of ALS is accepted in instances of LMN findings in the arms and UMN in the legs, cervical spondylotic myelopathy must be excluded.
On rare occasions when the diagnosis of ALS proves difficult to establish, a muscle biopsy may be performed to confirm the presence of acute and chronic denervation and to rule out evidence for inflammatory or toxic myopathy that might simulate ALS.

**Electrophysiologic evaluation**

Electrophysiology is the centerpiece of the diagnostic evaluation. According to the El Escorial revised criteria [6], there are three reasons for performing the EMG in the patient with suspected ALS: (1) to confirm LMN dysfunction in clinically affected regions; (2) to detect electrophysiological evidence of LMN dysfunction in clinically uninvolved regions; and (3) to exclude other pathophysiological processes.

There are two major components of the electrophysiologic assessment of the peripheral nervous system in the patient with suspected ALS: nerve conduction studies and the concentric needle electrode examination (NEE). Motor nerve conduction and sensory studies are considered first.

**Nerve conduction studies**

Sensory studies comprise conventional assessments of sensory nerve action potential amplitudes, distal latencies, conduction velocities and H reflexes. Motor studies comprise conventional assessments of evoked motor response amplitudes (with careful attention to the possibility of partial
conduction block), distal latencies, nerve conduction velocities, F-wave latencies, and sequential evoked motor amplitudes with repetitive nerve stimulation. An additional technique used to monitor motor neuron degeneration in ALS is motor unit number estimation (MUNE) that attempts to estimate the number of motor units innervating a given muscle.

The revised El Escorial criteria [6] pertaining to nerve conduction studies for the diagnosis of ALS indicate that both sensory and motor studies “should generally be normal or near normal.” They indicate further “that the studies are required principally to define and exclude other disorders of peripheral nerve, neuromuscular junction and muscle that may mimic or confound the diagnosis of ALS.” The next few sections discuss nerve conduction study findings in greater detail.

Sensory conduction studies

Because ALS is essentially a pure motor disorder, it is expected that routine sensory studies will be normal. In fact, a normal sensory nerve action potential in the face of severe muscle atrophy is the hallmark of a motor neuronopathy or neuropathy. Nonetheless, there are instances of abnormal sensory electrophysiology that may be encountered in ALS. Some elderly patients with ALS may be expected to lose sensory responses in the legs (sural and superficial peroneal responses may be attenuated or absent) and have absent H-reflexes bilaterally because of the effects of aging. Entrapment neuropathies commonly coexist with ALS and the involved nerves may have abnormalities in one or more parameters. Finally, mild axonal sensory polyneuropathies may also occur in ALS patients. Indeed, two kinds of subtle sensory abnormality have been found in some clinically definite ALS patients without risk factors for a peripheral sensory disorder [10]. First, the amplitude of the sensory action potential may be reduced. Second, the conduction velocity of the slowest conducting component of the sensory fiber action potential (known as the minimum conduction velocity) may be reduced. The latter may reflect a mild “dying back” axonopathy of peripheral sensory fibers in ALS [11]. In a prospective clinical and electrophysiological study, Gregory et al [12] found that sensory nerve dysfunction progresses in parallel with motor decline.

Excluding the aging effect, the H-reflex is usually obtainable in ALS since the sensory component (IA spindle afferent fibers) remains intact and the excitability of the motor neuron pool that can be activated by the H-reflex pathway is increased [13]. This latter phenomenon, relating to clinical signs of upper motor neuron involvement, increases the H response amplitude and thus tends to increase the ratio of the H to the M maximum amplitudes (Hmax/Mmax) [14].

If substantially reduced or absent sensory action potentials are elicited in the patient with suspected ALS, particularly in the early stages, and aging and entrapment have been excluded as causes, then consideration should
turn to diagnoses other than ALS. These include a sensory axonopathy or neuronopathy in the context of bulbospinal neuronopathy (Kennedy’s syndrome) as well as other neuromuscular disorders such as polyradiculoneuropathies including chronic inflammatory demyelinating polyneuropathy [13].

Motor conduction studies

Evoked motor responses are usually normal in the early stages of ALS, although sometimes there are asymmetric reductions of the evoked compound muscle action potentials (CMAPs) at initial presentation, reflecting early focal or multifocal, predominantly distal limb muscle weakness and atrophy. As the disease progresses with its attendant progressive loss of motor units, one typically finds CMAP amplitude reductions to be widespread.

When CMAP amplitudes are normal or only mildly decreased, motor conduction velocities and distal latencies are typically normal, but as muscle weakness and atrophy progress and spread, there is a mild increase in distal motor latencies, a mild decrease of motor conduction velocities, and a mild prolongation of F-wave latencies. This association of low CMAP with reduced motor nerve conduction velocity stems from the loss of the motor units with the fastest conducting myelinated motor fibers. Accordingly, the myelinated motor fibers that remain conduct relatively slowly, but their minimum velocity is 35 meters/second or approximately 75% of the lower limit of normal [15]. Velocities slower than this fall in the range of acquired demyelination and with occasional exceptions (see below) are inconsistent with the diagnosis of ALS.

Lambert and Mulder [16] observed that the changes in motor conduction velocity in 100 ALS patients were generally minor compared to findings in “chronic peripheral neuropathy or polyneuropathies such as the Guillain-Barré syndrome or Charcot-Marie-Tooth disease.” They noted that the conduction velocity of the ulnar nerve was within the normal range in 90% of the 100 patients and was seldom less than 75% of the average conduction velocity in a group of normal patients. In a larger study of 322 ALS patients, Lambert [17] showed that the mean conduction velocity of the ulnar nerve in the forearm segment was 55 meters/second, 8% below the normal mean; and, for the peroneal nerve in the foreleg segment, 44 meters/second, 16% below the normal mean. As the ulnar CMAP amplitudes fell in the ALS patient group, the ulnar motor conduction velocities gradually declined; CMAP amplitudes less than 1 mV were associated with a mean conduction velocity of 48 meters/second. In only 2.5% of all subjects did the mean values fall below 40 meters/second, the lowest being 33 meters/second. Also, the distal latency prolongation correlated inversely with the CMAP amplitude.

Cornblath et al. [18] sought to determine the limits of abnormality in motor nerve conduction parameters for the ulnar, median and peroneal nerves evoked from atrophic muscles in a group of 61 patients who met a
strict clinical definition of ALS. They related conduction velocity, distal latency and F-wave latency to distal CMAP in the three nerves. They found that distal latency was rarely greater than 125% of the upper limit of normal and that higher values occurred in only 4% of measurements. Motor nerve conduction velocity was never less than 70% of the lower limit of normal and was rarely (1% of observations) below 80% of the lower limit of normal. For the F-wave, Cornblath et al. [18] found that only 1% of values was greater than 125% of the upper limit of normal.

The experience with F-waves in ALS is that their response frequency is usually reduced with 50% of delivered stimuli failing to elicit an F-wave [19]. Ultimately, with progressive loss of motor units and the resulting reduction of CMAP amplitudes, F-wave responses cannot be elicited.

Felice [20] reported that comparisons between 13 ALS and 10 normal subjects did not disclose a significant difference in median distal motor latencies and motor conduction velocities. However, using automated F-wave analysis for the investigation of single thenar motor unit conduction velocity, he found significant reductions in ALS units compared to controls. He postulated that the motor nerve slowing occurred at proximal sites and was related possibly to impairment of axonal transport due to neurofilament accumulation and axonal swelling that have been described at these proximal levels [21].

Behnia and Kelly [22] caution that interpretation of motor conduction velocity may be difficult in limbs with low CMAP amplitudes recorded from atrophic muscles. First, motor conduction is likely to be excessively slowed by the presence of degenerating or regenerating, thinly myelinated axons. Second, despite warming, the reduced muscle mass and lack of movement may lead to erroneously slowed conduction velocity because of difficulty maintaining ideal temperature in deeper tissues, in the vicinity of the nerve. Accordingly, these authors suggest that accurate determination of motor conduction parameters should be performed on nerves with relatively well preserved CMAP amplitudes of at least 50% of the lower limit of normal. Likewise, F-wave latencies should be performed in nerves with similar CMAP amplitudes.

Care must also be taken in the interpretation of prolonged distal motor latencies in the setting of pronounced muscle atrophy with attendant low CMAPs [19]. Distal motor latencies may also be prolonged out of proportion to the degree of conduction slowing because of cool atrophic extremities, local entrapments and nerve terminal sprouting; the latter associated with incompletely myelinated new collateral sprouts conducting nerve impulses inefficiently, thereby increasing distal latency.

The issue of whether or not definite partial conduction block is present in the patient with suspected ALS is complex, yet critically important from the diagnostic standpoint. There are two aspects to consider. First, patients with a relatively benign or potentially treatable disorder—multifocal motor neuropathy with conduction block—may present clinically in a fashion that
may strongly resemble ALS with a lower motor neuron onset ([23–25] (see later discussion) and patients with ALS per se may demonstrate a greater amplitude difference between distal and proximal stimulating sites than is seen in individuals without ALS, simulating partial conduction block. The latter phenomenon results from phase cancellation and the mild slowing of motor conduction velocity that is common in ALS when CMAP amplitude is reduced to less than 50% [26]. Consensus criteria for probable and definite partial conduction block have been developed and the reader should consult this document [27] for a full treatment of the subject. To highlight just one among several consensus criteria—probable partial conduction block over a segment of 3 cm or less requires reduction in amplitude and area by 10% without significant temporal dispersion.

**Repetitive nerve stimulation**

Abnormalities may also be found in repetitive nerve stimulation (RNS) studies in ALS patients. Bernstein and Antel [28] found a significant decrement of the CMAP recording the abductor digiti minimi in response to 2-Hz RNS of the ulnar nerve at the wrist in patients with rapidly progressive disease, not in patients with slowly developing ALS. Subsequent studies have found some decrement in more than half of patients with ALS, usually less than 10%, with the same characteristics of the decrement seen in myasthenia gravis [26,29]. The pathogenesis of the decrement is likely related to the reduced safety factor in neuromuscular junctions of reinnervated muscle fibers. The more pronounced decrement in rapidly progressive disease may correlate with instability of neuromuscular transmission in collateral nerve terminal sprouts in this form of ALS [22,26] (see later discussion).

Table 4 reviews the key points pertaining to routine conduction studies, and Table 5 summarizes the changes in nerve conduction study parameters at different stages of ALS.

**Motor unit number estimate**

Motor unit number estimate (MUNE) is an electrophysiological technique that measures the approximate number of LMNs innervating a single muscle or a small group of muscles [30]. The MUNE count is determined through division of the supramaximal CMAP amplitude or area by the mean surface-recorded motor unit potential amplitude or area. Gooch and Harati [31] point out that the technique enables a quantitative estimate of the number of functional motor units and allows tracking of the progressive loss of motor units over months to years. In a longitudinal study of ALS the decrease in MUNE over a 6-month interval was significantly greater than the decrease in CMAP (or grip strength) [32]. This result indicates that following MUNE over time provides a more sensitive measure of the rate of progression of ALS than monitoring CMAP or grip strength over time. Although not employed routinely in the electrodiagnostic process, MUNE
has potential in studies of the natural history of ALS and of the response to experimental treatment [30].

**Needle electrode examination**

We now turn to a consideration of the needle electrode examination (NEE) in the patient with suspected ALS. It is the most important diagnostic method for providing evidence of generalized motor neuron degeneration, even early in the course of the illness in apparently unaffected limbs.

**Table 4**

<table>
<thead>
<tr>
<th>Features consistent with ALS</th>
<th>Features inconsistent with ALS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor conduction times should be normal, unless the CMAP is small</td>
<td>Evidence of motor conduction block</td>
</tr>
<tr>
<td>Sensory nerve conduction studies can be abnormal in the presence of entrapment syndromes and coexisting peripheral nerve disease</td>
<td>Motor conduction velocities lower than 70%, and distal motor latencies over 30%, of the lower and upper limit of normal values, respectively</td>
</tr>
<tr>
<td>Lower extremity sensory nerve responses can be difficult to elicit in the elderly</td>
<td>Abnormal sensory nerve conduction studies&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>F-wave or H-wave latencies more than 30% above established normal values</td>
</tr>
<tr>
<td></td>
<td>Decrements greater than 20% on repetitive nerve stimulation at 2 Hz</td>
</tr>
</tbody>
</table>

<sup>a</sup> With the exception of age, entrapments, and coexisting sensory polyneuropathy (see text).

**Table 5**

<table>
<thead>
<tr>
<th>Study</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Early</td>
</tr>
<tr>
<td><strong>Motor NCS</strong></td>
<td></td>
</tr>
<tr>
<td>CMAP amplitude</td>
<td>N or ↓</td>
</tr>
<tr>
<td>Conduction velocity</td>
<td>N</td>
</tr>
<tr>
<td>Distal latency</td>
<td>N</td>
</tr>
<tr>
<td><strong>Sensory NCS</strong></td>
<td></td>
</tr>
<tr>
<td>SNAP amplitude</td>
<td>N</td>
</tr>
<tr>
<td>Conduction velocity</td>
<td>N</td>
</tr>
<tr>
<td>H-reflex</td>
<td>N</td>
</tr>
</tbody>
</table>

**Abbreviations:** NCS = nerve conduction studies; N = normal; ↓/↑ = decreased/increased; one arrow = mild; two arrows = moderate.

The revised El Escorial criteria note that "features of LMN dysfunction in a particular muscle are defined by electromyographic concentric needle examination to provide evidence of active and chronic denervation including fibrillations and fasciculations." The revised criteria further delineate the signs of active denervation—fibrillation potentials and positive sharp waves, and of chronic denervation—large motor unit potentials, reduced recruitment, and unstable motor unit potentials (Table 6). As we have seen, nerve conduction studies are required to recognize peripheral neuropathy, mononeuropathy, and polyradiculopathy all of which could produce the NEE findings seen in ALS. Indeed these NEE signs are nonspecific, shared by "every subacute lesion of motor neurons or axons". It is the distribution of these acute and chronic signs in the patient with suspected ALS beyond the innervation territory of single nerve roots or peripheral nerves, or outside of a purely distal polyneuropathic pattern that raises the index of suspicion for the disease.

The revised El Escorial criteria describe the topography of active and chronic denervation required to support a diagnosis of ALS—that is, EMG signs of LMN dysfunction should be found in at least two of the four CNS regions (brainstem, cervical, thoracic, or lumbosacral) (Table 7). For the brainstem region to be involved, EMG signs may be found in one muscle (e.g., the tongue, facial or jaw muscle). For the thoracic spinal cord region to be considered positive, EMG signs must be found in either paraspinal muscles at or below T6 or in the abdominal muscles. (Because the thoracic region is rarely affected by spondylotic disease, the NEE of the thoracic paraspinal muscles is especially valuable electrodiagnostically; in fact it is deemed "strategic in the diagnosis of ALS" [34]. Findings of active and chronic denervation

<table>
<thead>
<tr>
<th>Electrophysiological sign</th>
<th>Description</th>
</tr>
</thead>
</table>
| Active denervation        | Fibrillation potentials  
                          Positive sharp waves |
| Chronic denervation       | Large MUPs: increased duration, amplitude, and phases/turns  
                          Reduced interference pattern (reduced recruitment) with firing rates >10 Hz (unless there is a significant UMN component when rates may be <10 Hz)  
                          Unstable MUPs |
| Fasciculation potentials  | Tend to be of long duration and polyphasic and almost always detectable |

LMN = lower motor neuron; MUP = motor unit potential.

in thoracic paraspinal muscles are strongly supportive of anterior horn cell involvement.) Finally, for the cervical and lumbosacral spinal cord regions to be deemed affected by the disease process, EMG signs must be demonstrated in two muscles innervated by different roots and peripheral nerves.

