American Association of Neuromuscular & Electrodiagnostic Medicine


# Numbness, Tingling, Pain, and Weakness:

## A Basic Course in Electrodiagnostic Medicine

Anthony A. Amato, MD

Lawrence R. Robinson, MD

Kathryn A. Stolp, MD, MS

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Timothy R. Dillingham, MD, MS

2005 AANEM COURSE A

AANEM 52ND Annual Scientific Meeting

Monterey, California

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# Numbness, Tingling, Pain, and Weakness: A Basic Course in Electrodiagnostic Medicine

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Dr. Amato is the vice-chairman of the Department of Neurology and the director of the Neuromuscular Division and Clinical Neurophysiology Laboratory at Brigham and Women's Hospital in Boston. He is also an associate professor of neurology at Harvard Medical School. Dr. Amato is an author or co-author on over 80 published articles, 36 book chapters, and 2 books, and is co-author on the second edition of Electrodiagnostic Medicine with Drs. Dumitru and Zwarts. He has been involved in clinical research trials involving patients with amyotrophic lateral sclerosis, peripheral neuropathies, neuromuscular junction disorders, and myopathies.


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### Peter D. Donofrio, MD

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Dr. Donofrio is a graduate of The Ohio State University School of Medicine in Columbus, Ohio. He completed an internal medicine residency at Good Samaritan Hospital in Cincinnati, Ohio, and a neurology residency and neuromuscular fellowship at the University of Michigan in Ann Arbor. Presently, he is professor of neurology and vice-chairman of the Department of Neurology at Wake Forest University School of Medicine. His major research interests are amyotrophic lateral sclerosis, peripheral neuropathy, and the electrodiagnosis of peripheral neuropathy. Dr. Donofrio is associate chief of Professional Services of North Carolina Baptist Hospital.


### Timothy R. Dillingham, MD, MS

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Dr. Dillingham is professor and chairman of the Department of Physical Medicine and Rehabilitation at the Medical College of Wisconsin, in Milwaukee, Wisconsin. Dr. Dillingham graduated from the University of Washington School of Medicine in Seattle, Washington in 1986. In 1990, he completed his internship and residency training in physical medicine and rehabilitation at the University of Washington. During his residency he earned a Master of Science degree in gait biomechanics. Following his post-graduate training, he served in the United States Army from 1990 to 1994 at Walter Reed Army Medical Center in Washington, D.C. After completing his service obligation, Dr. Dillingham joined the faculty of the Johns Hopkins University School of Medicine and became an associate professor in the Department of Physical Medicine and Rehabilitation. Dr. Dillingham's electrodiagnostic research assessed needle electromyography in persons with suspected radiculopathy. Health services research and epidemiology are areas of research interest for him as well. He also serves as chair of the AANEM Research Committee.

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## Kathryn A. Stolp, MD, MS

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Dr. Stolp received her medical degree from the University of Minnesota. She trained in a physical medicine and rehabilitation residency followed by a fellowship in neuromuscular disease and electromyography at the University of Michigan. She also received a Masters of Science degree in clinical research design and experimental analysis from the University of Michigan's School of Public Health. She has been a member of the Mayo Clinic Rochester Department of Physical Medicine and Rehabilitation (PM&R), served as director of the Mayo Clinic Spinal Cord Injury Program, Mayo PM&R residency program, and as associate dean in the Mayo School for Graduate Medical Education. She is presently an associate professor of PM&R and department chair. She serves on the Board of Directors for both the Association of Academic Physiatrists and the American Association of Neuromuscular & Electrodiagnostic Medicine and is currently president-elect of the latter organization. Research interests include healthcare costs for the disabled, spasticity management, and neuromuscular disease.

*Authors had nothing to disclose.*

# Numbness, Tingling, Pain, and Weakness: A Basic Course in Electrodiagnostic Medicine

## Contents



**OBJECTIVES** This basic review will cover a range of neuromusculoskeletal disorders from a practical clinical perspective moving from patient assessment and differential diagnosis to the electrodiagnostic (EDX) evaluation. After attending this course, the participant will gain (1) improved clinical skills and strategies, including the judicious and selective application of EDX studies, in assessing the patient with generalized weakness and/or fatigue; (2) improved understanding of the clinical assessment and EDX evaluation of the patient who presents with focal sensory and/or motor impairment due to an entrapment mononeuropathy; (3) improved understanding of the differential diagnosis of patients with generalized sensory disturbance and/or weakness due to peripheral neuropathy including the role of EDX studies in the evaluation process; and (4) insight into the process of clinical examination and EDX consultation for patients with neck or low back pain due to spinal pathology, who may or may not have radiculopathy.

**PREREQUISITE** This course is designed as an educational opportunity for residents, fellows, and practicing clinical EDX physicians at an early point in their career, or for more senior EDX practitioners who are seeking a pragmatic review of basic clinical and EDX principles. It is open only to persons with an MD, DO, DVM, DDS, or foreign equivalent degree.

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

**CME CREDIT** The AANEM designates attendance at this course for a maximum of 3.75 hours in category 1 credit towards the AMA Physician's Recognition Award. This educational event is approved as an Accredited Group Learning Activity under Section 1 of the Framework of Continuing Professional Development (CPD) options for the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada. Each physician should claim only those hours of credit he/she actually spent in the activity. The American Medical Association has determined that non-US licensed physicians who participate in this CME activity are eligible for AMA PMR category 1 credit. **CME for this course is available 9/05 - 9/08.**

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# Approach to Patients With Neuromuscular Disorders

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## INTRODUCTION

The approach to patients with neuromuscular disorders is challenging. As in other neurological diseases the key to arriving at the correct diagnosis is careful localization of the lesion. Weakness can be the result of central lesions (brain or spinal cord processes—e.g., brainstem infarct, central pontine myelinolysis, transverse myelopathy), anterior horn cell disease (e.g., amyotrophic lateral sclerosis [ALS], poliomyelitis), peripheral neuropathy (e.g., Guillain-Barré syndrome [GBS]), neuromuscular junction defects (botulism, Lambert-Eaton myasthenic syndrome [LEMS], myasthenia gravis [MG]), or myopathic disorders. The most important aspect of assessing individuals with neuromuscular disorders is taking a thorough history of the patient's symptoms, disease progression, and past medical and family history as well as performing a detailed neurologic examination. This is not to say that the electrodiagnostic (EDX) examination, laboratory data, and muscle biopsies are not important, but the physician's clinical acumen based on the historical aspects of the disease and the clinical examination provide the guiding force for performing the most appropriate confirmatory tests to most expeditiously arrive at a correct diagnosis.

