Current Approaches to Common Neuromuscular Problems

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Authors had nothing to disclose.

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The ideas and opinions expressed in this publication are solely those of the specific authors and do not necessarily represent those of the AANEM.
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Current Approaches to Common Neuromuscular Problems

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OBJECTIVES After attending this session, participants will (1) obtain the conceptual framework for patient history and physical examination for common neuromuscular disorders, (2) understand the strengths and limitations of the needle EMG examination in the evaluation of these disorders, and (3) understand the anatomy and physiology of peripheral nerve and muscle and the pathophysiologic changes that occur with common neuromuscular disorders.

PREREQUISITE This course is designed as an educational opportunity for physicians.

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INTRODUCTION

Patients with symptoms of weakness are commonly referred for a nerve conduction study (NCS) and electromyogram (EMG) to look for the one of many different peripheral neuromuscular disorders that may account for their symptoms. The identifiable etiologies are distributed among myopathies, motor neuron diseases, polyradiculoneuropathies, and neuromuscular junction disorders. Since identifiable causes of weakness make up only 11% of patients seen in an EMG laboratory, a well-defined approach should be available when they do appear. A clinical history to define the temporal course, distribution of symptoms, previous testing, previous treatments, and treatment outcomes should be combined with a focused neurological examination. Testing cranial nerves, strength, gait, tone, reflexes, and sensation before starting the study allows a much more focused and efficient study. Among these weakness is particularly important for planning the testing.

Generalized weakness in the outpatient or inpatient settings can have very different clinical pictures and approaches to the problems. Fatigue, weakness, cramps, and myalgia are common complaints in the outpatient setting, often without definitive findings on clinical examination. Hospitalized patients usually have more prominent deficits; in the intensive care unit they may be close to quadriplegic. Thus careful assessment of the clinical weakness is needed to identify the clinical problems that must be considered.

Patients with weakness are often referred by other physicians for EMG and NCS to assess for a specific disorder of concern to them. Weakness can occur with both central and peripheral diseases that are usually readily distinguished clinically. Occasional patients with unrecognized central disorders are referred for an EMG and NCS, such as foot drop in a stroke or paraparesis with a spinal cord lesion. The electrodiagnostic (EDX) physician should therefore do a limited evaluation to assure that the process is not central in origin.

EMG and NCS are a major part of the full evaluation of a patient with each of the peripheral causes of weakness: myopathy, neuromuscular junction disorder, peripheral neuropathy, polyradiculopathy, and motor neuron disease. EMG and NCS include a wide range of different tests for these disorders that cannot all be performed on every patient. The EDX physician must select those tests that will most reliably and efficiently define the underlying disorder. While a referring physician's concern about specific clinical entities must be given high priority in determining the tests to select, the referring physician usually does not have the expertise and experience of an EDX physician. The EDX physician should therefore perform a clinical examination to determine the tests that will be performed focusing particularly on signs of objective weakness.

### TABLE 1 
Distribution of electromyography diagnoses during 1 year in an academic electromyography laboratory

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No abnormalities</td>
<td>3634</td>
<td>26%</td>
</tr>
<tr>
<td>Focal nerve disorders</td>
<td>6098</td>
<td>43%</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>1934</td>
<td>14%</td>
</tr>
<tr>
<td>Weakness</td>
<td>1480</td>
<td>11%</td>
</tr>
<tr>
<td>Myopathy</td>
<td>590</td>
<td>4%</td>
</tr>
<tr>
<td>Motor neuron disease</td>
<td>377</td>
<td>3%</td>
</tr>
<tr>
<td>Polyradiculoneuropathy</td>
<td>348</td>
<td>3%</td>
</tr>
<tr>
<td>Demyelinating neuropathy</td>
<td>101</td>
<td>1%</td>
</tr>
<tr>
<td>Neuromuscular junction</td>
<td>64</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>
CHARACTERIZATION OF OBJECTIVE CLINICAL WEAKNESS FOR PLANNING EMG AND NCS TESTING

A neurologic examination is critical to planning the EMG and NCS that would most efficiently and accurately define the underlying disorder in a patient with weakness. Basic strength testing can guide the testing by suggesting the likelihood of possible underlying diseases. Reflex and sensory testing are helpful in selected situations.

Within the group of myopathies, as well as in other neuromuscular diseases, there can be quite different clinical pictures. For example, a myopathy may be distal as well as proximal, or neuromuscular junction diseases may get weaker (myasthenia gravis) or stronger (Lambert-Eaton myasthenic syndrome) with exercise. And there may be mixtures: polyradiculopathy often occurs in association with peripheral neuropathy, and is referred to as a polyradiculoneuropathy. The occurrence of such combinations will be identified as equal likelihood of polyradiculopathy and peripheral neuropathy. None the less, there is sufficient similarity of the diseases within each of these categories to classify them separately in defining the appropriate testing.

The distribution of the weakness assists in defining the likelihood of each of the major types of peripheral neuromuscular disease. The determination of likelihood is based on the usual clinical picture of a category of disease and the frequency of its occurrence in the population.

Each of the diseases could present distribution of the weakness with any one of the distributions, but the likelihood varies with the specific type of disease. The major disease groups will be referred to with abbreviations: myopathy (Myop), neuromuscular junction (NMJ), peripheral neuropathy (PN), polyradiculopathy (PolyRad), motor neuron disease (MND). Likelihood is defined by the greater than (“>”) signs.

Generalized distribution – clear evidence of weakness in many areas

Diffuse = similar weakness in all limb and trunk muscles

Myop > PolyRad = PN > NMJ > MND

Proximal = predominantly in proximal, limb-girdle muscles

Myop >> PolyRad > NMJ > MND > PN

Distal = predominantly in distal limb muscles

PN = PolyRad > MND > Myop > NMJ

Cranial = predominantly in cranial muscles

MND > NMJ > Myop > PolyRad > PN

Asymmetrical = greater weakness on one side, but not focal

(see below)

MND > NMJ > Myop > PolyRad > PN

Focal = specific, usually unilateral area, not just asymmetrical

Focal weakness is most commonly a mononeuropathy, limited to the distribution of individual nerves, such as carpal tunnel syndrome or ulnar neuropathy.

Radiculopathies and plexopathies are also typically focal in their distribution, a single root or a component of the brachial or lumbo-sacral plexus.

Muscle – rarely, focal weakness may be due to a muscle disease

With the exception of certain rare muscle disorders, focal processes require specific approaches to EMG and NCS that will not be discussed in this manuscript.

While there are exceptions, the time course of the disease often provides clues to the specific nature of a peripheral neuromuscular disease. Acute processes suggest toxic neuropathies or myopathies; subacute onset over days to weeks is likely an inflammatory disorder such as myositis and Guillain-Barre syndrome. Transient disorders are often metabolic, while fluctuating weakness is typical of myasthenia gravis. Disorders evolving over years generally are genetic or “degenerative” such as the dystrophies and MND.

Patient examples will be used to demonstrate approaches to weakness in different clinical settings.

Case 1: 67-year-old woman with leg weakness

- 8-year history of slowly progressive, painless weakness
  - 8 years ago - trouble arising from floor
  - 4 years ago - trouble arising from chair
  - 2 years ago - falls, give way of left leg
- Denies atrophy, fasciculations, muscle pain, sensory symptoms, or any upper extremity or trunk symptoms
- Previous EMG and NCS normal

Clinical Examination: Uses upper extremities to arise from seated position.

- -2 weakness quadriceps with mild, bilateral atrophy
- -1 to -2 weakness left>right finger flexors and wrist flexors
- Remainder of neurologic examination is normal, including reflexes and sensory examination

EMG/NCS and report- see insert

This patient demonstrates the importance of the clinical examination and the information that EDX studies can provide. Each of these should be kept in mind in performing EDX studies. An EMG report will be enhanced for the referring physician by commenting on these.

- Confirm clinical impression
- Disease type
- Disease location
- Define severity
- Identify subclinical disease
- Define course
- Identify other associated disease

TOOLS FOR TESTING PERIPHERAL NEUROMUSCULAR DISORDERS

A patient with objective weakness in one of the defined distribution listed above on clinical examination will help to determine the type and extent of testing that is needed. The following EDX tools should
be considered for testing. Their specific applications are discussed separately below.

- NCS
- Repetitive nerve stimulation
- EMG
- Single fiber EMG (SFEMG)
- Interference analysis
- Turn/amplitude

**NCS**

Motor NCS - Patients with weakness may demonstrate a number of abnormalities on motor NCS that assist in localizing the process along the peripheral neuraxis. A low compound muscle action potential (CMAP) can occur in any of the neuromuscular diseases, but are less common in myopathy and NMJ disorders. Slow conduction, temporal dispersion, or conduction block are signs of demyelination that suggest acute or chronic, acquired demyelinating polyradiculopathies (AIDP or CIDP) or a multifocal motor neuropathy. Repetitive stimulation with exercise often shows the decrement and/or facilitation of a defect of neuromuscular transmission.

Late responses - Prolonged F-wave latencies or R1 blink latencies are signs of the proximal slowing seen in patients with weakness due to polyradiculopathies, particularly early in the course when other abnormalities on NCS may not be evident.

Sensory NCS - Low amplitude sensory responses and/or slow conduction, especially in the sural or medial plantar nerves in patients with weakness without sensory findings, suggest the possibility of a subclinical peripheral neuropathy as might occur in diabetes, myopathies such as inclusion body myositis. However, some disorders, such as amyloidosis or sarcoidosis, may affect nerve and muscle (neuromyopathies).

**Repetitive Nerve Stimulation**

Repetitive nerve stimulation testing should be considered in all patients who complain of generalized weakness, as they will occasionally identify an unsuspected NMJ disorder. The extent of testing depends on the level of suspicion of a NMJ disorder; if the suspicion is high, distal and proximal nerve-muscle testing before and after exercise should be performed in the limbs with greatest weakness. A decrement is evidence of a disorder of the NMJ; repair 2–3 minutes after exercise suggests myasthenia gravis. Marked facilitation is typical of Lambert-Eaton myasthenic syndrome, especially if the CMAP amplitudes are low. Repetitive CMAP suggest congenital which requires more extensive complicated, testing that will not be reviewed here.

**EMG**

Testing muscle with a needle recording electrode is the single most useful study of patients with weakness. Examination of weak muscles can define the underlying pathology in most patients. A normal study makes a neuromuscular disorder an unlikely cause of weakness. Short duration, low amplitude motor unit action-potentials are typical of a myopathy. Combined with fibrillation potentials and an excess of polyphasic MUAPs, these findings suggest muscle fiber necroses and/or regeneration, which can occur in many myopathies, but especially inflammatory. Myopathies typically show an increased turn/amplitude ratio with interference pattern analysis.

Variation in the size and shape of a single MUAP with or without short duration is a sign of NMJ disease, but can also occur in neurogenic disorders with denervation and ongoing reinnervation. Unstable individual MUAPs should be sought in each patient with weakness.

More precise identification of the severity of a disorder is aided by quantitation of the duration, amplitude, and phases of 30 or more individual MUAPs. Quantitation of an interference pattern with a mixture of superimposed MUAPs can be analyzed by interference pattern analysis in which the amplitude and turns are measured at a fixed force.

Reduced MUAP recruitment with long duration, polyphasic MUAPs are evidence of a neurogenic disorder. The presence of fibrillation potentials and unstable MUAPs indicate a progressing disorder, or less likely, ongoing reinnervation. Neurogenic disorders typically show decreased turn/amplitude ratio with interference pattern analysis.

**SFEMG**

Specialized needle EMG recordings with a 500 Hz filter and more rapid sweep settings allow the isolated recording of individual muscle fibers. Variation in the interval between two fibers in a single MUAP (jitter) can provide very sensitive evidence of a NMJ disorder. Increased jitter with normal or mildly short duration MUAPs is the most sensitive test for NMJ disorders, and may be seen in muscles without decrement in myasthenia gravis. Increased jitter with long duration, polyphasic MUAPs is evidence of a progressing neurogenic disorder such as MND.

**Case 2:** 20-year-old college student 2 weeks progressive generalized weakness

- Day 1  Myalgia, headache, sore throat, fever
- Day 10  Student Health: penicillin for “strept throat”, persistent emesis
- Day 11  Emergency Room - Urinary retention, lethargy, unsteady
- Day 12  Diplopia, mild proximal weakness, brisk deep tendon reflex (DTR), bilateral Babinski
- Day 13  Reduced reflexes, progressive weakness, shortness of breath (SOB), tachycardia
- Day 14  Hospitalized: Head computed tomography and magnetic resonance imaging scans normal; Cerebrospinal fluid (CSF) cells and protein increased
Diagnosis – Guillain–Barré with myelopathy, polyradiculoneuropathy, and autonomic neuropathy

Treatment Plan: Start 5 days intravenous immunoglobulin (IVIg)

EMG/NCS #1 and report – see insert
EMG/NCS #2 and report – see insert
EMG/NCS #3 and report – see insert

Case 2 demonstrates the evolution of a clinical disorder in which EMG provides valuable clinical guidance for both prognosis and clinical guidance. All the EMG/NCS abnormalities found in neuromuscular diseases evolve over time. These changes should be kept in mind in interpreting findings. The typical evolution of EMG findings in a patient with weakness from an acute axonal loss is shown in Table 2.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Evolution of electromyography findings in an acute neurogenic disorder</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>1 week</td>
</tr>
<tr>
<td>Fibrillation Potentials</td>
<td>None</td>
</tr>
<tr>
<td>Recruitment</td>
<td>Reduced</td>
</tr>
<tr>
<td>Phases</td>
<td>Normal</td>
</tr>
<tr>
<td>Duration</td>
<td>Normal</td>
</tr>
<tr>
<td>Other</td>
<td>None</td>
</tr>
</tbody>
</table>

The remainder of this review will include a brief summary of the approach to weakness in each of the major groups of neuromuscular disease followed by a detailed review of the considerations in assessing a patient for possible myopathy.

**TESTS TO CONSIDER IN A PATIENT WITH SUSPECTED MND**

Evaluation of MND is complicated by the variety of initial presentations both in distribution and clinical manifestations. Amyotrophic lateral sclerosis (ALS), the most common MND, typically presents with focal signs that may be one arm, one leg, bulbar, respiratory or trunk in that order of frequency. Presentation may be with purely lower motor neuron, purely upper motor neuron, or a mixture of signs in each area. Two reliable clues to ALS are: presence of motor with no sensory findings, EMG abnormalities outside the distribution of clinical findings. ALS should be considered in every patient with focal deficit if there are no sensory findings, such patients 1) with foot drop, but no pain or sensory loss, hand weakness, but no pain or sensory loss, difficulty swallowing, but no pain or sensory loss, etc. Other signs can be helpful in suggesting specific MND. Facial fasciculations suggest Kennedy’s disease; very long standing, minimally progressive, symmetrical, predominantly proximal weakness suggests a spinal muscular atrophy. Asymmetric distribution of widespread neurogenic MUAPs with a minimum of fibrillation can be residuals of poliomyelitis.

**EMG**

While EMG or NCS testing could be performed first, in a patient with suspected MND it is often more efficient to begin with EMG testing, sampling weak muscles in the weakest limb in the distributions of different nerves and roots. If the abnormalities are outside the distribution of a single nerve or root, it is most efficient to then move to muscles in another limb, e.g., anterior tibial, medial gastrocnemius and vastus medialis in the leg, or first dorsal interosseous, biceps, and triceps in the arm. If abnormality is found in two limbs, thoracic paraspinal muscles at two levels can be sampled with a goal of finding abnormalities at three levels of the neuraxis. If changes are found at only two levels, or if there is bulbar weakness, cranial innervated muscles like the trapezius, masseter, or tongue should be tested. Unstable, polyphasic MUAPs can provide evidence of denervation early in the course of the disease when fibrillations may be minimal. If necessary, diaphragm EMG should be considered.

**NCS**

If changes of MND are found on EMG, NCS can be limited to the limb with greatest weakness to be sure there is not a superimposed mononeuropathy or peripheral neuropathy. A critical finding in distinguishing the changes of a mononeuropathy from MND is normal sensory potentials with low amplitude motor responses.

**TESTS TO CONSIDER IN A PATIENT WITH SUSPECTED POLYRADICULOPATHY**

PolyRad are often demyelinating disorders with significant slowing of conduction or conduction block. NCS testing provides the most definitive evidence of a PolyRad. NCSs are generally performed first with particular attention to motor NCSs. NCSs in a pure axonal PolyRad will be less informative, but necessary to demonstrate the extent of axonal loss.

**NCS**

Starting with the most involved limb, median, ulnar, peroneal, and tibial nerves are tested with particular attention to F-wave latencies and distal latencies. If conduction velocity is slowed at all distally, the F-wave latency should be compared with an estimated F-latency. PolyRad will typically show more slowing proximally with a longer F-wave latency than F-wave latency estimate. If proximal slowing is not clearly shown by distal nerve testing, proximal conduction is most efficiently tested with blink R1 latency. Although technically more difficult, proximal slowing can also be identified by percutaneous, needle stimulation of the nerve “root” (spinal nerve) with recording from the hypothenar, biceps, abductor hallucis, or extensor digitorum brevis muscles.

**EMG**

If clear evidence of PolyRad is found on NCS, the purpose of EMG becomes to determine the extent and distribution of axonal loss.
(fibrillation potentials). Selected weak muscles in one arm and leg, and paraspinal muscles are usually sufficient.

**TESTS TO CONSIDER IN A POSSIBLE PERIPHERAL NEUROPATHY**

Despite the wide variety of forms of PN the approaches are similar with a focus on NCS. Both the axonal and demyelinating forms are identified by similar testing. The criteria for distinguishing them should be familiar to the EDX physician, but will not be discussed in this manuscript.

**NCS**

Since the disorder is typically distal and length dependent, testing the leg on the most involved side first (or the least involved if there is severe atrophy) including peroneal/anterior tibial, if there are no responses distally. F-wave testing is important to identify combined PN and PolyRad. If both disorders are present the F-wave latency and F-wave latency estimate will be similar; if there is no PolyRad, the F-wave latency will be shorter than the estimate. It is particularly important to compare proximal and distal amplitudes and configuration. Significantly lower amplitude with proximal stimulation can identify a focal conduction block (distinct from focal slowing); an irregular spreading of the CMAP shape identifies temporal dispersion, another sign of a demyelinating process.

**EMG**

The purpose of EMG is primarily to confirm the extent and distribution of axonal loss (fibrillation potentials), and should test distal, proximal and paraspinal muscles if there are any clinical or NCS signs of proximal involvement. EMG of distal arm muscles often demonstrates axonal loss with not clinical signs, usually only long duration motor unit potentials. If no fibrillation potentials are found in standard muscles, intrinsic foot muscles (abductor hallucis and dorsal interossei) will often show abnormality.

**TESTS TO CONSIDER IN A POSSIBLE MYOPATHY WITH A FOCUS ON INFLAMMATORY MYOPATHIES**

While either EMG or NCS testing could be performed first, in a possible myography it is often more efficient to begin with EMG testing, sampling weak muscles in the weakest limb in the distributions of different nerves and roots.

The following needle EMG protocol is recommended:

- Test two or three of the weakest muscles and a less involved muscle searching for fibrillation potentials, unstable MUAPs and short duration and/or polyphasic potentials
- Examine multiple areas within a muscle since findings may be scattered, giving particular attention to superficial layers where abnormalities are often more prominent in inflammatory myopathies
- If abnormalities are not found in the limbs, test thoracic paraspinal muscles at two levels and test cranial muscles with significant weakness
- If abnormalities are found in one limb, compare at least one muscle in the other ipsilateral limb to fully define the distribution
- Quantitate MUAPs in the weakest muscles if clear abnormalities are not found

The following NCS protocol is recommended:

Test the weakest limb with motor NCS and F-waves. If weakness is particularly prominent in radial or musculocutaneous innervated muscles, test radial and/or musculocutaneous nerves for focal slowing or conduction block to exclude multifocal motor neuropathy with conduction block

If there is a history of fatigable weakness, look for NMJ disorders by testing repetitive stimulation before and after exercise in clinically weak muscles, (e.g., accessory/trapezius, musculocutaneous/biceps, axillary/deltoid, femoral/rectus femoris).

**Findings in Myopathy**

The distribution of abnormality in many myopathies, especially inflammatory is proximal and paraspinal, but often with prominent changes in the anterior tibial muscle. A few myopathies, especially fascio scapulo humeral (FSH) dystrophy and DM2 myotonic dystrophy may have different findings in muscles near each other or be asymmetrical. These require more sampling to identify. A limited number of myopathies have distal weakness, especially the relatively common inclusion body myositis (Table 3).

<table>
<thead>
<tr>
<th>Table 3 Myopathies with predominantly distal weakness</th>
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<tbody>
<tr>
<td>o Inclusion body myositis - usually</td>
</tr>
<tr>
<td>o Polymyositis - infrequently</td>
</tr>
<tr>
<td>o Centronuclear myopathy (dynamin 2)</td>
</tr>
<tr>
<td>o Nebulin distal myopathy</td>
</tr>
<tr>
<td>o Central core myopathy</td>
</tr>
<tr>
<td>o Myotonic dystrophy</td>
</tr>
<tr>
<td>o Distal dystrophies</td>
</tr>
<tr>
<td>o Amyloid</td>
</tr>
</tbody>
</table>

MUAPs in a myopathy become shorter in duration and lower in amplitude as muscle fibers are destroyed by the disease. The changes are typically proportional to the weakness. In severe disease MAUPs may have only a tiny potential from one remaining fiber in the MUAP. Increased MUAP turns and phases results from differential fiber conduction velocity with loss of synchrony because of fiber atrophy or small regenerating fibers. SFEMG also shows abnormalities with increased jitter due to reinnervation, and in-
creased fiber density due to fiber splitting and reinnervation. Early in the course of a myopathy, the findings may be patchy or subtle, requiring widespread and thorough sampling of muscles. Keep in mind each of the neuromuscular disorders that may show short duration MUAPs (Table 4).

**Table 4** Disorders that can result in short duration MUAPs

- Myopathy with muscle fiber destruction
- Neuromuscular junction disorders with severe block or end plate destruction
- Periodic paralysis and other membrane disorders
- Neuropathy with primarily nerve terminal damage
- Late stage, severe neurogenic disorder
- Early regeneration after a severe neurogenic process

MUAPs = motor unit action potentials

EMG is limited in its ability to distinguish between different etiologies. Although the findings reflect the underlying muscle fiber pathology and physiology, pathologic changes in different disorders may produce similar EMG changes such that the findings are not specific for individual diseases. The absence of abnormal MUAP changes in a clearly weak muscle can occur in some endocrine or metabolic myopathies, especially steroid myopathy.

Fibrillation potentials occur by a number of mechanisms, including segmental necrosis of fibers, fiber splitting, and from regenerating muscle fibers. Fibrillation potentials may be few in number and scattered. They tend to fire slowly at less that 4 Hz. Positive waveform fibrillation potentials are often seen. Muscle fiber atrophy results in very tiny MUAPs in long-standing disease. Myopathies with fibrillation potentials are listed in Table 5.

**Table 5** Myopathies with fibrillation potentials

- All inflammatory myopathies
- Inclusion body myositis - often with a mixture of short and long duration motor unit action potentials
- Critical illness myopathy
- Congenital myopathies - centronuclear, nemaline, congenital fiber-type disproportion
- Muscular dystrophies - dystrophinopathies, fascio capulohumeral, myotonic dystrophy DM1 and DM2, some limb-girdle muscular dystrophy (LGMD), most distal dystrophies
- Toxic: acute alcoholic myopathy, lipid lowering drugs
- Metabolic: acid maltase, other glycogen storage diseases after an attack, hyperkalemic periodic paralysis, paramyotonia, K-sensitive myotonia
- Rhabdomyolysis – may be quite prominent
- Muscle trauma – including previous surgery and injections

The common occurrence of fibrillation potentials in an inflammatory myopathy and the much greater incidence of inflammatory myopathy than other myopathies, make inflammatory myopathy far more likely in a patient with weakness, short duration MUAPs and fibrillation potentials. There are differences in density of fibrillation potentials among the myopathies as shown in Table 6.

**Table 6** Major Categories of Inflammatory Myopathies Listed by Density of Fibrillation

<table>
<thead>
<tr>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polymyositis</td>
</tr>
<tr>
<td>Dermatomyositis</td>
</tr>
<tr>
<td>Inclusion body myositis</td>
</tr>
<tr>
<td>Overlap syndromes</td>
</tr>
<tr>
<td>Connective tissue diseases sometimes with neuropathy</td>
</tr>
<tr>
<td>Scleroderma</td>
</tr>
<tr>
<td>Sjogren's</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
</tr>
<tr>
<td>Rheumatoid</td>
</tr>
<tr>
<td>Penicillamine</td>
</tr>
<tr>
<td>Amyloid</td>
</tr>
<tr>
<td>Bacterial myositis - Clostridia, tuberculosis, Lyme, syphils, Whipple’s disease</td>
</tr>
<tr>
<td>Viral myositis - human immune deficiency virus, Coxackie, influenza</td>
</tr>
<tr>
<td>Parasitic myositis - trichinosis, toxoplasmosis, cystercycosis, echinococcus</td>
</tr>
<tr>
<td>Sarcoid myopathy</td>
</tr>
<tr>
<td>Eosinophilia-myalgia syndrome</td>
</tr>
<tr>
<td>Focal myositis</td>
</tr>
<tr>
<td>Vasculitis</td>
</tr>
</tbody>
</table>

Other discharges have varying significance. Complex repetitive discharges indicate long duration of disease, but do not suggest a specific type. A limited number of myotonic discharges can be seen in many myopathies and in long-standing neurogenic processes. If they are more prominent, specific diseases listed in Table 7 should be considered.