In the next few sections of this review, we explore the development of and rationale for these criteria and discuss further the abnormal electrophysiologic signs in ALS. Table 8 depicts the NEE changes at different stages of ALS.

Electrophysiologic diagnostic criteria: an historical perspective

There is a tension inherent in the diagnostic approach to the patient with suspected ALS. On one hand is the reluctance to make a diagnosis of an incurable disease unless there is a high level of certainty in the diagnosis

Table 7
Topography of active and chronic denervation in ALS: Signs of LMN dysfunction should be found in at least 2/4 regions to support diagnosis of ALS

<table>
<thead>
<tr>
<th>Region of CNS</th>
<th>Considered positive when</th>
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<tbody>
<tr>
<td>Brainstem</td>
<td>One muscle is involved (eg, tongue)</td>
</tr>
<tr>
<td>Thoracic spinal cord</td>
<td>Paraspinal muscles at or below T6 or abdominal muscles are involved</td>
</tr>
<tr>
<td>Cervical spinal cord</td>
<td>At least two muscles innervated by different roots and peripheral nerves are involved</td>
</tr>
<tr>
<td>Lumbosacral spinal cord</td>
<td>At least two muscles innervated by different roots and peripheral nerves are involved</td>
</tr>
</tbody>
</table>


Table 8
Needle electrode examination changes at different stages of ALS

<table>
<thead>
<tr>
<th>Stage</th>
<th>Study</th>
<th>Early</th>
<th>Clinically obvious</th>
<th>Advanced</th>
</tr>
</thead>
<tbody>
<tr>
<td>At rest</td>
<td>Fasciculations</td>
<td>N or +</td>
<td>N to ++</td>
<td>N to ++</td>
</tr>
<tr>
<td></td>
<td>Insertional PSWs</td>
<td>+ or ++</td>
<td>+ to +++</td>
<td>+ to +++</td>
</tr>
<tr>
<td></td>
<td>Fibrillations</td>
<td>N or +</td>
<td>+ to +++</td>
<td>+ to +++</td>
</tr>
<tr>
<td>MUPs</td>
<td>Recruitment</td>
<td>N or ↓</td>
<td>↓ or ↓↓</td>
<td>↓↓ or ↓↓</td>
</tr>
<tr>
<td></td>
<td>Duration</td>
<td>N or ↑</td>
<td>↑ or ↑↑</td>
<td>↑↑ or ↑↑</td>
</tr>
<tr>
<td></td>
<td>Amplitude</td>
<td>N</td>
<td>↑ or ↑↑</td>
<td>↑↑ or ↑↑</td>
</tr>
<tr>
<td></td>
<td>Complexity</td>
<td>N</td>
<td>+ or ++</td>
<td>+ or ++</td>
</tr>
</tbody>
</table>

MUPs = motor unit potentials; N = normal/none; ↓/↑ = decreased/increased; one arrow = mild; two arrows = moderate; three arrows = marked. + = mild; ++ = moderate; +++ = marked.

and every other condition that could in any way resemble ALS has been excluded. On the other hand, however, for several reasons there is the need to establish the diagnosis as expeditiously as possible. First, it is difficult to live with uncertainty; from the patient’s perspective, the unknown may be as stressful as the fact of diagnosis itself. Second, today patients may be treated with current and emerging therapies that might be most efficacious when instituted in the initial stages of the illness. Third, because in the initial phases of the disease nutritional status is good and neurological/respiratory function are still relatively well preserved, early diagnosis facilitates the enrollment of patients into increasingly available treatment trials [35].

The first topographic criteria for the diagnosis of ALS elaborated by Lambert and Mulder [16] were demanding. In an era without clinical trials or therapy for ALS there was little pressure to make the diagnosis early in the course of the illness; the overriding concern was to achieve diagnostic certainty and to rule out ALS-mimics. Lambert and Mulder [16] stipulated that the NEE findings comprise “fibrillation and fasciculation potentials in muscles of the lower as well as the upper extremities or in the extremities as well as the head.” Over the years it has become customary to consider the NEE component of the “Lambert criteria” satisfied if there are fibrillation potentials in at least three extremities or two extremities and cranial muscles (the head and neck considered an extremity) [26,36,37]. Table 9 lists the full “Lambert criteria” (including the requirements for nerve conduction studies discussed earlier) that have been used for the electrophysiologic assessment of the patient with suspected ALS for nearly 50 years [38].

In 1991 Behnia and Kelly [22] reviewed the role of electrodiagnostic testing in 133 patients with the clinical diagnosis of ALS and found that 30% of the patients did not fulfill the Lambert NEE criteria. Typically, these

<table>
<thead>
<tr>
<th>Table 9</th>
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<tr>
<td>Lambert criteria for the EMG diagnosis of ALS</td>
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<tr>
<td>Needle electrode examination criteria</td>
</tr>
<tr>
<td>Fibrillation and fasciculation potentials in muscles of the lower and the upper extremities, or in the extremities and the head</td>
</tr>
<tr>
<td>Reduction in number and increase in amplitude and duration of motor unit action potentials</td>
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EMG = electromyography.
patients were found to have active denervation in one or two limbs or the bulbar muscles but not elsewhere; the findings were at least indicative of focal motor neuron disease, but not a generalized denervating disorder. Yet 37% of these patients had evidence of widespread chronic denervation, suggesting the presence of a diffuse disease. The authors proposed accepting the presence of “enlarged, polyphasic motor unit potentials with reduced recruitment (chronic denervation) as evidence of denervation with compensatory reinnervation if conduction studies in these limbs were normal” [22]. With this modification of the Lambert criteria, the non-diagnostic rate was reduced from 38% to 27%.

In 1990, in El Escorial, Spain, electrophysiologic features required for the diagnosis of ALS were proposed (in the context of a broad array of clinical and laboratory criteria) to enhance clinical studies and therapeutic trials [7]. These features required that confirmation of the diagnosis of ALS “depends on finding electrophysiologic evidence of LMN degeneration in at least two muscles of different root or spinal nerve and different cranial or peripheral nerve innervation in two or more of the four regions.” Additionally, for each muscle examined there were NEE requirements to qualify for the diagnosis of definite, probable, or possible ALS. Wilbourn [38] later highlighted selected aspects of these criteria for reappraisal, including the alteration in motor unit potential firing pattern in the case of UMN involvement, the usefulness of detecting fasciculation potentials, and the requirements for the distribution of NEE abnormalities.

This brings us to the revised ALS criteria developed at Airlie House in 1998, described earlier in this review (see earlier discussion, Table 2). The consensus document was reviewed and posted on the World Federation of Neurology ALS web site and was recently published [6]. The diagnostic criteria take into consideration some of the criticisms alluded to above, and they also include a new level of diagnostic certainty not present in 1994: “probable ALS–laboratory supported.” For this level, NEE findings qualify as evidence of LMN involvement as we explain later.

This new level of diagnostic certainty derives from the experience of Ross and colleagues [35]. They were motivated to relax the 1994 El Escorial criteria for establishing the diagnosis of ALS so that patients might have the opportunity to participate in clinical trials (in this instance, ciliary neurotrophic factor) in the early phases of their illness. They noted that early diagnosis might not be possible if it required widespread UMN and LMN disease since the clinical manifestations of ALS are often focal in the early stages. They cited the work of Chaudhuri et al. [39] who observed that when clinical features were correlated with postmortem neuropathologic findings that 25% of ALS patients died of the illness without meeting El Escorial criteria for definite or probable ALS.

To facilitate early diagnosis, less restrictive criteria were created: UMN signs were required in at least one region, and EMG signs of LMN involvement (fibrillation potentials) in at least two limbs. The fibrillation potential
activity was supposed to be found in at least two muscles innervated by different peripheral nerves and nerve roots. In addition, the “Ross et al. criteria” incorporated neuroimaging, electrodiagnostic, and laboratory studies to further define ALS and exclude alternative diagnoses. All patients who met the criteria were given the diagnosis of ALS without further division into subcategories. Using these criteria, the diagnosis of ALS was made at a mean time of 9.7 months from onset of symptoms, which compared favorably with the 12-month period cited in the literature. At the end of the clinical trial, the authors believed that based on clinical grounds the diagnosis of ALS was accurate in every patient, but there was no pathological confirmation. Therefore, confidence in these criteria appeared to be justified and led to “probable ALS–laboratory supported” being added to the revised WFN criteria [40].

**Active denervation changes**

Active denervation changes, also known as pathological or abnormal spontaneous activity (Table 6)—fibrillation potentials and positive sharp waves—have long been regarded as the hallmark of acute neurogenic disease and their presence is essential for the diagnosis of ALS (Fig. 1). They are however nonspecific, found in necrotizing myopathic disorders and rarely in long-standing disease of the neuromuscular junction. In the context of the evaluation for suspected ALS, fibrillation potentials and positive sharp waves are reliable indicators of ongoing loss of the anterior horn cell, representing the spontaneous discharge of single muscle fibers that have lost their innervation [26]. Fig. 2 depicts the morphological correlate of acute denervation—the angulated atrophic muscle fiber. Insertional positive sharp waves are probably the earliest indicators of denervation [19]. Fibrillation potentials are short in duration (0.5–2.0 msec) and low in amplitude (50–150 μV) compared to motor unit potentials [13]. Lambert [16] noted that in ALS, fibrillation potentials are found in almost all muscles with less than normal strength but also in about 25% of clinically unaffected muscles. Troger and Dengler [33] observe that in the early stages of ALS, fibrillation potentials and positive sharp waves are often found focally and asymmetrically, generalizing as the disease progresses. They describe an especially high probability of finding fibrillation potentials and positive sharp waves in the tibialis anterior, first dorsal interosseous, abductor pollicis brevis, deltoid, and thoracic paraspinal muscles. Yet, the probability of finding pathologic spontaneous activity in the biceps brachii or vastus lateralis muscles was only 50%.

**Chronic denervation changes**

The revised criteria list three signs of chronic denervation (Table 6): large motor unit potentials, reduced interference pattern, and unstable motor unit potentials. We begin with a consideration of the pathophysiology underlying
the development of large, sometimes unstable motor units (so-called motor unit potential remodeling) followed by discussion of changes in interference pattern (or recruitment).

*Motor unit potential remodeling.* Early on in the course of the illness, or in patients with slowly progressive ALS, fibrillation potentials, and positive sharp waves may be “limited in number and scattered in distribution” [26]. In fact, up to one half of the anterior horn cells can be lost before prominent fibrillation potentials develop. This presumably relates to reinnervation [41]: the effect of collateral sprouts from surviving motor units making contacts with denervated muscle fibers before they begin to fibrillate [26].
This compensatory physiologic process, initiated by the loss of anterior horn cells, leads to enlarged motor unit potentials; the clinical correlate of this process is preserved muscle strength. This process continues until the capacity for terminal collateral sprouting has been exhausted [42]. Dengler [43] has shown in studies of the contraction force of the motor units in ALS that more than 50% of motor units can be compensated for by collateral sprouting. Presumably, as anterior horn cell loss continues beyond this point, the process of reinnervation by remaining motor neurons cannot keep up with denervation and muscle strength decreases [42].

The incorporation of previously denervated muscle fibers into an established motor unit may be referred to as motor unit remodeling [19]. The enlargement of surviving motor units is reflected in motor unit potentials of increased duration, increased amplitude and often an increased number of phases (four or more). This latter phenomenon (the development of polyphasic motor unit potentials) is secondary to the asynchrony of firing of new muscle fiber components belonging to the reinnervated motor unit and is an early finding in virtually all patients with ALS [26]. There are two reasons for this asynchronous activation [26,42]: first, because nerve conduction velocity will be slowed along immature sprouts that are incompletely myelinated; and

Fig. 2. Muscle biopsy showing early denervation. There are small groups of angulated, atrophic muscle fibers of both histochemical types. Type II fibers are darkly staining, and type I fibers are lightly staining. ATPase (pH 9.4) × 215 (before reduction). (Courtesy of TW Smith, MD, University of Massachusetts Medical Center; from Mitsumoto H, Chad DA, Pioro EP. Amyotrophic lateral sclerosis. Philadelphia: FA Davis; 1998. p. 122–33, with permission.)
second, because the conduction velocity of muscle action potentials will be slowed along the atrophic muscle fibers of the reinnervated motor unit.

Polyphasic motor unit potentials may also be low in amplitude. There are two scenarios in which one encounters these potentials in ALS: in the rapidly progressive form of the disease, and late in the course of the illness. In the first instance, there may be insufficient time for collateral reinnervation, and in the latter case, when there are few residual anterior horn cells, the remaining motor units may decompensate [42]. These low-amplitude, polyphasic, sometimes short duration ("spikey") potentials resemble the motor units seen in myopathic disorders, and in the company of fibrillation potentials might suggest a necrotizing myopathy, one form of which (inclusion body myositis) may simulate ALS (see later discussion).

Another phenomenon that results from reinnervation by an immature sprout is moment-to-moment variation in the appearance of a motor unit potential, also designated an unstable motor unit potential. There are two reasons for this EMG sign that results from the action potentials of certain muscle fibers coming in and out of the summated motor unit action potential: first, intermittent conduction block along an incompletely myelinated collateral sprout; second, inadequate release of acetylcholine at newly formed neuromuscular junctions. The presence of unstable motor unit potentials even after sufficient time (3 months) has elapsed for improvements in myelination and neuromuscular transmission is indicative of active disease and points to more rapidly progressive course [19,26]. Unstable motor unit potentials correlate with increased jitter and blocking measured in single fiber EMG studies. Jitter is the interval between action potentials of two repeatedly firing muscle fibers that belong to the same motor unit [19]. Increased jitter and blocking are electrophysiological manifestations of tenuous and failed neuromuscular transmission, respectively (Fig. 3).

When the disease is less aggressive (more slowly evolving), the collateral sprouts have the opportunity to mature, and reinnervated muscle fibers are able to regain their size. This leads to an increase in terminal nerve fiber conduction velocity and a more robust conduction velocity of muscle action potentials, respectively. As a result, there is greater synchrony of firing of individual muscle fiber components of the motor unit. With the reinnervated motor unit having gained more muscle fibers than it had originally, the result is an increase in both its amplitude and duration. As expected, fiber density, or the packing density of muscle fibers, assessed by single fiber EMG and measuring the number of muscle fibers innervated by one anterior horn cell increases because of collateral sprouting [44]. When studied longitudinally, fiber density was significantly increased in those patients with longer survival, suggesting that the capability for greater collateral sprouting is associated with better prognosis [32]. In advanced cases, decline in fiber density has been noted, possibly reflecting decompensation of the reinnervation process in the later phases of ALS [26].
Altered interference pattern (changes in recruitment). Normal recruitment refers to the orderly activation of more motor units as the effort and firing rate of individual units increases [26]. Recruitment frequency, or firing rate, is “the frequency of firing of a unit when the next unit is recruited or begins to discharge” [45]. This rate is typically 5–15 Hz for motor units in a normal muscle during mild contraction. The progressive loss of anterior horn cells during the course of ALS leads to a reduction in the number of motor units that may be activated during voluntary muscle contraction (reduced recruitment) along with an increase in firing rate of surviving motor unit potentials (Fig. 4). As the disease progresses, the NEE of weakened muscles might disclose a marked decrease in motor unit potential number with an considerable increase in firing rate; in advanced cases, two or three motor units firing at frequencies of 20 Hz [26].

Another description of the alteration in motor unit potential firing pattern in ALS, and one used in the El Escorial criteria [6], is “reduced interference pattern,” which has the same significance as reduced recruitment [46]. It indicates that some of the individual motor unit potentials can be clearly identified from the electrical activity recorded during full voluntary effort.
In contrast, the description “full interference pattern” refers to the electrical pattern in normal muscle wherein no individual motor unit potential can be clearly identified because there has been no drop out in motor units.