It is usually not difficult to distinguish generalized weakness secondary to a cerebral or brainstem insult from other causes of muscle weakness, because in these central disorders weakness is accompanied by impaired consciousness. Myelopathies can be more troublesome to diagnose. Compressive lesions of the involving spinal cord and the nerve roots can result in a combination of upper and lower motor neuron abnormalities which can mimic ALS and vice-versa. Acute transverse myelitis can be associated with rapid quadriparesis in which the deep tendon reflexes (DTRs) are initially absent from a "shocked cord." Such cases are not uncommon initially as GBS. Although both conditions are usually associated with sensory loss, a true sensory level is not evident in GBS but should be present in transverse myelitis and other structural abnormalities involving the spinal cord.

The presence of motor and sensory symptoms and signs are helpful in distinguishing peripheral neuropathies from anterior horn cell disorders, myopathies, and neuromuscular junction disorders. However, some types of peripheral neuropathy are predominantly or purely motor and thus can be difficult to distinguish these other disease processes. Most neuropathies are associated with distal greater than proximal weakness. However, significant proximal weakness can be seen in certain peripheral neuropathies (e.g., GBS, chronic inflammatory demyelinating polyradiculoneuropathy [CIDP]). Further, although usually associated with proximal weakness, certain myopathies and rarely even neuromuscular junction disorders can manifest with primarily distal weakness.

Amyotrophic lateral sclerosis is the result of degeneration of upper and lower motor neurons. The degeneration of lower motor neurons leads to muscle weakness, atrophy, and fasciculations, which typically begins focally. Upper motor neuron involvement manifests as spasticity and pathologically brisk DTRs. While most patients over time develop both upper and lower motor neuron deficits, some patients continue to have pure lower motor neuron abnormalities, while others have only upper motor neuron signs. Some of the hereditary spinal mus-

cular atrophies present with generalized symmetrical, proximal greater than distal, weakness and can be difficult to distinguish from myopathic disorders.

The key in distinguishing neuromuscular junction defects from myopathies is the fluctuation in symptoms and signs in the former. Patients with MG usually fatigue during repetitive activity while patients with LEMS can actually improve with continued physical exertion. Neuromuscular junction disorders have a predilection to affect the extraocular muscles which are less commonly affected in myopathies.

The following discussion is a reasonable approach to evaluating patients with neuromuscular complaints.

## MEDICAL HISTORY

While obtaining the medical history, the clinician should attempt to define onset and course of the illness as well as the distribution of symptoms. The differential diagnosis of generalized weakness presenting in infancy (Table 1) is different from that presenting later in childhood or early adult life (Table 2) and those disorders manifesting in late adulthood (Table 3). The rate of disease progression is important to pursue with the patient. Certain disorders progress acutely over days or weeks (Table 4), while others evolve more slowly over months (Table 5). The course of the disease may be chronic and progressive, mono-phasic, or relapsing. The increasing health consciousness of some individuals presents a good opportunity to gauge the rate of disease progression with respect to distance previously run, weight lifted, or games played. A steady reduction in these exercise-related parameters may be important clues for establishing a pattern of gradual and progressive physical decline.

The patients' presenting symptoms are dependent upon the muscle groups that are predominantly affected. Early manifestation of proximal lower extremities weakness is progressive difficulty climbing stairs and in arising from a chair, commode, or the floor. The patient may note that the upper extremities may now be required to provide assistance in pulling them up the stairs with a hand rail or in pushing them up from a seat. Weakness of the anterior compartment of the distal lower extremity results in foot drop. These patients will complain of frequent tripping or stubbing of the toes because of the inability to dorsiflex the foot when walking. Involvement of the posterior compartment of the distal legs leads to difficulty standing on one's toes.

Weakness about the shoulder girdles may impact on the patient's ability to perform activities of daily living, such as brushing hair and lifting objects. Distal upper extremity weakness usually presents with progressive difficulty with grip. Patients will describe difficulty opening jar tops and twisting or turning door knobs.

A patient with neck weakness will often complain of difficulty lifting their head off a pillow. Further, sudden braking or accelerating in a car can cause the head to jerk back and forth. Involvement of cranial muscles may result in ptosis, diplopia, dysarthria, or difficulty chewing and swallowing.

**Table 1** Differential diagnosis of the floppy infant

- **Central nervous system disorders (most common etiology)**
- **Anterior horn cell**
  - Spinal muscular atrophy type I and II
- **Peripheral neuropathy**
  - Congenital hypomyelinating/amyelinating neuropathy
  - Charcot-Marie-Tooth (CMT) III (Dejerine-Sottas)
  - CMT type I and CMT type II (rare)
  - Giant axonal neuropathy
- **Neuromuscular junction**
  - Infantile botulism
  - Infantile myasthenia gravis
  - Congenital myasthenia
- **Myopathy**
  - Congenital myopathies (all of them can present in infancy)
  - Muscular dystrophies
    - Congenital muscular dystrophies
    - Dystrophinopathy/sarcoglycanopathy (rare)
    - Congenital myotonic dystrophy
  - Metabolic myopathies
    - Glycogen storage defects
      - Acid maltase deficiency
      - Debrancher deficiency
      - Branching enzyme deficiency
      - Myophosphorylase deficiency (rare)
    - Disorders of lipid metabolism
      - Carnitine deficiency
      - Fatty acid-Acyl-CoA dehydrogenase deficiencies
  - Mitochondrial myopathies
    - Benign and fatal infantile myopathy
    - Leigh's syndrome
  - Endocrine myopathies (e.g., hypothyroidism)

**Table 2** Weakness presenting in childhood or early adulthood

- **Anterior horn cell**
  - Spinal muscular atrophy type III
  - Poliomyelitis
  - Amyotrophic lateral sclerosis
- **Peripheral neuropathy**
  - Acute or chronic inflammatory demyelinating polyneuropathy
  - Hereditary neuropathies
- **Neuromuscular junction**
  - Botulism
  - Myasthenia gravis
  - Congenital myasthenia
  - Lambert-Eaton myasthenic syndrome
- **Myopathy**
  - Congenital myopathies
    - Central core
    - Multicore
    - Centronuclear
    - Nemaline
    - Myofibrillar
  - Muscular dystrophies
    - Dystrophinopathy (Duchenne or Becker)
    - Limb-girdle muscular dystrophies
    - Congenital muscular dystrophy (partial merosin deficiency)
    - Myotonic dystrophy
    - Other dystrophies (e.g., FSHD, EDMD)
  - Metabolic myopathies
    - Glycogen storage defects
      - Acid maltase deficiency
      - Debrancher and branching enzyme deficiency
    - Disorders of lipid metabolism
      - Carnitine deficiency
      - Fatty acid-Acyl-CoA dehydrogenase deficiencies
  - Mitochondrial myopathies
  - Periodic paralysis
  - Electrolyte imbalance
    - Hyperkalemia
    - Hypokalemia
    - Hypophosphatemia
    - Hypercalcemia
  - Endocrine myopathies
  - Toxic myopathies
  - Inflammatory myopathies
    - Dermatomyositis
    - Polymyositis (after age 20)
    - Infectious myositis