**Table 7** Myopathies with myotonic discharges

- Myotonic dystrophy, both DM1 and DM2
- Paramyotonia congenita
- Myotonia congenita
- Hyperkalemic periodic paralysis
- Potassium sensitive myotonia
- Centronuclear myopathy
- Hypothyroid myopathy
- Statin-associated myopathy
- Acid maltase deficiency
- Amyloid

The two forms of myotonic dystrophies, DM1 and DM2 differ clinically with myalgia and asymmetry in DM2. Differences in response to repetitive stimulation and the character of the myotonic discharges allow them to be distinguished from each other and more important from an inflammatory myopathy.

A number of reports have shown that the distribution of myotonic discharges in DM2 is more prominent and may be limited to proximal in the legs. It is therefore important to look there. In addition while both DM1 and DM2 have myotonic discharges in DM2 they generally wane rather than wax and wane. The end of slow-waning discharges in DM2 has characteristics that are similar to fibrillation potentials. The limited distribution of DM2 and the difference in
pattern can result in a patient having what appears to be fibrillation potentials with short duration MUAPs, like an inflammatory myopathy. A more extensive search for myotonic discharges is needed in some patients with myalgia and minimal weakness who might have DM2.

The abnormalities in inflammatory myopathy evolve over time. Early on the findings are patchy or subtle, requiring thoroughness and widespread sampling for the short MUAPs and fibrillation potentials. The MUAPs become more polyphasic with disease progression to where they have some features of a chronic neurogenic process, including reduced recruitment and long-duration MUAPs. In chronic stages, MUAPs become more polyphasic with satellite potentials with mixed short-and long-duration MUAPs. Mild NCS changes may appear. A long standing inflammatory myopathy cannot be readily distinguished from inclusion body myositis, whose apparent incidence is increasing as specific biopsy staining for the disorder has become more prominent.

Before concluding that a patient’s clinical and EMG/NCS findings are due to an inflammatory myopathy, attempts should be made to assure that other mimic disorders are excluded (Table 8).

<table>
<thead>
<tr>
<th>TABLE 8 Disorders to rule out in a suspected inflammatory myopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Other Myopathies</strong></td>
</tr>
<tr>
<td>Enzyme deficiencies</td>
</tr>
<tr>
<td>Congenital myopathies</td>
</tr>
<tr>
<td>Necrotizing myopathies</td>
</tr>
<tr>
<td>Toxins and drugs</td>
</tr>
<tr>
<td>Alcohol</td>
</tr>
<tr>
<td>Ischemia</td>
</tr>
<tr>
<td>Heat</td>
</tr>
<tr>
<td>Injections</td>
</tr>
<tr>
<td>Hypokalemia</td>
</tr>
<tr>
<td>Paraneoplastic</td>
</tr>
<tr>
<td><strong>Other neuromuscular disease</strong></td>
</tr>
<tr>
<td>Neuromuscular junction disorders</td>
</tr>
<tr>
<td>Polyradiculopathy</td>
</tr>
<tr>
<td>Spinal muscular atrophy</td>
</tr>
<tr>
<td>Amyotrophic lateral sclerosis</td>
</tr>
</tbody>
</table>

NCSs in myopathies are usually normal, or show only low amplitude responses if the weakness is sufficiently severe, but others should be considered as well (Table 9).

Slow motor conduction or sensory NCS abnormalities suggest the additional presence of a neuropathy. While long-duration MUAPs can occur with chronic myopathies, neuromyopathies are disorders that involve both nerve and muscle directly, and must be considered when these combinations are found. They occur most commonly in connective tissue diseases, but do occur in other myopathies, particularly drugs or toxins as listed in Table 10.

<table>
<thead>
<tr>
<th>Table 9 Myopathies more likely to have low compound muscle action potentials amplitudes on nerve conduction studies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inflammatory</strong></td>
</tr>
<tr>
<td>* Inclusion body myositis</td>
</tr>
<tr>
<td>* Severe polymyositis</td>
</tr>
<tr>
<td><strong>Dystrophies</strong></td>
</tr>
<tr>
<td>* Distal muscular dystrophies</td>
</tr>
<tr>
<td>* Distal myopathies</td>
</tr>
<tr>
<td>* Myotonic dystrophy</td>
</tr>
<tr>
<td>* Facioscapulohumeral dystrophy</td>
</tr>
<tr>
<td>* Emery-Dreifuss muscular dystrophy</td>
</tr>
<tr>
<td><strong>Enzyme deficiencies</strong></td>
</tr>
<tr>
<td>* Debrancher enzyme deficiency</td>
</tr>
<tr>
<td>* Acid maltase deficiency</td>
</tr>
<tr>
<td><strong>Other myopathies</strong></td>
</tr>
<tr>
<td>* Congenital myopathy</td>
</tr>
<tr>
<td>* Nemaline myopathy</td>
</tr>
<tr>
<td>* Central core myopathy</td>
</tr>
<tr>
<td>* Centronuclear myopathy</td>
</tr>
<tr>
<td>* Myofibrillary myopathy</td>
</tr>
</tbody>
</table>

Among the most difficult muscle problems for the EDX physician are patients with myalgia and fatigue who have no weakness or other clinical deficits. They are often classified and treated as fibromyalgia, but it must be recalled that some myopathies may have these as primary symptoms (Table 11). Some of them can be readily identified with EMG and muscle biopsy, but others will require more specific testing.
Clinical Examples of the Application of These Principles

**Case 3:** 65–year-old woman with fatigue

- 2 years of difficulty with household chores, “tired”
- Difficulty squatting during exercise
- EMG 1 year ago – normal NCS and EMG
- Limited improvement on Sertaline
- Examination - mild proximal weakness; normal reflexes, cranial nerves, sensation, gait

**EMG/NCS and report** – see insert

**Case 4:** 29-year-old woman with muscle aches

- Healthy - 5 years muscle aches
- Mild elevations of creatine kinase (300 - 550)
- Examination normal
- Mild weakness, limited to left triceps
- Normal NCS

**EMG/NCS and report** – see insert

**Case 5:** 45–year-old interior designer with 3 months generalized weakness

- Diplopia brain stem astrocytoma-stable 2 yrs after radiation therapy
- Temporal lobe herpes simplex virus (HSV) encephalitis-better 1 year after Acyclovir
- Bulbar dysfunction from tumor-dexameth asme and Temazolamide
- 2 mo progressive weakness with no other symptoms or signs
- CSF and EMG performed at home - axonal and demyelinating neuropathy
- Hospital transfer - quadriparetic with deep vein thrombosis
- Normal reflexes and sensation
- MRI 10 mm mass and residuals of HSV

**EMG/NCS and report** – see insert

**Case 6:** 84-year-old woman with weakness

- Diabetes mellitus and hypothyroidism with 2 months of painless arm weakness
- Examination: Proximal symmetric arm weakness, normal reflexes
- NCS - normal

**EMG/NCS and report** - see insert
INTRODUCTION

Cervical and lumbosacral radiculopathies are conditions involving a pathological process affecting the spinal nerve root. Commonly, this is a herniated nucleus pulposis that anatomically compresses a nerve root within the spinal canal. Another common etiology for radiculopathy is spinal stenosis resulting from a combination of degenerative spondylolisthesis, ligament hypertrophy, and spondylolisthesis. Inflammatory radiculitis is another pathophysiological process that can cause radiculopathy. It is important to remember, however, that other more ominous processes such as malignancy and infection can manifest the same symptoms and signs of radiculopathy as the more common causes.

This manuscript deals with the clinical approach used in an electrodiagnostic (EDX) laboratory to evaluate a person with neck pain, lumbar spine pain, or limb symptoms which are suggestive of radiculopathy. Given the large differential diagnosis for these symptoms, it is important for EDX physicians to develop a conceptual framework for evaluating these referrals with a standard focused history and physical examination and a tailored EDX approach. Accurately identifying radiculopathy by EDX whenever possible provides valuable information for treatment and minimizes other invasive and expensive diagnostic and therapeutic procedures.

SPINE AND NERVE ROOT ANATOMY: DEVIATIONS FROM THE EXPECTED

The anatomy of the bony spine, supporting ligamentous structures, and neural elements provides a unique biomechanical system that allows tremendous strength, yet flexibility. The interested reader can consult standard anatomy texts for further discussions. The important structural issues that relate to radiculopathy are addressed in this manuscript.

In the lumbar spine, the attachment and shape of the posterior longitudinal ligament predisposes the nucleus pulposis to herniation in a posterolateral direction where it is the weakest. The dorsal root ganglion (DRG) lies in the intervertebral foramen and this anatomical arrangement poses major implications for clinical EDX of radiculopathy. Intraspinal lesions can cause weakness due to their effects on the motor axons which originate in the anterior and lateral gray matter and pass through the lumbar spine as spinal roots. These roots form the “cauda equina,” or horse’s tail, the name used to describe this anatomical structure. Intraspinal lesions can also produce sensory loss by damaging the dorsal roots, which are composed of central processes from the sensory nerve cell bodies in the DRG, as they project to the spinal cord. Electrophysiologically, severe axonal damage intraspinally results in spontaneous activity on needle electromyography (EMG) and possibly reduced compound muscle action potentials (CMAPs). However, the sensory nerve action potentials (SNAPs) are preserved. This anatomical relationship provides a mechanism for further confirming whether or not a lesion is radicular (intraspinal). A destructive intramedullary (spinal cord) lesion at T11 can produce EMG findings in muscles innervated by any of the lumbosacral nerve roots and manifest the precise findings on needle EMG as those seen with a herniated nucleus pulposis at any of the lumbar disc levels. For this reason, the EDX physician cannot determine for certain the anatomic location of the lumbar intraspinal lesion producing distal muscle EMG findings in the lower limbs. EMG can only identify the root or roots that are physiologically involved, but not the precise anatomic site of pathology within the lumbar spinal canal.

In a prospective study of 100 patients with lumbosacral radiculopathy who underwent lumbar laminectomy, EMG precisely identified the involved root level 84% of the time. EMG failed to accurately identify the compressed root in 16% of patients. However, at least half of the failures were attributable to anomalies of innervation.
Another component to this study involved stimulating the nerve roots intraoperatively with simultaneous recording of muscle activity in the lower limb using surface electrodes. These investigators demonstrated variations in root innervations, such as the L5 root innervating the soleus and medial gastrocnemius in 16% of a sample of 50 patients. Most subjects demonstrated dual innervations for most muscles.68

Regarding the cervical nerve roots and the brachial plexus, there are many anatomic variations. Perneczky described an anatomic study of 40 cadavers where in all cases there were deviations from accepted cervical root and brachial plexus anatomy.47 Levin, Maggiano, and Wilbourn examined the pattern of abnormalities on EMG in 50 cases of surgically proven cervical root lesions.39 A range of needle EMG patterns was found with EMG demonstrating less specificity for the C6 root level, but more specificity and consistent patterns for C8, C7, and C5 radiculopathies. In subjects with C6 radiculopathies, half the patients showed findings similar to those with C5 radiculopathies and the other half demonstrated C7 patterns.

These findings underscore the limitations of precise localization for root lesions by EMG. The EDX physician should maintain an understanding of these anatomic variations to better convey the level of certainty with respect to diagnostic conclusions.

**COMMON MUSCULOSKELETAL DISORDERS MIMICKING CERVICAL RADICULOPATHY**

The symptoms of radiculopathy are nondescript and not specific for radiculopathy. Many other neurologic and musculoskeletal conditions can produce pain, weakness, and sensory symptoms. In addition to the standard peripheral neurologic examination, one of the most helpful maneuvers is to ask the patient where it hurts, then carefully palpate that area. If pain is reproduced by this palpation then the examiner should have a heightened suspicion for a musculoskeletal disorder. However, whereas a musculoskeletal disorder identified on examination makes a normal EDX study more likely, the presence of a musculoskeletal disorder does not exclude an abnormal EDX study with reliability or specificity. Common musculoskeletal disorders that produce symptoms similar to those produced by a cervical radiculopathy are shown in Table 1.

Shoulder impingement, lateral epicondylitis, and de Quervain’s tenosynovitis are easily identifiable conditions that are extraordinarily common. Even with a positive EDX test showing an entrapment neuropathy or radiculopathy, treatment of a concomitant musculoskeletal disorder can often improve overall symptoms.

Common entrapment neuropathies can present with symptoms similar to radiculopathy. Median neuropathy at the wrist and ulnar neuropathy at the elbow are common conditions for which patients are referred for EDX, and complicate the EDX assessment for radiculopathy. Plexopathies such as idiopathic brachial neuritis can pose diagnostic dilemmas for the EDX consultant as pain, weakness, and sensory loss are all common symptoms in bothplexopathies and radiculopathies.

**COMMON MUSCULOSKELETAL DISORDERS MIMICKING LUMBOSACRAL RADICULOPATHY**

Conditions that present with symptoms similar to those of lumbosacral radiculopathy are shown in Table 2. In this author’s opinion, one of the most readily treatable, yet under-recognized conditions is trochanteric bursitis and illiotibial band syndrome. The illiotibial band originates at the iliac crest and has tendinous contributions from the gluteus maximus and tensor fascia latae. It runs the length of the thigh and crosses the knee joint inserting on the lateral condyle of the tibia. This band is part of the fascia lata, a layer of dense strong connective tissue enveloping the thigh.

### Table 1  Musculoskeletal conditions that commonly mimic cervical radiculopathy

<table>
<thead>
<tr>
<th>Condition</th>
<th>Clinical symptoms/signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibromyalgia syndrome</td>
<td>Pain all over, female predominance, often sleep problems, tender to palpation in multiple areas</td>
</tr>
<tr>
<td>Polymyalgia rheumatica</td>
<td>&gt;50 years old, pain and stiffness in neck shoulders and hips, high ESR</td>
</tr>
<tr>
<td>Sternoclavicular joint arthropathy</td>
<td>Pain in anterior chest, pain with shoulder movement (adduction), pain on direct palpation</td>
</tr>
<tr>
<td>Acromioclavicular joint arthropathy</td>
<td>Pain in anterior chest, pain with shoulder movement (adduction), pain on direct palpation</td>
</tr>
<tr>
<td>Shoulder bursitis, impingement syndrome, bicipital tendonitis</td>
<td>Pain with palpation, positive impingement signs, pain in C5 distribution</td>
</tr>
<tr>
<td>Lateral epicondylitis “tennis elbow”</td>
<td>Pain in lateral forearm, pain with palpation and resisted wrist extension</td>
</tr>
<tr>
<td>De Quervain’s tenosynovitis</td>
<td>Lateral wrist and forearm pain, tender at abductor pollicis longus or extensor pollicis brevis tendons, positive Finkelstein test</td>
</tr>
<tr>
<td>Trigger finger, stenosing tenosynovitis</td>
<td>Intermittent pain and locking of a digit in flexion of finger flexor tendons</td>
</tr>
</tbody>
</table>

ESR = erythrocyte sedimentation rate
like a stocking. It is extremely strong laterally where it becomes the iliotibial band. Where it crosses the hip, trochanteric bursitis can occur. The lateral femoral condyle of the knee can also be a site of tendinitis as well, particularly in runners. Trochanteric bursitis and iliotibial band syndrome are two conditions which respond well to corticosteroid injections and a rehabilitation program aimed at stretching this musculotendinous band. They are commonly mistaken for lumbosacral radiculopathy.

Pain at the bottom of the foot with symptoms of burning and tingling is frequently plantar fasciitis. Dorsiflexing the foot and palpating the plantar fascia will identify taut painful tendinous bands if plantar fasciitis is present.

Neuralgic amyotrophy from diabetes is a condition that is often difficult to distinguish from lumbosacral radiculopathy. It often presents with thigh pain and on EMG appears more like proximal lumbosacral plexus mononeuropathies with frequent involvement of the femoral nerve. Diabetic thoracic radiculopathy is a distinct syndrome with abdominal wall or thoracic wall pain, and weight loss, but has a good prognosis. In diabetic thoracic radiculopathy, intra-abdominal and intra-thoracic conditions must first be excluded. The EMG findings of denervation in the abdominal or thoracic wall musculature are consistent with this clinical entity.

Mononeuropathies such as peroneal, tibial, and femoral, pose diagnostic challenges and the EDX consultant should sample enough muscles with EMG in different peripheral nerve distributions to confirm that findings are not localized to a particular peripheral nerve distribution.

**PHYSICAL EXAMINATION**

The EDX examination is an extension of the standard clinical examination. The history and physical examination are vital initial steps in determining what conditions may be causing the patient’s symptoms. Most radiculopathies present with symptoms in one limb. Multiple radiculopathies such as are seen in cervical spinal stenosis or lumbar stenosis, may cause symptoms in more than one limb. A focused neuromuscular examination that assesses strength, reflexes, and sensation in the affected limb and the contralateral limb provides a framework for EDX assessment.

An algorithmic approach to utilizing physical examination and symptom information to tailor the EDX evaluation is shown in Figure 1. In this approach, the patient’s symptoms, and physical examination signs of sensory loss and weakness create a conceptual framework for approaching these sometimes daunting problems. Admittedly, there are many exceptions to this approach with considerable overlap in conditions which might fall in multiple categories. Radiculopathies and entrapment neuropathies are examples of such conditions with a variety of clinical presentations and physical examination findings, such that they are included in both focal symptom categories with and without sensory loss. In the case of a person with lumbosacral radiculopathy, a positive straight leg raise test may be noted in the absence of motor, reflex, or sensory changes. Conditions such as myopathies and polyneuropathies better fit this algorithmic approach given that symptoms and physical examination signs are somewhat more specific. Figure 1 also contains musculoskeletal disorders and denotes how they fall into this conceptual framework. The EDX physician must be willing to modify the EDX examination in response to nerve conduction and EMG findings and adjust the focus of the examination in light of new information.

The implications of symptoms and signs on EDX findings were investigated by Lauder and colleagues for cohorts of patients with upper or lower limb symptoms as well suspected cervical and lumbosacral radiculopathies. Even though physical examination findings were better at predicting who would have a radiculopathy, many patients with normal examinations had abnormal EMG studies, indicating that clinicians should not curtail EDX testing simply because the physical examination is normal. For lower limb

### Table 2 Common musculoskeletal disorders mimicking lumbosacral radiculopathy

<table>
<thead>
<tr>
<th>Condition</th>
<th>Clinical symptoms/signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibromyalgia syndrome and polymyalgia rheumatica</td>
<td>As in Table 1</td>
</tr>
<tr>
<td>Hip arthritis</td>
<td>Pain in groin, anterior thigh, pain with weight bearing, positive Patrick’s test</td>
</tr>
<tr>
<td>Trochanteric bursitis</td>
<td>Lateral hip pain, pain with palpation on lateral and posterior hip</td>
</tr>
<tr>
<td>Iliotibial band syndrome</td>
<td>Pain along outer thigh, pain with palpation</td>
</tr>
<tr>
<td>Knee arthritis</td>
<td>Pain with weight bearing</td>
</tr>
<tr>
<td>Patellofemoral pain</td>
<td>Anterior knee pain, worsened with prolonged sitting</td>
</tr>
<tr>
<td>Pes anserinus bursitis</td>
<td>Medial proximal tibia pain, tender to palpation</td>
</tr>
<tr>
<td>Hamstring tendinitis, chronic strain</td>
<td>Posterior knee and thigh pain, can mimic positive straight leg raise, common in runners</td>
</tr>
<tr>
<td>Baker’s cyst</td>
<td>Posterior knee pain and swelling</td>
</tr>
<tr>
<td>Planter fasciitis</td>
<td>Pain in sole of foot, worsened with weight bearing activities, tender to palpation</td>
</tr>
<tr>
<td>Gastrocnemius-soleus tendinitis,</td>
<td>Calf pain, worsened with sports activities, usually limited range of motion compared to asymptomatic limb, chronic strain</td>
</tr>
</tbody>
</table>
Evaluating the Patient With Suspected Radiculopathy

AANEM Course

Symptoms, loss of a reflex or weakness dramatically increased the likelihood of having a radiculopathy by EMG. Losing the Achilles reflex for instance, resulted in an odds ratio of 8.4 (p<0.01)—eight times the likelihood of having a radiculopathy (S1 level) by EMG with this physical examination finding. Weakness in any leg muscle group resulted in about 2.5 times greater chance of identifying a lumbosacral radiculopathy on EMG. Similar findings were noted for upper limb symptoms. For instance, if a reflex was lost or weakness was noted, the likelihood of having a cervical radiculopathy confirmed by EMG was about 4 times more likely. Combinations of findings, particularly weakness plus reflex changes, resulted in a 9-fold greater likelihood of cervical radiculopathy.

Guidelines for Radiculopathy Evaluation

The American Association of Neuromuscular & Electrodiagnostic Medicine’s (AANEM) guidelines recommend that for an optimal evaluation of a patient with suspected radiculopathy, a needle EMG screen of a sufficient number of muscles and at least one motor and one sensory nerve conduction study (NCS) should be performed in the involved limb. The NCSs are necessary to exclude polyneuropathy. The sufficiency of the EMG screen and a recommended number of muscles is discussed in detail below. An EMG study is considered confirmatory for a radiculopathy if EMG abnormalities are found in two or more muscles innervated by the same nerve root and different peripheral nerves, yet muscles innervated by adjacent nerve roots are normal. This definition assumes that other generalized conditions such as polyneuropathy are not present.

Bilateral limbs are often necessary to study, particularly if a single limb shows EMG findings suggestive of radiculopathy and the patient has symptoms in both the studied and the contralateral limb. If bilateral limbs are involved, the EDX physician should have a low threshold for studying selected muscles in an upper limb (if the lower limbs are abnormal on EMG) or a lower limb (if both upper limbs are abnormal), to exclude a generalized process such as polyneuropathy or motor neuron disease. Likewise, additional NCSs are appropriate to exclude other suspected conditions and the EDX consultant should have a low threshold for expanding the study.

H Reflexes, F Waves, and Nerve Conduction Studies

Nerve conduction studies, H reflexes, and F waves are not very useful for confirming radiculopathy. They are useful, however, to exclude polyneuropathy or mononeuropathies.
H Reflexes

H reflexes have commonly been used to determine whether a radiculopathy demonstrates S1 involvement. It is a monosynaptic reflex that is an S1 mediated response and can differentiate to some extent to determine if L5 from S1 radiculopathy. Many researchers have evaluated their sensitivity and specificity with respect to lumbosacral radiculopathies and generally found a range of sensitivities from 32-88%. However, many of these studies suffered from lack of a control group, imprecise inclusion criteria, or small sample sizes.

Marin and colleagues prospectively examined the H reflex and the extensor digitorum brevis reflex in 53 normal subjects, 17 patients with L5, and 18 patients with S1 radiculopathy. Patients included in the study had all of the following: (1) radiating low back pain into the leg; (2) reduced sensation or weakness or positive straight leg raise test; and (3) either EMG evidence of radiculopathy or structural causes of radiculopathy on magnetic resonance imaging (MRI) or computed tomography (CT) imaging. The H-reflex maximal side-to-side latency difference was 1.8 ms as derived from the normal group. They analyzed the sensitivity of the H reflex for side-to-side differences greater than 1.8 ms or a unilaterally absent H reflex on the affected side. The H reflex only demonstrated a 50% sensitivity for S1 radiculopathy and 6% for L5 radiculopathy, but had a 91% specificity. Amplitudes were not assessed in this study. These results suggest that the H reflex has a low sensitivity for S1 root level involvement.

H reflexes may also be useful to identify subtle S1 radiculopathy, yet there are a number of shortcomings related to these responses. They can be normal with radiculopathies, and because they are mediated at the spinal cord level. They can be abnormal due to polyneuropathy, sciatic neuropathy, or plexopathy. They are most useful in the assessment for polyneuropathy.

In order to interpret a latency or amplitude value and render a judgement as to the probability that it is abnormal, precise population-based normative values encompassing a large age range of normal subjects must be available for NCS comparisons. Falco and colleagues demonstrated in a group of healthy elderly subjects (60-88 years old), that the tibial H reflex was present and recorded bilaterally in 92%. Most elderly subjects are expected to have normal H-reflex studies and when abnormalities are found in these persons, the EDX consultant should critically evaluate these findings and the clinical scenario before attributing H-reflex abnormalities to the aging process.

F Waves

F waves are late responses involving the motor axons and axonal pool at the spinal cord level. They can be assessed and classified by using the minimal latency, mean latency, and chronodispersion or scatter. As in the case of H reflexes, they demonstrate low sensitivities and are not specific for radiculopathy, rather they are a better screen for polyneuropathy. Published sensitivities range from 13-69%, however these studies suffer from many of the shortcomings described for H-reflex studies.

The AANEM guidelines examined the literature and concluded that somatosensory evoked potentials (SEPs) may be useful for cervical spondylosis with cord compression. Likewise, in lumbosacral spinal stenosis, dermatomal somatosensory evoked potentials (DSEPs) may be useful in defining levels of deficits.

Physiological evidence of multiple or single root involvement in lumbosacral spinal stenosis can be documented with DSEPs and may be useful in the case where spinal canal narrowing is minimal and the patient has symptoms. This testing also complements standard needle EMG. Snowden and colleagues found that for single and multilevel lumbosacral spinal stenosis, DSEPs revealed 78% sensitivity relative to spinal imaging. In this well-designed prospective study, DSEP criteria as well as inclusion criteria were precisely defined. The predictive value for a positive test was 93%.

Yiannikas, Shahani, and Young demonstrated that SEPs may be useful for cervical myelopathy. In this study, in 10 patients with clinical signs of myelopathy, all 10 had abnormal peroneal SEPs and 7 had abnormal median SEPs.
Maertens de Noordhout and colleagues examined motor and SEPs in 55 persons with unequivocal signs and symptoms of cervical spinal myelopathy. In this group 87% showed gait disturbances, and 82% showed hyperreflexia. MRI was not the diagnostic standard as these authors felt that MRI was prone to overdiagnosis; metrizamide myelography showed unequivocal signs of cervical cord compression for all patients. Magnetic stimulation of the cortex was performed and the responses measured with surface electrodes. In these subjects 89% demonstrated abnormalities in motor evoked potentials (MEP) to the first dorsal interosseous muscle and 93% had one MEP abnormality. At least one SEP abnormality was noted in 73%. This study demonstrated the potential usefulness of these techniques for identifying subtle cord compression.