If the only target of the disease process in ALS were the anterior horn cell, then motor unit potential firing might be reliably described as “reduced interference pattern with firing rates higher than 10 Hz” as noted in Table 6. The normal basal firing rate is 5–10 Hz and if firing exceeds this window, it indicates a drop out of motor units. By definition, however, “ALS has an
UMN component that causes both a reduction in number of motor unit potentials because fewer units can be recruited, but also a reduction in the firing frequency of those motor units that can be activated’’ [38]. Wilbourn points out that in the setting of both UMN and LMN pathology, the UMN component dictates the motor unit potential firing pattern. Accordingly, the revised criteria (Table 6) stipulate that “firing rate may be lower than 10 Hz if there is a significant UMN component.”

**Fasciculation potentials**

Fasciculation potentials are spontaneous, irregularly discharging motor unit potentials that are often associated with a visible muscle twitch [19]. (In the clinical context, they are found in nearly all ALS patients, but are an uncommon presenting manifestation.) Except for motor neuropathy and amyloid polyneuropathy, diffuse fasciculation potential activity is strongly suggestive of disordered function of the motor neuron cell body [47]. In fact Lambert [17] observed that “fasciculations occur so regularly in ALS that one rarely accepts the diagnosis unless fasciculations are demonstrated.” Fasciculation potentials also occur in otherwise healthy individuals, as so-called “benign fasciculations.” Benign fasciculations are an isolated NEE finding without accompanying fibrillation potential activity, enlarged or unstable motor unit potentials; and clinically, weakness and wasting are conspicuously absent.

Fasciculation potentials in ALS are typically more complex and less stable than similar discharges in healthy individuals (Fig. 1) [48,49]. It is likely that these potentials become enlarged in the process of denervation and reinnervation, as described in the discussion of chronic denervation (see earlier discussion in this article). The origin of fasciculation potentials has been debated, but they can probably arise from the anterior horn cell, nerve trunk, and distal nerve terminals [5,49]. It is possible that they arise in the more proximal portion of the motor unit early in the disease and in more distal motor axons in the later stages [48,49].

**Differential diagnostic highlights**

We turn now to some of the disorders, and their electrophysiological signatures, that tend to come up for consideration with some regularity in the differential diagnosis of ALS [5].

**Spondylotic myelopathy**

Spondylotic myelopathy may lead to spinal cord compression with or without nerve root compromise. Neck pain is a common but not invariable clinical feature. Some patients with myelopathy develop UMN signs in the legs and if there is coexisting central gray matter or nerve root involvement
or both a subset of patients may have additional LMN signs in the arms, simulating ALS. In fact, in the experience of the Eleanor and Lou Gehrig Center at the New York Institute, Rowland reports that 5% of patients with ALS have had cervical (or lumbar) laminectomies early in their course [47]. Although the NEE may disclose active and chronic denervation in both arms in cervical spondylosis (and the legs if there is coexisting lumbosacral spondylosis disease), the NEE of bulbar and thoracic paraspinal muscles should be normal, in contrast to the frequent abnormal NEE findings in ALS.

The presence of lower and upper extremity proprioceptive loss and sphincter abnormalities often accompanies the clinical picture of motor weakness in spondylotic myelopathy, however, and suggest a structural abnormality of the cervical spine. Neuroimaging of the cervical cord is necessary to help establish the diagnosis.

**Bulbospinal neuronopathy**

Bulbospinal neuronopathy or Kennedy’s syndrome is an X-linked disorder that results in slowly progressive, symmetric, bulbar and proximal limb muscle weakness, cramps and atrophy without UMN features. Fasciculations are prominent in perioral facial muscles and the tongue. Deep tendon reflexes are depressed or absent. In more than 50% of patients, there are signs of partial androgen deficiency like gynecomastia and infertility. The creatine kinase is typically elevated to a higher degree than would be seen in a purely denervating disorder. The NEE shows evidence of a LMN disorder (active and chronic denervation) but the sensory evoked potentials are reduced or even absent suggesting involvement of sensory axons or dorsal root ganglia neurons [50], a finding that raises serious questions about the validity of the diagnosis of ALS. The diagnosis may be established definitively by genetic testing, demonstrating an expansion of the cytosine-adenine-guanine trinucleotide repeat within the translated portion of the androgen receptor gene.

**Benign monomelic amyotrophy**

Benign monomelic amyotrophy is a sporadic disorder that presents with focal weakness involving a single limb and affects men five times more frequently than women. The age of onset is between 15 and 30 years and most of the patients described have been from Japan and India. Most often, weakness begins in the hand intrinsic muscles and then spreads centripetally for 1 to 2 years to involve the forearm flexors and extensors. After this slow progression the condition usually stabilizes. Deep tendon reflexes are usually normal or reduced. UMN signs and bulbar involvement are not encountered. The electrophysiologic findings parallel the clinical signs in revealing evidence for a restricted LMN disorder. Routine nerve conduction studies are generally normal except for the presence of low motor amplitudes when recording from atrophic hand muscles. Modest reductions in sensory potentials are found in 30% of cases. The NEE reveals fibrillation potentials and
positive sharp waves in less than half the patients, whereas recruitment is invariably reduced in a pattern corresponding to areas of weakness and atrophy [51]. The NEE of muscles in the limb that appears to be uninvolved typically discloses features of chronic denervation, suggesting more widespread LMN disease than is apparent clinically. Magnetic resonance imaging (MRI) of the cervical spine may disclose focal atrophy of the spinal cord.

Multifocal motor neuropathy with conduction block

Multifocal motor neuropathy with conduction block (MMNCB) is arguably the most important condition in the differential diagnosis of ALS [47]. This is because it “can simulate ALS clinically but differs because it is responsive to immunotherapy” [47]. The disorder affects men primarily at a relatively young age (<45 years) and usually presents as slowly progressive, painless, remarkably focal weakness and amyotrophy involving the small hand muscles [24,25]. Weakness begins typically unilaterally, progresses for a number of years, and then appears in the contralateral limb. Clinical deficits correspond to individual peripheral nerves and remain restricted in their anatomic distribution for years. The examination discloses marked atrophy of the intrinsic hand and forearm muscles; the humeral and shoulder girdle muscles are less frequently affected. Lower extremity weakness is infrequent and cranial nerve involvement is rare. Fasciculations and cramps are common. Deep tendon reflexes may be attenuated, especially in weak limbs, but occasionally they are normally active or unexpectedly brisk for the degree of muscle atrophy and weakness. Most remarkable is the preservation of sensation, even in regions where muscles are markedly atrophic. Diagnosis rests on the findings from electrophysiologic study that show evidence of a LMN disorder, but in contrast to ALS, the defining abnormality is partial conduction block (Fig. 5) along focal segments of motor fibers in regions not usually susceptible to compression [52]. Additional features of multifocal motor demyelination are also found including temporal dispersion, segmentally reduced motor nerve conduction velocity, prolonged distal motor latency, and prolonged F-wave latency. In some series, conduction block per se is found only in 30% of patients, but virtually all patients have nerve conduction study evidence for demyelination [53]. Fifty to sixty percent of patients have high titers of antibody reacting with the GM1 ganglioside, whereas in the vast majority of patients with ALS this autoantibody is either not detected or is present in low titer. As noted, the condition is responsive to immunotherapy including cyclophosphamide and intravenous gamma globulin.

Diseases of the neuromuscular junction

When myasthenia gravis presents with dysarthria, dysphagia, drooling, and head drop with no ocular symptoms or signs it may simulate bulbar onset ALS. When Lambert-Eaton myasthenic syndrome (LEMS) presents with limb girdle weakness and fatigability, it may suggest ALS with a
LMN onset. These diseases of the neuromuscular junction have well known abnormal serological test results (acetylcholine receptor antibody positivity and voltage-gated calcium channel antibody positivity for myasthenia gravis and LEMS, respectively) and characteristic electrophysiologic findings that help make the distinction from ALS. In myasthenia gravis there is typically a decremental motor response of >10% as well as an increase in jitter between two muscle fibers innervated by the same motor unit. Although these findings may be encountered in weakened muscles of patients with ALS, electrophysiologic evidence for LMN degeneration is lacking in myasthenia gravis. In LEMS, the diagnostic finding is very low initial motor evoked responses that increase by more than 200% after a brief (15-second) period of exercise. Although initial motor evoked responses are also low in ALS, the post-activation facilitation response does not occur.

**Inclusion body myositis**

Inclusion body myositis (IBM) is an inflammatory myopathy most often seen in older men. It tends to present in an asymmetric, patchy fashion with a predilection for weakness and atrophy of the forearm flexors, triceps,
biceps, and quadriceps. It may resemble a limb onset LMN form of ALS [54]. The CK is typically elevated to a modest degree and the muscle biopsy is diagnostic. The electrophysiologic findings usually suggest a necrotizing myopathy (evidence for active denervation with early recruited low-amplitude, short duration, polyphasic motor unit potentials), but when IBM is in its later discussion phases, the NEE may show motor unit potentials and recruitment characteristics of chronic denervation, features seen in the context of ALS. Complicating the diagnostic process is the NEE finding of fasciculation potentials in some patients with IBM [54].

Helping to make the distinction between ALS and IBM are specific clinical features in the latter disorder, especially early weakness of finger flexors, weakness of the quadriceps, slow progression, lack of UMN signs, and rarity of clinically visible fasciculations. Quantitative electromyography may provide evidence for a myopathic disorder even when routine NEE does not show a myogenic disorder [54]. A muscle biopsy should be obtained in circumstances that are diagnostically ambiguous looking for evidence of an inflammatory myopathy with rimmed vacuoles, the morphological hallmark of IBM.

Overview of the electrodiagnostic approach to the patient with suspected ALS

As we have seen, the electrodiagnostic study is important for several reasons, most notably to confirm the diagnosis and to exclude diseases of the peripheral nervous system that might mimic some clinical aspect of ALS. The study also assists in defining the severity, rate of progression, and prognosis of ALS [19,26]. In this concluding section of the review we summarize the parts of the electrophysiologic study most often employed in the evaluation of the patient.

We typically begin with sensory conduction studies—median, ulnar, radial, sural, and superficial peroneal—evaluating sensory amplitudes, distal latencies, and conduction velocities, ensuring maintenance of skin temperature at (33°C hand; 30°C foot) a challenge in the patient with thin, atrophic limbs [36]. As already described, the expectation is for essentially normal sensory evoked responses, distal latencies, and conduction velocities (Table 4) until the advanced stages of the disease (Table 5). Although a disorder of peripheral nerves might well co-exist with ALS (most commonly focal nerve entrapments), significant and generalized abnormalities must increase the index of suspicion for a peripheral neuropathy or neuronopathy and cast doubt on the diagnosis of ALS. In the face of such sensory abnormalities, we raise our diagnostic antennae to detect a peripheral neuropathy (specifically chronic inflammatory demyelinating polyneuropathy) during the remainder of the study.
The next step is to evaluate *motor conduction parameters* (amplitudes, distal latencies, conduction velocities, and F-wave latencies) for upper and lower extremity nerves comprising the median, ulnar, peroneal, and posterior tibial (Table 4). A critically important task is to look for partial motor conduction block and other electrophysiologic signatures for acquired demyelination, such as one might encounter in multifocal motor neuropathy with conduction block. Although reductions in motor amplitudes are expected as the disease progresses, low CMAPs in a widespread distribution especially in the early stages of the disease, coupled with essentially normal sensory studies should suggest several possibilities [13,19]. First, we consider Lambert-Eaton myasthenic syndrome, a diagnosis that may be corroborated by showing post-exercise facilitation of evoked motor responses. Second is the possibility of severe polyradiculopathy (in the setting of combined cervical and lumbar spinal stenosis with root involvement), which typically spares thoracic roots and lead to an essentially normal NEE of paraspinal or abdominal muscles. The third possibility is a severe myopathy whose NEE signature is abnormal in affected limb and paraspinal muscles (early recruitment of short duration, low amplitude polyphasic motor unit potentials) but is typically normal in bulbar muscles.

We then turn to the NEE taking care to evaluate muscles in the most clinically involved limb first, testing proximal and distal muscles innervated by different nerve roots and peripheral nerves [26]. A region is considered involved when reduced recruitment, large motor unit potentials, and fibrillation potentials are found in one muscle (for the bulbar or thoracic regions) or two limb muscles with different innervation (for the cervical and lumbo-sacral regions) (Table 7). From the most involved limb we move to other limb or thoracic paraspinal muscles reserving the bulbar region for last (because it is more difficult to evaluate and interpret) and typically necessary only if the diagnosis cannot be supported from the findings referable to non-bulbar regions.

For the upper extremity examination, suggested muscles include [19] the first dorsal interosseus, abductor pollicis brevis, extensor pollicis indicis (C8/T1 roots; ulnar, median, radial nerves, respectively); flexor pollicis longus, pronator teres (C7 root; median nerve); biceps (C5/C6 roots; musculocutaneous nerve); triceps (C6/C7/C8; radial nerve); and low cervical paraspinals (C6/C7/C8/T1 roots). In the lower extremity, suggested muscles include the extensor digitorum brevis, (L5 root; peroneal nerve); abductor hallucis, gastrocnemius (S1 root; tibial nerve); tibialis anterior, flexor digitorum longus (L4/L5 roots; peroneal and tibial nerves, respectively); vastus later discussionalis (L2/L3/L4 roots; femoral nerve); gluteus medius (L5 roots; superior gluteal nerve); and high sacral paraspinals (L4/L5/S1 roots). For the bulbar region suitable muscle selections include the tongue (cranial nerve XII), frontalis and orbicularis oculi muscles (cranial nerve VII); and the masseter (cranial nerve V). The thoracic region is best evaluated by examination of thoracic paraspinal muscles. To support the diagnosis of
ALS, signs of LMN dysfunction should be found in at least two of four regions (Table 7).

References

Electrodiagnostic approach to the patient with suspected neuromuscular junction disorder

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The neuromuscular junction (NMJ) is the anatomical site affected by myasthenia gravis (MG), Lambert-Eaton myasthenic syndrome (LEMS), botulism, and congenital myasthenic syndromes [1]. The NMJ is designed for rapid translation of the electrical impulse of the nerve to the muscle using the chemical acetylcholine (Ach). The NMJ is a specialized structure consisting of the motor nerve terminal, the post-synaptic muscle surface, a specialized basal lamina, and an associated Schwann cell. Depolarization of the nerve plasma membrane leads to opening of primarily P/Q-type voltage-gated calcium channels (VGCCs), which initiates a complex machinery of synaptic proteins that ultimately leads to fusion of synaptic vesicles with the nerve terminal’s plasma membrane. Each synaptic vesicle releases from 5,000 to 10,000 Ach molecules into the synaptic cleft with an action potential triggering the release of 50 to 300 vesicles. The release sites lie in direct opposition to the tops of the secondary synaptic folds of the postsynaptic muscle membrane, which have high concentrations of AchRs. The concentration of AchRs in the end plate region is 1000-fold higher than other muscle membrane regions. Skeletal muscle sodium channels are concentrated at the depths of the synaptic folds. In the basal lamina of the synaptic cleft, acetylcholinesterase (AchE) is anchored. AchE hydrolyzes most of the...
Ach and prevents repeated binding of Ach to the AchR. Consequently, AchRs are normally activated only once in response to Ach released by a nerve terminal action potential. Inactivation of AchE prolongs the duration of action of Ach and slows the decay of the end plate current.

The electrodiagnostic (EDX) examination in patients with suspected NMJ disorder constitutes the most advanced and complex type of EDX studies. Understanding the anatomy and physiology of neuromuscular transmission is prerequisite for the comprehension and planning of EDX studies in patients with suspected NMJ disorders. In addition to routine nerve conduction studies and conventional needle electromyography (EMG), the EDX studies that are most useful in the diagnosis of NMJ disorders include repetitive nerve stimulation (RNS) and single fiber EMG.