EDMD = Emery-Dreifuss muscular dystrophy; FSHD = facioscapulohumeral muscular dystrophy

The examiner should ask about the presence of extreme fluctuations in strength during the day or associated with physical activities. Such fluctuations in strength are more typical of neuromuscular junction disorders. Observant patients may also detect a progressive loss of muscle bulk about various aspects of their body, particularly involving the anterior thigh, shoulder, and occasionally face and small intrinsic hand muscles. Alternatively, some muscle groups may be noted to be enlarged. Some disorders are associated with fasciculations, myalgias, cramps, stiffness or myotonia, periodic paralysis, and myoglobinuria. If these symptoms are not offered by the patient, their presence should be inquired by the clinician.

It is important to inquire about sensory symptoms. Patients may complain of feeling "numb," but this word has different meanings for different people. If not offered by the patient, the examiner should specifically ask the patient about the presence or absence of sensory loss or tingling, prickly, or burning pain.

Fatigue is also a non-specific complaint. Most patients referred to a neuromuscular clinic or the neurophysiology laboratory for evaluation of fatigue do not have a primary neuromuscular disorder. Their symptoms are best characterized as asthenia or the subjective loss of energy. Although such patients often complain of "feeling weak all over," examination of muscle strength is typically normal or limited by give-way. This is not to say that patients with neuromuscular disorders do not experience fatigue. Certainly, pathologic fatigue can be demonstrated in patients with certain neuromuscular disorders by electrophysiologic testing (e.g., repetitive stimulation) or by provocative exercise testing. However, in organic disorders as opposed to psychosomatic illness, fatigue is usually accompanied by objective muscle weakness.

Likewise, muscle pain (myalgias) is a common symptom in patients referred to a neuromuscular clinic. Most neuromuscular disorders, including myopathies, are not associated with severe

**Table 3** Weakness presenting in middle to late adulthood

**Anterior horn cell**
- Spinal muscular atrophy type III
- Kennedy's disease
- Poliomyelitis
- Amyotrophic lateral sclerosis

**Peripheral neuropathy**
- Hereditary neuropathies
- Acute or chronic inflammatory demyelinating polyneuropathy
- Drug-induced or toxic neuropathies
- Diabetic neuropathy
- Amyloid
- Vasculitis

**Neuromuscular junction**
- Botulism
- Myasthenia gravis
- Lambert-Eaton myasthenic syndrome

**Myopathy**
- Congenital myopathies
  - Myofibrillar myopathy
  - (Others types are uncommon)
- Muscular dystrophies
  - Dystrophinopathy (Becker)
  - Limb-girdle muscular dystrophies
  - Oculopharyngeal dystrophy
  - Bent spine/dropped head syndrome
- Metabolic myopathies
  - Glycogen storage defects
    - Acid maltase deficiency
    - Debrancher deficiency
  - Disorders of lipid metabolism (rare)
- Mitochondrial myopathies
- Periodic paralysis
  - Familial hypoKPP manifests within the first 3 decades
  - Familial hyperKPP usually manifests in the first decade
- Electrolyte imbalance
  - Hyperkalemia
  - Hypokalemia
  - Hypophosphatemia
  - Hypercalcemia
- Endocrine myopathies
- Toxic myopathies
- Myopathy associated with systemic disease (e.g., cancer), poor nutrition, disuse
- Amyloid myopathy
- Inflammatory myopathies
  - Inclusion body myositis (most common inflammatory myopathy after the age of 50)
  - Dermatomyositis
  - Polymyositis (after age 20)
  - Infectious myositis

hyperKPP = hyperkalemic periodic paralysis; hypoKPP = hypokalemic periodic paralysis

muscle pain or tenderness. Some patients with various forms of muscular dystrophy or inflammatory myopathy will describe mild or sometimes moderate myalgias. The pain associated with these disorders myopathies is typically described as a deep, aching discomfort in the muscles and is seldom severe enough to warrant analgesics. Usually the pain is diffuse rather than localized and is not tender. However, severe myalgias and tenderness can accompany fasciitis, myositis related to infections, and rhabdomyolysis/myoglobinuria caused by various metabolic myopathies, electrolyte disturbances, and toxins.

In many patients referred for evaluation of severe muscle pain, the symptoms are psychosomatic rather than organic in etiology. Such patients typically describe severe generalized muscle pain and tenderness unrelieved by analgesic medications. The symptoms of severe muscle pain are usually accompanied by complaints of generalized weakness or fatigue as previously described. In addition, the patients frequently describe exquisite tenderness even to light touch. Despite these severe symptoms, there is no objective evidence of a neuromuscular disease on clinical examination, laboratory testing, electrophysiological studies (electromyography/nerve conduction study [EMG/NCS]), or muscle biopsy.

The past medical history of patients should be addressed because various medical diseases are associated with neuromuscular disorders. For example, inflammatory myopathies may be seen in patients with connective tissue disease; concurrent autoimmune disorders may be present in patients with MG; LEMS is associated with small cell lung cancer; and neuropathies are common

**Table 4** Neuromuscular disorders presenting with acute or subacute proximal weakness

| |
|---|
| **Anterior horn cell** |
| Poliomyelitis |
| **Peripheral neuropathy** |
| Guillain-Barré syndrome |
| Porphyria |
| Diphtheria |
| Tick paralysis |
| Toxic neuropathies |
| Diabetic amyotrophy |
| Vasculitis |
| Carcinomatous infiltration (e.g., leukemia, lymphoma) |
| Paraneoplastic neuropathy |
| **Neuromuscular junction** |
| Botulism |
| Lambert-Eaton myasthenic syndrome |
| Myasthenia gravis |
| **Myopathy** |
| Periodic paralysis |
| Electrolyte imbalance |
| Endocrinopathies |
| Inflammatory myopathies |
| Dermatomyositis |
| Polymyositis |
| Infectious myositis |
| Note: Inclusion body myositis does not present acutely |
| Toxic myopathies |
| Metabolic myopathies |
| Glycogen and lipid disorders in association with myoglobinuria |