Tavy and colleagues examined whether MEPs or SEPs assisted in identifying persons with radiological evidence of cervical cord compression but who were without clinical markers for myelopathy. All patients had clinical symptoms of cervical radiculopathy, but not myelopathy. In this group MEPs were normal in 92% and SEPs were normal in 96%. These investigators concluded that MEPs and SEPs are normal in most cases of persons with asymptomatic cervical stenosis. This indicates that abnormal MEPs and SEPs are likely to be true positive findings and not false positives related to mild asymptomatic cord compression. It is important to remember that cervical spondylosis is a process that causes a continuum of problems including both radiculopathy and myelopathy.

The inherent variability and difficulty in determinations as to what constitutes normal evoked potentials prompted investigation. Dumitru and colleagues examined the variations in latencies with SEPs. In 29 normal subjects, they examined the ipsilateral intertrial variations, arithmetic mean side-to-side differences and maximum potential side-to-side differences with stimulation of the superficial peroneal sensory nerve, sural nerve and L5 and S1 dermatomes with respect to P1 and N1 latencies and peak-to-peak amplitudes. Considerable ipsilateral intertrial variation was observed and side-to-side comparisons revealed a further increase in this inherent variation regarding the above measured parameters. They suggested an additional parameter with which to evaluate SEPs: the maximum side-to-side latency difference.

Dumitru and colleagues, in a study involving persons with unilateral and unilevel L5 and S1 radiculopathies, evaluated dermatomal and segmental somatosensory evoked potentials. History, physical examination, imaging studies, and EDX medicine evaluations clearly defined patients with unilateral/unilevel L5 or S1 nerve root compromise. Regression equation analysis for cortical P1 latencies evaluating age and height based on comparable patient and control reference populations revealed segmental and dermatomal sensitivities for L5 radiculopathies to be 70% and 50%, respectively, at 90% confidence intervals. Similar sensitivities were obtained for 2 standard deviation mean cortical P1 latencies. Side-to-side cortical P1 latency difference data revealed segmental and dermatomal sensitivities for S1 radiculopathies to be 50% and 10%, respectively, at two standard deviations. These investigators questioned the clinical utility of both segmental and dermatomal SEPs in the evaluation of patients with suspected unilateral/unilevel L5 and S1 nerve root compromise, finding little utility for these tests in persons with single level lumbosacral radiculopathy.

**PURPOSE OF EDX TESTING**

EDX testing is expensive and uncomfortable for patients, therefore, it is important to understand why it is performed and the expected outcomes. EDX testing serves several important purposes:

- It effectively excludes other conditions that mimic radiculopathy such as polyneuropathy or entrapment neuropathy. Haig and colleagues demonstrated that the referring diagnostic impression is often altered with EDX testing.
- EDX testing can to some extent suggest severity, or extent of the disorder beyond the clinical symptoms. Involvement of other extremities can be delineated or the involvement of multiple roots may be demonstrated, such as in the case of lumbosacral spinal stenosis.
- There is utility in solidifying a diagnosis. An unequivocal radiculopathy on EMG in an elderly patient with nonspecific or mild lumbar spondylosis or stenosis on MRI reduces diagnostic uncertainty and identifies avenues of management such as lumbar corticosteroid injections or decompression surgery in certain situations.
- Outcome prediction may be possible. If surgical intervention is planned for a lumbosacral radiculopathy, a positive EMG preoperatively improves the likelihood of a successful outcome postoperatively. This is an area that deserves more research attention.

**EMG AND DIAGNOSTIC SENSITIVITIES**

The need for EMG, particularly in relationship to imaging of the spine, has been recently highlighted. Needle EMG is particularly helpful in view of the fact that the false positive rates for MRI of the lumbar spine are high, with 27% of normal subjects having a disc protrusion. For the cervical spine the false positive rate for MRI is much lower with 19% of subjects demonstrating an abnormality, but only 10% showing a herniated or bulging disc. Radiculopathies can occur without structural findings on MRI, and likewise without EMG findings. The EMG only evaluates motor axonal loss or motor axon conduction block and for these reasons a radiculopathy affecting the sensory root will not yield abnormalities by EMG. If the rate of denervation is balanced by reinnervation in the muscle, then spontaneous activity is less likely to be found.
The sensitivity of EMG for cervical and lumbosacral radiculopathies has been examined in a number of studies. The results of some of these studies are tabulated in Table 3. Table 3 lists the “gold standards” against which these EMG findings were compared. Studies using a clinical standard may reflect a less severe group, whereas those using a surgical confirmation may indicate a more severely involved group. The sensitivity for EMG is unimpressive, ranging from 49-92% in these studies. EMG is not a sensitive test, yet it likely has a higher specificity. The issue of specificity and its value in EDX was underscored by Robinson. It is apparent that EMG is not a good screening test. In terms of screening tests, MRI is better for identifying subtle structural abnormalities, with EMG to assess their clinical relevance and exclude other disorders.

PARASPINAL MUSCLE EXAMINATION

Paraspinal muscles are important to study for a variety of reasons but there are some important caveats regarding their examination. In one study, Date and colleagues demonstrated that lumbar paraspinal muscles in asymptomatic subjects over 40 years old showed denervation potentials approximately 30% of the time. Nardin and colleagues similarly noted up to 48% of normal subjects having fibrillations or positive sharp waves in at least one site with the prevalence higher for those over 40 years of age.

In sharp contrast to these findings, Dumitr u, Diaz, and King examined the lumbosacral paraspinal muscles and intrinsic foot muscles with monopolar EMG. These investigators recorded potentials and found that there were irregularly firing potentials with similar waveform characteristics as fibrillations and positive sharp waves (PSW). By excluding irregularly firing potentials (atypical endplate spikes) they found much lower false positive paraspinal findings than the investigators above, with only 4% of their normal subjects showing regularly firing fibrillations or PSW potentials. They felt that the higher prevalences of spontaneous activity previously reported were due to not fully appreciating the similarity between innervated and denervated spontaneous single muscle fiber discharges. This quantitative study underscores the need to assess both firing rate and rhythm as well as discharge morphology when evaluating for fibrillations and positive waves in the lumbar paraspinal muscles. Electrodiagnostic physicians should take care not to over-diagnose paraspinal muscle EMG findings by mistaking irregularly firing endplate spikes for fibrillations.

Paraspinal muscles (PM) may be abnormal in patients with spinal cancers, amyotrophic lateral sclerosis, and following spinal surgery or puncture. Investigations over the last decade have provided insights into better quantification and examination of lumbosacral paraspinal muscles. The lumbar paraspinal muscle examination has been refined through investigations that used a grading scale for the findings. The “mini PM” score provides a quantitative means of deriving the degree of paraspinal muscle denervation. It distinguishes normal findings from EMG findings in persons with radiculopathy. This novel and quantitative technique may prove useful in identifying subtle radiculopathies or spinal stenosis with greater precision.

IDENTIFICATION AS A SEPARATE CONCEPT FROM SENSITIVITY

Because EDX is a composite assessment composed of various tests, a fundamental question is when the point of diminishing returns has been reached. Some radiculopathies cannot be confirmed by needle EMG, even though the signs and symptoms along with imaging results suggest that radiculopathy is the correct diagnosis. A screening EMG study involves determining whether or not the radiculopathy can be confirmed by EMG. If the radiculopathy cannot be confirmed, then presumably no amount of muscles can identify the radiculopathy. If it can be confirmed, then the screen should identify this possibility with a high probability. The process of identification can be conceptualized as a conditional probability: Given that a radiculopathy can be confirmed by needle EMG, what is the minimum number of muscles which must be examined in order to confidently recognize or exclude this possibility? This is a fundamentally different concept from sensitivity. It involves understanding and defining the limitations of a composite test (group of muscles).

HOW MANY AND WHICH MUSCLES TO STUDY

The concept of a screening EMG encompasses identifying the possibility of an EDX-confirmable radiculopathy. If one of the muscles in the screen is abnormal, the screen must be expanded to exclude other diagnoses, and to fully delineate the radiculopathy level. Because of the screening nature of the EMG exam, EDX physicians with experience should look for more subtle signs of denervation, and if present in the screening muscles, then expand the study to determine if these findings are limited to a single myotome or peripheral nerve distribution. If they are limited to a single muscle, the clinical significance is uncertain.

The Cervical Radiculopathy Screen

Dillingham and colleagues conducted a prospective multi-center study evaluating patients referred to participating EDX laboratories with suspected cervical radiculopathy. A standard set of muscles were examined by needle EMG for all patients. Those with electrodiagnostically confirmed cervical radiculopathies, based upon EMG findings, were selected for analysis. The EMG findings in this prospective study also encompassed other neuropathic findings: (1) positive sharp waves, (2) fibrillation potentials, (3) complex repetitive discharges, (4) high-amplitude, long-duration motor unit action potentials, (5) increased polyphasic motor unit action potentials, or (6) reduced recruitment. There were 101 patients with EDX confirmed cervical radiculopathies representing all cervical root levels. When paraspinal muscles were one of the screening muscles and neuropathic findings were assessed, five muscle screens identified 90-98% of radiculopathies, six muscle screens identified 94-99% and seven muscle screens identified 96-100%
A prospective multicenter study was conducted at five institutions by Dillingham and colleagues.\textsuperscript{10} Patients referred to participating EDX laboratories with suspected lumbosacral radiculopathy were recruited and a standard set of muscles examined by needle EMG. Patients with EDX-confirmed lumbosacral radiculopathies were selected for analysis. As described above for the prospective cervical study, neuropathic findings were analyzed along with spontaneous activity. There were 102 patients with EDX confirmed lumbosacral radiculopathies representing all lumbosacral root levels. When paraspinal muscles were one of the screening muscles, 4 muscle screens identified 88-97\%, 5 muscle screens identified 94-98\%, and 6 muscle screens 98-100\% (Tables 6, 7, and 8). When paraspinal muscles were not part of the screen, identification rates were lower for all screens and eight distal muscles were necessary to identify 90\%. As with cervical radiculopathy screens, assessing for neuropathic findings increases identification rates. If only four muscles can be tested due to limited patient tolerance, as seen in Table 6, and if one of these muscles are the paraspinals, few EDX-confirrmable radiculopathies will be missed. A large retrospective study noted similar findings, concluding that five muscles identified most electrodiagnostically confirmable radiculopathies.\textsuperscript{37}

The Lumbosacral Radiculopathy Screen

Dillingham and Dasher\textsuperscript{9} re-analyzed data from a study published by Knutsson almost forty years earlier.\textsuperscript{29} In this detailed study, 206 patients with sciatica, underwent lumbar surgical exploration. All subjects underwent a standardized 14 muscle EMG evaluation by the author (Knutsson) using concentric needles. The examiner was blinded to other test results and physical examination findings. In addition to the EMG and surgical information, myelogram and physical examination data were derived. In this re-analysis, screens of four muscles with one being the lumbosacral paraspinal muscle yielded (1) an identification rate of 100\%, (2) a 92\% sensitivity with respect to the intraoperative anatomical nerve root compressions, and (3) an 89\% sensitivity with respect to the clinical inclusion criteria.\textsuperscript{9} This study, using data from 4 decades ago, confirmed that a 4 muscle screen provides high identification. These findings are consistent with contemporary work showing that screens with relatively few muscles (five or six) are sufficient.

As described above, recent research efforts were undertaken to refine and streamline the EMG examination. The strongest studies, contemporary prospective multicenter investigations, provide the best estimates of a sufficient number of muscles.\textsuperscript{10,11} In summary, for both cervical and lumbosacral radiculopathy screens the optimal number of muscles appears to be six muscles which include the paraspinal muscles and represent all root level innervations. When paraspinal muscles are not reliable, then eight nonparaspinal muscles must be examined.
Another way to think of this:

To minimize harm, six in the leg and six in the arm.

If one of the six muscles studied in the screen is positive with a neuropathic finding, there exists the possibility of confirming EDX that a radiculopathy is present. In this case, the examiner must study additional muscles. Nerve conductions should be undertaken as well to determine if this muscle finding is due to a mononeuropathy. If more extensive EMG testing reveals that the findings are limited to a single muscle, and NCSs exclude mononeuropathy, then the single muscle finding remains inconclusive and of uncertain clinical relevance.

If none of the six muscles are abnormal, the examiner can be confident in not missing the opportunity to confirm by EDX that a radiculopathy is present, and can curtail additional painful EMG studies. The patient may still have a radiculopathy, but other tests such as MRI will be necessary to confirm this clinical suspicion. This logic is illustrated in Figure 2.

### Table 4: Five muscle screen identifications of patients with cervical radiculopathies

<table>
<thead>
<tr>
<th>MUSCLE SCREEN</th>
<th>NEUROPATHIC</th>
<th>SPONTANEOUS ACTIVITY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Without Paraspinals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>deltoid, APB, FCU, triceps, PT</td>
<td>92%</td>
<td>65%</td>
</tr>
<tr>
<td>biceps, triceps, EDC, FCR, FDI</td>
<td>85%</td>
<td>54%</td>
</tr>
<tr>
<td>deltoid, triceps, EDC, FDI, FCR</td>
<td>84%</td>
<td>58%</td>
</tr>
<tr>
<td>biceps, triceps, PT, APB, FCU</td>
<td>91%</td>
<td>60%</td>
</tr>
<tr>
<td><strong>With Paraspinals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>deltoid, triceps, PT, APB, PSM</td>
<td>98%</td>
<td>80%</td>
</tr>
<tr>
<td>biceps, triceps, EDC, FDI, PSM</td>
<td>95%</td>
<td>73%</td>
</tr>
<tr>
<td>deltoid, EDC, FDI, PSM, FCU</td>
<td>90%</td>
<td>73%</td>
</tr>
<tr>
<td>biceps, FCR, APB, PT, PSM</td>
<td>95%</td>
<td>77%</td>
</tr>
</tbody>
</table>

The screen detected the patient with cervical radiculopathy if any muscle in the screen was one of the muscles which were abnormal for that patient. Neuropathic findings for non-paraspinal muscles included positive waves, fibrillations, increased polyphasic potentials, neuropathic recruitment, increased insertional activity, CRDs, or large amplitude long duration motor unit action potentials. For paraspinal muscles the neuropathic category included fibrillations, increased insertional activity, positive waves, or CRDs. Spontaneous activity referred only to fibrillations or positive sharp waves.

APB = abductor pollicis brevis; CRD = complex repetitive discharge; EDC = extensor digitorum communis; FCR = flexor carpi radialis; FCU = flexor carpi ulnaris; FDI = first dorsal interosseous; PSM = cervical paraspinal muscles; PT = pronator teres. (Adapted with permission, Dillingham and colleagues. Identification of cervical radiculopathies: optimizing the electromyographic screen. Am J Phys Med Rehabil 2001;80:84-91.)

### Table 5: Six muscle screen identifications of the patients with cervical radiculopathies (muscle identification criteria described in Table 2)

<table>
<thead>
<tr>
<th>MUSCLE SCREEN</th>
<th>NEUROPATHIC</th>
<th>SPONTANEOUS ACTIVITY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Without Paraspinals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>deltoid, APB, FCU, triceps, PT, FCR</td>
<td>93%</td>
<td>66%</td>
</tr>
<tr>
<td>biceps, triceps, EDC, FCR, FDI</td>
<td>87%</td>
<td>55%</td>
</tr>
<tr>
<td>deltoid, triceps, EDC, FCR, FDI</td>
<td>89%</td>
<td>64%</td>
</tr>
<tr>
<td>biceps, triceps, EDC, PT, APB, FCU</td>
<td>94%</td>
<td>64%</td>
</tr>
<tr>
<td><strong>With Paraspinals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>deltoid, triceps, PT, APB, EDC, PSM</td>
<td>99%</td>
<td>83%</td>
</tr>
<tr>
<td>biceps, triceps, EDC, FDI, PSM</td>
<td>96%</td>
<td>75%</td>
</tr>
<tr>
<td>deltoid, EDC, FDI, PSM, FCU</td>
<td>94%</td>
<td>77%</td>
</tr>
<tr>
<td>biceps, FCR, APB, PT, PSM, triceps</td>
<td>98%</td>
<td>79%</td>
</tr>
</tbody>
</table>

APB = abductor pollicis brevis; CRD = complex repetitive discharge; EDC = extensor digitorum communis; FCR = flexor carpi radialis; FCU = flexor carpi ulnaris; FDI = first dorsal interosseous; PSM = lumbar spinal paraspinal muscles; PT = pronator teres.

### LUMBAR SPINAL STENOSIS

There are fewer studies examining spinal stenosis and EMG. For lumbosacral spinal stenosis, Hall and colleagues showed that 92% of persons with imaging confirmed stenosis had a positive EMG. They also underscored the fact that 46% of persons with a positive EMG study did not demonstrate paraspinal muscle abnormalities, only distal muscle findings. For 76% of patients, the EMG showed bilateral myotomal involvement.

### LIMITATIONS OF THE NEEDLE EMG SCREEN

These cervical and lumbosacral muscle screens should not substitute for a clinical examination and differential diagnosis formulation by the EDX physician. Rather, the information from investigations described earlier in the article allows the EDX consultant to streamline the EMG evaluation and make more informed clinical decisions regarding the probability of missing an EDX-confirmable radiculopathy when a given
Performing a focused history and physical examination is essential, and these screens should not supplant such clinical assessments or a more detailed EDX study when circumstances dictate.

It is important to remember that the EMG screens for cervical and lumbosacral radiculopathies were validated in a group of patients with limb symptoms suggestive of radiculopathies. These screens will not provide sufficient screening power if a brachial plexopathy is present or if a focal mononeuropathy such as a suprascapular neuropathy is the cause of the patient's symptoms. The EDX physician should always perform EMG on weak muscles to increase the diagnostic yield. The six muscle EMG tests do not sufficiently screen for myopathies or motor neuron disease. It is incumbent upon the EDX physician to formulate a differential diagnosis and methodically evaluate for the diagnostic possibilities, further refining the examination as data are acquired.

### Table 6
Four muscle screen identifications of patients with lumbosacral radiculopathies.

<table>
<thead>
<tr>
<th>muscle Screen</th>
<th>Neuropathic</th>
<th>Spontaneous Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Four Muscles Without Paraspinals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATIB, PTIB, MGAS, RFEM</td>
<td>85%</td>
<td>75%</td>
</tr>
<tr>
<td>VMED, TFL, LGAS, PTIB</td>
<td>75%</td>
<td>58%</td>
</tr>
<tr>
<td>VLAT, SHBF, LGAS, ADD</td>
<td>52%</td>
<td>35%</td>
</tr>
<tr>
<td>ADD, TFL, MGAS, PTIB</td>
<td>80%</td>
<td>67%</td>
</tr>
<tr>
<td><strong>Four Muscles With Paraspinals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATIB, PTIB, MGAS, PSM</td>
<td>97%</td>
<td>90%</td>
</tr>
<tr>
<td>VMED, LGAS, PTIB, PSM</td>
<td>91%</td>
<td>81%</td>
</tr>
<tr>
<td>VLAT, TFL, LGAS, PSM</td>
<td>88%</td>
<td>77%</td>
</tr>
<tr>
<td>ADD, MGAS, PTIB, PSM</td>
<td>94%</td>
<td>86%</td>
</tr>
</tbody>
</table>

The screen identified the patient if any muscle in the screen was abnormal for that patient. The muscle either demonstrated neuropathic findings or spontaneous activity. Neuropathic findings for non-paraspinale muscles included positive waves, fibrillations, increased polyphasic potentials, neuropathic recruitment, increased insertional activity, CRDs, or long duration motor unit action potentials. Spontaneous activity referred only to fibrillations or positive sharp waves. For paraspinal muscles the neuropathic category included fibrillations, increased insertional activity, positive waves, or CRDs.

### Table 7
Five muscle screen identifications of patients with lumbosacral radiculopathies

<table>
<thead>
<tr>
<th>Screen</th>
<th>Neuropathic</th>
<th>Spontaneous Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Five Muscles Without Paraspinals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATIB, PTIB, MGAS, RFEM, SHBF</td>
<td>88%</td>
<td>77%</td>
</tr>
<tr>
<td>VMED, TFL, LGAS, PTIB, ADD</td>
<td>76%</td>
<td>59%</td>
</tr>
<tr>
<td>VLAT, SHBF, LGAS, ADD, TFL</td>
<td>68%</td>
<td>50%</td>
</tr>
<tr>
<td>ADD, TFL, MGAS, PTIB, ATIB</td>
<td>86%</td>
<td>78%</td>
</tr>
<tr>
<td><strong>Five Muscles With Paraspinals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATIB, PTIB, MGAS, PSM, VMED</td>
<td>98%</td>
<td>91%</td>
</tr>
<tr>
<td>VMED, LGAS, PTIB, PSM, SHBF</td>
<td>97%</td>
<td>84%</td>
</tr>
<tr>
<td>VLAT, TFL, LGAS, PSM, ATIB</td>
<td>97%</td>
<td>86%</td>
</tr>
<tr>
<td>ADD, MGAS, PTIB, PSM, VLAT</td>
<td>94%</td>
<td>86%</td>
</tr>
</tbody>
</table>

ADD = adductor longus; ATIB = anterior tibialis; CRD = complex repetitive discharge; LGAS = lateral gastrocnemius; MGAS = medial gastrocnemius; PSM = lumbosacral paraspinal muscles; PTIB = posterior tibialis; RFEM = rectus femoris; SHBF = short head biceps femoris; TFL = tensor fascia lata; VLAT = vastus lateralis; VMED = vastus medialis. (Adapted with permission from Dillingham and colleagues. Identification of cervical radiculopathies: optimizing the electromyographic screen. Am J Phys Med Rehabil 2001;80:84-91) 

### SPECIFICITY OF THE EMG SCREEN

Tong and colleagues examined the specificity in persons age 55 and older who were asymptomatic. A standardized EDX study was conducted by a blinded EDX physician using a monopolar needle to assess five leg muscles and the paraspinal muscles.

There were 30 subjects with a mean age of 65.4 yrs (SD 8.0). When only positive sharp waves or fibrillations were counted as abnormal, the specificity was 100% when the appropriate diagnostic criteria were used. The specificity for plexopathy was 100% when only positive sharp waves or fibrillations were used, and it remained 100% when increased polyphasia was added. This study demonstrated that needle EMG has excellent specificity for lumbosacral radiculopathy and plexopathy when the appropriate diagnostic criteria are used.

### SYMPTOM DURATION AND THE PROBABILITY OF FIBRILLATIONS

Previously, a well-defined temporal course of events was thought to occur with radiculopathies despite the absence of studies that support such a relationship between symptom duration and the probability of spontaneous activity in a muscle. It was a common belief that in acute lumbosacral radiculopathies, the paraspinal muscles denervated first, followed by distal muscles, and that later reinnervation began with paraspinal muscles and then with distal muscles. This paradigm
was recently challenged by a series of investigations.\textsuperscript{12,13,14,48} For both EDX confirmed lumbosacral and cervical radiculopathies, symptom duration had no significant relationship to the probability of finding spontaneous activity in paraspinal or limb muscles.

The findings from these investigations underscored the fact that the pathophysiological processes involved with cervical and lumbosacral radiculopathies are complex.\textsuperscript{12,13,14,48} Diagnostic EMG findings, manifested as a result of these processes, cannot be predicted by this overly simplistic, symptom-duration explanation. Symptom duration should not be invoked to explain the presence or absence of paraspinal or limb muscle spontaneous activity in persons suspected of having a radiculopathy.

**IMPLICATIONS OF AN ELECTRODIAGNOSTICALLY CONFIRMED RADICULOPATHY**

It is important that the EDX physician not forget that EMG does not indicate the exact cause of the symptoms, only that axonal loss is taking place. A spine tumor, herniated disc, bony spinal stenosis, inflammatory radiculitis, or severe spondylolisthesis can all yield the same EMG findings. This underscores the need to image the spine with MRI to assess for significant structural causes of electrodiagnostically confirmed radiculopathy. A negative EMG test should not curtail obtaining an MRI if clinical suspicion for radiculopathy is high. Given the low sensitivities of needle EMG, it is not an optimal screening test, but rather a confirmatory and complementary test to spinal imaging.

There are few studies that examine outcomes and the usefulness of EDX in predicting treatment success, the exception being surgical outcomes for lumbar discectomy. Tullberg and colleagues evaluated 20 patients with lumbosacral radicular syndromes who underwent unilevel surgery for disc herniations.\textsuperscript{63} They evaluated these patients before surgery and 1 year later with lower limb EMG, NCS, F waves, and SEPs. They showed that the EDX findings did not correlate with the level defined by computerized tomography for 15 patients. However, those patients in whom EDX testing preoperatively was normal were significantly more likely to have a poor surgical outcome (p<0.01). In spite of the fact that the sample size in this study was small, the significant correlation of a normal EDX study with poor outcome suggests that this may be a true relationship.

Spengler and Freeman described an objective approach to the assessment of patients preoperatively for laminectomy and discectomy for lumbosacral radiculopathy.\textsuperscript{57} Spengler and colleagues confirmed and underscored these previous findings regarding objective methods to assess the probability of surgical success preoperatively.\textsuperscript{58} In this preoperative screening evaluation, the EMG findings were combined with imaging, clinical, and psychological assessments. The EMG findings figured prominently (one quarter of the scale) — those patients with positive EMGs were more likely to have better surgical outcomes. This was particularly true when the EMG findings correlated with the spinal imaging findings in a person without psychological or dysfunctional personality issues.

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**Suspected Radiculopathy**

- Six muscles (with PSM) - lumbar screen
- Six muscles (with PSM) - cervical screen

If one muscle is positive, expand study
Determine if EMG reflects:
1) Radiculopathy (which level),
2) Entrapment neuropathy,
3) Generalized condition, or
4) Findings that are of uncertain relevance

If all muscles are negative, stop EMG exam in this limb
*The patient will not have an electrodiagnostically confirmable radiculopathy*

They may:
1) Not have a radiculopathy, or
2) Have a radiculopathy but you will not confirm this with EMG. Other diagnostic tests must be utilized such as MRI.