Repetitive nerve stimulation

Basic concepts

The understanding of RNS depends on a few important concepts inherent to the NMJ that dictate the type and frequency of RNS utilized in the accurate diagnosis of NMJ disorders:

- **Quantum.** A quantum is the amount of Ach packaged in a single vesicle. Each quantum (vesicle) released results in an approximate 1 mV change of postsynaptic membrane potential. This occurs spontaneously during rest and forms the basis of the miniature end plate potential (MEPP).

- The number of quanta released after a nerve action potential depends on the number of quanta in the *immediately available (primary) store* and the probability of release, that is, \( m = P \times n \), where \( m \) = the number of quanta released during each action potential, \( P \) = the probability of release (effectively proportional to the concentration of calcium and typically about 0.2, or 20%), and \( n \) = the number of quanta in the immediately available store. In normal conditions, the number of quanta released after a single nerve action potential is about 60 vesicles. A single nerve action potential triggers the release of 50–300 vesicles (quanta) with an average equivalent to about 60 quanta (60 vesicles).

- **End plate potential (EPP).** EPP is the potential generated at the postsynaptic membrane following a nerve action potential and neuromuscular transmission. Since each vesicle (quantum) released causes a 1 mV change in the postsynaptic membrane potential, this results in about 60 mV change in the amplitude of the membrane potential.

- **Safety factor.** The safety factor of neuromuscular transmission is simply defined as the difference between the EPP and the threshold potential for initiating an action potential. As long as the threshold potential is achieved, the action potential initiates muscle contraction. In normal conditions, the number of quanta (vesicles) released at the NMJ at
the presynaptic terminal (about 60 vesicles) far exceeds the postsynaptic membrane potential change required to reach the threshold needed to generate a postsynaptic muscle action potential (7 to 20 mV). Hence, a nerve action potential results in an EPP that always reaches threshold and results in an all-or-none muscle fiber action potential (MFAP) [2]. Also, the safety factor prevents NMJ failure despite repetitive action potentials. Several factors contribute to the safety factor. Quantal release, AchR conduction properties, AchR density, and AchE activity contribute to the EPP [1]. Postsynaptic folds form a high resistance pathway that focuses end plate current flow on voltage-gated sodium channels concentrated in the depths of the folds. Both these factors reduce the action potential threshold at the end plate and serve to increase the safety factor. Human junctions are smaller and with more extensive folding than other mammals, suggesting an evolutionary pressure towards postsynaptic modifications to enhance safety factor. All disorders of neuromuscular transmission are characterized by a compromise of the safety factor [1].

- **Calcium influx.** Following depolarization of the presynaptic terminal, VGCCs open leading to calcium influx. Through a calcium-dependent intracellular cascade, vesicles are docked into active release sites (called active zones), and releases their Ach molecules. Then, calcium diffuses slowly out of the presynaptic terminal in 100–200 msec. In RNS, the rate at which motor nerves are stimulated dictates whether calcium plays a role in enhancing the release of Ach or not. At slow rate of RNS (more than every 200 msec, or a stimulation rate of <5 Hz), calcium role in Ach release is not enhanced and subsequent nerve action potentials reach the nerve terminal long after calcium has dispersed. In contrast, with rapid RNS (more than every 100 msec, or stimulation rate >10 Hz), calcium influx is greatly enhanced and the probability of release of Ach quanta increases.

- **Acetylcholine storage.** An immediately available (primary) store of Ach is placed beneath the pre-synaptic nerve terminal membrane. A secondary (or mobilization) store is located toward the axon and starts to replenish the immediately available store after 1–2 seconds of repetitive nerve action potentials. A large tertiary (or reserve) store is also available in the axon and cell body [3].

- The compound muscle action potential (CMAP) is the summation of all MFAPs generated in a muscle following supramaximal stimulation of all motor axons while recording via surface electrode placed over the belly of a muscle.

**Technical aspects**

The techniques of RNS should be mastered by electromyographers and technologists to avoid false positive and false negative results, which may
lead to erroneous diagnoses or may miss diagnoses of NMJ disorders. Limb
temperature should be maintained at around 33°C, because a CMAP decre-
ment may be masked in a cool limb. The limb tested should be immobilized
as best as possible. Patients on AchE inhibitors (such as pyridostigmine)
should be asked to withhold their medication for 12–24 hours before
RNS, if medically not contraindicated.

RNS often follows a routine motor nerve conduction study (NCS). A
good grasp of the techniques of the various motor NCSs is an essential
prerequisite to a reliable RNS [3,4]. The stimulator should be as close as
possible to the nerve and should not move during RNS. A supramaximal
stimulation is secured by delivering a stimulus intensity of 10–20% above
the intensity level needed for a maximal response. Long duration and
unnecessary high intensity stimuli should be avoided since they are painful
and may result in movement artifact. The stimulus rate and number of
stimuli are dictated by the clinical problem and the working diagnosis
(see below).

**Slow repetitive nerve stimulation**

After establishing a supramaximal CMAP, slow RNS is usually per-
formed by applying 3–5 stimuli to a mixed or motor nerve at a rate of 2–3
Hz. This rate is low enough to prevent calcium accumulation, but high
enough to deplete the quanta in the immediately available store before the
mobilization store starts to replenish it. A total of 3–5 stimuli are adequate
since the maximal decrease in Ach release occur after the first four stimuli.
Exceeding 9–10 stimuli does not add any diagnostic benefit and is painful.
Stimulation at rest may be repeated after an interval of one minute to con-
firm a normal or abnormal response. If there is a reproducible decrement
(≥10%), slow RNS should be repeated after the patient exercises for 10 sec-
onds to demonstrate repair of the decrement (“post-exercise facilitation”). If
there is no decrement or an equivocal decrement (≤10% decrement) with slow
RNS at rest, the patient should perform maximal voluntary exercise for
1 minute (exercise for 30 seconds, rest for 5 seconds and exercise for another
30 seconds). Then, slow RNS should be done immediately and at 1, 2, 3, 4,
and 5 minutes after exercise. Since the amount of Ach released with each sti-
minus is at its minimum 2 to 5 minutes after exercise, slow RNS after exercise
provides a higher chance in detecting a defect of transmission at the NMJ by
demonstrating a worsening CMAP decrement (“postexercise exhaustion”).

The choice of nerve to be stimulated and muscle to be recorded from
depends on the patient’s manifestations. Most useful nerves for slow RNS
are the median, ulnar, and spinal accessory nerves recoding abductor pollicis
brevis, abductor digiti minimi, and upper trapezius respectively [3,4]. The
median and ulnar nerves are easily immobilized during RNS, and the stimu-
lations are well tolerated and are accompanied by minimal movement arti-
facts. However, the recording muscles are distal and may be spared in some
NMJ disorders (such as MG). RNS of the spinal accessory nerve is the most popular RNS of a proximal nerve. It is the least painful and subject to little movement artifact compared to other proximal nerves such as the musculocutaneous or axillary nerves, recording the biceps and deltoid muscles respectively. Facial nerve RNS is indicated in patients with bulbar and ocular weakness when other RNS are normal or equivocal. However, the facial CMAP is low in amplitude and often plagued by large stimulation artifacts. This renders measurements of CMAPs and decrement difficult and subject to error.

Calculation of the decrement with slow RNS, requires comparing the baseline (first) CMAP amplitude to the lowest CMAP amplitude (usually the third or fourth) \([3,5]\). By the fifth or sixth response, the CMAP decrement plateaus or begins to improve, due to the mobilization store resupplying the immediately available store. The CMAP decrement is expressed as a percentage and calculated as follows:

\[
\text{% Decrement} = \frac{\text{Amplitude(1st response)} - \text{Amplitude(3rd/4th response)}}{\text{Amplitude(1st response)}} \times 100
\]

For example, if the first CMAP amplitude is 10 mV and the fourth CMAP is the lowest and is 8 mV in amplitude, the decrement is

\[
\frac{10 - 8}{10} \times 100 = 20\%
\]

In normal conditions, slow RNS does not abolish any MFAPs, because neuromuscular transmission at all fibers remains above threshold due to the safety factor (Fig. 1). Although the second to fifth EPPs fall in amplitude, they remain above threshold (due to the normal safety factor), and ensure generation of MFAPs with each stimulation \([4]\). In addition, the secondary store begins to replace the depleted quanta after the first few seconds with a subsequent rise in the EPP. Thus, with slow RNS, all muscle fibers generate MFAPs, and the CMAP does not change.

In postsynaptic NMJ disorders (such as MG), the safety factor is reduced because there are fewer Ach receptors resulting in less binding of Ach. Hence, the baseline EPP is reduced but usually still above threshold. Slow RNS results in the loss of EPPs at many end plates, and as EPPs become subthreshold, there is a decline in the number of MFAPs, leading to a decline in the CMAP (decrement) \([4,6,7]\).

In presynaptic NMJ disorders (such as LEMS), the baseline EPP is low, with many end plates often not reaching threshold. Hence, many muscle fibers do not fire, resulting in a low amplitude baseline CMAP. With slow RNS, there is further CMAP decrement, due to the further decline of Ach
release with the subsequent stimuli, resulting in further loss of many EPPs and MFAPs [4].

**Rapid repetitive nerve stimulation**

Rapid RNS is most useful in patients with suspected presynaptic NMJ disorders such as LEMS or botulism. The optimal frequency is 20–50 Hz for 2–10 seconds. A typical rapid RNS applies 200 stimuli at a rate of 50 Hz (i.e., 50 Hz for 4 seconds). Calculation of CMAP increment after rapid RNS is as follows:

$$\% \text{ Increment} = \frac{\text{Amplitude (highest response)} - \text{Amplitude (1st response)}}{\text{Amplitude (1st response)}} \times 100$$
For example, if the first CMAP amplitude was 4 mV and the highest was 10 mV, then the increment is:

\[
\frac{10 - 4}{4} \times 100 = 250\%
\]

A brief (10-second) period of maximal voluntary isometric exercise has the same effect as rapid RNS at 20–50 Hz, is much less painful, and can substitute for rapid RNS in cooperative subjects. Hence, a single supramaximal stimulus is applied to generate a baseline CMAP. Then, the patient performs a 10-second maximal isometric voluntary contraction that is followed by another stimulus and a post-exercise CMAP. In patients who could not exercise (e.g., infants, comatose patients, patients with severe weakness), rapid RNS are necessary. Calculation of CMAP increment after a brief (10-second) voluntary contraction is similar to the calculation of the increment following rapid RNS, as follows:

\[
\% \text{Increment} = \frac{\text{Amplitude of postexercise response}}{\text{Amplitude of preexercise response}} \times 100
\]

For example, if the baseline (pre-exercise) CMAP is 5 mV and the post-exercise CMAP is 15 mV, then the increment is:

\[
\frac{15 - 5}{5} \times 100 = 200\%
\]

With rapid RNS or postexercise CMAP evaluation, there are two competing forces that are acting on the nerve terminal:

1. Stimulation tends to deplete the pool of readily-releasable synaptic vesicles. This depletion effect reduces transmitter release by reduction of the number of vesicles that are released in response to a nerve terminal action potential.
2. Repeated stimulation however, causes calcium to accumulate within the nerve terminal, thereby increasing the probability of synaptic vesicle release.

In a normal nerve terminal, the effect of depletion of readily releasable synaptic vesicles predominates, so that with rapid RNS, the number of vesicles released decreases; however, the EPP does not fall below threshold due to the safety factor [4]. Hence, the supramaximal stimulus generate MFAPs at all end plates and no decrement of CMAP amplitude occurs (Fig. 2). In fact, rapid RNS or a brief (10-second) exercise in normal subjects often leads to a slight physiological increment of the CMAP which does not
Exceed 25% to 40% of the baseline CMAP. This is likely caused by increased synchrony of MFAPs following tetanic stimulation ("post-tetanic pseudofacilitation").

In a presynaptic disorder (such as LEMS), very few vesicles are released so that depletion of vesicles is not a prominent effect. Thus, the baseline CMAPs obtained during routine motor NCSs are low in amplitude since many muscle fibers do not reach threshold due to inadequate release of quanta (vesicles) after a single stimulus. With rapid RNS, the local calcium concentrations in the nerve terminal can rise high enough to stimulate synaptic vesicle fusion for a sufficient number of synaptic vesicles to result in an EPP capable of action potential generation [1,9]. This leads to many muscle fibers reaching threshold required for the generation of MFAPs. Thus, more MFAPs are generated and hence the increment of the CMAP. The increment in LEMS is often higher than 200% [8,10], and is about 30–100% in patients with botulism [11,12,14,26].

In a postsynaptic disorder (such as MG), rapid RNS causes no change of CMAP because the depleted stores are compensated by the calcium influx.
In severe postsynaptic blockade (such as during myasthenic crisis), the increased quantal release cannot compensate for the marked NMJ block resulting in a drop in EPP amplitude. Hence, fewer MFAPs are generated along with an associated CMAP decrement.

**Nerve conduction studies**

Sensory NCSs are normal in all NMJ disorders. Motor NCSs are usually normal in postsynaptic disorders due to the intact safety factor. After a single stimulus, and despite Ach receptors blockade, EPPs reach threshold and generate MFAPs in all fibers, which results in normal CMAP. Occasionally, such as during myasthenic crisis, the CMAPs may be borderline, particularly recording proximal muscles, due to severe postsynaptic neuromuscular blockade. In presynaptic disorders, motor NCSs often show low CMAP amplitudes with normal distal latencies, conduction velocities, and F-wave minimal latencies. The CMAP amplitude (and area) is low because the baseline EPP is low, often not reaching threshold, and many muscle fibers do not fire.

**Needle electromyography**

Conventional needle EMG is usually normal in NMJ disorders. However, three non-specific changes, that are often observed in other neuromuscular disorders such active myopathies or neurogenic disorders, may be associated with severe NMJ disorders.

1. **Short duration, low amplitude, and polyphasic motor unit action potentials (MUAPs).** These are similar to the MUAPs seen in myopathies, and are seen primarily in proximal muscles. Such MUAPs are caused by physiological blocking and slowing of neuromuscular transmission at many end plates during voluntary activation. This leads to exclusion of many MFAPs from the MUAP (hence the short duration and low amplitude) and delay of neuromuscular transmission of other fibers (hence the polyphasia).

2. **Moment to moment variation of unstable MUAPs.** In healthy individuals, MUAPs are stable with little, if any, variation in amplitude and configuration [5]. However, in NMJ disorders, individual MUAP amplitude can vary significantly during activation (Fig. 3). Care should be taken not to record from more than a single MUAP at a time, since MUAP overlap may lead to an erroneous assumption of moment-to-moment variation.

3. **Fibrillation potentials.** These potentials are rarely seen in MG or botulism [13,14]. They are usually inconspicuous and present mostly in proximal muscles. Their presence should raise the suspicion of an alternate diagnosis or associated illness. The mechanism of fibrillation potentials in NMJ disorders is likely persistent transmission block, resulting in “effective” denervation of individual muscle fibers.
Single fiber electromyography

Technical aspects

Single fiber EMG (SFEMG) is the selective recording of a small number of MFAPs (usually two or three) innervated by a single motor unit [15,16]. SFEMG recording requires the following:

1. A concentric single fiber needle electrode with a small recording surface (25 µm) to restricts the number of recordable MFAPs and results in an effective recording area of 300 m² (as compared with a concentric conventional needle electrode that records from approximately 1 cm³).
2. A 500 Hz low frequency filter to attenuate signals from distant fibers (more than 500 µm from the electrode).
3. An amplitude threshold trigger and delay line to allow recording from a single MFAP by triggering on it on a screen with a delay line capability.
4. A computerized equipment with an ability to calculate individual and mean interpotential intervals (IPIs) and jitters (see below).