**Table 5** Differential diagnosis of chronic progressive proximal weakness

| |
|---|
| **Anterior horn cell** |
| Amyotrophic lateral sclerosis |
| Spinal muscular atrophy type III |
| Kennedy's disease |
| **Peripheral neuropathy** |
| Chronic inflammatory demyelinating polyneuropathy |
| Multifocal motor neuropathy |
| Toxic neuropathies |
| Neuropathy associated with systemic disorders |
| Connective tissue disease (e.g., vasculitis) |
| Diabetes mellitus |
| Amyloidosis |
| Paraneoplastic |
| Carcinomatous infiltration (e.g., leukemia, lymphoma) |
| **Neuromuscular junction** |
| Lambert-Eaton myasthenic syndrome |
| Myasthenia gravis |
| **Myopathy** |
| Periodic paralysis |
| Electrolyte imbalance |
| Endocrinopathies |
| Inflammatory myopathies |
| Dermatomyositis |
| Polymyositis |
| Infectious myositis |
| Note: Inclusion body myositis does not present acutely |
| Toxic myopathies |
| Metabolic myopathies |
| Glycogen and lipid disorders in association with myoglobinuria |

in patients with diabetes mellitus. The review of symptoms should assess systemic complaints that may be associated with a specific neuromuscular disorder (e.g., arthralgias to assess for underlying connective tissue disease). A careful family history is also vitally important in attempting to define the possible mode of inheritance or degree of genetic penetrance. When a hereditary disorder is suspected, it is valuable to examine affected family members. Some patients may claim a family history of a particular disorder but upon examining affected family members a different disease may be diagnosed. In addition, some family members who are asymptomatic may be found to have mild signs of disease on a thorough examination. Thus, the past medical and family history as well as a pertinent review of symptoms provide insights into the type of disorder potentially affecting the patient.

In patients with progressive weakness, a history regarding possible toxin exposures is important. These exposures may come from the work or home environment or from medications. Such toxins can result in damage of the peripheral nerves, neuromuscular

junction, or muscle. The severity of the clinical manifestations often depends upon the type of toxin as well as the dose and duration of the exposure.

When children are concerned, the parents must be questioned with great care and sensitivity. The heightened concern of the parents may cause them to unconsciously omit important details of the patient's status as related to various other associated childhood illnesses or just to being a "clumsy child." Also, parents may bring a considerable amount of guilt to the examination and the physician must be aware of this potential problem. The parents' fears and associated guilt should be dealt with and not ignored. If necessary, professional counseling should be offered in addition to treating the patient. Often, when a child is ill, the entire family is affected, which can in turn have profound physical and psychological repercussions on more than just the patient.

## PHYSICAL EXAMINATION

Following the above acquired medical history, a complete neurological examination should be performed. The distribution of symptoms and pattern of weakness is of utmost importance. Most myopathies preferentially affect the proximal more than distal muscles, while distal muscles are more severely involved than proximal muscles in most types of peripheral neuropathy. However, the distal muscles can be weaker than the proximal muscles in certain neuromuscular disorders other than peripheral neuropathy (Table 6). Likewise, significant proximal weakness can be seen in disorders other than myopathies (ALS, spinal muscular atrophy [SMA], GBS, chronic inflammatory demyelenating polyneuropathy [CIDP], MG, LEMS). Certain neuromuscular disorders can predominantly affect or have an early predilection for the ocular muscles (Table 7).

The physical examination actually begins during the taking of the history. Extraocular, facial, jaw, pharyngeal, tongue, and neck weakness may be apparent by just observing the patient during the interview. For example, a mitochondrial myopathy or MG should be considered in patients observed to have ptosis or ophthalmoparesis. Patients with myotonic dystrophy often have facial weakness, temporalis muscle wasting, and frontal balding. A characteristic rash is typically present in patients with dermatomyositis. Thus, specific neuromuscular disorders can be diagnosed or at least strongly suspected by casually observing the patient while taking their medical history.

**Table 6** Differential diagnosis of distal weakness

| |
|---|
| **Cervical disease** |
| Multilevel radiculopathy (C7, C8, T1) |
| Lower trunk brachial plexopathy |
| Syringomyelia |
| Tumor of the cord |
| **Lumbosacral disease** |
| Tumor of the conus medularis |
| Polyradiculopathy (L4, L5, S1, S2) |
| Lumbosacral plexopathy |
| **Motor neuron disorders** |
| Distal spinal muscular atrophy |
| Amyotrophic lateral sclerosis |
| **Neuromuscular junction** |
| Myasthenia gravis (rare) |
| Congental myasthenia gravis (e.g., slow ion channel defect) |
| **Peripheral neuropathies** |
| Charcot-Marie-Tooth disease and related hereditary neuropathies |
| Multifocal demyelinating motor or sensorimotor neuropathies |
| Vasculiltis |
| Toxic/metabolic neuropathies |
| **Intrinsic muscle disorders** |
| Distal myopathies/dystrophies |
| Facioscapulohumeral muscular dystrophy |
| Scapuloperoneal syndromes |
| Emery-Dreifuss muscular dystrophy |
| Oculopharyngodistal muscular dystrophy |
| Myotonic dystrophy |
| Acid maltase deficiency |
| Debrancher enzyme deficiency |
| Phosphorylase b kinase deficiency |
| Myofibrillar myopathy |
| Central core disease |
| Centronuclear myopathy |
| Nemaline myopathy |
| Inclusion body myositis |
| Focal myositis |

**Table 7** Neuromuscular causes of ptosis or ophthalmoplegia

| |
|---|
| **Peripheral neuropathy** |
| Guillain-Barré syndrome |
| Miller-Fisher syndrome |
| **Neuromuscular junction** |
| Botulism |
| Lambert-Eaton myasthenic syndrome |
| Myasthenia gravis |
| Congenital myasthenia |
| **Myopathy** |
| Mitochondrial myopathies |
| Kearn-Sayres syndrome |
| Progressive external ophthalmoplegia |
| Oculopharyngeal and oculopharyngodistal muscular dystrophy |
| Myotonic dystrophy (ptosis only) |
| Congenital myopathy |
| Myotubular |
| Nemaline (ptosis only) |
| Hyperthyroidism/Grave's disease (ophthalmoplegia without ptosis) |