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Figure 2 Implications of a positive or negative electromyography (EMG) screening evaluation. Note that a positive result will usually warrant further EMG testing to fully define the pathology, and a negative test could lead to nerve conduction or other testing to consider other diagnoses. PSM = paraspinal muscles; MRI = magnetic resonance imaging; SNRB = selective nerve root block. (Modified from Dillingham TR. Electrodiagnostic approach to patients with suspected radiculopathy. Phys Med Rehabil Clin N Am 2002;13:567-588, with permission.)
It has become apparent over the last 2 decades that the natural history of both lumbosacral radiculopathy and cervical radiculopathy, with or without structural findings on MRI, is very favorable. A classic investigation by Henrik Weber showed that surgery for a herniated nucleus pulposis causing sciatica was more effective at pain control at 1 year, but beyond that conservative treatment had equal results compared to the surgically managed group. Of particular note was the fact that weakness did not correlate with outcome and even for persons with motor weakness, a good outcome with conservative treatment was the norm, and surgery did not improve motor return. Other investigators in cohort outcome studies demonstrated that the majority of persons suffering lumbosacral radiculopathy can resolve their symptoms. In fact, on follow-up MRI studies, lumbosacral disc herniations and disc fragments resolve in 76% of patients.

The outcomes for cervical radiculopathy are generally good in the absence of myelopathy.

Saal, Saal, and Yurth demonstrated that persons with cervical disc herniations have a similar favorable clinical course as persons with lumbosacral radiculopathy. These patients were managed with pain management strategies incorporating medications, rehabilitation with cervical traction and exercises, and epidural or selective nerve root injections if medications failed to control pain. In this series, the majority of patients (24 of 26) achieved successful outcomes.

**SUMMARY**

One cannot minimize the importance of the clinical evaluation and differential diagnosis formulation by the EDX physician to guide testing. The needle EMG examination is the most useful EDX test but is limited in sensitivity. EMG screening examinations using six muscles are possible that optimize identification yet minimize patient discomfort. EMG findings must be interpreted relative to the patient’s clinical presentation, and the consultant should tailor the EDX study to the clinical situation. Electromyography complements spinal imaging and often raises other diagnostic possibilities in addition to confirming clinical suspicions.

**REFERENCES**

8. Dillingham and colleagues TR, Lauder TD, Andary M, Kumar S, Pezzin LE, Stephens RT, Shannon S. Identification of cervical ra-

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**Table 8** Six muscle screen identifications of patients with lumbosacral radiculopathies

<table>
<thead>
<tr>
<th>Screen</th>
<th>Neuropathic</th>
<th>Spontaneous Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Six Muscles Without Paraspinals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATIB, PTIB, MGAS, RFEM, SHBF, LGAS</td>
<td>89%</td>
<td>78%</td>
</tr>
<tr>
<td>VMED, TFL, LGAS, PTIB, ADD, MGAS</td>
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<td>70%</td>
</tr>
<tr>
<td>VLAT, SHBF, LGAS, ADD, TFL, PTIB</td>
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<td>62%</td>
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<tr>
<td>ADD, TFL, MGAS, PTIB, ATIB, LGAS</td>
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<td>79%</td>
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<tr>
<td><strong>Six Muscles With Paraspinals</strong></td>
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<td></td>
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<tr>
<td>ATIB, PTIB, MGAS, PSM, VMED, TFL</td>
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<td>93%</td>
</tr>
<tr>
<td>VMED, LGAS, PTIB, PSM, SHBF, MGAS</td>
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<td>87%</td>
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<tr>
<td>VLAT, TFL, LGAS, PSM, ATIB, SHBF</td>
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<td>ADD, MGAS, PTIB, PSM, VLAT, SHBF</td>
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<tr>
<td>VMED, ATIB, PTIB, PSM, SHBF, MGAS</td>
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<td>VMED, TFL, LGAS, PSM, ATIB, PTIB</td>
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<tr>
<td>ADD, MGAS, PTIB, PSM, SHBF, ATIB</td>
<td>100%</td>
<td>93%</td>
</tr>
</tbody>
</table>

ADD = adductor longus; ATIB = anterior tibialis; CRD = complex repetitive discharge; LGAS = lateral gastrocnemius; MGAS = medial gastrocnemius; PSM = lumbosacral paraspinal muscles; PTIB = posterior tibialis; RFEM = rectus femoris; TFL = tensor fascia lata; SHBF = short head biceps femoris; VLAT = vastus lateralis; VMED = vastus medialis.


INTRODUCTION

Symptoms of numbness and tingling are common neurologic complaints. The evaluation of a peripheral neuropathy (PN) can seem daunting given the long list of potential causes and the number of available diagnostic tests, including antibody and genetic test panels. However, the evaluation is manageable using a structured approach. This manuscript presents elements of such an approach based on a systematic evaluation of symptoms and signs and electrodiagnostic (EDX) findings (Table 1). Clinical characterization is achieved by asking direct historical questions and conducting thoughtful clinical tests. The role of EDX testing is stressed because it provides unique information on the pathologic features of the neuropathy not otherwise available from symptoms and clinical signs. The process is divided into 7 steps. With a full characterization, the list of potential causes becomes shorter and the appropriate selection of informative tests more manageable. This approach, in various forms, has been described elsewhere.11,12,14

As clinical features are elicited, it is important to appreciate that not all symptoms of numbness, sensory loss, and weakness are due to peripheral nerve disease. The exercise of neurologic localization is an essential element to assure peripheral nervous system (PNS) pathology. The most common errors in localization are failure to diagnose central nervous system pathology and somatization. Clinical features suggestive of a myelopathy include numbness that does not follow a stocking-glove or dermatomal distribution (numbness involving both legs to the waist or above), numbness affecting one limb or side of the body, and pathologic tendon reflexes. In these circumstances, other diagnostic tests can help confirm central nervous system involvement.

Sensory symptoms attributable to somatization are common but challenging because the clinician does not want to miss a neurologic disease. However, it is equally inappropriate to carry forward a tentative neurologic diagnosis that is not tenable. One approach is to determine whether the symptoms make sense anatomically (based on the organization of the peripheral or central nervous systems) or pathophysiologically (based on types of peripheral nerve and central nervous system pathology). EDX studies can determine the presence of PNS involvement. If there is no evidence for a neurologic basis for the symptoms, a gentle but frank discussion into issues in a patient’s life is appropriate.

This manuscript will focus on peripheral neuropathies. Disorders primarily affecting other portions of the PNS, such as radiculopathies and plexopathies, will not be considered.

PERTINENT PERIPHERAL NERVOUS SYSTEM ANATOMY

A simple working view of PNS anatomy is useful when evaluating for a peripheral neuropathy. The PNS can be divided into autonomic and somatic components. Autonomic nerve fibers markedly outnumber somatic fibers, but symptoms and signs of autonomic nerve dysfunction are rare compared to those associated with somatic nerve dysfunction. When present, prominent autonomic signs provide an important clue to specific causes of a neuropathy, but most diagnostic efforts focus on somatic nerves.

Step 1

The first step when evaluating a patient with suspected PN is determining if there is involvement of sensory nerves, motor nerves, or both. The distribution of nerve involvement may not be obvious from symptoms, but can be determined accurately by EDX studies. This can be explained by the fact that damage to sensory nerves results in more frequent symptoms than damage to motor nerves.
Step 2

The second step is determining the distribution of involvement (Table 2). Peripheral neuropathies most commonly follow one of several general patterns. Polyneuropathies are roughly symmetric in distribution and tend to affect nerves in a length dependent manner, with longest nerves first (stocking-glove distribution). Polyradiculoneuropathies include nerve roots as well as peripheral nerves, leading to diffuse symptoms in both proximal and distal distributions. Mononeuropathies involve the distribution of a single nerve with motor and sensory disturbance in a nerve distribution. Mononeuritis multiplex may become confluent and relatively symmetric, but a step-wise progression can usually be elicited from the history. Neuropathies that do not follow these patterns are important to recognize, and the pathology may be identifiable based on their unusual pattern.

Table 2 Patterns of peripheral nerve involvement and examples of neuropathies.

<table>
<thead>
<tr>
<th>Symmetric, length dependent distribution</th>
<th>Diabetes</th>
<th>Drugs</th>
<th>Toxins</th>
<th>Metabolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symmetric, proximal and distal distribution</td>
<td>Acute inflammatory demyelinating polyradiculoneuropathy</td>
<td>Chronic inflammatory demyelinating polyradiculoneuropathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymmetric, nerve or plexus distribution</td>
<td>Diabetic amyotrophy</td>
<td>Idiopathic plexopathy</td>
<td>Mononeuritis multiplex</td>
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<tr>
<td>Asymmetric, unusual</td>
<td>Polychondritis</td>
<td>Leprosy</td>
<td>Tangier disease</td>
<td>Multifocal motor conduction block neuropathy</td>
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<tr>
<td>Autonomic, unusual</td>
<td>Porphyria</td>
<td>Leprosy</td>
<td>Tangier disease</td>
<td>Amyloidosis</td>
</tr>
</tbody>
</table>

TIME COURSE

Step 3

Every disease has a momentum or time course. The third step is determining the time course to help focus the differential diagnosis (Table 3). Acute neuropathies progress over days to several weeks, while chronic neuropathies progress over many months to years, and may have an insidious onset.
SUMMARY OF DIAGNOSTIC STEPS 1-3

The site of initial involvement, the distribution of involvement, and the pattern of progression can be combined. For example, a pattern suggesting acute inflammatory demyelinating polyradiculoneuropathy (AIDP), also known as Guillain-Barré syndrome, includes symptoms involving both distal and proximal limbs with progression over 2 to 4 weeks. A similar distribution of distal and proximal symptoms and signs, but progressing over several months, suggests chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). Acute onset of asymmetric painful proximal neuropathy in the setting of symmetric distal sensory loss suggests diabetic neuropathy. Mononeuritis multiplex is suggested by a stepwise progression involving single nerve distributions. The majority of neuropathies will be chronic. A symmetric motor and sensory neuropathy with an ill-defined insidious onset raises the question of a familial neuropathy, and it is important to seek evidence for involvement in childhood and other family members.

CLINICAL FEATURES

Step 4

The fourth step in the evaluation is determining the clinical features, including symptoms and signs, physical aspects, identification of potential underlying medical conditions, drug use, and family history.

Symptoms

Elicitation of a full spectrum of symptoms is helpful in narrowing diagnostic possibilities and guiding symptomatic treatment. Neuropathic symptoms may be positive or negative in nature (Table 4). Positive symptoms imply spontaneous discharges in nerve fibers, while negative symptoms imply loss of normally conducted discharges. Positive sensory symptoms are easily recognized and are frequently volunteered by the patient as chief complaints. Positive motor symptoms may not be recognized by the patient, and should be actively sought because they may be the only clinical manifestation of motor nerve involvement. The discrepancy between patient perception of sensory and motor symptoms is due to two factors. First, collateral reinnervation occurs with loss of motor fibers, which tends to preserve muscle strength, whereas the same degree of sensory fiber loss is essentially permanent and symptomatic. Second, mild weakness of distal muscles (intrinsic foot muscles) does not usually affect motor function to a noticeable degree.

Sensory Signs

Clinical testing of sensory function is a subjective endeavor. Although attempts are made to assess a number of individual sensory modalities and nerve fiber types, distinctions between modalities and fiber types may be more apparent than real. While there are examples of large fiber neuropathies (Friedreich’s ataxia) and small fiber neuropathies (Tangier’s disease), most sensory modalities (light touch through pain) can be conveyed by both large and small diameter fibers. Further, clinical testing (light touch, stroking, sharp instruments) usually activates a variety of receptor types. An important clinical variable is patient attention. It is advisable to develop an individual set of tests that are informative. It is important to not become bogged down in incongruities during the examination with a large battery of tests.

The following information is offered as a guide to selecting a set of clinical sensory tests. Findings from formal psychophysical laboratory testing of sensory perception should be combined with a set of informative clinical tests of sensory function. A variety of cutaneous receptor types subserve low-threshold mechanoreception, and mechanoceptors are most sensitive to moving stimuli. In formal testing, controlled stimuli are applied to restricted areas of skin. In contrast, clinical testing of mechanoreception may include touch or stroking, and likely activates a variety of receptor types. Psychophysical testing for vibration perception confirms equal sensitivity for frequencies from 64 Hz to 512 Hz. Nociceptive stimulation is perhaps the most challenging. It is difficult to separate stimulus properties of nociception from pressure and it is possible for a subject to distinguish a sharp from a dull stimulus without feeling pain. Nociceptive stimuli are felt to be conveyed by “small fibers,” but some nociceptive
receptors are innervated by myelinated fibers. Formal testing of noxious stimuli has been by hot and cold stimuli using special equipment, and it is not clear how well temperature detection can be assessed with clinical testing using the cold end of a tuning fork.

Reliable and informative results can be obtained from the clinical tests listed below.

**Touch threshold.** Patient detection of the lightest touch or stroking on the dorsum of the hand and foot represents a measure of low threshold sensory perception. Use of a 10 g filament is another method to distinguish light touch thresholds.

**Vibration threshold.** Patient perception of when a tuning fork applied to a finger or toe dies out is a measure of vibration threshold. Vibration perception is felt to represent large fiber function. A 128 Hz tuning fork dies out more slowly than a 256 Hz fork and is easier to use. The patient must understand the need to indicate complete disappearance. The time interval (in seconds) from when the vibration extinguishes in the patient compared to the observer is a measure of impairment.

**Sharp stimulus threshold.** A patient’s ability to distinguish between the lightly applied “pokey” feeling from the sharp end of a safety pin compared to the similarly lightly applied dull end likely represents discrimination of more noxious stimuli from light touch.

**Position threshold.** Patient perception of changes in joint position is usually exquisite. Any errors in direction, or false perception of movement, are abnormal.

The tests of light touch, the distinguishing the sharp end of the safety pin, and position sense should be performed with the patient blinded to the exercise.

The sensory examination can be focused to answer several useful clinical questions. Most information about the neuropathy should come from the patient's history, and the sensory examination should be confirmatory. Two questions to consider for a symmetric polyneuropathy are the presence of a distal-to-proximal gradient, and the severity of nerve damage. Patients can contribute to determining sensory gradient and severity. It is surprising how readily a patient can mark a point on their limb below which sensation is abnormal and above which it is normal. The gradient can be confirmed clinically by asking if light touch is perceived less strongly at a distal point compared to a proximal point. Severity of light touch loss can be addressed by asking the patient to estimate the relative percent value of light touch sensation at the involved site compared to the face. Severity of vibration loss can be estimated by the time difference between vibration extinguishing for the patient compared to the examiner.

Questions to consider for an asymmetric neuropathy are whether the sensory loss follows a nerve distribution, a radicular distribution, or a complex pattern best explained by a plexopathy.

**Tendon reflexes.** An objective measure of sensory nerve function is the deep tendon reflex. The deep tendon reflex is a monosynaptic reflex arc with sensory and motor nerve components, but the arc is much more vulnerable to sensory nerve damage. As an example, ankle plantar flexion strength is relatively preserved in all but the most severe neuropathies, yet ankle reflexes are lost early on. Accordingly, an absent Achilles tendon reflex is an objective indication of a significant degree of sensory nerve damage. It is important to be assured that the reflex is truly absent by performing a number of reinforcing maneuvers while testing.

**Motor Signs**

Motor signs include muscle atrophy and weakness. Mild distal atrophy can be appreciated by assessing the prominence of extensor tendons in the feet and finding a thin foot. Prominent tendons and thin feet suggest loss of intrinsic foot muscle bulk. A certain amount of denervation and atrophy occur with age, which must be considered. Weakness can be appreciated by testing muscles that can just overcome in normal individuals. Accordingly, flexion and extension of the lesser toes and extension of the great toe are informative when weakness is subtle. Ankle dorsiflexion weakness will occur with greater severity of the neuropathy, but it is rare for plantar flexion to be weak until very late in a neuropathy. The angle between the shin and the foot is a clue to distal weakness: in normal individuals it is about 130 degrees, but with weakness of anterior muscles, the angle increases and can be 180 degrees in the setting of a neuropathy. Fallen arches also suggest intrinsic foot weakness. In the hands, atrophy of the first dorsal interosseous muscle and weakness of finger abduction are informative.

**Orthopedic Signs**

Inspection of the foot for high arches and hammertoes is informative because it suggests a long-standing neuropathy. The shape of the foot is determined by the interplay of muscular forces acting on the various bones in the foot. Weakness of extensor muscles leads to a foreshortened foot (high arches) and hammertoes.

**Autonomic Signs**

As discussed earlier, autonomic nerve fibers make up the majority of fibers in a nerve but account for a minority of symptoms. Evidence for autonomic nerve dysfunction comes from symptoms of orthostatic dizziness and impotence in men. Clinical signs of autonomic dysfunction are an orthostatic blood pressure change. Dry and scaly skin on the feet is a clue to autonomic dysfunction. Dry eyes and mouth (sicca syndrome) represent reduced tear and salivary gland activity, and raise the question of Sjögren’s syndrome that can be associated with sensory neuropathies.

**PN NERVE PATHOLOGY**

**Step 5**

Underlying pathologic processes are poorly understood for most neuropathies. However, the consequences of the processes can be viewed clinically as causing three patterns of peripheral nerve
damage: primary axonal, primary demyelinating, and a combination of the two. The fifth step is determining the predominant pathologic process. Primary axonal damage usually follows a distal predominant pattern because longer nerves tend to be affected first.\(^2^1\) This results in symptoms and signs in a distal-to-proximal gradient that can be demonstrated clinically by a stocking-glove distribution, with more pronounced abnormalities distally than proximally within a limb, and more in legs than in arms. Primary demyelination can occur at multiple foci along nerves, leading to both distal and proximal involvement at onset or early in the course, that can be demonstrated clinically by finding both distal and proximal weakness and sensory disturbance.\(^2^1\) In addition, demyelinating polyradiculoneuropathies involve roots of nerves innervating both proximal and distal muscles and skin. Demyelinating neuropathies usually include a variable degree of axonal damage, and the distinction between primary demyelination and a combination of demyelination and axonal damage can be challenging. EDX studies are helpful in making this distinction.

Mononeuropathies generally have axonal pathology. An exception is asymmetric neuropathies characterized by focal conduction block. The distinction between axonal and conduction block mononeuropathies can be made with EDX testing.

Collateral reinnervation represents an important compensatory mechanism in peripheral neuropathies. Loss of motor nerve axons initiates sprouting of terminal branches from intact axons to reinnervate denervated muscle fibers. This compensates and preserves muscle strength until 50% or more motor axons degenerate, at which time reinnervation can not keep up and the muscle becomes clinically weak. This means that muscle strength is not a sensitive measure of whether motor nerves are involved in a peripheral neuropathy. Needle electromyography (EMG), however, is sensitive to the process of reinnervation.

**EDX Features**

Perhaps the most important element in the diagnostic evaluation is EDX testing because nerve conduction and needle EMG studies provide objective information on the peripheral nervous system not available from the history and clinical examination. Characterization by EDX features can thus narrow the differential diagnostic list.\(^6\) EDX test results are considered from two directions: by the EDX physician conducting the study, and by the consultant reviewing an existing study. The performance and interpretation of EDX studies can be optimized for both the performer and reviewer by following several principles. The EDX test should be used as a direct extension of the neurologic examination to answer specific questions: (1) Confirm which portions of the peripheral nervous system are involved; sensory only, motor only, or both. In this regard, step 5 complements step 1; (2) Confirm the distribution of involvement: symmetric polyneuropathy, single nerves, or another pattern; (3) Determine the pathologic mechanism: primary axonal, primary demyelination, or a mixture; (4) Determine the severity and time course: mild or severe, recent or chronic.

**Nerve Conduction Studies**

**Primary axonal loss and demyelination.** The question of underlying pathology is the most challenging question to answer. Distinctions are based primarily on motor nerve conduction velocity values. Nerve conduction measures of distal latency, conduction velocity and F-wave latency focus on the fastest conducting fibers. Experience indicates that severe axonal loss has relatively little effect on nerve conduction. Changes in conduction can be expressed as percentages of the laboratory limits of normal: lower limits of normal (LLN) for conduction velocity, and upper limits of normal (ULN) for distal latency and F-wave latency. Thus in amyotrophic lateral sclerosis, as an example of a pure and severe axonal motor neuropathy, distal latencies are rarely longer than 125% of the ULN, conduction velocities rarely slower than 70% of the LLN, and F-wave latencies rarely longer than 125% of the ULN.\(^7\)

The distinction between demyelinating and axonal pathology is based on showing a degree of slowed conduction greater than expected for axonal loss alone. Just how slow is slower than expected has been the subject of controversy. Several sets of nerve conduction limits for primary demyelination have been proposed and tested.\(^6\) The problem of sensitivity and specificity looms large because some demyelinating neuropathies are mild, and nerve conduction values will overlap with normal values and abnormal values encountered in axonal neuropathies. Table 5 lists nerve conduction guidelines for considering primary demyelination.

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Limits of Axonal Pathology</th>
<th>Limits of Demyelinating Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal latency</td>
<td>(&lt;120%) ULN</td>
<td>(&gt;130%) ULN</td>
</tr>
<tr>
<td>Conduction velocity</td>
<td>(&gt;70%) ULN</td>
<td>(&lt;70%) ULN</td>
</tr>
<tr>
<td>Proximal: distal amplitude</td>
<td>(&lt;50%)</td>
<td>(&gt;50%)</td>
</tr>
<tr>
<td>Abnormal temporal dispersion</td>
<td>Smooth waveform</td>
<td>Irregular waveform</td>
</tr>
<tr>
<td>F-wave latency</td>
<td>(&lt;130%) ULN</td>
<td>(&gt;130%) ULN</td>
</tr>
</tbody>
</table>

**Demyelination and conduction block.** Although distal latency, conduction velocity, and F-wave latency measure the speed of the fastest conducting fibers, it is possible to assess the conduction speed of the remainder of the fibers in the response by looking for abnormal temporal dispersion. Quantitatively, temporal dispersion can be assessed by the duration of the negative compound muscle action potential (CMAP) waveform. Temporal dispersion represents the spectrum of arrival times of nerve impulses from the range of nerve fiber conduction velocities. Abnormal temporal dispersion is caused by a greater degree of slowing of individual nerve fibers due to
demyelination. Abnormal temporal dispersion leads to a greater degree of phase cancellation in the waveform leading to a reduction of the amplitude of the CMAP to more proximal stimulation compared to the amplitude following more distal stimulation. If individual nerve fibers slow to a halt, i.e., conduction block, there will also be a reduction of the CMAP amplitude to more proximal stimulation, and thus a drop in amplitude of the proximal response by greater than 50% indicates increased temporal dispersion and greater phase cancellation, or conduction block, or both. There are guidelines to help distinguish between abnormal temporal dispersion and conduction block (Table 6).\textsuperscript{17,28} In abnormal temporal dispersion there will be an amplitude reduction of the proximal response but little change in the areas of the response. In addition, there will be a prolongation of the negative peak duration. In conduction block there will be a reduction of both amplitude and area with little change in the negative peak duration. However, many clinical examples include a combination of abnormal temporal dispersion and conduction block. What is most important is that abnormal temporal dispersion and conduction block suggests a demyelinating pathology.

Table 6  Nerve conduction value guidelines to help distinguish between abnormal temporal dispersion, conduction block, or a combination of the two

<table>
<thead>
<tr>
<th></th>
<th>CMAP Amplitude</th>
<th>CMAP Negative Peak Area</th>
<th>CMAP Negative Peak Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conduction block</td>
<td>&lt;50%</td>
<td>&lt;50%</td>
<td>≤30%</td>
</tr>
<tr>
<td>Conduction block/ Abnormal temporal dispersion</td>
<td>&lt;50%</td>
<td>&lt;50%</td>
<td>&gt;30%</td>
</tr>
<tr>
<td>Temporal dispersion</td>
<td>&lt;50%</td>
<td>&gt;50%</td>
<td>&gt;30%</td>
</tr>
</tbody>
</table>


Abnormal temporal dispersion can be assessed qualitatively because it will also affect the smooth shape of the CMAP waveform, and wave form irregularities should be sought by inspection (Figure 1). Assessing for abnormal temporal dispersion is important because a group of hereditary neuropathies, Charcot-Marie-Tooth type 1, are characterized by slow conduction velocity but no abnormal temporal dispersion (Figure 2).\textsuperscript{18}

**Needle EMG**

The needle EMG examination is important because it is the most sensitive measure of motor nerve involvement. CMAP amplitude is a measure of axonal loss, but collateral reinnervation will compensate early for mild degrees of loss, and CMAP amplitude will not be a sensitive measure of early loss. The presence of abnormal temporal dispersion (fibrillation potentials and positive waves) is sensitive signs of denervation. Reduced motor unit recruitment indicates a neuropathic cause of denervation. The chronicity of

**Figure 1** Differences between normal and abnormal temporal dispersion stimulating at the wrist, elbow, and axilla.

Left set of waveforms: Normal changes in motor responses with greater conduction distances due to normal temporal dispersion. Right set of waveforms: Marked changes in motor responses with greater conduction distances due to abnormal temporal dispersion. Note initial low response amplitude with further loss with greater conduction distances, and irregularities of the waveform. Oscilloscope settings: 5 ms/div and 5 mV/div.

**Figure 2** Motor nerve conduction study stimulating at the wrist and elbow showing slow conduction velocity with normal temporal dispersion in Charcot-Marie-Tooth hereditary neuropathy type 1A.

Top set of waveforms: Slow velocity (18 m/s) from subject with Charcot-Marie-Tooth hereditary neuropathy type 1A with normal changes in waveforms reflecting normal temporal dispersion. Bottom set of waveforms: Normal velocity (52 m/s) with normal changes in waveforms reflecting normal temporal dispersion. Oscilloscope settings: 5 ms/div and 5 mV/div.
motor nerve loss can be assessed by the degree of complexity of the motor unit action potentials; highly complex or polyphonic potentials support an ongoing enervating process, while high amplitude but simple potentials support a very longstanding enervating process. In the latter situation, a longstanding and slowly progressive denervation lends support for a hereditary neuropathy.