SFEMG is performed by inserting single fiber concentric needle into a muscle. Filter settings should be set at 500 Hz for the high pass filter, and 10–20 kHz for the low pass filter [3,4]. Selected single MFAPs should have a rise time of 300 seconds and a preferable peak-to-peak amplitude of 200 V or more.

Voluntary single fiber electromyography

Voluntary (conventional or recruitment) SFEMG is the most commonly used method for activating motor units: the patient activates and maintains...
the firing rate of the motor unit. This technique is not possible if the patient cannot cooperate (e.g., child, dementia, coma, severe weakness), and is difficult if the patient is unable to maintain a constant firing rate (e.g., tremor, dystonia, spasticity). With minimal voluntary activation, the needle is positioned until two muscle potentials (a pair) from a single motor unit are recognized. When a muscle fiber pair is identified, one fiber triggers the oscilloscope (triggering potential) and the second precedes or follows the first (slave potential). With voluntary activation, fifty consecutive discharges of a single pair is recorded. The interpotential interval (IPI) of the pair is then measured and a mean consecutive difference (MCD or jitter) of that pair is calculated as follows:

\[
\text{MCD} = \frac{(\text{IPI}_1 - \text{IPI}_2) + (\text{IPI}_2 - \text{IPI}_3) + \ldots + (\text{IPI}_N - 1 - \text{IPI}_N)}{N - 1}
\]

wherein \(\text{IPI}_1\) is the interpotential interval of the first discharge, \(\text{IPI}_2\) of the second discharge, and so forth, and \(N\) is the number of discharges recorded. Finally, after analyzing twenty muscle fiber pairs, a mean jitter (MCD) is reported.

**Neuromuscular jitter** is defined as the random variability of the time interval between two MFAPs innervated by the same motor unit. In normal subjects, there is a slight variability in the amount of acetylcholine released at the synaptic junction from one moment to another. Though, a nerve action potential will result in a MFAP at all times, the rise of EPP is variable, resulting in a small variation of the muscle pair’s IPI (Fig. 4). The diagnostic yield of jitter analysis is increased by examining affected muscle(s) performed by an experienced electromyographer on a fully cooperative patient. Though SFEMG may be done on any muscle, the most desired muscles are the extensor digitorum communis, frontalis and orbicularis oculi [4,16]. These muscles are ideal since most patients are able to control and sustain their voluntary activity to a minimum for a long period. Normal values for jitter differ between muscles, and tend to increase with age (Table 1) [17].

**Neuromuscular blocking** is defined as the intermittent failure of transmission of one potential of the two potentials. This reflects the failure of one of the muscle fibers to transmit an action potential due to the failure of EPP to reach threshold. Blocking represent the most extreme abnormality of the jitter. Blocking is measured as the percentage of discharges of a motor unit in which a single fiber potential does not fire. For example, in an 100 discharges of the pair, if a single potential is missing 30 times, the blocking is 30%. In general, blocking occurs when the jitter values are significantly abnormal.

The results of SFEMG jitter study is expressed by: (1) the mean jitter of all potential pairs, (2) the percentage of pairs with blocking, and (3) the percentage of pairs with normal jitter. Jitter is considered abnormal if (1) the mean jitter value exceeds the upper limit of the normal jitter value for that
Table 1
Reference values for jitter measurements during voluntary muscle activation (μSec): 95% confidence limits for upper limit of mean jitter/95% confidence limits for jitter values of individual fiber pairs (adapted from Gilchrest [17])

<table>
<thead>
<tr>
<th>Muscle/Age</th>
<th>10 years</th>
<th>20 years</th>
<th>30 years</th>
<th>40 years</th>
<th>50 years</th>
<th>60 years</th>
<th>70 years</th>
<th>80 years</th>
<th>90 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontalis</td>
<td>33.6/49.7</td>
<td>33.9/50.1</td>
<td>34.4/51.3</td>
<td>35.5/53.5</td>
<td>37.3/57.5</td>
<td>40.0/63.9</td>
<td>43.8/74.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orbicularis oculi</td>
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<td>39.8/54.7</td>
<td>40.0/54.7</td>
<td>40.4/54.8</td>
<td>40.9/55.0</td>
<td>41.8/55.3</td>
<td>43.0/55.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orbicularis oris</td>
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<td>34.7/52.7</td>
<td>34.9/53.2</td>
<td>35.3/54.1</td>
<td>36.0/55.7</td>
<td>37.0/58.2</td>
<td>38.3/61.8</td>
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<td>42.5/74.2</td>
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<td>33.6/50.2</td>
<td>34.8/52.5</td>
<td>36.8/56.3</td>
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<td>44.0/70.0</td>
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<td></td>
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<td>29.8/46.8</td>
<td>30.8/48.8</td>
<td>32.5/52.4</td>
<td>34.9/58.2</td>
<td>38.4/62.3</td>
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<td>32.9/44.5</td>
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<td>33.0/44.8</td>
<td>33.0/45.1</td>
<td>33.1/45.6</td>
<td>33.2/46.1</td>
<td>33.3/46.9</td>
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<tr>
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<td>29.6/45.2</td>
<td>29.6/45.4</td>
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<td>30.1/46.2</td>
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<td>31.0/48.0</td>
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<td>Extensor digitorum</td>
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<td>35.4/51.3</td>
<td>35.9/52.5</td>
<td>36.6/54.4</td>
<td>37.7/57.2</td>
<td>39.1/61.1</td>
<td>40.9/66.5</td>
</tr>
<tr>
<td>communis</td>
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<tr>
<td>Abductor digiti minimi</td>
<td>44.4/63.5</td>
<td>44.7/64.0</td>
<td>45.2/65.5</td>
<td>46.4/68.6</td>
<td>48.2/73.9</td>
<td>51.0/82.7</td>
<td>54.8/96.6</td>
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<tr>
<td>Quadriceps</td>
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<td>36.0/48.0</td>
<td>36.5/48.2</td>
<td>37.5/48.5</td>
<td>39.0/49.1</td>
<td>41.3/50.0</td>
<td>44.6/51.2</td>
<td></td>
<td></td>
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<tr>
<td>Tibialis anterior</td>
<td>49.4/80.0</td>
<td>49.3/79.8</td>
<td>49.2/79.3</td>
<td>48.9/78.3</td>
<td>48.5/76.8</td>
<td>47.9/74.5</td>
<td>47.0/71.4</td>
<td>45.8/67.5</td>
<td>44.3/62.9</td>
</tr>
</tbody>
</table>
muscle, (2) more than 10% (more than two pairs) exhibits jitter values above the upper limit of the normal jitter, or (3) there is any neuromuscular blocking.

Jitter analysis is highly sensitive but not specific. Although it is frequently abnormal in MG and other NMJ disorders, it may also be abnormal in a variety of neuromuscular disorders including motor neuron disease, neuropathies, and myopathies. Thus, the value of jitter has to be considered in the contest of the patient’s clinical manifestations, nerve conduction studies, and needle EMG findings.

**Stimulation single fiber electromyography**

Stimulation (axonally-stimulated) SFEMG is an alternative method of motor unit activation. It has the advantage of not requiring patient participation and, thus, may be completed on children, uncooperative or comatose patients. It is performed by inserting another monopolar needle electrode near the intramuscular nerve twigs, and stimulating at a low current and constant rate [15]. This technique is more demanding since the electromyographer has to manipulate two electrodes, a stimulating and recording electrode. The IPI is calculated between a stimulus artifact and a single potential generated by stimulating a motor unit near the end plate zone. In contrast to voluntary SFEMG, where jitter is calculated as the variation in IPIs between two MFAPs (since one potential is time-locked by the trigger, all the variation of both end plates is expressed by the jitter of the other potential), the IPI in stimulated SFEMG is measured as the latency between the stimulation artifact and the single MFAP. As jitter values obtained by stimulation SFEMG are calculated on the basis of one end plate, the normal values are lower than those obtained by voluntary activation. To calculate the normal stimulation jitter value, it is recommended that the reference data for voluntary activation is multiplied by 0.80 [15].

**Findings in neuromuscular junction disorders**

**Myasthenia gravis**

MG is an organ-specific autoimmune disease, caused by an antibody-mediated attack primarily on the postsynaptic nicotinic AchRs [18]. The immune-mediated damage of MG leads to a loss of AchR at the NMJ. The primary mechanism involves complement-mediated lysis of the postsynaptic membrane. Antibody cross-linking of AchR leads to their increased internalization, and antibody-binding to the AchR compromises channel function. In addition to the AchR loss of MG, secondary synaptic folds are simplified. This structural feature would be expected to reduce the focus of current on skeletal muscle sodium channels, thereby compromising safety factor further. Finally, skeletal muscle sodium channels are also reduced, in all likelihood, secondary to the loss of post-synaptic membrane. There is no
evidence of a direct immune attack on the sodium channels, but antibodies against a muscle-specific kinase have been identified among some seronegative patients and may be of pathogenic importance [19].

The manifestations of MG are remarkably varied, though they all center around muscle weakness and fatiguability. The weakness is usually worse
with activity and improves after rest. Generally, patients do much better in the morning than the evening. Fatiguable diplopia or ptosis or both are extremely common symptoms. Bulbar symptoms (dysarthria, dysphagia and chewing difficulties) are also frequent. When generalized, there is usually neck extensor and proximal limb weakness. Rarely, the generalized weakness involves the respiratory muscles resulting in respiratory failure (myasthenic crisis).

Improvement in strength after intravenous injection of edrophonium (Tensilon®), an AchE inhibitor, helps to confirm the diagnosis. By inhibiting Ach degradation, edrophonium allows the Ach released into the junction, to interact repeatedly with the decreased number of nicotinic receptors. After a test dose of 1–2 mg, a total dose of 10 mg is administered intravenously. A positive response is expected within five minutes. False positive and false negative results are rare. The ice pack test may also improve ptosis since cooling improves neuromuscular transmission. Elevated serum Ach receptor antibodies occur in about 85–90% of patients with generalized MG, but only in about 50% of patients with ocular myasthenia.

The differential diagnosis of generalized MG includes LEMS, congenital myasthenic syndromes, hyper- and hypothyroidism, glucocorticoid excess, adrenal insufficiency and chronic fatigue syndrome. Ocular myasthenia should be distinguished from thyroid orbitopathy, Kearns Sayre syndrome, congenital myasthenic syndromes, brain stem lesion, and intracranial mass compressing cranial nerves.

The EDX study of patients with suspected MG is often useful and should be tailored to the patient symptomatology. At least one sensory and one motor NCSs should be performed in one lower and one upper extremities, along with a needle EMG emphasizing proximal muscles, to exclude other neuromuscular disorders such as polyneuropathies or myopathies. RNSs are an essential part of the EDX study of patients with suspected MG. They are extremely useful in patients with seronegative disease, negative tensilon test, or equivocal neurological findings. The EDX findings in patients with MG may be summarized as follows:

1. **Baseline CMAP.** The baseline CMAP amplitudes (as well as routine motor nerve conduction studies) are normal in MG. A single supramaximal stimulus to a motor nerve results in Ach release and postsynaptic EPPs which always reach the threshold required to initiate an action potential. Hence, MFAPs are generated in all fibers resulting in a normal CMAP.

2. **Slow repetitive nerve stimulation.** The functional effect of reduced AchRs is a decreased EPP. Depending on the physiological circumstances, the EPP may be adequate; however, if quantal release is lowered, as occurs with slow RNS, the EPP may fall below threshold and the MFAP will not be generated (Fig. 1). In contrast, decreased temperature or inhibition of AchE produces an increase in EPP, which may be adequate to
achieve threshold. In the diagnosis of MG, this property is exploited by the ice pack and Tensilon tests.

Slow RNS results in a progressive decrease in quantal release due to the depletion of the immediate Ach stores. This causes progressive loss of MFAPs since many EPPs do not reach threshold. The end result is a decremental CMAP on slow RNS. The greatest decrease in CMAP amplitude occurs between the first and the second responses but the decrement continues till fourth or fifth responses. Afterwards, the decrement levels off (or sometimes slight improves) due to the mobilization of the secondary stores resulting in no further loss of MFAPs [6,7].

A CMAP decrement of >10% is considered abnormal and eliminates false positive. This should be reproducible and shows the typical decrement described above (maximal at the 3rd to 5th CMAP and plateau after the 5th or 6th CMAP). The diagnostic yield of slow RNS in MG is increased by the following strategy:

a. Obtaining slow RNS following exercise looking for post-exercise exhaustion. After performing slow RNS at rest, patients are asked to contract the tested muscle for one minute. Then, slow RNS is repeated every 30–60 seconds for 3–5 minutes (Fig. 5). Post-exercise exhaustion usually lasts 3–5 minutes and is particularly useful in patients with suspected MG and equivocal (<10%) CMAP decrement at rest. Tetanic stimulation (30–50 Hz) may be substituted for voluntary contraction, but this is extremely painful and should be reserved to comatose or sedated patients.

b. Recording from clinically weakened muscles. This often includes recording from a proximal muscle (such as trapezius) in generalized MG, or from a facial muscle (such as orbicularis oris or nasalis) in ocular or bulbar MG. The diagnostic sensitivity is clearly higher for slow RNS recording proximal muscles than distal (Figs. 5 and 6) [2].

c. Warming the extremity studied (hand skin temperature should be above 32°C). This decreases false negative results, because cooling improves neuromuscular transmission and may mask the decrement.

d. Discontinuation of AchE inhibitors for 12–24 hours (if clinically possible). This also decreases false negative results of slow RNS.

3. **Rapid repetitive nerve stimulation.** Rapid RNS is not useful in the diagnosis of MG. It is mainly indicated when a presynaptic NMJ disorder (such as LEMS or botulism) is considered in the differential diagnosis and need to be eliminated. With rapid RNS, the depleted stores in MG are usually compensated by the accumulation of calcium resulting in no change of CMAP amplitude [4]. In severe myasthenics, rapid RNS may cause a decrement when the increased Ach release cannot compensate for the marked postsynaptic NMJ blockade. In contrast to MG, rapid RNS results in a CMAP increment in patients with LEMS or botulism (see below).
Fig. 5. Slow repetitive nerve stimulation (2 Hz) at rest. (A) Stimulating the median nerve in a normal control. (B) Stimulating the median nerve in a patient with severe myasthenia gravis. Note the significant decrement of CMAP (35% decrement comparing first and fourth CMAP). (C and D) Stimulating the median and spinal accessory nerves in another patient with myasthenia gravis. Note that the decrement stimulating the spinal accessory nerve (D) with 33% decrement comparing first and fourth CMAP) is much more prominent than stimulating the median nerve (C) with 13% decrement comparing first and fourth CMAP). Adapted from Katirji B. Electromyography in Clinical Practice. A Case Study Approach. St Louis: Mosby; 1998, with permission.
4. *Single fiber EMG*. Evaluation of neuromuscular transmission in patients with suspected MG is the most common indication for performing SFEMG. SFEMG is most useful in the diagnosis, but is also helpful in the management, of MG. In patients with MG, abnormal jitter values
are common and frequently accompanied by neuromuscular blocking (Fig. 7). Commonly tested muscles in patients with suspected MG are the extensor digitorum communis, orbicularis oculi and frontalis, but it is important to customize the muscle(s) tested depending on patient’s symptoms. SFEMG is the most sensitive diagnostic study in MG, with a sensitivity ranging from 90–99% (see Fig. 6) [2,15]. A normal SFEMG jitter study in a weak muscle virtually excludes the diagnosis of MG. In contrast to sensitivity, abnormal jitter is nonspecific since it is often abnormal in a variety of neuromuscular disorders. Hence, SFEMG should always be correlated with the history, examination, and entire EDX study.