It is essential that the patient undress except for undergarments and a gown for an adequate examination. The patient's posture while sitting, standing, and walking should be assessed. Weakness of the spine extensor may require the patient to lean forward on their arms or rest against the examining table to maintain an upright posture particularly for more than a few minutes. Some patients may have head drop related to neck extensor weakness. When standing, the patient should be observed from the side as well as the front and back. On side viewing, the clinician can detect excessive lumbar lordosis, hyperextension of the knee (genu recurvatum), and ankle contractures in patients with proximal muscle weakness. An excessive lordosis implies the hip extensors are too weak to maintain the center of gravity in its normal position without accessory muscle assistance. The weight line is purposefully brought posterior to the hip joints so that the patient can rest on the hip ligaments. This is all accomplished through the previously noted compensatory excessive lumbar lordosis. With quadriceps weakness, the knee extensors may become unable to resist the normal knee flexion moment during stance with a potential for falling secondary to buckling at the knee. The patient attempts to compensate for this problem by shifting the weight line anterior to the knee. This hyperextension of the knee (known as genu recurvatum or back-kneeing) provides stability to the knee while standing and walking. An exaggerated lumbar lordosis and genu recurvatum can result in an unfavorable dorsiflexion moment at the ankle, which is compensated by plantar flexion and slight heel rise (patient is seen to stand on his/her tip-toes).

During ambulation the patient with proximal leg weakness may be observed to have a wide-based waddling gait with the above noted hyperlordosis, genu recurvatum, and toe walk. The waddling gait is essentially a result of hip abductor weakness which is incapable of preventing the pelvis from dropping excessively, i.e., a positive Trendelenburg during ambulation. Compensatory abnormal shoulder motions can also be seen as a result of attempting to control gravity throughout the gait cycle and prevent falling. With disease progression, the patient begins to fall more frequently and display associated signs of bruises and superficial skin lesions about the knees and hands. Patients with weakness of the anterior compartment of the distal lower extremity will have foot drop and the so-called steppage gait. Instead of a normal heel-strike, the patient lands flat-footed or strikes the ground with the toes first. To avoid tripping, the patient lifts the knee higher than normal in order for them to clear the ground during the swing phase of ambulation. Distal lower extremity strength should also be assessed by having the patient walk on their heels and toes.

Weakness of the shoulder girdle can result in winging of the scapula. In addition, a "trapezius hump" caused by the scapula rising up the shoulder secondary to poor fixation may be noted, particularly in patients with facioscapulohumeral muscular dystrophy. Proximal arm weakness also may result in drooping of the shoulders and inward rotation of the arms. In addition, shoulder girdle weakness can cause the horizontal or downward rotation of the clavicles, diagonal or horizontal displacement of the anterior axillary lines, and the dorsum of the hands to face forwards rather than to the side.

During both quiet standing and ambulation, the muscles should be inspected for any signs of wasting or hypertrophy not only in the extremities, but also about the head and neck. The clinician should observe for fasciculations, which are signs of motor neuron or peripheral nerve disease. Visible muscle cramping and the presence of continuous muscle activity (e.g., myokymia) should be noted. Muscles should be palpated for tone and tenderness.

Muscles can be percussed in the upper and lower extremity as well as the face, including the tongue. Percussion of the muscle directly may reveal a pronounced contraction of a small portion with a delayed relaxation (percussion myotonia). Myotonia can predominantly affect proximal or distal muscles depending on the specific myopathy. Myotonia typically can be demonstrated distally and in the tongue in myotonic dystrophy, while proximal extremity muscles are affected in proximal myotonic myopathy (PROMM). Action myotonia can also be assessed by having the patient sustain a grip for a brief period and then

release the grip. One sees a slow relaxation with action myotonia. Myotonia generally improves with repetition. In contrast, paramyotonia worsens with repetitive activity. This is best demonstrated in patients with paramyotonia congenita by having them repeatedly open and close their eyes; eventually patients have difficulty completely opening their eyes. When myotonia or paramyotonia is elicited, the physician should inquire about the patient's response to activity and cold temperatures because these conditions worsen the symptoms in specific myotonic disorders. Other abnormalities can be noted on percussion. A peculiar wave of muscle contraction emanating from the site of percussion is seen in so-called rippling muscle disease. Occasionally, a "mounding" of the muscle as opposed to a contraction indentation can be observed. This phenomena is referred to as myoedema and can be observed in patients with hypothyroidism.

Manual muscle testing is extremely important and the author recommends using the Medical Research Council (MRC) scale for uniformity and hence understandability from one physician to another: Grade 0: no visible contraction; Grade 1: trace contraction; Grade 2: full movement across the joint with gravity eliminated; Grade 3: full movement across the joint against gravity; Grade 4: full movement against gravity plus some resistance; Grade 5: normal strength. A modification of this scale is usually employed by adding plus (e.g., 4+) or minus signs (e.g., 3–) next to the numbers for a finer distinction or degrees of muscle weakness between those larger grades. The MRC scale has been demonstrated to have excellent intraobservor and interobservor reliability. Face, neck, and upper and lower extremity muscles should be tested and documented in the patient's chart so as to provide an ability to document any changes over time. The author routinely grades the strength of the orbicularis oculi; jaw; tongue; neck flexion and extension; shoulder abduction, flexion, and extension; elbows flexion and extension; wrist flexion and extension; finger and thumb flexion, extension, and abduction; hip flexion, extension, and abduction; knee flexion and extension; ankle dorsiflexion; plantar flexion, inversion, and evasion; and toe flexion and extension. As the MRC scores reflect movement against gravity, muscle groups must be tested against gravity. Thus, neck flexion should be assessed with the patient supine; neck extension, hip extension and knee flexion with the patient prone; and hip abduction with the patient on their side. Examining the patient in these positions is essential in accurately assessing their strength and can detect weakness not noted if the patient were examined only in a seated position.

A functional assessment of motor strength should be assessed. To evaluate patients with possible hip girdle weakness, the clinician should observe the patient arise from the floor without grabbing onto nearby objects. A rather characteristic sequence of events is seen to occur with weak patients first assuming a position on the hands and knees and progressing up their legs, i.e., the so-called Gower's sign or maneuver. One can also observe the patient perform a deep knee bend, arise from a squat or a chair, climb stairs, run, or hop on one foot to detect subtle weakness. Recording the time it takes to perform specific tasks (e.g., climbing 10 steps or walking 30 feet) is helpful, especially in monitoring a functional response to a particular therapy or in following the natural progression of the disorder. In patients with myasthenia gravis, it is useful to measure and record the time it takes for ptosis to appear after sustained upgaze.