SUMMARY OF DIAGNOSTIC STEPS 1-5

At the conclusion of the clinical and EDX evaluation (steps 1-5), a full characterization of the peripheral neuropathy should emerge (Table 7). The differential diagnostic list is relatively short under each type of neuropathy.8 At this point, a review of the medical and family histories can be incorporated to give a complete characterization and a meaningful series of laboratory tests can be ordered.

MEDICAL HISTORY

Step 6

There are long lists of medical conditions and drugs that cause or predispose to peripheral neuropathy, but careful review reveals that some associations are rare and may reflect chance occurrences. Step 6 is to assess possible factors. In practical terms, a limited number of systemic diseases relate to peripheral neuropathies. Diabetes is the most common underlying disease, not only for frank diabetes, but also for undocumented diabetes (impaired glucose tolerance).23 Renal failure is also a cause of neuropathy, but not until the creatinine level is over 5 mg/dl.2 Medication use, both current and past, should be sought for a number of compounds. Cancer chemotherapeutic drugs such as cisplatin, vincristine, and the taxols are neurotoxic. There is a question whether previous exposure to neurotoxic chemotherapeutic drugs can be a predisposing factor for neuropathies from another cause, and has been shown to occur for vincristine in the setting of Charcot-Marie-Tooth type 1A hereditary neuropathies.14 Among commonly used drugs, nitrofurantoin and amiodarone can be neurotoxic. Infrequently used neurotoxic drugs include disulfiram, gold, and isoniazid. Recreational inhaled compounds, including n-hexane in glue sniffing should also be considered.25

Table 7

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
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</tr>
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<tbody>
<tr>
<td></td>
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<td></td>
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<td>Segmental demyelinating, motor &gt;</td>
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<td></td>
<td>sensorimotor polyneuropathy</td>
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MEDICAL HISTORY

Step 7

It is likely that hereditary neuropathies account for a larger than appreciated percentage of mild and very chronic idiopathic neuropathies. Step 7 assesses this possibility.9 Interestingly, among large families with known hereditary neuropathies, only 20% of affected family members seek medical attention because of symptoms. Accordingly, a full family history with detailed queries to the patient and relatives (if necessary over the telephone) about symptoms and signs that may suggest a hereditary neuropathy can be fruitful (Table 8).

Table 8

<table>
<thead>
<tr>
<th>Questions pertinent to a long-standing (familial) neuropathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulty with running, sports, or military activities</td>
</tr>
<tr>
<td>High arched feet</td>
</tr>
<tr>
<td>Hammer or curled-up toes</td>
</tr>
<tr>
<td>Surgery for hammer toes</td>
</tr>
<tr>
<td>Claw hands</td>
</tr>
<tr>
<td>Wasting of muscles</td>
</tr>
<tr>
<td>Foot troubles, foot ulcers</td>
</tr>
<tr>
<td>Use of braces</td>
</tr>
<tr>
<td>Arthritis or poliomyelitis (incorrect diagnosis)</td>
</tr>
<tr>
<td>Difficulty walking on heels and toes</td>
</tr>
</tbody>
</table>
OTHER DIAGNOSTIC TESTS

A number of ancillary diagnostic tests are available for special circumstances. These tests should be used when there is evidence from the history and examination findings that they will be informative. Lumbar puncture for cerebral spinal fluid can be informative for evidence of breakdown of the blood-nerve barrier by elevated protein when root involvement is suspected, as in AIDP and CIDP. Abnormal cells can suggest other processes, such as an infectious process. Peripheral nerve biopsy can provide evidence for vasculitis, amyloidosis, and infiltrative conditions. Skin biopsies can confirm damage to intraepidermal nerve endings. Recently, tests for antibodies against various gangliosides and for paraneoplastic conditions have become widely available. Antibody tests should be ordered with caution because the diagnostic yield of these tests is low.

SUMMARY

At the conclusion of the evaluation that includes a full characterization and a rational set of diagnostic tests a diagnosis should be forthcoming. However, it should be kept in mind that despite best efforts, it is important to appreciate that a good percentage of neuropathies, perhaps 20%, will remain undiagnosed despite an exhaustive evaluation. Ordering more laboratory tests is seldom informative, and may lead to false positive findings. A periodic review of a patient’s history and inquiry for new symptoms may be helpful.

REFERENCES

LOCALIZATION OF THE PROBLEM USING HISTORY AND EXAMINATION

Numbness can be the result of a disease process located in the central nervous system (CNS) or the peripheral nervous system (PNS). It can often be localized by the patient's history alone. It is important to recognize both the timing and onset of the patient's symptoms and the distribution of the patient's signs and symptoms. Localizing a patient's deficits to a specific area of the nervous system frequently can be accomplished with attention to the distribution of symptoms (e.g., right versus left, arm versus leg, proximal versus distal, symmetric versus asymmetric, and the presence of facial involvement). Determining the characteristics of symptoms (sensory and motor or sensory) and the temporal features (acute or chronic, or static or progressive) is also helpful.

Obtaining a clear history is important. The patient's complaints of “numbness” can include a range of sensory disturbances. The patient can describe “tingling,” “burning,” or a true loss of sensation simply as “numbness.” It is important to be specific when questioning the patient to clearly define the range of symptoms. This will help in identifying the etiology of the disease process. The simultaneous evaluation of the distribution of these complaints can significantly refine the differential diagnosis. Recognition of the common symptoms may have a major impact on appropriate treatment and may allow early management which can minimize long-term residual deficits for the patient. The use of a questionnaire with a human figure is helpful in defining the symptoms and their distribution (Figure 1).

The extent and characteristics of the patient's symptoms are related to the specific portion of the nervous system injured. Different populations of neurons are vulnerable in specific disease processes. The vulnerability may arise from the effect of a disease on a specific vascular territory (e.g., stroke, vasculitis, aneurysm), a space occupying lesion (e.g., tumor, herniated disk) or an autoimmune, inflammatory attack on the nervous system. Taking the patient’s history can frequently help the physician determine the localization (Tables 1 and 2).
A Practical Approach to the Patient Presenting With Numbness

The distribution of lesions affecting the CNS are usually distinct from those affecting the PNS (Table 3). This manuscript explores the possible disorders that can cause numbness along the neuroaxis, starting at the brain and moving out to the spinal cord and then peripheral nerves.

**BRAIN**

Numbness may be secondary to a lesion of the parietal lobe or thalamus (ventral posteromedial nucleus). Thalamic lesions produce contralateral sensory loss and numbness, but these may be painful. An abrupt onset suggests a cerebral vascular event and may be seen with lacunar infarcts secondary to hypertension. The patient would typically have sudden onset of contralateral sensory loss without other weakness. A magnetic resonance imaging (MRI) scan may confirm the presence of a lacunar infarct or a hemorrhagic infarction. Relative to other brain regions, the thalamus is more vulnerable to hemorrhage resulting from hypertension in the brain.

Parietal lobe lesions cause contralateral numbness associated with loss of discriminatory sensation. The patient may feel touch but may not localize it well. Patients may experience weakness as well as numbness but sensory complaints are more prominent.

**SPINAL CORD**

Lesions in the spinal cord resulting only in numbness are not common. Most cause both numbness and weakness. This is due to the close proximity of motor and sensory neurons and their pathways in the spinal cord and existing nerve roots. Inflammatory lesions can selectively affect sensory pathways. This can result in profound sensory disturbances that are typically bilateral. Disorders such as acute myelitis and multiple sclerosis can present as primarily sensory disturbances.

**NERVE ROOT/DORSAL ROOT GANGLION**

Sensory and motor nerve roots are separate as they exit the spinal cord but combine at the level of the dorsal root ganglion. The most common cause of nerve root injury is due to a herniated vertebral disk. This typically results in radiating pain frequently with both motor and sensory fibers involved. The involvement in the dermatome of multiple nerve roots suggests a problem other than a structural lesion. Consideration must be given to an inflammatory, neoplastic, or infectious process.

Selective involvement of the dorsal root ganglion cells causes a profound sensory loss. The differential diagnosis of a dorsal root ganglionopathy is a short list which includes heavy metals and paraneoplastic syndromes.

| Table 1 Patient's description of sensory loss likelihood of the localization |
|-----------------------------|----------------|
| Tingling                   | PNS > CNS   |
| Burning                    | PNS > CNS   |
| Total loss of feeling      | CNS* > PNS**|
| Poor coordination***       | CNS = PNS   |

CNS = central nervous system; PNS = peripheral nervous system

* Localization to the central nervous system would most commonly involve unilateral signs and symptoms except with spinal cord lesions where symptoms are usually bilateral.

** Peripheral nervous system lesions can be either multifocal or, commonly, bilateral and symmetric. Early signs in a neuropathy may involve only one extremity (usually the feet) but peripheral involvement would be much less likely with all unilateral complaints.

*** Poor coordination can result from either central (cerebellar, brainstem) or peripheral (impaired proprioception, nerve, dorsal root ganglion) pathology.

| Table 2 Distribution and characteristics of patient complaints along the neuraxis |
|-----------------------------|----------------|
| Distribution | Facial Involvement | Characteristic | Pain |
| Brain         | Unilateral       | often          | sensory + motor | no          |
| Spinal Cord   | Bilateral        | no             | sensory + motor | poss.       |
| Nerve Root    | Unilateral       | no             | sensory + motor | yes         |
| Nerve         | Unilateral or    | possible       | sensory, motor,  | yes         |
|               | Bilateral        |                | autonomic or combo |            |
| Neuromuscular | often bilateral  | yes, but not always | motor | no |
| Junction      | Bilateral        | rare           | motor | rare |

References:

Peripheral nerve injury is the most common reason for sensory disturbances, especially numbness. However, peripheral nerve injury frequently presents with both motor and sensory symptoms. The causes for a predominantly sensory neuropathy can be better understood if upon presentation the salient features of the patient’s sensory complaints are recognized. The goal is to distinguish between small fiber sensation (e.g., light touch, pain, and temperature) and large fiber sensation (e.g., position sensation and partial vibratory sensation). The list of possible etiologies that result in sensory neuropathy is long. It is also important to recognize some distinguishing features of the patient’s sensory disturbance, such as past history and family history. Diabetes, alcohol abuse, chronic use of medication or vitamins, and history of similar sensory problems in the family are significant clues to identifying a proper etiology. In the United States and many European countries, diabetes is the most common cause of neuropathy. However, leprosy remains the most common cause of neuropathy worldwide. The etiologies can be categorized as toxic, immune, metabolic, inherited, or mechanical.

HISTORY OF THE PRESENT ILLNESS

Knowing the timing of the onset of the symptoms as well as the family history and any occupational exposures can be helpful in understanding the disease process and fine-tuning the evaluation.

Onset

A slow, progressive numbness or sensory disturbance is frequently described as distal numbness or tingling in the toes. This may progress proximally into the feet and then up the legs and involve the hands as well (i.e., a stocking/glove distribution). The most distal segments of the nerve are most dependent upon axonal transport for delivery of vital proteins and neurotransmitters. Any process that interrupts axonal flow will be recognized by the patient as a symptom in the most distal aspects of the affected nerve. A slow progression from distal to proximal would strongly suggest a peripheral neuropathy in the differential diagnosis. Sensory complaints due to nerve root compression or irritation can also progress slowly. However, these lesions are commonly characterized by pain in the affected root distribution. The sensory complaints from a nerve root injury or generalized neuropathy can be episodic, particularly earlier in their course. Sensory disturbances from brain or spinal cord injury (typically vascular events) usually evolve more acutely. Numbness or paresthesias due to multiple sclerosis typically happens over days and may be episodic.

An acute or subacute onset with rapid progression of sensory complaints, accompanied usually by weakness, is consistent with localization to the brain, spinal cord, nerve root, or nerve. Typically, ischemic injury is associated with sudden onset of sensory symptoms. Inflammatory disorders can develop quickly and progress over several days and can affect any part of the neuraxis. In the brain, acute onset of sensory symptoms is typically accompanied by weakness and/or encephalopathy. The differential diagnoses would include stroke, multiple sclerosis, cancer (lymphoma, metastasis), and infection. In the nerve root, acute sensory symptoms are likely due to compression from a disk or trauma. In the peripheral nerve, the possible etiologies are more extensive but some require timely and appropriate management. Acute inflammatory demyelinating polyneuropathy often requires prompt management to maintain the airway and initiate treatment. Arsenic, thallium, tick paralysis, and porphyria are other problems that start with numbness but may result in a rapidly progressive disability for the patient and require urgent treatment (Table 4).
Family History

Family history can be helpful in identifying the etiology of neuropathy, particularly if a family member has had symptoms similar to the patient’s problems. The genetics of inherited neuropathy has significantly improved over the last decade and has increased the understanding of the normal biology of nerve tissue. The hereditary motor and sensory neuropathies (i.e., Charcot-Marie-Tooth neuropathies) are now better understood and represent a group of disorders with overlapping clinical characteristics but distinct pathology. Some can be identified by currently available commercial laboratory tests. Inherited disorders affecting only sensation (e.g., hereditary sensory neuropathy) are quite rare. They may involve either small fiber sensory loss (pain and temperature) or loss of larger sensory fibers (proprioception, vibration). Identifying the type of sensory loss on examination can help refine the differential diagnosis.

Occupational Exposure

Incidental exposure to agents that are toxic to nerve may be easily missed on a routine history and review of systems. Contact with solvents, glues, fertilizer, oils, and lubricants can result in a neuropathy that cannot be distinguished from other causes of idiopathic or hereditary etiology.

Medications

Injury to nerve caused by medications or vitamins is sometimes overlooked. Over-the-counter oral preparations can result in a predominantly sensory neuropathy (even at therapeutic doses). Patients with a neuropathy from some other cause may have an exacerbation of their symptoms when taking some over-the-counter medications (Table 5).

<table>
<thead>
<tr>
<th>Table 5</th>
<th>Selected medications associated with a sensory or a sensory predominant neuropathy which should be avoided in patients with a pre-existing peripheral neuropathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloramphenicol</td>
<td>Metronidazole</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>Nitrous oxide</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>Nucleosides</td>
</tr>
<tr>
<td>Glutathione</td>
<td>Didanosine</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>Dideoxycytosine</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>Stavudine</td>
</tr>
</tbody>
</table>

EXAMINATION

In addition to the body diagram, the physical examination can be helpful in localizing the site of injury. Evaluation of deep tendon reflexes examines both an afferent component to carry input from the muscle tendon to the spinal cord and an efferent component to produce a muscle twitch during a reflex. The reflex is affected by descending cortical-spinal inputs that mitigate or enhance the reflex arc. The arc reflects a specific root level and can be helpful in the localization of the process.

Pathology in the CNS is characterized by pathologically brisk reflexes and extensor plantar reflexes. Additionally there can be increased tone and spasticity. Pathology in the PNS would result in diminished or absent reflexes along with atrophy and/or reduced muscle tone. Asymmetric or absent reflexes suggest a focal neuropathy or radiculopathy. In a predominantly sensory neuropathy, the type of sensory loss can help indicate the nerve fibers involved (i.e., small fiber versus large fiber, or a mixed picture). The modalities of sensory loss which should be tested include those listed in Table 6.

<table>
<thead>
<tr>
<th>Table 6</th>
<th>Sensory modalities which should be included on a thorough examination and their anatomic correlates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modality</td>
<td>Fiber type (Periphery)</td>
</tr>
<tr>
<td>Light touch</td>
<td>Small fiber</td>
</tr>
<tr>
<td>Temperature</td>
<td>Small fiber</td>
</tr>
<tr>
<td>Pinprick</td>
<td>Small fiber</td>
</tr>
<tr>
<td>2-point discrimination</td>
<td>Small fiber</td>
</tr>
<tr>
<td>Proprioception</td>
<td>Large fiber</td>
</tr>
<tr>
<td>Vibration</td>
<td>Both small and large fiber</td>
</tr>
</tbody>
</table>

The most useful information from the sensory examination results from the distribution of the deficit (symmetric versus asymmetric) and the quality of the sensory loss.

Sensory loss and neuropathy frequently can be associated with systemic diseases such as diabetes and several connective tissue disorders. Clinical signs on the general examination can be helpful if there is evidence of multiple organ systems disorders. Autoimmune, inflammatory, metabolic, and neoplastic disease are some of the types of systemic illness which can present with peripheral nerve involvement resulting in numbness, paresthesia, and/or weakness. Careful attention to key clinical signs on general examination can result in the underlying disease as well as the etiology for the neuropathy.

Evaluation: Work-Up

One of the primary goals in patient work-up is to identify a treatable underlying process. Evaluation should include serologic and radiographic evaluation where appropriate to clarify the differential diagnosis and treatment plan (Table 7).

CNS

Sensory loss or numbness localized to the CNS is most typically associated with stroke or inflammatory disease. Evaluation of a patient with a suspected stroke, primarily involving sensation, should include screening risk factors such as hypertension, diabetes, cholesterol, tobacco use, and arrhythmia. An MRI of the brain is usually indicated. Ischemic or inflammatory disease thought to be localized to the spinal cord should be evaluated by an MRI.
and a lumbar puncture. The presence of elevated protein and an increased number of white blood cells in the cerebrospinal fluid suggests inflammation (myelitis). It is more difficult to define the specific etiology. Viral pathogens such as varicella, human T cell lymphotropic virus type 1, and human immunodeficiency virus have been demonstrated by high viral titers. Multiple sclerosis is a clinical diagnosis requiring multiple signs and symptoms at more than one point in time and MRI frequently can demonstrate plaques.

Electrodiagnosis

The evaluation of the functional health of peripheral nerves by nerve conduction studies (NCSs) and of affected muscles by needle electromyography (EMG) is often an essential component of the work-up. These tests can help localize nerve/muscle pathology and suggest an etiology. NCSs especially are helpful in identifying treatable causes of neuropathy by demonstrating primary demyelinating processes. Impairment of conduction velocity or evidence of conduction block in a focal region or in multiple regions can help define a demyelinating neuropathy. On the other hand, a reduced amplitude of the evoked response is more characteristic of an axonal neuropathy. It is important to note that axonal loss can be the result of a primary pathologic process attacking the axon or may be secondary to demyelination.

The EMG examination assesses the rate, amplitude, and frequency of electrical impulses being transmitted by the muscle. While NCSs can differentiate demyelinating versus axonal, the EMG is able to distinguish between the presence of denervation versus a primary muscle disease (myopathic process). The role of EMG in assessing a patient with only numbness is limited since it is only testing the motor nerves. However, a patient complaining of sensory loss in a radicular pattern may not be aware of any motor weakness (and the physical examination may be normal), but the EMG may demonstrate some motor axon involvement as the EMG can detect abnormalities with much greater sensitivity than the physical examination. It would take a 50% loss motor fibers to detect weakness on physical examination while a loss of only 5% can be detected by EMG. The added sensitivity in detecting abnormalities of motor units can implicate a combined motor-sensory etiology.

**BIBLIOGRAPHY**

CROSSFIRES: Controversies in Neuromuscular and Electrodiagnostic Medicine

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CROSSFIRES: Controversies in Neuromuscular and Electrodiagnostic Medicine

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Dr. Morris A. Fisher disclosed he has done consulting work for NeuroMetrix. Any conflict has been resolved according to ACCME guidelines.

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The ideas and opinions expressed in this publication are solely those of the specific authors and do not necessarily represent those of the AANEM.
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Please be aware that some of the medical devices or pharmaceuticals discussed in this handout may not be cleared by the FDA or cleared by the FDA for the specific use described by the authors and are "off-label" (i.e., a use not described on the product's label). "Off-label" devices or pharmaceuticals may be used if, in the judgement of the treating physician, such use is medically indicated to treat a patient's condition. Information regarding the FDA clearance status of a particular device or pharmaceutical may be obtained by reading the product's package labeling, by contacting a sales representative or legal counsel of the manufacturer of the device or pharmaceutical, or by contacting the FDA at 1-800-638-2041.
CROSSFIRES: Controversies in Neuromuscular and Electrodiagnostic Medicine

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OBJECTIVES After attending this session, participants will develop an understanding of, and be able to incorporate into their practice, arguments in favor of and against the following: (1) the use of F waves in disorders of the peripheral nervous system and nerve roots as well as the central nervous system; (2) the circumstances in which performing a needle EMG adds useful information in the evaluation of suspected carpal tunnel syndrome; and (3) the role of diagnostic ultrasound in the evaluation of neuromuscular disorders.

PREREQUISITE This course is designed as an educational opportunity for physicians.

ACCREDITATION STATEMENT The AANEM is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education (CME) for physicians.

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INTRODUCTION

Whether a physician should seriously consider learning neuromuscular (NM) ultrasound (US) and use it as part of the routine evaluation of patients seen in an electrodiagnostic (EDX) laboratory is debatable. An argument affirming the use of US is based on an analysis of the scientific evidence and an evaluation of the future of US. The evidence shows that US offers valuable contributions in regards to several common disorders in which EDX testing is currently used for diagnostic confirmation, and that there is considerable promise for other unique applications in NM disorders. The evolution of US imaging also strengthens the argument for using US.

COMMON ENTRAPMENT NEUROPATHIES IN WHICH US IS USEFUL

There are perhaps 50 citations in PubMed that focus on the sensitivity of US in carpal tunnel syndrome (CTS). The data can be summarized fairly simply; US is robustly specific and sensitive in the diagnosis of CTS. The relative quality of these studies is not uniform, but there is considerable weight in the multiplicity of studies performed. Depending on the study, the quality is of greater, lesser, or equivalent specificity and sensitivity to EDX testing, depending on how CTS is defined, and which types of US and EDX parameters for diagnosis are used. Since EDX techniques have been perfected for diagnosing CTS for the last five decades, it probably maintains a slight edge in this regard, but the data is not conclusive. There are clear instances where EDX tests can confirm CTS when US is normal, and clear instances where US can diagnose the disorder where EDX studies are normal.

In ulnar neuropathy at the elbow, similar findings prevail, although there is a significantly fewer number of studies. Again, studies show that US is a robust technique for identifying ulnar neuropathy at the elbow, but none of these studies are adequate in terms of head-to-head comparisons of US with nerve conduction studies (NCSs).

Experience with radial nerve palsy at the spiral groove and peroneal neuropathy at the fibular head have yielded similar findings, but the studies are fewer than those for ulnar neuropathy at the elbow with a smaller number of patients studied. Interestingly, peroneal nerve palsies, particularly if not associated with weight loss or known leg crossing, have a fairly high incidence of association with sonographically evident cysts.

CHALLENGES OF COMPARATIVE STUDIES

Will it be possible to establish US or NCSs as superior in terms of specificity and sensitivity in diagnosing entrapment neuropathies? There are at least four plausible reasons to assume that this will not occur.

First, currently there is no single golden standard for the diagnosis of entrapment neuropathies, so it is futile to expect certainty with any comparative study of diagnostic tests for these problems. As such, there will always be an error factor for any computed specificity and sensitivity for any technique. Second, at this time, there is no uniform consensus as to which of the many available EDX tests generates the best specificity and sensitivity for CTS, the most common entrapment neuropathy. It could be mixed palmar, multiple sensory nerve comparisons, inching, near nerve
studies, or a combination of these and electromyography (EMG). Since experts cannot agree on the ideal EDX tests for CTS, it is problematic to compare EDX testing to another technique (or if a comparison is performed, some experts will be dissatisfied with the choice of EDX protocol). There is similar debate regarding the precise EDX techniques needed to diagnose other entrapment neuropathies.

Third, in like manner, it is difficult to determine which US technique is optimal for diagnosing an entrapment neuropathy. Measuring nerve enlargement, although conceptually simple, involves a number of choices. The physician must decide if it should be measured by using the cross sectional area of the nerve, its thickness (diameter) \(^4\) or flattening ratio.\(^{10,17}\) The measurement site must also be determined. This could be a pre-ordained anatomic site, but there is debate as to which site should be used. For example, for the median nerve at the wrist, should it be placed at the distal wrist crease or the level of the hook of the hamate?\(^{20}\) Is it preferable to evaluate the nerve over several centimeters and record the area of maximal swelling? Is it better to use a ratio\(^{12}\) to measure the thickness of the nerve at the involved site and compare it to the contralateral side or an uninvolved site that is more proximal?\(^{8,12}\) Should a trace method or some other method be used for calculating cross sectional area?\(^{3}\) Should hypoechoic changes in the nerve be graded subjectively or measured precisely with some sort of quantitative program?\(^{25}\) How important is including an assessment of nerve mobility in terms of sagittal sliding, diving among the tendons with wrist flexion, or subluxation at the elbow?\(^{25}\) Should US values be corrected for factors such as age and body size which may correlate with nerve cross sectional area?\(^{26,78}\) Until there is a consensus about which EDX and US protocols are optimal for identifying entrapment neuropathies, it will be difficult to design a comparative study that provides truly conclusive results.

Fourth, it is not known what level of variation exists across EDX laboratories in terms of qualifications of the technicians and physicians involved, and standardization in the techniques employed. For example, there are still a number of laboratories that do not routinely check the temperature of the extremities before performing NCSs. Unfortunately, it is not known how much variation exists in conducting US techniques. However, clearly there is variation and it is likely to be significantly greater for US and EDX testing than for other specific types of procedures with test results that are based on hard copy images or blocks of tissue amenable to peer review by other experts at subsequent intervals. Therefore, a comparison of techniques in an optimal single laboratory setting would not predict the amount of variance in technical accuracy of a procedure being performed in multiple laboratories.

In selecting a diagnostic test, it is important to consider the advantages one may have over another in regards to sensitivity, specificity, as well as other such factors. Greater certainty in diagnosis is needed most in disorders in which therapeutic options carry considerable risks. The discomfort of a biopsy is appropriate for the evaluation of a potentially malignant nerve or muscle tumor. In entrapment neuropathies, because treatment is often elective and intervention typically carries low morbidity, slight improvements in diagnostic specificity or sensitivity are unlikely to significantly improve outcomes from current standard practices, which already incorporate a healthy appreciation of imperfect diagnostic certainty.