5. **Needle EMG.** Conventional needle EMG studies in MG are often normal; however, variation in MUAP configuration with consecutive dischargers (MUAP moment to moment variation) may be apparent (Fig. 3). This is due to intermittent blocking of synaptic transmission of some of the fibers that comprise the MUAP. Similar to SFEMG, however, this finding is nonspecific and is seen with presynaptic NMJ defect (such as LEMS), as well as neurogenic disorders associated with

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1 = **Slow RNS recording distal (hand) muscle**

2 = **Slow RNS recording proximal (shoulder) muscle**

3 = **Single Fiber EMG of forearm muscle (extensor digitorum communis)**

4 = **Single Fiber EMG of facial muscle (frontalis)**
reinnervation (such as motor neuron disease). Short duration, low amplitude, and polyphasic MUAPs, similar to those encountered in myopathies, may also be seen in MG. Fibrillation potentials are rarely seen in MG, usually in bulbar and paraspinal muscles of patients with late-onset disease [13]; however, when fibrillation potentials are encountered, other neuromuscular diagnoses should be investigated.

Fig. 7. Abnormal voluntary jitter analysis of a muscle fiber pair with blocking, recording frontalis muscle, in a patient with ocular myasthenia gravis. Adapted from Katirji B. Electromyography in Clinical Practice. A Case Study Approach. St Louis: Mosby; 1998, with permission.
Lambert-Eaton myasthenic syndrome

LEMS is an autoimmune disorder caused by a presynaptic NMJ defect. LEMS is a paraneoplastic syndrome in about 60% of cases, often due to a small cell lung carcinoma [8,10]. An autoimmune etiology of LEMS is indicated by the following: (1) the primary autoimmune LEMS responds to corticosteroid treatment, (2) LEMS is associated with other autoimmune disorders, (3) immunosuppressive therapy improves neoplastic and primary autoimmune LEMS, (4) IgG from LEMS patients injected into animals reproduces the electrophysiologic abnormality, (5) patients with LEMS, but not occurring with cancer, have a major histocompatibility locus associated with DRB1 and DQB1, and (6) calcium channel antibodies are found among most LEMS patients [9,20].

Patients usually present with proximal muscle weakness (especially lower extremities), minor ocular and bulbar weakness, and fatiguability. The deep tendon reflexes are characteristically absent or reduced but may be transiently enhanced after brief exercise [9,10]. Autonomic complaints such as dry mouth are common. The diagnosis of LEMS requires a high index of suspicion, particularly in men, smokers, and patients with a known malignancy. At times, LEMS may be confused, clinically and electrophysiologically, with MG (Table 2), and about one fifth of patients with LEMS are originally misdiagnosed as MG [21].

Elevated antibodies towards VGCCs occur in patients with LEMS, and this finding is diagnostic in the appropriate clinical setting. Hence, the

Table 2
Clinical and electrodiagnostic differential diagnosis between generalized myasthenia gravis and Lambert-Eaton myasthenic syndrome (LEMS)

<table>
<thead>
<tr>
<th></th>
<th>Myasthenia gravis</th>
<th>LEMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocular involvement</td>
<td>Prominent</td>
<td>Less prominent</td>
</tr>
<tr>
<td>Bulbar involvement</td>
<td>Common, prominent</td>
<td>Uncommon, subtle</td>
</tr>
<tr>
<td>Myotatic reflexes</td>
<td>Normal</td>
<td>Absent or depressed</td>
</tr>
<tr>
<td>Sensory symptoms</td>
<td>None</td>
<td>Paresthesia is common</td>
</tr>
<tr>
<td>Autonomic involvement</td>
<td>None</td>
<td>Dry mouth is common, but also</td>
</tr>
<tr>
<td>Tensilon test</td>
<td>Frequently positive</td>
<td>May be positive</td>
</tr>
<tr>
<td>Serum antibodies directed against</td>
<td>Postsynaptic acetylcholine receptors</td>
<td>Presynaptic voltage-gated calcium channels</td>
</tr>
<tr>
<td>Baseline CMAPs</td>
<td>Normal</td>
<td>Low in amplitude</td>
</tr>
<tr>
<td>Postexercise CMAPs</td>
<td>No change</td>
<td>Significant facilitation</td>
</tr>
<tr>
<td>Slow repetitive stimulation</td>
<td>Decrement</td>
<td>Decrement</td>
</tr>
<tr>
<td>Rapid repetitive stimulation</td>
<td>No change or decrement</td>
<td>Increment</td>
</tr>
<tr>
<td>Single fiber EMG</td>
<td>Increased jitter with blocking</td>
<td>Increased jitter with blocking</td>
</tr>
<tr>
<td>Rapid rate simulation jitter</td>
<td>Does not change or worsens jitter</td>
<td>Improves jitter</td>
</tr>
</tbody>
</table>

LEMS = Lambert-Eaton myasthenic syndrome; CMAP = compound muscle action potential; EMG = electromyography. (Adapted from Katirji B. Electromyography in clinical practice. A case study approach. St. Louis: Mosby; 1998; with permission)
EDX examination is an important diagnostic test in LEMS and constitutes the mainstay of diagnosis. In fact, the electromyographer may be the first to diagnose LEMS in the EMG laboratory by evaluating post-exercise CMAP in patients with universally low CMAP amplitude referred for a variety of reasons (see below). The EDX findings in LEMS are summarized as follows:

1. **Baseline CMAP.** The CMAPs at rest (as well as during routine motor conduction studies) are low in amplitude since many end plates do not reach threshold due to inadequate release of quanta (vesicles) after a single stimulus. Thus, less MFAPs are generated leading to a low amplitude CMAP. This finding occurs in all muscles resulting in diffuse low CMAPs (Table 3).

2. **Rapid repetitive nerve stimulation.** Rapid RNS (usually 20–50 Hz) and postbrief exercise CMAP evaluation enhances calcium influx into the presynaptic terminal, which result in larger releases of quanta and larger EPPs. With many end plates not reaching threshold after the first stimulus, rapid RNS results in many muscle fibers reaching threshold required for the generation of MFAPs (Fig. 2). Thus, more MFAPs are summated with rapid RNS resulting in a CMAP increment (Figs. 8 and 9). The post-tetanic facilitation should exceed 50% and preferably 100% to be diagnostic and specific for a presynaptic defect. This increment is more than 100% in 90% of patients with LEMS, is often more than 200% and may reach as high as 2000%\(^{[8,22]}\). A postbrief exercise CMAP evaluation of at least two motor nerves is a good and sensitive screening test for LEMS\(^{[23]}\). This should be performed also on all patients with universally low (or borderline) CMAPs during routine motor conduction studies, particularly if unexplained. If there is a CMAP increment following a brief exercise, then a rapid RNS should be obtained for confirmation on a single motor nerve.

<table>
<thead>
<tr>
<th>NMJ Disorder</th>
<th>NMJ defect</th>
<th>CMAP amplitude</th>
<th>Slow RNS</th>
<th>Rapid RNS(^a)</th>
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<tbody>
<tr>
<td>Myasthenia gravis</td>
<td>Postsynaptic</td>
<td>Normal</td>
<td>Decrement</td>
<td>Normal or decrement</td>
</tr>
<tr>
<td>Lambert-Eaton myasthenic syndrome</td>
<td>Presynaptic</td>
<td>Low in all muscles</td>
<td>Decrement</td>
<td>Marked (&gt;200%) increment in all muscles</td>
</tr>
<tr>
<td>Botulism</td>
<td>Presynaptic</td>
<td>Low in proximal and weak muscles</td>
<td>Decrement</td>
<td>Modest increment in weak muscles (50–100%)</td>
</tr>
</tbody>
</table>

NMJ = neuromuscular junction; CMAP = compound muscle action potential; RNS = repetitive nerve stimulation \(^a\) or postexercise CMAP amplitude. (Adapted from Katirji B. Electromyography in clinical practice. A case study approach. St Louis: Mosby; 1998; with permission)
3. Slow repetitive nerve stimulation. Slow RNS (usually 2–3 Hz) is not useful in LEMS since it results in decrement of the CMAP, similar to postsynaptic disorders such as MG. With slow RNS, ACH release is reduced further because of the depletion of the immediately available stores, and calcium does not accumulate in the presynaptic terminal. The end result is further loss of many MFAPs and a decrement of CAMP amplitude.

4. Single fiber EMG. Abnormal jitter and blocking, typical of defective neuromuscular transmission, is seen in all LEMS patients. While this
technique is highly sensitive, it lacks specificity; it is abnormal in MG as well as a variety of other neuromuscular disorders. However, with the stimulation SFEMG technique, the jitter may improve with increasing discharge rate, that is, with rapid rate stimulation (20–50 Hz) compared to the slow rates (2–5 Hz) [23,24]. This finding is caused by the same mechanism as CMAP increment following brief exercise or RNS, that is enhancement of Ach release by the influx of calcium into the presynaptic terminal. Decreased jitter with high rate of stimulation is specific for a presynaptic disorder and is useful in distinguishing LEMS from MG [25].

5. Needle EMG. Conventional needle EMG is often normal in patients with LEMS. Short duration, low amplitude and polyphasic MUAPs may be seen occasionally, particular with significant neuromuscular blockade. Similar to postexercise CMAP increment in LEMS, MUAP amplitudes may increase with sustained brief contraction.

Botulism

Botulinum toxins are produced by the anaerobic bacterium Clostridium botulinum. They are extremely potent muscarinic and nicotinic cholinergic presynaptic toxins, with human lethal doses as small as 0.05 to 0.1 micrograms. Botulinum toxins bind to various plasma membrane and vesicle proteins essential for docking of the presynaptic vesicles at the presynaptic active zones of the nerve terminals, resulting in failure of Ach release and ultimate destruction of the presynaptic terminals.
Botulism is rare but may be fatal [11,12,14,26]. Clinically, there are three distinct types of botulism: Food born, infantile and wound botulism. It often presents with a rapid, usually descending, muscular weakness (ocular to bulbar to extremities) with autonomic symptoms (pupillary dilatation, constipation, dry mouth, urinary retention). The differential diagnosis of botulism includes MG, LEMS, Guillain-Barré syndrome (including the Miller-Fisher syndrome), tick paralysis, and diphtheritic polyneuropathy. The diagnosis is confirmed by electrophysiological testing (see below), identification of toxin in serum and stool, or identification of organism in stool cultures (in infantile and wound botulism).

The EDX studies in patients with suspected botulism provides a rapid and readily available method of diagnosis in patients whom bioassay studies for botulinum toxin are pending or stool cultures are negative. The EDX findings are compatible with a presynaptic defect of NMJ but differs from LEMS in that they may vary from day to day, may be normal during the first few days and may be only present in weakened muscles. The findings may summarized as follows:

1. Low CMAP amplitudes is the most consistent finding and is present in 85% of cases, particularly when recording from weak muscles (usually proximal).
2. Rapid RNS, or CMAP following 10 seconds of isometric exercise, results in a CMAP increment consistent with a presynaptic defect (Fig. 10). However, the increment seen in botulism is modest, often ranging between 30 to 100%, when compared to the increment in LEMS which often surpasses 200% (Table 3). This increment may be absent, especially in severe cases such as those caused by type A toxin, presumably due to severe presynaptic blockade.
3. Slow RNS may be normal or reveals a decremental CMAP response; however, this decrement is often mild and does not exceed 8–10%.
4. Needle EMG often reveals increase in the number of small, short polyphasic MUAPs, and occasional fibrillation potentials [14].
5. Increase jitter with blocking on single fiber EMG is a consistent finding. Stimulation SFEMG may improve jitter with a rapid stimulation rate.

Congenital myasthenic syndromes

Congenital myasthenic syndromes are caused by genetic defects of the presynaptic or postsynaptic apparatus [9,27]. Patients have fatigable weakness and ptosis, which may often be traced to birth. Antibodies towards the AchR are not present, and symptoms do not respond to immunosuppressive therapies. Patients may have siblings with a myasthenic disorder, but cases may be sporadic. In newborns, congenital myasthenic syndromes should be differentiated from neonatal MG, which is caused by maternal transfer of anti-ACHR antibodies across the placenta, and may occur in babies of asymptomatic mothers.
Many congenital myasthenic syndromes, regardless of primary etiology, demonstrate a degeneration of the post-synaptic region and simplification of junctional folds often with a concomitant reduction of AchRs. The cause of the membrane damage has been hypothesized to result from the prolonged depolarization of the end plate. The AchR is permeable to calcium, and mechanisms that prolong the time or frequency of channel openings would increase calcium influx. Excess calcium influx could lead to activation of calcium-sensitive proteases and inhibition of mitochondrial respiration. Activation of nitric oxide synthase that is concentrated at the neuromuscular junction could also contribute to free radical damage of the end plate.

Fig. 10. Increment of CMAP in a patient with food-born botulism. (A) Baseline CMAP (1) and CMAP following 10 seconds of maximal voluntary isometric exercise (2), stimulating the median nerve. Note the 90% CMAP increment following exercise. (B) Following rapid repetitive nerve stimulation (50 Hz) of the spinal accessory nerve. Note the 100% CMAP increment. Adapted from Katirji B. Electromyography in Clinical Practice. A Case Study Approach. St Louis: Mosby; 1998, with permission.
Prolonged depolarization of the end plate region may also lead to inactivation of sodium channels that are concentrated in the depths of the junctional folds.

Given the similar anatomic pathology of all the congenital myasthenic syndromes, slow RNS often produces a decremental response. The decrement may be absent during rest and only elicited after several minutes of exercise. In cholinesterase deficiency and slow-channel syndrome, the best characterized of the congenital myasthenic syndromes, a single electrical stimulation leads to repetitive CMAPs. In both these situations, depolarization of the membrane beyond the refractory period for action potential generation would lead to the observed repetitive CMAPs. The repetitive CMAPs is similar to what is seen in organophosphate poisoning and in patients taking AchE inhibitors. Hence, the latter should be discontinued at least 24 hours before testing.

**Suggested electrodiagnostic strategy in patients with suspected neuromuscular junction defect**

The EDX study of a patient with suspected NMJ disorder should start with a detailed history and comprehensive neurologic examination. Sensory and motor NCSs at least in two limbs (preferably and upper and a lower extremity) should be the initial studies. If the CMAP amplitudes are low, a presynaptic defect should be suspected and ruled out (Fig. 11) [5]. A postsynaptic defect is characterized by normal CMAP amplitudes and, hence, cannot be excluded without the appropriate RNS or SFEMG.

If the diagnosis of LEMS is clinically suspected, baseline and postexercise CMAPs of at least two distal motor nerves is a sufficient screening test [23].
In LEMS, CMAP increment often surpasses 200%. A rapid RNS of one distal nerve, which is extremely painful, should only be done for confirmation if there is a CMAP increment after exercise. If the diagnosis of botulism is considered, the choice of muscle should include weakened, often proximal muscles. In botulism the CMAP increment is usually 30–100%. Also, the study should be repeated in 1–2 days, particularly if the initial evaluation was done during the early phase of the illness.
If the diagnosis of MG is clinically suspected, slow RNS at rest and for 4–5 minutes following a one-minute exercise should be done on at least two motor nerves. The selection of nerves and muscles is dependent on the clinical manifestations with the goal to record from weakened muscles. I suggest performing slow RNS on a distal hand muscle (such as the abductor digit minimi or abductor pollicis brevis) to start, then moving on to a proximal muscle such as the upper trapezius. Facial RNS should be reserved to patients with oculobulbar symptoms and normal slow RNS recording distal and proximal muscles (see Fig. 11). SFEMG of one or two muscles (such as the frontalis, orbicularis oculi or extensor digitorum communis) should be considered if the diagnosis of MG is still considered despite normal RNS studies (and AchR antibodies).