Muscle tone is assessed as normal, decreased, or increased. Increased tone or spasticity is caused by upper motor neuron lesions. Muscle tone in most myopathies, neuromuscular junction disorders, and neuropathies is usually normal or sometimes decreased. Deep tendon or muscle stretch reflexes are graded as: 0 = absent, 1+ = decreased (usually requires reinforcement maneuvers to obtain), 2+ = normal, 3+ = brisk (spread to other muscle groups), 4+ = pathologically brisk (clonus). DTRs are brisk in patients with upper motor neuron lesions and are decreased in patients with lower motor neuron disease and peripheral neuropathy. Reflexes are normal in patients with myasthenia gravis but are usually diminished in patients with LEMS. During the early phases of myopathic disorders, DTRs are usually present, but as the disease progresses they may diminish or become unobtainable. Specific myopathies are associated with decreased or absent reflexes and may have a predilection for certain muscle groups. For example, the knee jerk is reduced early in the course of inclusion body myositis when other reflexes are still relatively normal. On the other hand, certain reflexes appear to be spared even late in the course of the disease (e.g., ankle jerks are frequently present in patients with Duchenne muscular dystrophy despite severe generalized weakness). Plantar responses are usually assessed by striking the sole of the foot and looking for pathological dorsiflexion or extension of the big toe (a positive Babinski sign). The normal response is plantar flexion of the toes. The pathologic extension of the big toe can also be demonstrated after striking the lateral aspect of the foot (Chaddock's sign), after rubbing the anterior aspect of the shin (Oppenheimer's sign), or after pricking the extensor aspect of the toe (Bing's sign). Plantar responses are extensor in patients with upper motor neuron lesions, otherwise they are normal. In patients with significant weakness of the toes, a plantar response may be unobtainable and therefore not interpretable.

Sensation to various modalities (temperature, pain, touch, vibration, and proprioception) should be assessed in all patients. Temperature and pain are conveyed by small-diameter nerve fibers, while deep touch, vibration, and proprioception are mainly conveyed by large-diameter sensory nerves. Some neuropathies predominantly affect small-diameter nerve fibers (e.g., amyloid neuropathy), while other neuropathies have a predilection for larger fibers (e.g., CIDP). The sensory examination should be normal in patients with pure motor neuron disease, myopathy, or MG unless the patient has a concurrent neuropathy. Mild sensory symptoms and signs may be seen in LEMS.

Examining children can be a challenge, particularly infants. Infants can be positioned prone to observe if they are capable of extending their head. An inability to do so suggests weakness of the neck extensor muscles. Most infants have considerable subcutaneous fat that makes muscle palpation quite difficult. Palpating neck extensor muscles is a good place to attempt this evaluation secondary to little subcutaneous fat overlying this muscle group. Neck flexion strength can be assessed as the child is pulled by the arms from a supine to sitting position. Crying during the examination allows the opportunity to assess the child's vocalization (e.g., presence of a weak cry) and fatigability to the physical examination. Muscle weakness in infants is usually characterized by overall decrease in muscle tone and many children with profound weakness are characterized as a "floppy infant." This terminology does not necessarily imply a neuromuscular disorder. In fact, most floppy infants exhibit decreased tone secondary to a central nervous system problem. It is important to examine the parents of floppy infants for possibility of a neuromuscular disorder. This is particularly important in children suspected of having myotonic dystrophy. The author has diagnosed a number of infants with congenital myotonic dystrophy by examining the mother who was asymptomatic. In addition, weakness can transiently develop in infants born to mothers with MG.

After obtaining a detailed medical history and physical examination, the site of the lesion (upper motor neuron, anterior horn cell, peripheral nerve, neuromuscular junction, or muscle) responsible for the neuromuscular symptoms and signs is usually apparent. In patients in whom the site is still unclear, further testing is required. Electrophysiological testing with EMG and NCS can be of considerable help in localizing the lesion to the anterior horn cell, peripheral nerve, neuromuscular junction, or muscle. Features on EMG/NCS can also help identify the specific disorder (e.g., MG, LEMS, and Charcot-Marie-Tooth disease type 1). Specific laboratory tests are ordered depending on the localization of the disease process to confirm the site of the lesion and to identify the specific neuromuscular disease. Early and correct diagnosis of a neuromuscular disorder is essential, particularly if it is treatable (e.g., inflammatory neuropathies and myopathies, MG, LEMS). Even in chronic disorders in which progression can not be halted (e.g., muscular dystrophy, ALS), diagnosis is important because there are therapies available to improve quality of life. Further, correct diagnosis is essential for genetic counseling. In the remainder of the discussion, the specific laboratory tests which are ordered when evaluating a patient with a neuromuscular complaint are outlined.

## LABORATORY TESTING

### Motor Neuron Disease

In patients suspected of having motor neuron disease (anterior horn cell disease), the author orders routine complete blood count (CBC) and blood chemistries. Hyperthyroidism and hyperparathyroidism may superficially resemble motor neuron disease because of the weakness associated with brisk DTRs and fasciculations. However, the weakness in these disorders have a myopathic basis. A serum protein electrophoresis is obtained because there may be an increase in various lymphoproliferative disorders in patients with ALS. Unfortunately, the relationship does not appear causative as treatment of the underlying lymphoproliferative does not change the course of the motor neuron disease. In patients with symmetrical and proximal greater than distal weakness, DNA analysis for hereditary SMA may be useful.

Much has been made in the literature about the utility of antiganglioside antibodies, in particular anti-GM-1 antibodies, in assessing for a treatable cause of motor neuron disease. However, the author has not found this laboratory test to be clinically useful. Anti-GM-1 antibodies can be present in a low concentration in a number of neuropathic conditions. In high titers, the presence of these antibodies is quite specific for multifocal motor neuropathy (MMN), which is a potentially treatable condition. Unfortunately, the sensitivity of antibody testing in MMN is low (as many as 50% of patients with MMN have absent titers). Further, MMN can usually be distinguished clinically from motor neuron disease. Weakness is in the distribution of specific nerves in MMN as opposed to a myotomal or nerve roots pattern of weakness in motor neuron disease. In addition, pathologically brisk DTRs and extensor plantar responses are not seen in MMN. The most useful test in assessing whether a patient has a potentially treatable motor neuropathy is an EMG/NCS. Patients with MMN have electrophysiological evidence of conduction block or other features of demyelination.