In selecting a diagnostic test to help confirm a suspected case of entrapment neuropathy, multiple factors influence the test choice. Key elements of such a decision are time (e.g., does the patient need to make a separate visit to have the test conducted), expense, and discomfort. At this time, US, which is painless, has a clear advantage in terms of comfort over EDX testing. Patients and referring physicians are particularly sensitive to the perceived pain of an EDX procedure. US is the first technology to offer a painless alternative to electrodiagnosis for evaluating common entrapment neuropathies. Additionally, US can be performed at a lower cost and is more time efficient. Generally, for the patient and referring physician, US need not establish diagnostic superiority, it simply needs to approximate that of EDX assessment for there to be a compelling case for its routine, or in select cases, perhaps exclusive use.

For example, some clinicians treat mild or mild to moderate CTS with splinting and steroid injections into the carpal tunnel, reserving surgery for those who fail these conservative measures. If the EDX consultant routinely performs needle EMG of the abductor pollicis brevis in cases of suspected CTS, they may quite reasonably decide that such cases should be initially referred for US evaluation. If the result is clearly abnormal, and an evaluation of patients in the author’s laboratory has shown that 100% of patients with cross sectional areas of the median nerve exceeding 0.2 cm\(^2\) have abnormal NCS findings indicative of CTS,\(^6\) then it might be reasonable to forgo further EDX testing and inject steroids into the carpal tunnel (perhaps using US guidance). If the patient failed therapy, at that point, further EDX tests might be warranted. In this case, it is logical that the steroid injection, although associated with a very low likelihood of other complications, would likely be associated with less discomfort than the needle EMG and multiple shocks.

It is important to determine what information EDX testing and US can provide that is not captured by a specificity and sensitivity analysis in the evaluation of entrapment neuropathies. One of the challenges with statistical assessment of diagnostic procedures such as EDX studies or NM US that generate complex information is that the information generated cannot be reduced to a single number. For example, in CTS, EDX tests provide information about the severity, may identify an entrapment neuropathy, determine the extent to which axons or myelin are involved, and reveal the relative health of nearby nerves. Furthermore, in cases of complete median neuropathy from CTS, EDX testing may provide sufficient evidence to help a surgeon decide not to operate because it would be unlikely that the disorder would improve enough to warrant surgical morbidity. Baseline studies are helpful for post-operative evaluations of failed surgical intervention.
US cannot be as specific as EDX tests with respect to axonal versus myelin damage or completeness of nerve injury, but it can provide some evidence as to muscle atrophy in the appropriate nerve distribution.\textsuperscript{21} It can precisely identify the location and extent of focal nerve swelling or identify nerve transaction.\textsuperscript{5} Additionally, it can provide information on the ability of the nerve to slide in the sagittal and axial planes (an observation that is key in certain rehabilitation protocols for CTS and its surgical repair),\textsuperscript{6} pathologic vascularity (using power Doppler),\textsuperscript{17} the extent to which the lumbricals or flexor digitorum muscles penetrate into the carpal tunnel during wrist flexion and extension (factors which may contribute to CTS and which may be amenable to surgical resection of small portions of problematic hypertrophic muscle),\textsuperscript{6,8} the echogenicity of the nerve (which may reflect increased fluid content and be associated with swelling or venous retention)\textsuperscript{6} the integrity of the transverse carpal ligament (of interest in patients with failed recent carpal tunnel release), anomalous nerve branching or splitting, the presence of cysts or tumors, and the relationship of the nerve to vascular structures, such as persistent median arteries.\textsuperscript{6} Obviously, it is unlikely that a standard statistical analysis of specificity and sensitivity will be able to incorporate the diversity of qualitative and quantitative information relevant to CTS obtained in EDX or US studies, nor is it sensible to make clinical decisions in regards to testing based on an incomplete analysis of the data available.

Both US and NCSs have fairly high specificity and sensitivity for CTS and for ulnar neuropathy at the elbow. Due to the absence of a gold standard for diagnosis, debate over optimal techniques, the difficulty in reducing complex information into single variables, and variations in practice patterns and quality across different laboratories, it would be difficult to confer convincing superiority to either technique in a way that is applicable to the diversity of laboratory settings.

THE FUTURE OF NEUROMUSCULAR US

Other Potential Uses of US in NM Medicine

US, as previously alluded to, can be used therapeutically to guide injections of steroids as well as guide therapeutic injections of botulinum toxin, particularly for electrically silent tissues such as the salivary glands.\textsuperscript{9} Another potential indication for US is in screening large populations of at-risk individuals for early signs of CTS, or to screen selected family members for hypertrophic hereditary neuropathy. The portability and non-invasiveness of the technique makes it more palatable to participants for such studies as compared to EDX testing. US may be able to accurately identify musculoskeletal disorders, which often mimic symptoms of entrapment neuropathies. Thus, if a patient has a negative EDX work-up for a suspected neurogenic process, US may be able to identify other treatable conditions such as tendonitis or bursitis. Currently, there is not a sufficient number of published studies on the use of US in this fashion. However, it seems likely it will become an informative direction of inquiry because US is a routinely accepted technique for diagnosing a variety of musculoskeletal ailments.

Another use of US is in the prevention of surgical complications. An interesting study recently showed that preoperative mapping of the sural nerve could be used to identify it before surgery, a process that could reduce the likelihood of its compromise in Achilles tendon repair.\textsuperscript{11} Another recent report showed that by identifying vascular anomalies commonly associated with an atypical anatomic course of the recurrent laryngeal nerve, the incidence of inadvertent injury to the nerve was reduced.\textsuperscript{13} Although it was never studied, it seems likely that mapping the course of the spinal accessory nerve before surgery in the area might prevent inadvertent injuries of this nerve, which is an not uncommon occurrence.\textsuperscript{19}

Developments in US Technology

One of the most compelling reasons for physicians to adopt US in their practice is related to the pace of technological advancement in sonographic imaging. Over the last decade, there has been a steady evolution in the quality and availability of high-resolution probes in clinical US. A reduction in the size of the equipment and cost of instrument operation, enhanced digital features that facilitate storing, sharing, and post-processing analyses, simplification of application, and newer techniques for image display, measurement of elastance,\textsuperscript{27} and innovations in contrast material are notable improvements. During the coming decade, further advances in US technology are likely to continue. EDX technology is fairly static and could still be performed on instruments available 40 years ago, and barring unexpected discoveries, it is unlikely to significantly change over the course of the next decade.

The Role of Electrodiagnosis and US

In the last 30 years, imaging has revolutionized the evaluation of disorders of the central nervous system (CNS). Much of the ability to understand newer imaging modalities (magnetic resonance imaging [MRI], positron emission tomography, and functional MRI) has come from correlation studies with pre-existing imaging techniques of angiography, plain radiographs, myelography, and computed tomography (CT). In the field of NM disorders, however, there is no solid corpus of experience with imaging. As such, the key techniques that currently provide the most helpful correlative interpretation of US images are the clinical evaluation and EDX testing. Fortunately, US technology is readily accessible to practitioners of electrodiagnosis, individuals who are skilled in the clinical evaluation of NM patients and skilled in the interpretation of EDX and other laboratory findings such as genetic tests, serology, and histopathology. It would be unthinkable to try to manage severe multiple sclerosis or recurrent cerebrovascular disease without imaging today, and given the continued advances in imaging technologies, this may be true of NM disorders in the future. The large community of involved physicians who are members of the American Association of Neuromuscular & Electrodiagnostic Medicine is uniquely positioned to elucidate the best strategies for applying imaging to best enhance the diagnosis and care of patients with NM disorders. By becoming involved now at this critical juncture of advancing and receding technologies, clinicians will be able to establish themselves as the experts in the emerging area of imaging in NM disease.
CONCLUSION

In conclusion, regarding the value of US, the following points should be able to obtain a broad consensus:

1) US and EDX testing are complementary diagnostic tests that can contribute to patient care.

2) MRI or CT alone, on current relatively low-resolution scanners without clinical or EDX correlation, are less likely to be informative than high-resolution US imaging with such correlation.

3) The discomfort of EDX testing may have had a negative impact on referrals to NM experts. The addition of a painless, informative, diagnostic technique may enhance referrals, particularly for those unusually sensitive to discomfort (e.g., children) and those in need of serial studies of complex NM problems.

4) Innovation in imaging technology is currently outpacing innovation in EDX technology.

5) In time, it seems likely that NM US will likely find unique diagnostic, preventative, and therapeutic indications beyond its use in the evaluation of common entrapment neuropathies.

For these reasons, US should be embraced by NM and EDX physicians.

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Neuromuscular Ultrasound is Not Ready for Prime-Time Use

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INTRODUCTION

High-resolution ultrasound (US) has made it possible to image peripheral nerves and muscle. The application of this technique to neuromuscular (NM) disorders has sparked considerable interest among NM clinicians. It provides clinicians with an imaging tool to evaluate anatomical detail at sites where disordered functions have been identified. US is noninvasive, painless, and less expensive than electrodiagnostic (EDX) studies, conventional computed tomography, or magnetic resonance imaging (MRI). However, the question remains as to whether NM US is ready for prime time as defined by its use in routine clinical practice outside academic centers. Though the use of US in musculoskeletal trauma or in interventions guiding peripheral nerve blocks or botulinum toxin injections will not be reviewed, the diagnostic value of US in common NM disorders will be addressed.

VALUE OF US IN THE DIAGNOSIS OF CARPAL TUNNEL SYNDROME

Carpal tunnel syndrome (CTS) results from an entrapment of the median nerve at the wrist and is the most frequent reason patients are referred for EDX studies. According to population studies, it is the most common entrapment neuropathy with a prevalence of 6% in women and 0.6% in men. The clinical diagnosis rests on typical core symptoms of wrist, arm pain, and hand paresthesia that is provoked by sleep or sustained hand grip and relieved by changes in hand posture or shaking of the hands. Additional core symptoms include sensory symptoms in digits 1, 2, 3, and part of the 4th digit, as well as thenar atrophy and weakness in more advanced cases. Provocative tests are based on eliciting paresthesia by tapping on the nerve at the wrist (Tinel’s sign) or by flexion of the wrist (Phalen’s sign). However, the clinical usefulness of these tests is limited due to the wide range of sensitivities (38% to 85%) and specificities (54% to 98%). The conditions associated with CTS are numerous, but most cases seen in routine practice are idiopathic. Underlying conditions frequently associated with CTS include diabetes, hypothyroidism, pregnancy, and rheumatoid arthritis.

EDX studies are used to confirm the clinical diagnosis of CTS, to define the severity of nerve damage, exclude other conditions producing similar symptoms such as proximal median nerve lesions, brachial plexopathy, and cervical radiculopathies (especially, C6 and C7), and uncover a co-existing polyneuropathy. A critical review of the literature of EDX studies in CTS provides scientific evidence that median motor and sensory nerve conduction studies are valid and reproducible studies that can confirm the clinical diagnosis of CTS with a high degree of sensitivity (>85%) and specificity (95%). Despite using more sensitive comparative median-ulnar studies, a small group of patients (10% to 15%) with clinical symptoms compatible with CTS will have normal EDX studies.

COULD IMAGING STUDIES USING US BE OF ADDITIONAL DIAGNOSTIC VALUE?

In 1993, the Quality Standards Subcommittee of the American Academy of Neurology stated that the benefits of diagnostic imaging techniques such as US had yet to be fully established. Since then, more than 200 citations of sonography or US and CTS have appeared in PubMed. Among NM physicians in the United States, US is not a universally accepted or widely applied test. High resolution US provides morphologic information of the content
Neuromuscular Ultrasound is Not Ready for Prime-Time Use

(i.e., the median nerve, deep and superficial finger flexor tendons, possible ganglion cysts, tumors, anomalous muscles, median artery) and surrounding tissues (flexor retinaculum and carpal bones) of the carpal tunnel. Four characteristic features have been described by US in patients with well-defined CTS: (1) increase of the cross sectional area (CSA) of median nerve at the entry of the carpal tunnel at the level of the pisiform bone; (2) increase in the CSA at the level of the pisiform bone compared to the CSA at the level of the distal radius; (3) increase in the flattening ratio determined as the ratio of the nerve’s major to minor axis at the level of the hook of the hamate; and (4) significant displacement or bowing of the flexor retinaculum.7

Case-controlled studies comparing US findings in patients with confirmed CTS to normal control subjects report on the pathological swelling of the median nerve by assessing the CSA at variable levels using different landmarks along the carpal tunnel.16,19 The cut off values of the CSA considered abnormal in these studies have ranged from 9.8 to 11 mm2, which overlap in part with normal control values (7.8 to 10.2 mm2). When selecting cases with confirmed CTS and control subjects, patients with borderline or mild disease are frequently omitted, resulting in unusual high diagnostic accuracy that cannot be expected in clinical reality.

Evaluating a new diagnostic test requires an independent blind comparison of the gold standard in consecutive patients with suspected CTS to reliably determine its accuracy and clinical validity. Among the more than 200 citations on sonography and CTS in PubMed, only four are prospective studies (Table 1). Three studies18,22,23 used clinical criteria supported by EDX studies, while Swen and colleagues17 used the beneficial response after operative treatment as the diagnostic gold standard. The four studies concluded that US is comparable to EDX studies in the diagnosis of CTS. US has an excellent power to rule in CTS for median nerve CSA greater than 12 mm2 with a post-test probability of greater than 90%.23 The kappa co-efficient, or ratio of actual to potential agreement beyond chance, for EDX studies using the median-ulnar distal sensory latency difference versus clinical evaluation was 0.64; that for US kappa was 0.69, indicating substantial agreement between both tests.18 Combining US and EDX studies did not significantly improve sensitivity and specificity.

Should EDX Studies be Abandoned in Favor of US in the Diagnosis Of CTS?

Each investigation yields different information. High resolution US offers the advantage of yielding structural information of the carpal tunnel and its content. In addition, it is less expensive, painless, and therefore, preferred by patients. On the other hand, sonography is an operator dependent test that requires special training. It takes about 6 months to train a rheumatologist to become an expert sonographer.17 Whether NM clinicians can achieve competency in a shorter training period is not known.

EDX studies are readily available in the United States and can be performed in community and academic centers according to established guidelines. EDX studies not only confirm the presence of CTS, but are also able to determine its severity and define demyelination versus axonal loss; differentiate CTS from other mimicking lesions such as C6 - C7 cervical radiculopathies, proximal median nerve and brachial plexus lesions; and detect an underlying polyneuropathy. Despite the higher cost and slight discomfort, EDX studies should not be abandoned in patients with suspected CTS. US should be considered a complementary study whenever structural abnormalities of the carpal tunnel are suspected, or when less invasive endoscopic surgical techniques are planned.

US IN THE DIAGNOSIS OF ULNAR NEUROPATHY AT THE ELBOW

Ulnar neuropathy at the elbow (UNE) is second only to CTS as the most common entrapment neuropathy affecting the upper

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients/wrists</th>
<th>Gold Standard</th>
<th>CSA mm2</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>+LR</th>
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<tr>
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<td>63</td>
<td>&gt;90% improvement after surgery</td>
<td>≥10</td>
<td>70</td>
<td>63</td>
<td>1.9</td>
</tr>
<tr>
<td>Wong</td>
<td>120/193</td>
<td>Clin +EDX; DML &gt; 4ms; M-U SLD &gt;0.4 ms</td>
<td>≥9</td>
<td>93</td>
<td>56</td>
<td>2.1</td>
</tr>
<tr>
<td>Zisweiler</td>
<td>71/101</td>
<td>Clin +EDX DML &gt;4.2 ms SCV &lt;41m/s</td>
<td>≥12</td>
<td>44</td>
<td>100</td>
<td>19.9</td>
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<tr>
<td>Visser</td>
<td>168/</td>
<td>Clin +EDX DML &gt;3.8 ms M-U SLD &gt;0.4 ms</td>
<td>≥10</td>
<td>82</td>
<td>87</td>
<td>6.3</td>
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</tbody>
</table>

CSA = cross sectional area of median nerve; DML = distal motor nerve latency; EDX = electrodiagnostic; +LR = positive likelihood ratio; M-U SLD = median ulnar sensory latency digit 4 difference; SCV = antidromic median sensory conduction velocity.

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US IN THE DIAGNOSIS OF ULNAR NEUROPATHY AT THE ELBOW

Ulnar neuropathy at the elbow (UNE) is second only to CTS as the most common entrapment neuropathy affecting the upper
extremity (UE). The ulnar nerve at the elbow may potentially be compressed at four sites that include (from proximal to distal): the medial intermuscular septum, the epicondylar groove, the humero-ulnar arcade (i.e., the arcuate ligament that joins the two heads of the flexor carpi ulnaris), and the exit of the nerve from the flexor carpi ulnaris muscle. The clinical spectrum of UNE ranges from paresthesias in the fourth and fifth digits to sensory impairment in the territory of the ulnar nerve with or without atrophy and weakness of ulnar innervated muscles. In contrast to CTS, localizing the ulnar nerve lesion at the elbow is more difficult and technically challenging with EDX studies. Unless partial motor conduction block or focal slowing of motor conduction velocity across the elbow can be documented, EDX studies may reveal nonlocalizing abnormalities in cases of pure axonal injury at the elbow. Needle electromyography (EMG) of ulnar innervated forearm muscles, such as flexor carpi ulnaris and flexor digitorum, may frequently be normal even in such proximal lesions because of fascicular sparing. In 1999, the American Association of Neuromuscular & Electrodiagnostic Medicine (AANEM) published guidelines to optimize EDX studies for UNE. The EDX studies have reported sensitivities ranging from 37% to 86%, and specificities of 95% or greater. Ulnar neuropathy at the wrist, C8 radiculopathy, lower trunk/medial cord brachial plexopathy, or even motor neuron disease can mimic UNE.

CAN DIAGNOSTIC US IMPROVE THE LOCALIZATION OF UNE?

A limited number of studies using diagnostic US have documented segmental ulnar nerve swelling along its course at the elbow. The focal nerve swelling has been measured using the maximal diameter of the ulnar nerve, its maximal CSA along the elbow, or a ratio of the nerve diameter between medial epicondyle and elbow joint level. Two case control studies of 14 and 33 UNE patients confirmed significantly increased ulnar nerve CSA as compared to healthy volunteers. One study reported a sensitivity of 93% and specificity of 95%, while the other reported a sensitivity of less than 50%. Applying the test in healthy control subjects to determine its specificity artificially increases the results because healthy volunteers are not part of the clinical spectrum of patients. Prospective studies of patients with suspected UNE are needed to evaluate the validity of US as a diagnostic test. A single prospective study of 123 patients with suspected UNE compared to 56 healthy control subjects confirmed an enlarged diameter of the ulnar nerve at the medial epicondyle. Additionally, the ulnar nerve diameter was significantly larger in patients with axonal lesions (3.3 mm2) compared to electrophysiologically defined demyelinating lesions (2.5 mm2). At the cut-off value of ≥ 2.5 mm for the largest ulnar nerve diameter (measured at the medial epicondyle, and 2 cm proximally & distally), the investigators reported a sensitivity of 80%, specificity of 91%, and positive likelihood ratio of 9. In the subgroup of patients who had nonlocalizing abnormalities on EDX studies, US confirmed ulnar nerve swelling at the elbow in 85% of subjects. If confirmed by additional studies, diagnostic US may replace MRI in the localization of ulnar nerve lesions in patients with nonlocalizing EDX abnormalities. Diagnostic US is a promising adjunct technique to EDX studies in the diagnosis of UNE. However, standardization of the techniques and additional well-designed prospective studies are needed before this test can be recommended for routine clinical practice.

US IN THE EVALUATION OF HYPERTROPHIC NEUROPATHIES

High resolution US is capable of identifying peripheral nerves and the brachial plexus in the UEs. Deeply situated nerves in the lower extremity are more difficult to depict. Problems that emerge while imaging nerves with US include difficulty in the identification of deeper situated nerves, nerves that are surrounded by fat or beneath bony structures, the imaging provides a relatively small field of view, and the quality of the image being operator dependent. US has the potential to identify focal, multifocal, and diffuse enlargement of peripheral nerves. The reference values of the CSA of peripheral nerves have recently been published. Diffusely enlarged nerves may be seen in hypertrophic neuropathies which include hereditary neuropathies (i.e., Charcot Marie Tooth disease types 1 and 3, Refsum’s disease, and neurofibromatosis), and acquired neuropathies such as chronic inflammatory demyelinating neuropathy, leprosy, and rarely multifocal motor neuropathy. Confirming enlarged peripheral nerves are of limited diagnostic value in patients with CMT1A or chronic inflammatory demyelinating polyneuropathy. Imaging studies are of much greater diagnostic importance in hypertrophic mononeuropathies, which are single nerves with focally enlarged segments. Perineuropathia, chronic inflammatory demyelinating mononeuropathy, leprosy, lymphoma, and peripheral nerve sheath tumors are the pathologic conditions producing focal hypertrophic mononeuropathy. MRI is used to identify the extent of the enlarged nerve and its signal characteristics. A targeted fascicular biopsy of the involved nerve by a skilled surgeon is often necessary to achieve a pathological diagnosis. To recommend a fascicular biopsy of a mixed nerve based on abnormal US images alone at this

Table 2 Prospective study of diagnostic ultrasound in ulnar neuropathy at the elbow

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients/Control subjects</th>
<th>Standard</th>
<th>UNE diameter mm</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>+ LR</th>
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<tr>
<td>Beekman5</td>
<td>123/56 control subjects</td>
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<td>Cut off = 2.5</td>
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<td></td>
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<td></td>
<td>(95% CI 74-87)</td>
<td>(95% CI 86-96)</td>
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CI = confidence intervals; Clin = clinical criteria; EDX = electrodiagnostic criteria similar to American Association of Electrodiagnostic Medicine (AAEM) recommendations; + LR = positive likelihood ratio. UNE = ulnar neuropathy at elbow; US = ultrasound. Highest diagnostic yield in ulnar nerve with nonlocalizable EDX studies = 86%.
time would be inappropriate. US offers the advantage of being a quick, less expensive screening examination. MRI provides a much wider field of view, is better in detecting tumors or inflammatory lesions by its signal characteristics, and most importantly, it is not operator dependent.

High resolution US will not replace EDX studies in the evaluation of disorders of peripheral nerves, but may be used as an additional tool to improve diagnostic localization in entrapment neuropathies and provide information on structural abnormalities.

MUSCLE US IN NM DISORDERS

NM disorders lead to changes in muscle morphology which can be detected with US. Both atrophy and hypertrophy, abnormal echo-intensity of muscles, and the presence of fasciculations can be readily assessed. Muscle infiltration with fat and connective tissue causes increased echo-intensity, which are either visually evaluated or quantified with computer assisted gray scale analysis. Myopathies can be distinguished from neurogenic muscle atrophy by different patterns of echo-texture. Myopathies cause a homogenous increase in echo-intensity, whereas neurogenic disorders have a more inhomogenous, moth eaten pattern that corresponds to groups of atrophic fibers. US is a valuable initial screening test of NM disorders in children who poorly tolerate the needle EMG examination. Prospective studies of children using quantitative muscle US have a more inhomogenous, moth eaten pattern that corresponds to groups of atrophic fibers. US is a valuable initial screening test of NM disorders in children who poorly tolerate the needle EMG examination. Prospective studies of children using quantitative muscle echo-intensity have detected a NM disorder with a sensitivity of 71% and specificity of 91%. The sensitivity is lower in children less than 3 years of age and in metabolic and mitochondrial myopathies.

The value of muscle US is limited in the diagnostic evaluation of adult NM disorders. Muscle echo-intensity is increased in inflammatory disorders. Inclusion body myositis has more atrophic muscles compared to other inflammatory myopathies. The sensitivity of US detecting biopsy proven disease was not significantly different from needle EMG and creatine kinase activity in a series of patients with inflammatory myopathies. Muscle US may describe the pattern of muscle involvement as accurately as a carefully performed NM examination can. Muscle US is rarely necessary to select a muscle for open biopsy.

In patients with amyotrophic lateral sclerosis (ALS), US demonstrates a combination of muscle atrophy, increased echo-intensity, and wide spread fasciculations. Increased echo-intensity has been found in muscles of three body regions (cranial, cervical and lumbar-sacral) in the early stages of ALS in a small series of patients. US appears to be more sensitive in detecting fasciculations in lower motor neuron disorders than visual inspection or needle EMG. Future studies using a prospective and blinded design are needed to establish the role of US in ALS.

Diagnostic US seems to be a valuable tool in the evaluation of NM disorders but warrants further study. Both EDX and US studies should be considered complementary, one dealing with functional aspects and the other with structural assessment. US is not yet ready for prime time use for the following reasons: (1) training guidelines and special certification of the US operators must be established; (2) standardization of techniques is necessary, and (3) more prospective studies according to Standards for Reporting of Diagnostic Accuracy criteria are required to establish its true diagnostic value in NM disorders.

REFERENCES

INTRODUCTION

The F wave is an interesting electrophysiological artifact produced by antidromic activation (“backfiring”) of motor neurons (MNs) following distal electrical stimulation of motor nerve fibers. Because they traverse the entire length of a peripheral nerve between the spinal cord and muscle, F waves provide a means of examining transmission between stimulation sites in the arm, leg, and in the related MNs in the cervical and lumbosacral cord. An adequate recording and interpretation of F waves requires an understanding of their physiology.

Physiology of the F Wave

F waves are the result of antidromic activation (“backfiring”) of MNs. The probability that any one motor unit (MU) in a particular MN pool will generate an F wave is small. Some stimuli in a train may not be followed by an F wave. Where F waves do follow the direct response, their shape and size usually changes from stimulus to stimulus (Figure) because the MUs and the associated motor unit action potentials (MUAPs) which generate the F wave, change with each successive stimulus.