If the CMAPs obtained on motor NCSs in a patient with suspected MG are low or borderline, postexercise CMAP screening should always be done to exclude LEMS. A misdiagnosis of MG is often made if postexercise CMAP evaluation is not done and a slow RNS shows a CMAP decrement. Similarly, postexercise CMAP screening is recommended for a patient with weakness associated with a malignancy (particularly a small cell lung cancer), or if the clinical situation could not clearly differentiate between LEMS and MG (see Table 2).

References


Electrodiagnostic approach to the patient with suspected myopathy

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Myopathies often pose a diagnostic challenge. These somewhat uncommon disorders have many potential causes. Yet, a precise diagnosis is important, since myopathies are often treatable or have genetic implications. Fortunately, much is known about the clinical manifestations and pathogenesis of many myopathies. Using this knowledge as a foundation, a clinician can build a rational approach to the patient with suspected myopathy.

First, the history and physical examination are used to narrow the diagnostic possibilities and to direct the rest of the evaluation. In particular, the pace and distribution of the illness, potential risk factors (especially systemic disorders and toxins), and family history must be ascertained. Next, the appropriate laboratory tests are requested. Genetic studies as well as measures of serum chemistries, endocrine, and immunologic functions may be obtained. In most patients, an electromyogram (EMG) is then performed to help confirm the diagnosis of myopathy, to further narrow the differential diagnosis, and often to help designate a muscle for biopsy. In fact, histologic evaluation of a muscle biopsy specimen is often the final step in this constructed approach.

This paper describes how these steps are utilized in approaching the patient with suspected myopathy, with an emphasis on the EMG findings.

Symptoms and signs of myopathy and differential diagnosis

The symptoms and signs of myopathy are listed in Table 1. Symptoms often precede the signs and are usually attributable to proximal weakness. Patients may have difficulty rising from a chair (Fig. 1), climbing stairs, or combing their hair. Most patients present with symmetric, painless, and progressive,
limb-girdle and neck flexor weakness. In addition, those with longstanding myopathies often exhibit a component of trunk weakness affecting paraspinal or abdominal muscles and leading to a hyperlordotic posture and the inability to perform a sit-up.

In some disorders such as mitochondrial myopathies, bulbar and extraocular muscle weakness may occur. Distal weakness is a prominent feature of only a few myopathies such as myotonic dystrophy, facioscapulohumeral dystrophy (FSHD), inclusion body myositis (IBM), distal dystrophies, congenital myopathies, myofibrillar myopathy [1], and limb-girdle muscular dystrophy 2G (with telethonin mutations) [2,3]. IBM and FSHD often also exhibit some asymmetry. Respiratory muscles may be weakened in severe inflammatory myopathies and in some inherited conditions, resulting in dyspnea and hypercapnic respiratory failure.

In contrast to neurogenic diseases, loss of muscle bulk and attenuation of tendon reflexes only occur late in the course of myopathies. On the other hand, calf pseudohypertrophy may be seen early in some muscular dystrophies. Fasciculations do not occur in diseases of muscle. Although there is no sensory loss, patients with myopathy occasionally have muscle pain. It is important to note, however, that most patients with myalgias and no weakness usually do not have an identifiable myopathy. In myopathies, pain can also occur in the form of cramps at rest or during exercise. Abnormal pain during exercise can be due to defects in glycogen or lipid metabolism or in mitochondrial function. Ischemia, spinal stenosis, and other disorders can also cause this symptom. Cramps also occur in other conditions, includ-

### Table 1

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
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<tbody>
<tr>
<td>Most common</td>
<td>Most common</td>
</tr>
<tr>
<td>Proximal muscle weakness</td>
<td>Limb-girdle weakness</td>
</tr>
<tr>
<td>(e.g. difficulty rising from a</td>
<td>Neck flexor weakness</td>
</tr>
<tr>
<td>chair, climbing stairs, walking,</td>
<td>Waddling gait</td>
</tr>
<tr>
<td>or using the arms above the head)</td>
<td>Trunk weakness</td>
</tr>
<tr>
<td>Less common</td>
<td>Less common</td>
</tr>
<tr>
<td>Myalgias</td>
<td>Muscle tenderness to palpation</td>
</tr>
<tr>
<td>Cramps</td>
<td></td>
</tr>
<tr>
<td>Uncommon</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Diplopia</td>
<td>Extraocular muscle weakness</td>
</tr>
<tr>
<td>Ptosis</td>
<td>Ptosis</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>Weak palate, tongue, or both</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>Nasal speech</td>
</tr>
<tr>
<td>Distal weakness (e.g., foot drop,</td>
<td>Footdrop; forearm or intrinsic hand muscle weakness</td>
</tr>
<tr>
<td>hand weakness)</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>Diaphragm weakness</td>
</tr>
<tr>
<td>Impaired grip release</td>
<td>Grip or percussion myotonia</td>
</tr>
</tbody>
</table>
ing neuropathy and anterior horn cell disease and in metabolic conditions such as electrolyte disturbances. Sometimes, cramping (or stiffness) is actually a manifestation of myotonia.

Patients with myopathy may experience fatigue. Worsening of fatigue and weakness can occur later in the day, but this diurnal variation tends to be less prominent than in neuromuscular junction (NMJ) disorders. However, it may not be possible to differentiate a myopathy from a NMJ disorder without laboratory and electrodiagnostic testing. Although the presence of ocular or oropharyngeal involvement would favor a NMJ disorder such as myasthenia gravis (MG), such involvement also occurs in some myopathies. Alternatively, rare patients with MG have a purely limb-girdle
presentation [4]. In addition, Lambert-Eaton myasthenic syndrome (LEMS) may be misdiagnosed as a myopathy. However, LEMS patients usually have reduced tendon reflexes and autonomic symptoms such as a dry mouth while myopathy patients do not.

Some patients with suspected myopathy are asymptomatic. They may be referred to the neurologist because an elevated serum creatine kinase (CK) was incidentally discovered, or because a family member was found to have an inherited myopathy and the patient is at risk. Occasionally, an astute ophthalmologist or internist realizes that systemic symptoms, such as early onset cataracts (in myotonic dystrophies), cardiomyopathy (in some dystrophies), or impaired bowel motility (in mitochondrial neurogastrointestinal encephalomyopathy) may be the presenting features of an inherited myopathy, and requests a neurological consultation.

**Laboratory testing**

Typically, the most useful laboratory test available for identifying patients with possible myopathy is the serum CK. Almost all of the MM components (and most of the total measures) are derived from skeletal muscle. The CK is more specific to muscle than the serum aldolase, which is usually not worth measuring. The CK is usually elevated if there is muscle necrosis or a muscle membrane leak. Therefore, the majority of patients with inflammatory myopathies and aggressive muscular dystrophies have an elevated CK level (the degrees of elevated CK are noted in Table 2). It is important to note the CK levels may be normal in 3–36% of patients with inflammatory myopathies, especially after treatment, even if the disease is active. In contrast, some muscular dystrophy patients are asymptomatic despite an elevated CK [5].

The CK level is also elevated in some toxic myopathies and in hypothyroid myopathy. During rhabdomyolysis related to drugs, enzyme defects, infections, and other processes, CK levels are often elevated more than 50-fold. A minority of patients with mitochondrial myopathies [6,7] and almost all patients with acid maltase and debrancher deficiencies have an elevated CK level (Table 2) [8,9]. In other glycogen storage diseases, CK levels may be mildly to moderately elevated [10]. In lipid storage diseases, CK levels are normal to mildly elevated at rest [11]. The CK levels are normal in congenital myopathies and in chronic corticosteroid myopathy.

CK levels may be elevated after excessive exercise, intramuscular injections, seizures, and muscle trauma, and in viral illnesses, motor neuron disease (mild elevation), and malignant hyperthermia trait [12]. The CK level should not be measured soon after an EMG because the level may be elevated transiently; such increases are typically of low magnitude [13,14]. Athletes with elevated CK levels should not exercise for 7–10 days before the enzyme levels are reassessed [12].
Patients are said to have idiopathic hyperCKemia if they have no muscle symptoms, normal strength, and normal electrodiagnostic and histological studies. In clinical practice, a muscle biopsy and even an EMG are considered optional in these patients depending upon one’s index of suspicion that

<table>
<thead>
<tr>
<th>Myopathy</th>
<th>Frequency of CK elevation</th>
<th>Degree of CK elevation</th>
<th>Typical EMG pattern (see text)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inflammatory/Infectious</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM/DM</td>
<td>+++-++++</td>
<td>+ to +++</td>
<td>1 or 2</td>
</tr>
<tr>
<td>IBM</td>
<td>++++</td>
<td>+ to ++</td>
<td>1 or 2&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Sarcooidosis</td>
<td>++</td>
<td>+ to ++</td>
<td>1 or 2</td>
</tr>
<tr>
<td>Viral</td>
<td>++++</td>
<td>++ to +++</td>
<td>1 or 2</td>
</tr>
<tr>
<td>Trichinosis</td>
<td>++++</td>
<td>+ to +++</td>
<td>1</td>
</tr>
<tr>
<td><strong>Endocrine</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothyroid</td>
<td>+++</td>
<td>+ to +++</td>
<td>1, 2, or 3</td>
</tr>
<tr>
<td>Hyperthyroid</td>
<td>0–&lt;sup&gt;a&lt;/sup&gt;</td>
<td>NA</td>
<td>2</td>
</tr>
<tr>
<td>Cushing’s syndrome</td>
<td>0–&lt;sup&gt;a&lt;/sup&gt;</td>
<td>NA</td>
<td>2, rarely 1</td>
</tr>
<tr>
<td>Parathyroid disorders</td>
<td>0–&lt;sup&gt;a&lt;/sup&gt;</td>
<td>NA</td>
<td>2</td>
</tr>
<tr>
<td><strong>Toxic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic steroid myopathy</td>
<td>0–&lt;sup&gt;a&lt;/sup&gt;</td>
<td>NA</td>
<td>2 or 4</td>
</tr>
<tr>
<td>Colchicine</td>
<td>++++</td>
<td>+ to +++</td>
<td>1 or 3 + neuropathy</td>
</tr>
<tr>
<td>Zidovudine/HIV</td>
<td>++++</td>
<td>+ to ++</td>
<td>1</td>
</tr>
<tr>
<td>Cholesterol-lowering agents</td>
<td>++++</td>
<td>to +++</td>
<td>1 or 3</td>
</tr>
<tr>
<td>Penicillamine</td>
<td>++++</td>
<td>+ to +++</td>
<td>1 or 2</td>
</tr>
<tr>
<td>Critical illness myopathy</td>
<td>++</td>
<td>+ to +++</td>
<td>1 or 2</td>
</tr>
<tr>
<td><strong>Dystrophies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dystrophinopathies</td>
<td>++++</td>
<td>+++&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1</td>
</tr>
<tr>
<td>Emery-Dreifuss</td>
<td>++++</td>
<td>+ to +++</td>
<td>2 or 1</td>
</tr>
<tr>
<td>Limb-Girdle</td>
<td>++++</td>
<td>++ to +++</td>
<td>2 or 1</td>
</tr>
<tr>
<td>FSHD</td>
<td>+–&lt;sup&gt;e&lt;/sup&gt;</td>
<td>+</td>
<td>2</td>
</tr>
<tr>
<td>Myotonic</td>
<td>+–&lt;sup&gt;e&lt;/sup&gt;</td>
<td>+</td>
<td>3</td>
</tr>
<tr>
<td>PROMM</td>
<td>+++&lt;sup&gt;e&lt;/sup&gt;</td>
<td>+</td>
<td>2</td>
</tr>
<tr>
<td>Oculopharyngeal</td>
<td>+–&lt;sup&gt;e&lt;/sup&gt;</td>
<td>+</td>
<td>2</td>
</tr>
<tr>
<td>Distal</td>
<td>+–&lt;sup&gt;e&lt;/sup&gt;</td>
<td>+</td>
<td>2 or 1</td>
</tr>
<tr>
<td>Congenital myopathies</td>
<td>+&lt;sup&gt;e&lt;/sup&gt;</td>
<td>+</td>
<td>2</td>
</tr>
<tr>
<td>Mitochondrial myopathies</td>
<td>+–&lt;sup&gt;e&lt;/sup&gt;</td>
<td>+</td>
<td>1, 4</td>
</tr>
<tr>
<td>Acid maltase and debrancher</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>deficiencies</td>
<td>++++</td>
<td>+–&lt;sup&gt;f&lt;/sup&gt;</td>
<td>1, 2, or 3</td>
</tr>
<tr>
<td>Other glycogen storage diseases</td>
<td>++++</td>
<td>+–&lt;sup&gt;f&lt;/sup&gt;</td>
<td>1, 2, or 3</td>
</tr>
<tr>
<td>Carnitine and carnitine palmitol transferase deficiencies</td>
<td>+</td>
<td>+&lt;sup&gt;f&lt;/sup&gt;</td>
<td>2 or 4</td>
</tr>
</tbody>
</table>

**Abbreviations:** DM, dermatomyositis; PM, polymyositis; IBM, inclusion body myositis; FSHD, facioscapulohumeral muscular dystrophy; PROMM, proximal myotonic dystrophy; NA, not applicable.

<sup>a</sup> 0 = never; + = <25%; ++ = 25–50%; +++ = 51–75%; ++++ = >75%.

<sup>b</sup> + = <fourfold; ++ = four- tenfold; +++ = >tenfold.

<sup>c</sup> Long-duration high amplitude motor unit potentials often appear to be present.

<sup>d</sup> Declines with age.

<sup>e</sup> Except centronuclear myopathy (exhibits pattern 1).

<sup>f</sup> Highly elevated during episodes of myoglobinuria.
A neuromuscular disease is present. Typically, these patients are males with 3- to 10-fold elevations in CK. Careful follow-up is indicated because about one-third of these patients are eventually diagnosed with a neuromuscular disorder [12].

In patients with a suspected myopathy, the other laboratory studies noted in the algorithm may be obtained (Fig. 2). Thyroid studies should be ordered in most patients. In patients with a suspicious body habitus or any other clinical features of Cushing's syndrome, a 24-hour urinary free cortisol level should be assessed. When a mitochondrial disorder is suspected, serum lactate and pyruvate should be measured. In selected patients, carnitine, vitamin E, and acid maltase (in WBCs) [8] could be assessed from blood samples. When an inflammatory myopathy is suspected, one can consider obtaining myositis-specific or myositis-associated antibodies, for example, anti-Jo-1 [15]. Human immunodeficiency virus (HIV) antibodies may be assessed in the appropriate setting. Ischemic exercise lactate testing may be useful in patients with exercise-induced myalgias or contractures if patients exercise appropriately during testing. However, the findings are nonspecific and a normal result does not exclude all inherited metabolic myopathies.

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**Fig. 2.** An algorithmic approach to the evaluation of a patient with a suspected myopathy

Other causes of weakness, such as neuromuscular junction disorders, central nervous system processes, disuse, connective tissue diseases, and orthopedic problems should also be considered initially. **Abbreviations:** c/w = consistent with; FH = family history; CK = creatine kinase; U = Urine; TFTs = thyroid function tests; ESR = erythrocyte sedimentation; ANA = antinuclear antibody; Abs = antibodies; IM = Inflammatory myopathy; Fibs = fibrillation potentials; Nl = normal; Inc = increased; ? = consider; + = present.
Based on the presence of any serologic abnormalities, a specific workup may be undertaken. For example, an elevation in calcium and reduction in phosphorus would prompt an evaluation for hyperparathyroidism. If a genetic disorder is highly suspected based on the clinical features, family history, and routine laboratory studies, DNA or protein testing may be the next appropriate test. For example, molecular testing is easily available on blood specimens for the following disorders: dystrophinopathies, myotonic dystrophy type 1, FSHD, oculopharyngeal dystrophy, and some mitochondrial syndromes. Molecular testing is available on a more limited basis for some glycogen storage diseases, calpain deficiency, and sarcoglycanopathies. For most other patients, EMG is the next step. Occasionally, musculoskeletal imaging is performed instead of or in addition to EMG.