### Neuropathies

In patients with generalized symmetric peripheral neuropathy, the author orders routine CBC, chemistries, urinalysis, thyroid function tests, $B_{12}$, folate, erythrocyte sedimentation rate (ESR), rheumatoid factor, antinuclear antibody (ANA), and serum protein electrophoresis (SPEP). In a patient suspected of a lymphoproliferative disease or amyloidosis or if the nerve conduction

studies are demyelinating, serum and urine immunofixation electrophoresis (IFE) rather than an SPEP (an IFE is more sensitive at identifying a monoclonal gammopathy) are ordered. Skeletal surveys are ordered in patients with acquired demyelinating neuropathies and M-spikes to look for osteosclerotic or lytic lesions. Patients with monoclonal gammopathy should also be referred to a hematologist for consideration of a bone marrow biopsy. In patients with a mononeuropathy multiplex pattern of involvement, the author orders a vascultitic workup to include the above laboratory tests as well as these: cryoglobulins, hepatitis serology, anticytoplasmic nuclear antibodies, Western blot for Lyme disease, human immunodeficiency virus (HIV), and occasionally a cytomegalovirus (CMV) titer.

There are many autoantibody panels (various antiganglioside antibodies) being marketed for screening routine neuropathy patients for a treatable condition. However, as noted in the discussion above, these autoantibodies have no proven clinical utility or added benefit provided one performs a good clinical examination and obtains detailed electrophysiological studies (EMG/NCS). The author typically does not order heavy metal screen, unless there is a history of possible exposure or features on the examination which are suspect (e.g., severe painful sensorimotor and autonomic neuropathy and alopecia: thalium; severe painful sensorimotor neuropathy with or without gastrointestinal (GI) disturbance and Mees lines: arsenic; wrist/finger extensor weakness and anemia with basophilic stippling of red blood cells: lead).

In patients with suspected GBS or CIDP, a lumbar puncture is important to look for an elevated cerebrospinal fluid (CSF) protein. In idiopathic cases of GBS and CIDP, there should not be a significant number of cells in the CSF. If cells are present, one should consider HIV infection, Lyme disease, sarcoidosis, or lymphomatous or leukemic infiltration of nerve roots. Some patients with GBS and CIDP have increased liver function tests (LFTs). In these cases, it is important to also check for hepatitis B and C, HIV, CMV, and Epstein-Barr virus infection. In patients with an axonal GBS (by EMG/NCS) or those with a suspicious coinciding history (e.g., unexplained abdominal pain, psychiatric illness, significant autonomic dysfunction), it is reasonable to screen for porphyria.

In patients with a severe sensory ataxia, a sensory ganglionopathy or neuronopathy should be considered. The most common causes of sensory ganglionopathies are Sjögren's syndrome and a paraneoplastic neuropathy. Neuropathy can be the initial manifestation of Sjögren's syndrome. Thus, one should always inquire about dry eyes and mouth in patients with sensory signs and symptoms. Further, some patients can manifest sicca complex without full-blown Sjögren's syndrome. In patients with sensory ataxia, the author orders a Sjögren's antibody test $SS_a$ and $SS_b$ in addition to the routine ANA. Further, the patients are referred to ophthalmology for a Rose Bengal stain and Schirmer's test. They are also referred to ear-nose-and-throat for biopsy of the lip or parotid gland to confirm a diagnosis of Sjögren's syndrome. To workup a possible paraneoplastic sensory or sensorimotor polyneuropathy, anti-Hu antibodies are ordered. These antibodies are most commonly seen in patients with small cell carcinoma of the lung. Importantly, the paraneoplastic neuropathy can precede the detection of the cancer and should lead to periodic imaging of the chest with computed tomography (CT) or magnetic resonance imaging.

### Neuromuscular Junction Disorders

In patients in whom a neuromuscular junction defect is a possibility, acetylcholine receptor antibodies (MG) and antibodies directed against the voltage-gated muscle calcium channel (LEMS) can be assayed. Although these antibodies are quite specific, they are not 100% sensitive and can be negative in patients with the neuromuscular disorder in question. A chest CT should be ordered in patients with MG to look for thymic hyperplasia (evident in 40%) or thymoma (present in 10%). A chest CT scan should also be performed on patients with LEMS because of the association with small cell carcinoma of the lung. Botulism is caused by the exotoxin of the bacteria, *Clostridium botulinum*. Infantile botulism is contracted by ingestion of bacterial spores (e.g., usually from contaminated honey) which subsequently colonize the gut and release the toxin. Wound botulism can occur following colonization of deep wounds such as those that occur in compound fractures or subcutaneous injection sites in drug addicts. Botulism can also arise from food poisoning resulting from the direct ingestion of the toxin from improperly canned and cooked foods. The toxin can be assayed in the serum and stool in suspected cases. Polymerase chain reactions can identify the organism in biological specimens and food.

### Myopathies

The single most useful blood test in a patient evaluated for weakness is a serum creatine kinase (CK) level. The upper limit of normal in the ambulatory population for serum CK is dependent on the sex and race of an individual and is typically higher than most established laboratory normative data. For instance, the upper limit of normal for serum in black males is in the low 500s IU/L; in black females, white males, and hispanics the CK can be in the 300s IU/L range; and in white females the upper limit of normal is in the 200s IU/L. Importantly, mild elevations in serum CK can be seen in neurogenic processes such as motor neuron disease or other rapidly denervating processes in which large amounts of muscle tissue acutely degenerate. However, the serum CK is rarely elevated above 1000 IU/L in these conditions. In addition, it is important to note that not all patients with myopathies have elevated serum CK levels. Further, the serum CK levels do not correlate with the degree of muscle weakness in any given patient.

It is important for clinicians to know that other enzymes which are routine screened for on routine laboratory tests (e.g., asparte amino transferase [AST], alanine amino transferase [ALT], and lactate dehydrogenase [LDH]) can also be elevated in muscle disorders. Many physicians initially suspect a liver disease upon seeing an elevated AST, ALT, and LDH. However, one must recall that AST, ALT, LDH, and aldolase are expressed in muscle as well as the liver. Unfortunately, it is not uncommon for patients with primary muscle disorders to have undergone liver biopsies before the correct diagnosis of a myopathy was made. In order to distinguish elevation of these enzymes due to liver disease versus a myopathic process, a serum CK which is specific for muscle disease and gamma glutamyl transferase (GGT) which is specific for liver disease should be obtained. In this regard, treatment of inflammatory myopathies with certain immunosuppressive agents (i.e., azathioprine and methotrexate) are hepatotoxic. In following the liver functions tests of such patients on treatment, it is essential to check to GGT and CK levels, not just the AST, ALT, or LDH as these later enzymes may become elevated from an exacerbation of the underlying myositis rather than from liver damage.