Physiological Factors Influencing the F wave

Electrical stimulation of peripheral nerves is associated with antidromic activity in motor nerve fibers and orthodromic activity in sensory fibers. They might influence the excitability of MNs and thereby increase the chance of an F wave. For example, antidromic activity caused by the invasion of collateral branches of the motor nerve fibers in the ventral horn will activate the inhibitory interneuronal Renshaw cells. The Renshaw cells will transynaptically change the excitability of neighboring MNs. Renshaw cells are distributed widely throughout a MN pool, respond to increasingly intense stimulation by increasing their discharge frequency, and preferentially inhibit smaller MNs. Other possible physiological influences of antidromic volleys include the induction of a large enough field potential within the ventral horn to change the excitability of the MNs, as well as inhibition by direct recurrent collaterals from one MN to another.

To have any influence on an F-wave discharge in a particular MN, an antidromic volley in motor nerve fibers or orthodromic activity in sensory fibers would have to reach that MN prior to its own antidromic activation. A time allowance must be made for the MUAPs to spread into the axonal collaterals within the ventral horn for synaptic activation of an interneuron, and then for the synaptic activation of the MN. Theoretically, this should be possible due to rise times for spinal cord MN excitatory postsynaptic potentials of at least 3 ms. This should also allow ample time for segmental inhibitory and excitatory influences.

The precise manner by which an antidromic action potential triggers a second orthodromic action potential in the same MN has been examined only indirectly. Nevertheless, it is reasonable to think that once the antidromic action potential reaches the somadendritic (SD) membrane, the transmembrane currents associated with the antidromic action potential might be sufficiently strong enough to electrotonically reactivate the initial segment (IS). This requires that sufficient time has elapsed for the IS to recover from a refractory state from the preceding antidromic action potential. Once regenerated in the IS, the MUAP then returns to the periphery to activate the corresponding MU, thereby generating an F wave.
Numbness, Tingling, Pain, and Weakness

This hypothesis for the generation of an F wave suggests that any factors tending to speed up the recovery of the IS or which delay and/or increase the magnitude of any antidromically induced depolarization of the SD membrane, might increase the chance of an F wave. In contrast, any factors which do the reverse might reduce the chance of an F wave.

Selectivity of MUs in the F wave

Since there is a wide range in the physiological properties of MUs, the question of selection bias in the generation of F waves is important. Since MN size directly correlates with axonal size and therefore, conduction velocity, selection could affect the size, and conductions in a series of F waves. However, all studies supporting the absence of bias in the selection of MUs in F waves have been performed at submaximal stimulation. The relevance of such studies to situations where supramaximal stimuli are used, as in the usual clinical setting, is unclear. Empirically, there are strong arguments for thinking there is selective activation of the larger, faster conducting MUs in F waves. The potential range of conductions in F waves should be large, and yet this range is usually relatively small (about 15%). This is true despite the small number of F waves usually recorded. Conduction velocities using F-wave latencies have produced data similar to that for standard motor nerve conduction studies (NCSs) accordant with a consistent and selective activation of the fastest conducting, and therefore, the largest MUs, in a series of F waves. In the author’s opinion, the evidence favors some bias toward preferential activation of larger MUs in F waves. Fortunately, whatever the theoretical issues, the observed variability in F-wave latencies is not as random or remarkable as to preclude their clinical use.

Methodology

F waves are ubiquitous in distribution. When recorded from distal muscles in the limbs, F waves are almost always separated from the direct M potential. With more proximal stimulation, F waves may be obscured by the preceding direct M response due to the shorter latency of the F waves. Collision techniques may be employed to cancel the effect of the direct M potential on the F waves and make it possible to measure the latencies of the F waves with proximal recordings.

F waves are usually recorded using surface electrodes in a belly-tendon fashion with the active electrode positioned over the innervation zone of the target muscle. When recording from calf muscles, both electrodes should be positioned over the muscle belly to reduce any pick up of late responses from more distant muscles. As when recording H reflexes from the calf muscles, the recording electrode can be positioned on the soleus, one-half the distance between the stimulation site in the popliteal fossa and the superior aspect of the medial malleolus. The stimulating cathode should be proximal to the anodal electrode to avoid anodal block. Because F waves may be affected by a previous conditioning stimulus and F wave, the rate of stimulation should be less than 0.5 Hz.

F waves may be present following submaximal stimulation, but they prove to be more prominent with supramaximal stimulations (i.e., 25% above that required for the maximum M wave) since the amplitudes of the F waves, as well as the frequency of occurrence (persistence) increases as the stimulus intensity increases. Supramaximal stimulation also provides a physiologically definable and uniform environment in which F waves will occur.

Analysis of F waves

F-wave latencies reflect the conduction times between the site of stimulation and the spinal cord. They also measure the time for...
MN reactivation and the time for the centrifugally conducted action potential to activate the MU. Individual F-waves are generated by the recurrent discharges from one to at the most a few MUs whose associated MUAPs and F-wave latencies differ from one another. Therefore, F waves are small, relative to the size of the direct M potential (generally < 5%), and inherently vary in size, latency, and shape from stimulus to stimulus (Figure). There is uncertainty about the “turnaround” time for individual MUs. This time is said to be approximately 1 ms, but latency variations of up to 3 ms for individual F waves have been noted in humans.

The inherent variability of F waves dictates that a number of them should be recorded to insure that accurate, reproducible data are obtained. In addition, because of the inherent variability of F waves, they are adequately evaluated only by analyzing a number of variables.

The most common F-wave variable reported is minimal latency. Given the frequent difficulty of accurately determining individual F-wave latencies and issues such as overlapping A waves, obvious problems occur. During the past 25 years, there has been at least one paper every 2 to 3 years that addresses this question. It has been concluded that other measures of F-wave latency such as mean latency measurements, should be used rather than minimal values.1 In addition, whatever latency measurement is used, it is critical for normative values to include the effect of limb size, latencydifferences between sides, as necessary in radiculopathies. A series of 20 F waves is adequate for measuring mean F/M amplitude ratios and the percentage of individual repeater waves. As few as two F waves may be adequate for establishing an abnormal chronodispersion if the separation in latency between these two responses is greater than normal. Accurate measurement of chronodispersion requires more than 20 stimuli, with the possible need for 50 to 60. As many as 100 stimuli may be required to determine the number of individual repeater waves.

**mean latency = M latency**

• APB=abductor pollicis brevis; ADM=abductor digiti minimi; EDB=extensor digitorum brevis; AH=abductor hallucis

• *a=age in years; d= distance in cm (for APB and ADM, C7 to superior aspect radial styloid; for soleus, mid popliteal fossa to superior aspect of the medial malleolus); ht= height in cm

• latencies and regression equations shown with standard deviations

• regression equations for APB, ADM, and soleus from [26]; for EDB and AH from [62] AQ – There are no references 26 and 62 – please insert citations here but do not add to references.

<table>
<thead>
<tr>
<th>Table 1 Suggested normative F-wave values (see text)</th>
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<tbody>
<tr>
<td>Latencies</td>
</tr>
<tr>
<td>Minimal</td>
</tr>
<tr>
<td>APB (median)</td>
</tr>
<tr>
<td>ADM (ulnar)</td>
</tr>
<tr>
<td>Soleus (tibial)</td>
</tr>
<tr>
<td>EDB (peroneal)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>AH (tibial)</td>
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</table>

The upper limit of normal values for mean F wave latency differences between sides are 2 ms for the hand, 3 ms for the soleus, and 4 ms for the foot.

* Mean latency = M latency

** mean F amplitude in µV, maximum M in mV

*upper limit of normal

Amplitudes (mean F/maximum M [mF/M] ratios)*

| APB | 22+10** |
| Soleus | 25+12 |

** mean+SD
Peripheral Neuropathies

The evaluation of polyneuropathies is one of the most important functions for electrodiagnosis. The latencies of F waves are characteristically prolonged in neuropathies and may be abnormal even when peripheral motor NCSs are normal. This may be due to the long length of nerve that is monitored by F waves. They may also be more sensitive than conventional motor NCSs in axonal neuropathies. F-wave latencies are the most stable and reliable measurement for sequential NCSs in the same subjects and are the most sensitive nerve conduction parameter in patients with diabetic neuropathies. Prolonged F-wave latencies that exceed 150% of the upper limit of normal have been considered highly suggestive of demyelinating neuropathies, as has the absence of F waves in the presence of relatively preserved maximum M potentials. With the exception of latency, F-wave parameters can provide additional valuable electrophysiological information. For example, the percentage of repeater waves is increased in neurogenic disorders, especially those associated with atrophy. Although a large number of F waves are required, increases in repeater waves have been reported to be a sensitive indicator of carpal tunnel syndrome. Increases in the durations of F waves may also be an early sign in diabetic neuropathies. Mean F/M amplitude ratios may be increased in neuropathies. This is most characteristic of axonal injuries and is consistent with the increased amplitudes of the F waves and reduced amplitudes of the maximum M potentials, which is so often a feature of these neuropathies.

F-wave abnormalities have been reported in more than 90% of nerves studied in patients with acute and chronic acquired demyelinating neuropathies. This is consistent with the demyelinating and focal proximal injury present in these patients. In these 90% of nerves, abnormal latencies were present in less than half of these nerves. Other meaningful F-wave findings have included absent responses as well as abnormal chronodispersion or persistent F-wave abnormalities in acquired demyelinating neuropathies that have been at least as frequent as motor NCS abnormalities. F-wave abnormalities are so frequent in these patients that one should be hesitant in making such a diagnosis electrodiagnostically without such findings.

Characteristic F-wave findings in axonal and demyelinating neuropathies are summarized in Table 2. What may be of greater importance is that F waves are usually critical in defining different patterns of electrophysiologic abnormalities that can be helpful in better establishing the etiology of a neuropathy.

<table>
<thead>
<tr>
<th>Polyneuropathies – Characteristic Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Axonal</strong></td>
</tr>
<tr>
<td>• Mildly prolonged F-wave latencies</td>
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<tr>
<td>• Increased mF/M values</td>
</tr>
<tr>
<td>• Increased repeater waves</td>
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<tr>
<td><strong>Demyelinating</strong></td>
</tr>
<tr>
<td>• Prominently prolonged F-wave latencies (i.e., &gt;150% of the expected value)</td>
</tr>
<tr>
<td>• Decreased persistence</td>
</tr>
<tr>
<td>• Absent F waves with relatively preserved M waves</td>
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</tbody>
</table>

mF/M = mean F/maximum M ratios

F waves in Radiculopathies

Experimentally, root injury is due to compression and inflammation. Demyelination would be produced and slowing of nerve conduction could be demonstrated. For this reason, one may expect that F waves might be of value in the electrophysiological evaluation of radiculopathies. In fact, the use of F waves in the radiculopathies has been controversial.

Criticism

The use of F waves in radiculopathies has been criticized because the injury may not involve all of the motor axons in that particular root. F waves are uniquely qualified to analyze radicular injury where there may be axons that are injured, while others may remain intact. F-wave parameters that can measure this range of normal versus abnormal conductions include mean, median, and maximum latencies, as well as chronodispersion. The same debate applies to arguments that F waves cannot be used because the recording muscles may have multiple root innervation.

Another theoretical criticism of the use of F waves in radiculopathies is based on the concept of “dilution”; namely, the relatively small latency delay that is associated with compressed nerve root that would be obscured by the much longer F-wave latency. Modeling F-wave latency changes in radiculopathies using signal detection theory indicates that absolute F-wave latency does not influence the accuracy of detecting focal lesions. In fact, the important variable is variance which makes the “dilution” argument irrelevant. This argument in regards to “dilution” also ignores the ability to use appropriately analyzed F-wave latencies (i.e., mean latencies) to reliably compare latency differences between sides and examine the information that may be obtained by analyzing other F-wave variables.

Finally, the use of F waves in radiculopathies has been criticized because the data essentially overlaps with that obtained with needle electromyography (EMG). This belief is not necessarily supported by available reports, based on the pathophysiology of root injury. Needle EMG requires axonal injury, while F-wave abnormalities can occur with demyelination.
The article most commonly cited in the criticism of F-wave use in radiculopathies cannot be defended methodologically by current standards. For example, the analysis was based on only a few F waves recorded from the antigravity antagonist extensor digitorum brevis, and at least 75% of the patients had S1 radiculopathies in muscles with unexpected abnormalities.

**Defense**

Up to 90% of radiculopathies occur at the lumbosacral level, and up to 80% involve the L5 and/or S1 roots. These roots innervate muscles that are commonly used for F-wave recordings, namely the calf or small foot muscles. In contrast, nearly 90% of cervical radiculopathies involve muscles innervated by roots (C5, C6, or C7) that are not commonly used for F-wave recordings. As a result, meaningful information regarding the use of F waves in cervical radiculopathies is not available.

Based on prolonged latencies or abnormal side to side differences, sensitivities of 50% to 80% were reported about 30 years ago for F waves used in the evaluation of lumbosacral radiculopathies. More recent studies using F-wave variables, in addition to minimal F-wave latencies, have reported a sensitivity in L5/S1 radiculopathies comparable to that for needle EMG. In addition to mean latencies and latency comparison between sides, F wave variables of importance have included chronodispersion and persistence. Blinded studies using multiparameter analyses including F wave and compound muscle action potentials have revealed a diagnostic specificity of 84.3% and a sensitivity of 83.3% in patients with lumbosacral radiculopathies. In such patients, similar multiparameter analyses when compared to traditional EMG studies have revealed comparable positive and negative likelihood ratios with blinded neuroradiological evaluations. A multiparameter approach has been recommended in other areas of EDX. 12 Several reports have noted meaningful increases in F-wave chronodispersion—up to 8 ms—in patients with lumbar spinal stenosis with standing, and a recent study reports a meaningful decrease in F-wave persistence following a program of exercise.14 Such observations support the idea that F waves can monitor physiological changes at the level of the roots.

**Conclusion**

There are no convincing theoretical arguments or convincing studies indicating that F waves cannot be helpful in lumbosacral radiculopathies. The current evidence would support the usefulness of F waves in the EDX evaluation of radiculopathies where such evidence of injury to the anterior rami could be helpful.

**Central Nervous System Disorders and F waves**

F waves provide a physiological window into a segmental MN pool excitability, even if not necessarily for short-term changes. In patients with upper MN syndromes due to central nervous system (CNS) lesions, antidromically activated MNs fire more frequently than those in normal individuals. At the same time, this is complicated by the fact that frequently backfired MNs will discharge less frequently with activation by muscle contraction, whereas MNs that discharge infrequently will increase their firing rate. Therefore, at times, an increased central excitability results in a decreased discharge of larger MNs in an F wave, owing to blockage at the still refractory initial segment of the MN. Despite this complexity, analyses of F waves are a valuable technique for monitoring central MN excitability. For example, F waves are decreased early after central motor system injury that is associated with decreased reflexes and tone, while increased F-wave persistence and amplitudes have been noted with well established upper MN syndromes.

**CONCLUSION**

If used appropriately, F waves can be an important tool for evaluating the normal and abnormal physiology of the peripheral nervous system and the CNS. Currently, although F waves are underutilized, they maintain a well-established role in the evaluation of peripheral nerve dysfunction with evidence to support their role in lumbosacral radiculopathies. With more sophisticated technology and the greater potential use of a multiparameter type of analyses, the importance of F waves in clinical EDX will likely increase.

**REFERENCES**


5. **Fisher MA, Hofen B, Hultman, C. Normative F-wave values and the number of recorded F-waves. Muscle Nerve 1994;17:1185-1189.**


F-Wave Studies are of Limited Clinical Value

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Medical College of Georgia
Augusta, Georgia

INTRODUCTION

The role of F-wave testing in the practice of clinical neurophysiology is one of heated debate. Some believe this test has been employed to a point of overutilization. While many clinical neurophysiologists believe the test has wide applicability and can be used in most clinical situations, others feel it is of limited value. The rationale for F-wave testing, the pitfalls in performing F-wave testing, and the role of F-wave testing in specific clinical situations will be examined.

The F wave has been advocated as a method to determine the health of a population of motor nerves throughout their entire course. The axons of motor nerves are stimulated antidromically, resulting in depolarization of their cell bodies. Following the absolute refractory period, a limited number (often a single cell body) will be depolarized above threshold and produce a small late motor response known as an F wave. Since the F-wave response is usually the evoked response of a single motor neuron, its size is small and its latency is variable since different motor neurons are usually activated with each stimulus. Many different measurements are used by neurophysiologists to assess F-wave normality. The most commonly used measurement is the minimum F-wave latency which is simply the shortest latency of 5 to 10 different F-wave responses. Since this value only represents the latency of a single nerve, many advocate using the mean F-wave latency to better reflect the nerve's function. Another method, called chronodispersion, measures the range between the shortest and longest F-wave latency. F-wave persistence, which is the number of definable F waves seen, then divided by the number of stimuli; and non-repeater F waves, which is the number of unique F waves seen in a series, are measurements that are less commonly used.

In theory, the F wave should be a valuable tool in the armamentarium of the clinical neurophysiologist. Unfortunately, this test in actual practice is of limited value and is clinically overutilized. The major problem with the F wave relates to the fact that the response is generated by a single motor unit (MU). Sampling problems often prevent small lesions from being detected clinically because the majority of the neurons in the nerve are normal. There are five major problems that limit the F-wave's value as a clinical test (Table 1). First, it is difficult to detect axonal damage with F waves since usually the latency of the fastest F wave will not be affected by axonal damage. Second, due to sampling problems, small demyelinating lesions will not affect the minimum F-wave latency. Third, an F wave will only assess the normality of the nerve or nerve root stimulated and will not be useful for detecting abnormalities of other nerves and roots. This point may seem obvious, but often F waves are used inappropriately in radiculopathy screens. The fourth problem is that adding several F waves to routine clinical studies will increase the likelihood of test errors. Finally, normal values for F-wave latencies may not be interpreted correctly.

<table>
<thead>
<tr>
<th>Table 1 Causes of F wave limitations</th>
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<tbody>
<tr>
<td>1) Wrong measurement obtained</td>
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<tr>
<td>2) Sampling problems</td>
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<tr>
<td>3) F waves are poorly applied clinically</td>
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<tr>
<td>4) Statistical errors</td>
</tr>
<tr>
<td>5) Interpretation errors due to poor normal values</td>
</tr>
</tbody>
</table>

F WAVES IN AXONAL DAMAGE OR CONDUCTION BLOCK

While many neuropathies are due to focal demyelination that produce slowing, others cause axonal damage that result in Wallerian degeneration. While a conduction delay will prolong the F wave, conduction blocks and axonal degeneration will interfere with F-wave conduction and result in no F-wave response. If the lesion
is incomplete, the F-wave latency may be normal. As a result, it is still possible to have a significant axonal lesion and have a normal F-wave latency. While F-wave persistence and repeater F-wave determinations may show abnormalities in these situations, these tests are difficult and time consuming to perform. As a result, they are rarely performed.

**SAMPLING PROBLEMS AND F WAVES**

In an incomplete lesion typically seen in a radiculopathy, only a small proportion of a root’s neurons are involved. The involved neurons may show conduction block, but the other uninvolved neurons will be normal. The minimum F-wave latency will measure the latency of a normal neuron, which in many lesions will make up the majority of the nerve. As a result, the F-wave latency will be normal. A mean F wave would better reflect these abnormalities but these are usually also normal in incomplete lesions such as a radiculopathy. F-wave chronodispersion might allow the involved neurons to be tested, but this technique is not uniformly performed in most clinical laboratories. Therefore, because of sampling problems, the F wave will be normal in most patients with small, incomplete lesions.

**TESTING THE WRONG NERVES**

F waves are often applied in situations where there is no possibility that they will be helpful. It may seem obvious that an F-wave abnormality in the medium nerve recording from the abductor pollicis brevis (APB) muscle will not give information about the C6 nerve root, but reports have been seen in which multiple F waves have been performed to rule out a C6 radiculopathy. Unfortunately, none of the nerves studied were innervated by the C6 root. While an F wave may be performed on any motor nerve, they are usually performed in only a few selected nerves. Generally, nerves that innervate distal muscles are chosen because they are relatively long and have ample separation between the M response and the F wave. Unfortunately, these nerves will only provide information for a small number of nerve roots. Often nerve roots of interest will innervate proximal muscles. These nerves may be studied, but because the F wave may overlap the M response, there is need for use of special, technically difficult, collision techniques. As a result, these nerves are rarely tested. There is little value in studying F waves in nerves where pathology is not suspected. Therefore, F waves should be applied judiciously and used only in situations where they can be of value.

**STATISTICAL ERRORS AND F WAVES**

As more clinical testing is performed, the likelihood of a result being abnormal by chance alone becomes greater. As a result, one must either limit themselves to highly specific and sensitive tests or require more than a single abnormality before making a diagnosis. Therefore, it is important to know which tests are most sensitive when checking for specific diagnoses. To conduct an endless number of tests without a clear plan will lead to error. Performing F waves will also increase the number of tests performed. Therefore, this could lead to a situation in which the probability of error by chance could become unacceptably high. For this reason, a single abnormal F wave should be interpreted cautiously.

**NORMAL VALUES AND F WAVES**

Whenever numeric values are used in a clinical test, it is important to understand how the normal values were determined. Unfortunately, the establishment of proper normal values is usually not given enough attention. Many laboratories use a static value for the upper limit of normal. This method is flawed because F-wave latency is related to height and age. These values must be considered when establishing normal values for F waves. If they are not considered, an F-wave latency in a very tall person may be considered prolonged when it is actually normal. Another variable to consider is nerve conduction velocity (NCV). It would be expected that if the conduction velocity of a nerve is slowed, its F wave would be prolonged. Often the question is whether or not a more proximal lesion exists. In these cases, it is important to factor out known NCV slowing to see if the F wave is longer than expected. In the case of a radiculopathy, it must be determined whether or not a proximal lesion exists at the root level that is the cause of the patient’s symptoms. If the NCV of a nerve is slowed, without factoring out its effects, it would not be known if the prolonged F-wave latency is due to distal slowing or a more proximal lesion. It was recently shown that correcting for NCV did not improve the F-wave sensitivity for radiculopathy. The problem is that all of the patients studied had normal NCVs. Only in patients with abnormal NCVs would correction of the normal values for NCV improve the ability of an F wave to detect a proximal nerve lesion. In the case of neuropathy, if the NCV is slowed, a prolonged F wave without correcting for NCV can provide no additional information. If corrected for NCV, a prolonged F wave will indicate that another more proximal lesion is present. While it is expected that with correction, the F wave will more often be normal, since the slowing that had been accounted for by the already known slowed NCV will be factored out, this method will allow previously undetected proximal lesions to be discovered.

**THE USE OF F WAVES IN SPECIFIC CLINICAL SITUATIONS**

**F Waves in Radiculopathy**

The F wave is used most often in the evaluation of suspected radiculopathies. They are often tested in nerve areas innervated by nerve roots other than those which are clinically relevant. Under these situations, the test has limited value. The sensitivity of the F wave in cervical radiculopathy ranges from 10% to 20%. In most series, either the needle examination is abnormal for the patient to be included or the needle electromyography (EMG) examination is abnormal more often than the F wave. Since the
F wave is rarely abnormal when the needle examination is normal, an F wave has limited clinical utility. In one study of patients with magnetic resonance imaging confirmed cervical radiculopathy, F waves were abnormal in 55% of patients compared to 75% with abnormal needle EMG. While 13% more patients were confirmed to have cervical radiculopathy if both the F waves and EMG were utilized, there are several problems with this study. The first problem revolves around the fact that subjects with C5 radiculopathy had been excluded, thereby a population of patients had been selected that were more prone to having F-wave abnormalities. Secondly, multiple F-wave determinations were performed. These authors studied minimum F wave, F-wave persistence, F-wave chronodispersion as well as their side-to-side comparisons, or a total of six F-wave measurements. It is difficult to be certain what the significance of a single F-wave abnormality is with this number of measurements.

Table 2 shows the results of 2093 patients studied at the Medical College of Georgia who had clinical symptoms of cervical radiculopathy and F-wave data. In this group of patients, 10% had abnormal F waves. In patients with no evidence of radiculopathy, the F wave was abnormal 3% of the time. In patients with good clinical symptoms and a normal EMG, 7% had abnormal F waves. Therefore, the F wave is abnormal twice as often in patients with clinical symptoms consistent with a radiculopathy. With an abnormal EMG, the likelihood of finding an abnormal F wave becomes greater and approaches 20% of patients with needle EMG exami

<table>
<thead>
<tr>
<th></th>
<th># in population</th>
<th>Abnormal F wave</th>
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<tbody>
<tr>
<td>Clinical symptoms of cervical radiculopathy</td>
<td>3324</td>
<td>16.0 %</td>
</tr>
<tr>
<td>Clinical symptoms and F-wave data</td>
<td>2093</td>
<td>10.0 %</td>
</tr>
<tr>
<td>Clinical symptoms and normal EMG</td>
<td>1200</td>
<td>5.8 %</td>
</tr>
<tr>
<td>Clinical symptoms and abnormal EMG</td>
<td>893</td>
<td>4.3 %</td>
</tr>
<tr>
<td>Clinical symptoms and EMG C8 radiculopathy</td>
<td>154</td>
<td>0.7 %</td>
</tr>
<tr>
<td>Normal clinical examination with F-wave data</td>
<td>1005</td>
<td>4.9 %</td>
</tr>
</tbody>
</table>

Table 2 F waves in cervical radiculopathy, Medical College of Georgia 1986-1996 (20,623 patients)

The use of F-wave values in a generalized neuropathy is of considerable interest. F waves would more likely be abnormal if their normal values were not corrected for NCV. With this correction, F waves would be abnormal less often, but testing would indicate abnormalities that are not explained by the already slowed NCV recorded over the nerve. For example, in a patient with a peroneal NCV of 32 m/s, the F-wave latency would be longer than if the patient had a NCV of 45 m/s. The prolonged F-wave latency in the patient with the slowed NCV is expected and it is not known whether there are additional proximal lesions unless a normal value that takes this slowed NCV into consideration is used. If the F-wave latency was slower than expected, this would indicate that an additional conduction delay is to be found proximally. If the F-wave latency was corrected for the nerve’s measured NCV, then it would be less likely to be abnormal. In the case where it was not corrected, it would provide no more information than can be obtained by standard NCSs. For this reason, an argument could be made that F waves should only be performed on nerves with normal NCV, or that one should take the NCV into consideration if it is expected that the F wave would provide additional information in a generalized neuropathy.
F Wave in Focal Neuropathies

F wave advocates support its use in the detection of focal neuropathies. Because the F-wave minimal latency measurement will be normal unless significant demyelination is present that involves most of the axons in the nerve, a small area of focal demyelination will usually not be detected by F-wave measurements. Therefore, if it is possible to directly stimulate across the suspected lesion, it is better to use this direct approach. There have been studies that show the utility of F waves in the diagnosis of carpal tunnel syndrome (CTS), but in all cases, the patients were already diagnosed by having abnormalities in other NCSs. In addition, an abnormal F wave would not localize the lesion to the carpal tunnel. It is rare that a prolonged median F wave would change a clinical decision about whether or not a patient has CTS. In very proximal lesions where there is no way to stimulate across the lesion, F waves may be of limited value. Unfortunately, as previously addressed, F-wave latency is a relatively insensitive test for an incomplete lesion. Other techniques such as chronodispersion, F-wave persistence, or repeater F waves may be more sensitive but more experience is needed before these tests become a routine part of an electrodiagnostic (EDX) evaluation. These tests are too difficult and time consuming to perform on a routine basis.