**Imaging studies**

Skeletal muscle imaging has some utility in the evaluation of myopathies, especially in children [16]. Ultrasound may be used to detect evidence of neuromuscular disease and to select a site for muscle biopsy. Computed tomography can define anatomy and identify atrophy and hypertrophy patterns, and fatty replacement. However, magnetic resonance imaging (MRI) is the best imaging modality for skeletal muscle. In addition to defining anatomy, patterns of atrophy, and fatty infiltration, MRI also images in multiple planes and can detect changes of edema, inflammation, or necrosis. There is high sensitivity (89%) [17] for detecting abnormalities in inflammatory myopathies. Unfortunately, the changes are not disease specific and usually only one body region is imaged. Thus, EMG may be more advantageous because multiple sites can be sampled at equally high sensitivity. Although EMG findings are also nonspecific, there are a number of patterns that further narrow the differential diagnosis.

**Electrodiagnostic testing**

Nerve conduction studies (NCS) in patients with suspected myopathy should include at least one motor and one sensory recording. We typically examine one motor and sensory nerve in both an arm and a leg. The NCS are usually normal in proximal myopathies, especially since recordings are typically from distal muscles. If there has been substantial loss of muscle underlying the recording electrode, however, a low compound muscle action potential (CMAP) may be elicited. In addition, low CMAP amplitude may be present if there is an associated abnormality in muscle membrane depolarization.

In patients with low CMAP amplitudes and normal sensory responses, NMJ disorders, especially LEMS, and motor neuropathies and neurogenic polyneuropathies must be excluded. The needle EMG examination findings should distinguish a motor axonopathy or motor neuronopathy from a myopathy.
To assess for a NMJ disorder, 2–3 Hertz repetitive stimulation should be performed at baseline and after exercise. In addition, a single supramaximal shock should be delivered to a motor nerve at rest and after 10 seconds of exercise (LEMS test). The studies for LEMS and MG should be performed even if the motor responses are normal when there is a high index of suspicion and if the needle electrode examination findings do not explain the patient’s weakness.

The needle EMG examination is the most important component of electrodiagnostic testing for myopathy; the four main components include assessment of (1) insertional activity, (2) spontaneous activity, (3) motor unit action potential (MUAP) morphology, and (4) recruitment [18]. The first two components are assessed with the muscle at rest. Damage to muscle fibers resulting from EMG needle movement leads to a brief electrical burst of insertional activity. Insertional activity can be abnormally prolonged if muscle is disconnected from the motor nerve terminal; (e.g., following denervation or muscle necrosis). It is also prolonged in some channelopathies, such as myotonic disorders, in the form of myotonic discharges [18]. Sometimes increased insertional activity is thought to be a normal variant, especially in muscular men [18]. Insertional activity can actually be decreased in periodic paralysis during an attack or if muscle is replaced by connective tissue as in chronic muscular dystrophies.

Except at the muscle endplate, spontaneous activity is abnormal and is due to the generation of action potentials from single muscle fibers that have lost their innervation (structurally or metabolically). It usually occurs in the form of positive waves and fibrillation potentials. Fibrillation potentials occur in denervating and myopathic diseases and are occasionally seen in NMJ and spinal cord disorders. They may also occur after muscle trauma. The types of myopathies in which fibrillation potentials occur tend to be more necrotizing, inflammatory, or both.

Complex repetitive discharges, (CRDs) due to ephaptic activation and discharge of groups of adjacent muscle fibers, are also a form of increased insertional activity. These occur in some chronic and inflammatory myopathies, but they are also seen in neurogenic disorders [18].

Evaluation of MUAPs is initially performed at low levels of voluntary activation so one or a few MUAPs are examined at a time. At least 20 MUAPs should be carefully examined. Each MUAP represents the summation of action potentials from a proportion of myofibers innervated by one axon from a single anterior horn cell (part of a motor unit). In myopathic processes, the duration of the MUAP is less than in normal muscles because of structural or functional loss of myofibers from a motor unit. For the same reason, the amplitude may also be reduced compared to normals. Due to a loss of synchrony in depolarization, the MUAPs are often polyphasic. In very chronic myopathies, such as IBM and chronic polymyositis, some long duration MUAPs may occur. Long duration MUAPs are more typical after reinnervation, but they may also be caused by desynchronization of single
fiber potentials within the motor unit, perhaps due to myofiber regeneration [19]. None of the above findings are specific to myopathy, but they are characteristic along with early recruitment (described later). NMJ disorders and nascent motor units undergoing early reinnervation, for example, may also exhibit short duration MUAPs.

It is relatively easy for an electromyographer to detect spontaneous activity. It is somewhat more difficult to recognize MUAP changes of myopathy. The findings are subtler in mild cases and in young patients in whom differences from normal to abnormal MUAP may not be profound. In addition, one must be familiar with normal MUAPs from many muscles from different age groups before knowing what is abnormal. This interpretation is generally subjective. Quantitative methods are available and will be discussed, but most EMG laboratories do not utilize such methods routinely.

The final component of the EMG is assessment of MUAP recruitment. In patients with myopathy, motor units are not lost; therefore, recruitment may be normal for a certain level of activation. In contrast to normals, however, more MUAPs are required to generate the same degree of force. Thus, recruitment of MUAPs may be early or rapid. Early recruitment is more recognizable subjectively as the degree of weakness increases. At the end stage of a myopathy, however, recruitment may actually be reduced.

Planning the EMG

The muscles that are most electrically affected are typically also the weakest. In most myopathies, these are the proximal muscles. Therefore, most studies should include several proximal muscles from an arm and a leg as well as a distal muscle. A paraspinal muscle, a most proximal muscle, should always be studied in patients with a suspected myopathy. Occasionally, paraspinals may also harbor myotonia and CRDs in patients with myotonic and glycogen storage disorders when limb muscles do not. We typically examine one or more thoracic paraspinal muscles and avoid lumbar paraspinals since the latter are more typically affected by radiculopathy and may provide false positive results. In patients with distal involvement, more distal muscles (such as finger or forearm flexors in IBM) also warrant extensive study. In all patients, a unilateral study should be performed, allowing a potential muscle biopsy to be performed on the contralateral limb.

Quantitative studies

Especially in cases in which the needle EMG findings are equivocal, and it is not certain if the MUAPs are short in duration, quantitative studies may be helpful. Typically, duration is the MUAP parameter that is measured in myopathies, but amplitude, turns, polyphasia, and recruitment may all be quantitated [23]. Methods of computer-assisted quantitation are now widely
available on more sophisticated EMG machines. MUAPs must still be carefully isolated and recorded with a stable baseline; the concentric needle electrode must be close to the fibers of the motor unit resulting in a rise time of less than 500 microsecond (μs); the individual MUAP is captured; and typically the cursors must be placed appropriately before the measures are obtained by the computer. Twenty MUAPs are assessed and then mean and standard deviations for the parameters under study are generated. Age-matched normative data must also be available for comparison. More sophisticated automatic digital systems for quantitative analysis of waveforms and recruitment is available and used most frequently in research (reviewed by Dorfman and McGill [23]).

**Single fiber EMG**

Single-fiber EMG is usually not performed in myopathy evaluations, but it might be performed when the differential diagnosis includes a NMJ disorder. Increased jitter and blocking may be identified in myopathies, especially with inflammatory and necrotizing processes. Fiber density can be normal or increased [24].

**EMG patterns with histopathologic correlation in various myopathies**

The EMG findings of myopathy are not specific. They complement the clinical examination and laboratory tests. In general, there is a concordance (about 80–95%) of EMG and muscle biopsy findings. The largest quantitative study of 188 patients with myopathy disclosed that 87% had EMG features of myopathy and 79% had myopathic histopathology [25]. In another study assessing the accuracy of clinical diagnosis using histopathological features as the gold standard, the overall accuracy was only about 50%. However, more than 68% of patients with either an elevated CK or myopathic EMG had myopathic histologic changes on muscle biopsy specimens [26].

Although a myopathic EMG is not specific, there are patterns that point toward a certain disorder or group of disorders. These patterns are also predictive of muscle histopathologic findings. In these described patterns, myopathic MUAPs will refer to short duration, low amplitude, polyphasic MUAPs. However, as noted above, myopathic MUAPs may occur in other conditions.

**Pattern 1: Myopathic MUAPs with fibrillation potentials (Table 2)**

This pattern is most commonly seen with idiopathic inflammatory myopathies such as polymyositis (PM), dermatomyositis (DM), and IBM (Figs. 3 and 4). Essentially all patients with IBM and 45% to 74% of patients with PM and DM exhibit this pattern; the rest exhibit Pattern 2 (described below) [27,28]. Myotonic discharges or CRDs are sometimes seen also [29]. These
disorders are differentiated based upon the histologic as well as EMG and clinical features. PM and IBM are both characterized by endomyal CD8 + inflammation. Vacuoles containing Congo red positive and filamentous material (ultrastructurally) occur in IBM (Fig. 4). DM is associated with a perivascular, perimysial B-cell inflammatory response and microangiopathy with perifascicular atrophy and degeneration.

Viral myositis, sarcoid myopathy [30], trichinosis [31], and penicillamine-induced inflammatory myopathy [32,33] might also exhibit this pattern, but childhood myositis from influenza may feature Pattern 2 [34]. Non-inflammatory necrotizing myopathies, such as cholesterol lowering agent myopathy [35], as well as hypothyroid myopathy, commonly produce Pattern 1 [36,37]. In hypothyroid myopathy, the fibrillation potentials are presumed to be due to sarcolemmal membrane instability. Fibrillation potentials are sometimes encountered in hyperthyroid myopathy [38], while histologic changes may be minimal. In patients with HIV infection with or without zidovudine treatment, Pattern One is seen [39–41]. In critical illness myopa-
thy, fibrillation potentials may or may not occur. When present, it is uncer-
tain if the fibrillation potentials are caused by myonecrosis or muscle mem-
brane dysfunction [42].

Of the inherited disorders, many muscular dystrophies exhibit this pat-
tern [43–47]. They are often ultimately distinguished by immunohistochem-
ical or molecular studies. Centronuclear myopathy is the only congenital
myopathy featuring Pattern 1 [48]. Pattern 1 is also seen mainly with exacer-
bations of inherited metabolic disorders such as McArdle’s Disease [10].

Additionally, patients with chronic inflammatory myopathies, especially
IBM and sometimes chronic PM and DM, exhibit a combination of longer
and short duration MUAPs (mixed pattern) in the same muscle (Fig. 4).
However, quantitative studies may only identify a myopathic pattern [49].
A mixed pattern is also occasionally noted in muscular dystrophies in which
long duration MUAPs are thought to be due to innervation of regenerating
muscle fiber segments [46]. The combination of short and long duration
MUAPs may also occur if there is a coexisting neurogenic process such as
in colchicine neuromyopathy, amyloidosis (Fig. 5), or vasculitis. In this sce-

Fig. 4. EMG and histopathologic correlation from a patient with inclusion body myositis. (A) Short duration, polyphasic MUAPs are recorded from the biceps brachii. Positive waves and fibrillation potentials were also noted (not shown). (B) A mixed population of MUAPs was present in the vastus lateralis. A low amplitude, short duration MUAP (short arrow) is depicted. A polyphasic MUAP (longer arrow) has a normal duration for age (13 ms), but it appears as a long duration MUAP (unless measured) when viewed adjacent to a short duration MUAP. (C) A muscle biopsy specimen from the biceps brachii reveals chronic changes (endomysial fibrosis and a variation in fiber sizes) and myofibers containing multiple rimmed vacuoles (arrow). (Gomori trichrome, cryostat section.) (D) Endomysial lymphocytic inflammation is shown on an H & E stained paraffin section.
nario, the long duration MUAPs tend to occur in the reinnervated muscles, and nerve conduction studies reveal sensory as well as motor abnormalities.

Pattern 1 is also seen in very unusual disorders such as adult rod body, myofibrillar, and amyloid myopathies, and in carnitine deficiency. These disorders may also exhibit Pattern 2. Often, these disorders are not expected clinically, and they are diagnosed pathologically. Overall, the likelihood of making a specific histopathological diagnosis is probably highest in patients with this EMG pattern [26].

*Pattern 2: myopathic MUAPs without fibrillation potentials (Table 2)*

This pattern is most commonly seen in non-inflammatory, nonnecrotizing myopathies, including most of the endocrine myopathies [36–38,50,51], congenital myopathies, mitochondrial, and other metabolic myopathies [7,52,53], toxic myopathies [42,54], and some muscular dystrophies. The dystrophies typically include the following: oculopharyngeal dystrophy, FSHD,
and some distal dystrophies [43,55,56]. Limb-girdle dystrophies, a heterogeneous group of autosomal dominant and recessive disorders, tend to be more indolent than the dystrophinopathies, and presumably are associated with less muscle necrosis. Hence, electrically, they exhibit Pattern 2 more often than Pattern 1 [57,58].

Treated inflammatory myopathies may also exhibit this pattern even if the myositis is active. Thus, Pattern 2 does not differentiate between active (partially treated) myositis and corticosteroid (CS) myopathy, but if Pattern 1 is seen in myositis patients treated with CS, then CS myopathy is excluded.

**Pattern 3: myopathic MUAPs with myotonic discharges (Table 2)**

This pattern is most commonly seen in myotonic dystrophies, either the classic myotonic dystrophy type 1 or the more recently identified proximal myotonic myopathy (PROMM) [59]. In these disorders, sarcolemmal membrane channel defects probably cause myotonia. However, the defects have not yet been clarified, especially in PROMM [60]. Myotonia, along with CRDs, is also seen more focally in acid maltase deficiency, especially in the paraspinal muscles. However, acid maltase deficiency often also manifests with Patterns 1 and 2 [8,61,62]. In infantile and childhood cases, pathologic studies reveal a myopathy with autophagic (acid phosphatase reactive) vacuoles containing glycogen. In adult cases, the biopsy findings may reveal a milder vacuolar myopathy, but normal findings are common [8,62]. The cause of the myotonia is not certain. Fiber splitting may lead to the CRDs. CRDs also occur with debrancher deficiency [52], and other glycogen storage diseases can exhibit this pattern focally [63].

Myotonia is also encountered focally in inflammatory myopathies, colchicine neuromyopathy [64,65], cholesterol-lowering agent, and less often hypothyroid myopathy. Myotonic discharges have also been reported in carnitine myopathy [11]. Myotonic discharges without myopathic MUAPs are seen in myotonia congenitas, paramyotonia congenita, and hyperkalemic periodic paralysis.

**Pattern 4: Normal electromyogram (EMG) (Table 2)**

About 35–50% of patients with mitochondrial myopathy have a normal EMG [6,7]. Normal studies may also occur in congenital myopathies, since subtle abnormalities may be harder to recognize due to the nature of the test and the difficulty performing extensive studies in children. Normal studies may also occur in lipid and glycogen storage disorders between attacks. Other myopathies sometimes associated with normal EMGs are listed in Table 2.

Clinical follow-up, a repeat EMG, or quantitative EMG is indicated in patients with a normal EMG and progressive or persistent weakness that could be of myopathic origin. Obtaining a muscle biopsy specimen is also a consideration (Fig. 2).
Summary

Uncovering the cause of a suspected myopathy may be challenging. However, a careful approach starts with utilizing the wealth of available information regarding the clinical and laboratory features of myopathy. Electrodiagnostic testing is then obtained (in most cases). Recognition of the pattern of EMG findings in light of the clinical and laboratory features should narrow the differential diagnosis and dictate the next steps in the evaluation. Histopathologic or molecular studies, or both may follow. Ultimately, this approach usually allows the clinician to make the correct diagnosis.

References

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