F waves in Generalized Conditions

F-waves have been shown to be abnormal in generalized neuropathic conditions such as amyotrophic lateral sclerosis (ALS). It is important to check F waves in ALS so that a diagnosis of multifocal motor neuropathy is not missed. While F-wave latencies may be slightly long in ALS, other F-wave measurements are often more likely to be abnormal. F-wave amplitude is increased because the MUs are larger in ALS. In addition, the number of nonrepeater F waves and F-wave persistence are reduced in ALS. At this point, the findings are supplemental to other EDX findings seen in this condition. While these findings are of interest, the main value of F waves, as well as other NCSs in ALS, is to exclude other diseases.

CONCLUSION

In conclusion, F-wave testing is currently overutilized in routine clinical practice. Their value in radiculopathies is limited at best. However, in most cases of generalized neuropathy, they are of value. In the case of focal demyelinating lesions, their use is limited to situations in which it is not possible to record across the suspected lesion. In these instances, the test is relatively insensitive. It is possible that other nonroutine methods of F-wave testing may increase the value of these tests. Currently, these methods are too time consuming and difficult to use on a routine basis. However, in the proper clinical situation, they may be of value.
INTRODUCTION

Carpal tunnel syndrome (CTS) is caused by entrapment of the median nerve as it passes from the distal forearm into the hand. The pathogenesis includes local demyelination and axon loss if the compression is more advanced.

Demyelination declares its presence by slowing conduction speed through the entrapped region. In CTS, this produces prolongation of the latency across the wrist. Conduction velocity is usually normal in the nerve proximal to the lesion, although in severe cases, the forearm segment can also be slowed due to retrograde atrophy of the compressed axons.

The presence of axon loss is generally considered to be indicative of a lesion which is more severe than one resulting from demyelination alone. Detection of axon loss in CTS might dictate a more aggressive approach to treatment such as promptly proceeding to surgical decompression. Although axon loss can be inferred from reduction of the amplitude of the sensory and motor responses in nerve conduction studies (NCSs) conduction block due to local demyelination could also produce low amplitude responses. Abnormalities found during the needle electromyography (EMG) examination are generally considered to be more robust indicators of axon loss. In the needle EMG, the presence of abnormal resting activity like fibrillation potentials and positive waves as well as abnormal voluntary activity like enlarged motor unit action potentials are indicators of axon loss.

TO NEEDLE OR NOT TO NEEDLE, THAT IS THE QUESTION

The “con” side of the argument that performing needle EMG should be a standard component of the evaluation of CTS is that the presence of CTS is electrodiagnostically established by demonstrating slowing of median nerve conduction across the wrist. This is most commonly accomplished by finding prolongation of the median nerve distal latency, or slowing of the transcarpal conduction velocity in laboratories that perform that calculation. Performing needle EMG without NCSs is insensitive in the identification of CTS. Needle EMG abnormalities are present in about 40% of currently reported patient series and up to half of those will have fibrillation potentials. Needle EMG of thenar and other hand muscles can be uncomfortable and decrease patient satisfaction with the testing. Performing the needle EMG also increases the cost of the study due to additional supplies required and professional component expenses. In a hospital-based laboratory, the base Medicare reimbursement for a single limb needle EMG examination is approximately $38 for the technical fee while the professional component costs an additional $77.

The “pro” side of the argument is that performing NCSs without needle EMG does not provide a direct assessment of the median nerve axons. Equally important is that conditions with potentially similar presentations like cervical radiculopathy, plexopathy, or proximal median neuropathies will not be detected by NCSs alone. Modern needle electrodes are available in diameters as small as 0.3 mm (30 gauge) and their use can significantly reduce patient discomfort.

Several published studies have examined the issue of what information needle EMG can contribute to the assessment of CTS. Werner and colleagues showed that the presence of needle EMG abnormalities correlated with reduction of the amplitudes of the compound muscle action potential (CMAP) and sensory nerve action potentials (SNAPs). However, abnormal needle EMG findings could be found in patients whose CMAP or SNAP values were still within a normal range, although below the normal mean. In the series of 480 patients, nearly half with CTS had needle EMG

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abnormalities and about half of those had fibrillation potentials. Needle EMG abnormalities correlated better with the degree of distal latency prolongation than response amplitude reduction. A report by Vennix and colleagues also showed that needle EMG abnormalities could be present in patients with CMAP amplitudes of 7 mv, a value which many laboratories would consider to be within the range of normal values. The study also showed that the presence of fibrillation potentials greatly increases when the distal CMAP amplitude drops below 4 mv. About 7% of patients in the latter series had needle EMG findings which identified additional peripheral nerve lesions like cervical radiculopathy or proximal median neuropathies.

Some physicians choose to perform the needle EMG in any patient referred for evaluation of CTS in whom NCS results showed abnormalities greater than just relative prolongation of latency in trans-carpal sensory conduction studies like “palmar” type testing. The test may be performed to “rule out” carpal tunnel and cervical radiculopathy.

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Appropriate Testing for Carpal Tunnel Syndrome

Needle EMG is NOT NEEDED

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INTRODUCTION

Carpal tunnel syndrome (CTS) is defined as a complex set of symptoms resulting from compression of the median nerve in the carpal tunnel. Some of these symptoms include pain, burning or tingling, paresthesias in the fingers and hands, and pain that sometimes extends to the elbows. Current electrodiagnostic (EDX) instrumentation will identify this peripheral nerve dysfunction. There can be NO EDX-negative CTS Today!

As recently as 1946, Gilliatt, one of the forefathers of EDX medicine, suggested that EDX and sweat tests were too “time consuming” to be used in a busy clinic for identifying CTS. In 1952, Marinacci used only needle electromyography (EMG) to diagnose CTS. Since more sophisticated technology has been developed, needle EMG has become less useful in the diagnosis and management of CTS.

In 1956, Dr. George Phalen, an orthopedist at the Cleveland Clinic, noted that it was not necessary to use EDX testing for diagnosing CTS. He believed that physical findings were used almost exclusively for CTS diagnosis. Others have reported the sensitivity and specificity of several tests used in the physical examination. Most valuable was the weakness of the thenar muscle. The other test that was seen as valuable was the interesting finding of the wrist ratio as both a sensitive and a specific test for CTS.

Motor latency of the median nerve became popular in the 1960s. Median sensory latencies became more widely employed as definitive techniques in the 1970s. Prior to the early 1960s, a motor latency greater than 5 ms was the objective test for CTS. Instruments became more sophisticated and eventually all signals were digitalized for greater accuracy. Antidromic sensory latencies were quicker and easier than orthodromic techniques and they gradually assumed primacy in the diagnosis of CTS. This provided a quick and precise method to compare the latency of the median nerve with those of radial and ulnar nerves. Latencies of mixed nerves, both median and ulnar, were compared across the carpal tunnel and proved to be an accurate and reliable measure of CTS.

As the understanding of the median nerve anatomy improved, more branches were studied across the carpal ligament. More techniques were developed and compared for sensitivity and specificity. The comparison of radial and median sensory nerve action potential (SNAP) to digit 1 has been studied extensively and has proven to be of great value as both sensitive and specific in CTS.

BEST PROCEDURE FOR CARPAL TUNNEL SYNDROME DIAGNOSIS

Clearly, with the current technology, if there is compromise of the median nerve within the carpal tunnel, there must be an abnormality found using EDX testing.

When compromise of the median nerve occurs in the carpal canal, only four things are possible: (1) axons are unaffected; (2) axons are dead and inexcitable; (3) myelin is mildly affected and slowing occurs; or (4) myelin is more severely compromised and conduction is blocked.

It is axiomatic that to best evaluate an entrapment of a peripheral nerve, one must stimulate the nerve both proximal and distal to the compromise. Furthermore, it becomes necessary to evaluate both sensory and motor axons on both sides of the entrapment.

Thus for CTS, the sensory axons of the median nerve can be stimulated at the wrist and midpalm with recording at digit 3 (long finger). Reference values are 3.1 ± .03 ms for latencies and 50 ± 6 µV at wrist stimulation (14 cm); 1.6 ± .02 ms and 60 ± 6 µV at midpalm (7 cm). Digit 3 is more sensitive than digit 2, which is more often the finger tested. More recently, studies have been performed to show the advantages of stimulating the motor axons of the median nerve both proximal and distal to the carpal tunnel.
Motor latency of the median nerve at wrist stimulation is $3.7 \pm .03$ ms and the amplitude is 5 mV to 20 mV (reference values from standard texts). At midpalm stimulation, the latency is irrelevant (over motor point) but the increase in amplitude normally is less than 10%. With blocking of motor axons in the carpal tunnel, the compound muscle action potential (CMAP) will be small when stimulating the median nerve at the wrist but will be increased at distal stimulation. Furthermore, the CMAP at distal stimulation will represent only the living and still conducting axons, a semi-quantitative measure of the severity of CTS. To identify how many axons are compromised, it is necessary to stimulate both proximal and distal to the carpal tunnel and to record motor and sensory fibers separately.

**MIXED NERVE STIMULATION**

The mixed median nerve contains both sensory and motor axons, so that depending on the proportion of dysfunctional axons, SNAP and CMAP are evoked when the median nerve is stimulated both proximal and distal to carpal ligament. Although some investigators have thought this to be the most sensitive technique, it is unable to separate sensory from motor compromise. For example, if the motor axons are unaffected and the latency is normal while the sensory latency is prolonged, a mixed nerve latency can be normal.

**ACUTE CARPAL TUNNEL SYNDROME**

Acute CTS occurs when a severe insult is suddenly presented to the median nerve in the carpal tunnel. Examples include a worker operating a paint sprayer continuously over several hours, an amateur playing hockey morning and afternoon every day for a week, or a worker continuously using a jackhammer for 4 to 5 hours.

In acute CTS the major EDX abnormality is an increase in SNAP or CMAP at stimulation, distal to the carpal ligament. This can be more than 100% even with normal values or with only a minimal increase in the latency. If there is still uncertainty in the diagnosis, the next recommendation is to stimulate the median and ulnar nerves at wrist (14 cm) (SNAP digit 4). The latencies should be equal to or less than .03 ms; amplitudes – median 30 µV, ulnar 25 µV. In the late 1980s, the transcarpal mixed nerve latencies were proposed as sensitive diagnostic studies for CTS. The following were the amplitudes and latencies for the transcarpal, median, and ulnar nerves: (8 cm)– median 1.8 ± .2 ms, 60 to 150 µV, ulnar 1.8 ± .2 ms, 20-40 µV same latency (difference ≤ .03 ms).

Needle EMG is generally not necessary for diagnosis unless there is any question about concomitant or other conditions. It is important to note that the term “double crush syndrome” is misleading. Cervical radiculopathy is not a direct or indirect cause of CTS. It is a consequence of multiple entrapments with underlying vulnerable nerves (e.g., diabetic peripheral neuropathy). A detailed history and a meticulous physical examination should be sufficient to determine if the cause of the patients symptoms is something other than CTS, or to identify a condition coexisting with CTS.

**NEEDLE EMG SHOULD NOT BE A SUBSTITUTE FOR A HISTORY AND PHYSICAL**

If concomitant conditions are excluded and the diagnosis of CTS is established, then needle EMG is unnecessary. It is important to remember that reduced recruitment does not distinguish between conduction blocking and axonal death. Positive waves and fibrillation potentials are only an indication of some axons’ death; they have little quantitative value due to sampling variability. Severity and prognosis are best determined by the most distal stimulation as it would be a reflection of the remaining functioning axons. If an underlying peripheral neuropathy is suspected (e.g., diabetic), the ulnar, radial, and distal median segment will provide clues to extend the EDX (i.e., sural, F waves, etc.). If these is a confirmed diagnosis of CTS, there is no reason to do a needle EMG.
**DISCUSSION**

Stimulation both proximally and distally to evaluate a peripheral nerve compromise is clearly indicated during the EDX evaluation of CTS.\(^\text{22}\) Certainly, both sensory and motor axons should be assessed separately for precise diagnosis. Because of the chronology of peripheral nerve injuries and the variability of nerve fiber damage, latencies do not provide sufficient information for complete evaluation. Amplitudes (CMAP, SNAP, and compound nerve action potential) both proximal and distal to the carpal ligament are the most important values in determining CTS severity and prognosis.

While there are ample studies comparing different techniques, there are only a few that compare the amplitudes of the SNAPs. This is probable because the SNAP is larger at distal stimulation (phase cancellation) and is affected more by temperature (i.e., it increases when cool).\(^\text{1}\) The temperature at distal palm can be measured easily with currently available instruments. Whether or not to warm the hand is controversial; in hands with overactive sympathetic fibers, continued stimulations will change the environment in spite of warming the hand. It is necessary to be aware of SNAP changes secondary to cooling during the EDX examination as a negative spike of SNAP will increase in duration and amplitude as well as cause the peak latency to increase.

The distal stimulation of median motor fibers is complicated by the proximity of the ulnar nerve and the ulnar innervation of the deep head of the flexor pollicis brevis in the thenar muscle group. Stimulation of the median nerve with a needle (e.g., monopolar needle electrode) will facilitate the procedure. The shape of the CMAP must be the same at both wrist and midpalm stimulation points to ensure that the ulnar nerve is NOT stimulated.

It is challenging to compare the median nerve values with those of the radial and ulnar nerves. Many studies have been performed and while some show varying results, it is fair to conclude:

- Digit 1 is the best and most sensitive digit to use when comparing radial to median SNAP. Besides its value in CTS diagnosis, there is additional value in identifying cervical radiculopathy (second to foraminal stenosis where the sensory axons will be compromised at or distal to the dorsal ganglion and would reduce the SNAP amplitude). One study suggested that the radial sensory branch was the least affected in diabetic neuropathy.\(^\text{4}\)

- Digit 3 is the best finger to study the median nerve SNAP both proximal and distal to carpal tunnel. This is probably because it is the longest portion of the median nerve.

- Digit 4 SNAP with stimulation of median and ulnar nerves is a useful technique to determine underlying neuropathy effects on CTS. Its advantage is that both nerves are being subjected to the same temperature variations.

- CMAP of an ulnar-innervated interosseus muscle compared to a median-innervated lumbrical I or II can be helpful in distinguishing CTS from an underlying neuropathy.\(^\text{2,19}\)

**SUMMARY**

In diagnosing CTS, one should first screen for CTS with median and radial SNAP to digit 1. The latency difference should be less than .03 ms. Next, stimulate the median nerve at the wrist (14 cm) and midpalm (7 cm), recording from digit 3. Allow for a SNAP amplitude increase of less than 30%. Then, stimulate the median nerve at the wrist and distal to carpal ligament recording from the abductor pollicis brevis. Allow for a CMAP increase of less than 1 mV.

If CTS diagnosis is still not confirmed, perform a transcarpal study (mixed nerve latency) and stimulate the median and ulnar nerve in midpalm and record over wrist (8 cm). Although Stevens\(^\text{22}\) suggests a difference of less than .2 ms, this author prefers .3 ms. Note that the amplitude of median CMAP is 80 to 150 µV while that of ulnar is only 20 to 40 µV. This is due to the superficial location of the median nerve at the wrist, while the ulnar nerve lies deep to the tendon of the flexor carpi ulnaris. Next, stimulate the median and ulnar nerves at the wrist (14 cm), recording from digit 4. The median SNAP is slightly larger (30 µV) and the latency difference is less than .3 ms. There is often a motor artifact when stimulating the ulnar nerve.

Finally, stimulate the median and ulnar nerves at the wrist (12 cm), recording over lumbrical I or II. Latencies differ less than .5 ms. Note that the CMAP of lumbrical I or II is only 1 to 2 mV, while that of ulnar interosseous muscle is 4 to 6 mV.

In a previously conducted study, 2\(^\text{0}\) 2/3 SNAPs were combined with different digits. This was found to increase the sensitivity of CTS diagnosis.

The principal objective of the EDX examination in CTS is to confirm the diagnosis and to establish the stimulation severity. This can only be determined by recording SNAP and CMAP of the median nerve both proximal and distal to the entrapment.

Needle EMG is unnecessary and causes additional discomfort for the patient. It should not be routinely included in CTS EDX.

**REFERENCES**


Case 1 – 67-year-old woman with leg weakness

8-year history of slowly progressive, painless weakness
- 8 years ago - trouble arising from floor
- 4 years ago - trouble arising from chair
- 2 years ago - falls, give way of left leg
- Denies atrophy, fasciculations, muscle pain, sensory symptoms, or any upper extremity or trunk symptoms
- Previous needle electromyography (EMG) and nerve conduction studies (NCSs) normal

Clinical Examination: Uses upper extremities to arise from seated
- -2 weakness quadriceps with mild, bilateral atrophy
- -1 to -2 weakness left-right finger flexors and wrist flexors
- Remainder of neurologic examination is normal, including reflexes and sensory examination

NCS – normal peroneal, tibial, and sural

COMMENT
Scattered, mytonic discharges in multiple muscles

REPORT
Summary - NCSs are normal. Needle EMG shows fibrillation potentials and myotonic discharges with a mixture of short and long duration, polyphasic, rapidly recruited motor unit action potentials (MUAPs) in proximal and distal muscles.

Interpretation – The findings are those of a chronic, severe, diffuse myopathy. Fibrillation potentials in myopathic disorders may indicate the presence of necrosis, splitting, or vacuolization of muscle fibers. Mixed MUAPs can be seen in disorders that affect both nerve and muscle or in very chronic myopathies such as inclusion body myositis (IBM), chronic polymyositis or some muscular dystrophies. IBM is most likely with this combination of EMG and clinical findings.

MUSCLE BIOPSY – IBM

COMMENT
The distribution of weakness is an important clue to IBM. Mixed MUAP changes are also typical, but can be seen in very chronic myositis.
Case 2: 20-year-old college student 2 weeks progressive generalized weakness

Day 1
1. Myalgia, headache, sore throat, fever
10. Student Health: penicillin for “strep throat”, persistent emesis
11. Emergency Room - Urinary retention, lethargy, unsteady
12. Diplopia, mild proximal weakness, brisk deep tendon reflex (DTR), bilateral Babinski
13. Reduced reflexes, progressive weakness, shortness of breath (SOB), tachycardia
14. Hospitalized: Head CT and MRI normal; Cerebrospinal fluid (CSF) cells & protein increased

Diagnosis – Guillain–Barré with myelopathy, polyradiculo neuropathy, and autonomic neuropathy

Treatment Plan: Start 5 days intravenous immunoglobulin (IVIg)

Day 14

NCS
All motor amplitudes were low with no dispersion
Median motor and peroneal responses absent
No F waves
Conduction velocities and blink reflexes normal
Repetitive stimulation normal

EMG
Poor or no activation
Two muscles with reduced recruitment
No fibrillation potentials

REPORT
Acute, severe, diffuse, axonal polyradiculopathy. A severe motor neuropathy with distal conduction block cannot be excluded, but is less likely. Repeat study in 7 - 10 days for more definitive information.

Day 21 Total paralysis. Pulse dose methylprednisolone; tracheostomy; percutaneous endoscopic gastrostomy (PEG); C. difficile colitis; GM1 < 250; viral t/c (-)

NCS
Motor and sensory responses all showed marked reduction from the study of 9 days ago, despite high-intensity stimulation. The remaining, very low-amplitude responses had markedly long distal latencies and reduction in amplitude with proximal stimulation. No blink reflexes could be recorded.

EMG
No voluntary MUAPs could be activated in any muscle tested. Minimal fibrillation potentials were recorded only in hand and cervical paraspinal muscles.

REPORT
There has been marked progression of the disorder. There is now much clearer evidence of a widespread, demyelinating neuropathy with distal involvement that could account for the paralysis.

Day 23 IVIg 5 days - slow improvement; antibiotics continued

Day 60

NCS
NCSs reveal markedly reduced or absent compound muscle action potentials throughout with markedly slowed conduction velocities and prolonged distal latencies. There is an ulnar conduction block in the forearm on the left. The blink reflex was present, but markedly prolonged.

EMG
There are fibrillation potentials throughout, but with clear MUAP activation of normal or mildly long duration in the proximal upper limb.

REPORT
The findings are now those of a severe polyradiculopathy with prominent demyelination, as well as moderate axon loss. There has been improvement since the previous study. Fibrillation potentials are more prominent, but this reflects the Wallerian degeneration that has occurred, and does not indicate a worsening.

3 months – Reflexes return; tracheostomy and PEG out
6 months – Return to school with good limb strength

COMMENT
The distinction between an axonal motor neuropathy (AMAN) and an acute demyelinating neuropathy is not always easy. Every attempt should be made to define the diagnosis and stop specific therapy too soon.

Case 3: 65-year-old woman with fatigue

• 2 years of difficulty with household chores, “tired”
• Difficulty squatting at “Curves”
• EMG 1 year ago - normal NCS and EMG
• Limited improvement on sertraline hydrochloride
• Examination - mild proximal weakness including difficulty swallowing. Normal reflexes, cranial nerves, sensation, and gait

NCS
Motor and sensory NCSs are normal in the arm and leg, including F-wave latencies. Slow repetitive stimulation of ulnar/hypothenar,
accessory/trapezius and peroneal/anterior tibial muscles before and after exercise is normal.

**EMG**

Needle EMG showed short duration MUAPs in several proximal muscles, including the genioglossus. A few fibrillation potentials were seen in the thoracic paraspinals.

**REPORT**

The findings are those of a very proximal myopathy. The absence of many fibrillation potentials argues against, but does not exclude, an active inflammatory myopathy.

**BIOPSY**

Sarcoidosis

**COMMENT**

While the clinical and EMG picture make an inflammatory myopathy most likely, a muscle biopsy should always be considered to obtain a more definitive diagnosis. Sarcoidosis may present initially with muscle involvement

**Case 4: 29-year-old woman with muscle aching**

- Healthy - 5 years muscle aching
- Mild elevations of creatine kinase (CK) (300 - 550)
- Examination normal
- Mild weakness, limited to left triceps

**NCS**

Motor and sensory NCSs normal in arm and leg. Normal repetitive stimulation.

**EMG**

Short duration MUAPs with mild, scattered fibrillation potentials in proximal muscles.

**REPORT**

The findings are mild, but consistent with a proximal myopathy, possibly inflammatory.

**BIOPSY**

Scattered, small, atrophic fibers with rare necrotic fibers. Consider myotonic dystrophy, Type 2.

**GENE TEST**

Myotonic dystrophy type 2 (DM2) showed CCTG repeat expansions (>12,100 bp). Confirmed in relatives.

**COMMENT**

Myotonic discharges in DM2 are more prominent proximal, predominantly wane, and may be few and far between.

**Case 5: 45 -year-old interior designer with 3 months generalized weakness**

- Brain stem astrocytoma-stable 2 yrs after radiation therapy
- Temporal lobe herpes simplex virus (HSV) encephalitis-better year after acyclovir
- Bulbar dysfunction from tumor-dexamethasone and temazolamide
- 2 mo progressive weakness with no other symptoms or signs
- CSF and EMG performed at home - axonal and demyelinating neuropathy
- Hospital transfer – flaccid quadriparesis with mild facial weakness and dyspnea
- Other cranial nerves, reflexes and sensation normal
- MRI 10 mm mass and residuals of HSV; with deep vein thrombosis (DVT)

**EMG**

Short duration, polyphasic, stable MUAPs with rapid recruitment in all muscles. Scattered fibrillation potentials

**NCS**

CMAPs are low amplitude and markedly long duration without dispersion. F-wave latencies are normal, but F waves are small. Normal sensory NCSs. Normal repetitive stimulation.

**ADDITIONAL STUDIES**

Low amplitude MUAP with direct muscle stimulation. Normal motor unit number estimates.

**REPORT**

The findings are those of a severe, generalized myopathy of the type seen with critical illness. This pattern can occur with high dose steroid medication.

No evidence of an additional, neurogenic process or defect of neuromuscular transmission was found.

**FOLLOW-UP**

Full return of strength after 4 months

**COMMENT**

Critical illness myopathy can be difficult to distinguish from neuropathy. Prolonged CMAP without dispersion and small MUAPs are important distinguishing features.
Case 6: 84- year-old woman with weakness

- Diabetes mellitus and hypothyroidism with 2 months of painless arm weakness
- Examination: Proximal, symmetric arm weakness; normal sensation and reflexes

NCS
Normal

EMG
Proximal and distal muscles of the arm and leg show rapid recruitment of short duration MUAPs primarily in the proximal, muscles, a bit more in the arm than leg. A few scattered myotonic discharges were seen, but no fibrillation potentials were found.

REPORT
The findings are those of a proximal myopathy. The findings do not clearly suggest an inflammatory or other specific muscle disorder. This pattern could be seen with a hypothyroid myopathy.

COMMENT
Severe hypothyroid myopathy often shows brief runs of myotonic like activity. Biopsy is nonspecific.