Other blood work which is routinely ordered in patients suspected of having a myopathy are routine electrolytes. Hyper- and hypokalemia can be caused by a number of conditions and can result in generalized weakness (Table 8). Likewise, hyper- and hypocalcemia may lead to generalized weakness. Thyroid function tests are obtained because both hyper- and hypothyroidism are associated with myopathies. In patients suspected of having an inflammatory myopathy, an ESR and antinuclear antibody are ordered to assess for an underlying connective tissue disease. A serum protein electrophoresis or immunofixation looking for a monoclonal gammopathy should be ordered to help exclude non-familial amyloidosis. With the explosion in our understanding of molecular genetics, there is an ever-expanding list of hereditary myopathies which can be diagnosed by way of deoxyribonucleic acid (DNA) testing. These include various types of muscular dystrophy, mitochondrial myopathy, congenital myopathy, and hereditary forms of periodic paralysis.

**Table 8** Etiologies of secondary hypokalemic and hyperkalemic paralyses

| |
|---|
| **Hypokalemic paralysis** |
| Thyrotoxic periodic paralysis |
| Renal tubular acidosis |
| Villous adenoma |
| Bartter's syndrome |
| Hyperaldosteronism |
| Chronic or excessive use of diuretics, corticosteroids, licorice |
| Amphotericin B toxicity |
| Alcoholism |
| Toluene toxicity |
| Barium poisoning |
| **Hyperkalemic paralysis** |
| Addison's disease |
| Hypoaldosteronism (hyporeninemic) |
| Isolated aldosterone deficiency |
| Excessive potassium supplementation |
| Potassium-sparing diuretics (e.g., spironolactone, triamterene) |
| Chronic renal failure |
| Rhabdomyolysis |

## ELECTRODIAGNOSTIC EXAMINATION

The EDX medicine examination is useful in localizing the site of the neuromuscular lesion, determining the pathogenic basis of the disease process, and occasionally identifying the specific disorder. Occasionally, an EDX medicine consultant may detect abnormalities not suspected by the referring physician because of the nature of the disease only manifesting electrically at the time of the patient's presentation, or suggest an entirely different list of disorders.

### Nerve Conduction Studies

Motor and sensory NCSs are invaluable in assessing patients with neuromuscular disorders. Routine NCSs are most useful in the evaluation of patients for a peripheral neuropathy. The abnormalities apparent on these NCSs can help assess whether the pathogenic process is targeting the nerve axon or myelin. In axonopathies, the amplitudes of sensory and motor responses are decreased, but the velocities are relatively normal or only slightly diminished. In demyelinating disorders, the conduction velocities are slowed, while the amplitudes of the responses are preserved. NCSs can also assess if the neuropathic process is generalized or multifocal, hereditary or acquired, and more importantly whether or not the neuropathy is potentially treatable. Sensory conduction studies are normal in motor neuron disease,

myopathies, and neuromuscular junction diseases. Motor studies can reveal decreased amplitudes in motor neuron disease, peripheral neuropathies, and LEMS.

### Repetitive Stimulation

Repetitive stimulation studies are useful in distinguishing neuromuscular junction disorders (i.e., botulism, LEMS, and MG) from myopathies, which they can resemble. In patients with MG, baseline motor responses are of normal amplitude. However, a decrementing response is seen following slow rates (2-3 Hz) of repetitive stimulation. Ten seconds of exercise may correct this decrement (post-exercise facilitation), while 1 minute of exercise will result in an increase of the decrement (post-exercise exhaustion). In botulism and LEMS the baseline motor amplitudes are low. Decrement may be seen following low rates of repetitive stimulation. An incrementing response may be seen following fast rates of repetitive stimulation (20-50 Hz). This is a painful procedure and is rarely necessary because 10 seconds of exercise can usually reproduce a significant increase in amplitude from baseline in these disorders.

### Needle Electromyography

The routine needle EMG examination is performed with particular attention paid to motor unit action potential duration, morphology, amplitude, and recruitment. It is also important to assess for the presence of abnormal insertional and spontaneous activity. A thorough examination of multiple muscles is necessary, especially in mild or moderately severe disease states. By assessing these various components, the EDX medicine consultant can usually determine whether the lesion is neuropathic or myopathic. Special techniques such as quantitative EMG may be required in difficult or borderline cases. Single-fiber EMG is useful in diagnosing patients with MG in whom repetitive stimulation, a tensilon test, and autoantibody testing were uninformative. Single-fiber EMG measures the "jitter" between two single muscle fibers belonging to the same motor unit. Jitter is increased in MG. However, increased jitter is not specific for MG as it can be seen in any pathological process involving remodeling of the neuromuscular junction (e.g., reinnervation in motor neuron disease, neuropathies, necrotizing myopathies).

## HISTOLOGICAL EVALUATION

An important decision a clinician must make is whom to send for a biopsy and what tissue to biopsy. In general, most patients with a myopathy will require a muscle biopsy. The clinical examination, laboratory workup, and electrophysiological studies can indicate a myopathy is present but usually does not indicate the exact type of myopathy. There are of course exceptions in which the clinical phenotype in combination with the appropriate laboratory and electrophysiological studies allows diagnosis without need for a biopsy (e.g., myotonic dystrophy). In contrast, the value of a nerve biopsy is limited. Nerve biopsies are warranted if one is suspicious for amyloid neuropathy or vasculitis. In most instances, the abnormalities present on biopsies do not help distinguish one form of peripheral neuropathy from another (aside from what is already apparent by clinical examination and the NCS). Unfortunately, nerve biopsies are limited by post-biopsy complications. Following a nerve biopsy, there is usually permanent numbness in the respective cutaneous distribution. Further, there can be significant neuropathic pain in the distribution of the nerve for several months and potential for growth of painful neuroma.

### Muscle Biopsies

Despite the fact that the physiology of muscle tissue is extremely complex, there is a limited number of ways in which muscle can react to disease. The manner in which these reactions are critically evaluated is through either an open (minor surgical procedure) or closed (needle/punch) muscle biopsy. Some authorities prefer open muscle biopsy because several large samples can be obtained and processed for routine and electron microscopy (EM), metabolic analysis, and protein analysis (Western blot). Others recommend needle muscle biopsies in which the individual samples sizes are small but many more areas of potentially affected muscle tissue can be assessed via smaller incisions. The author prefers open biopsy especially in multifocal processes, such as in inflammatory myopathies and in those myopathic disorders which require electron microscopy for confirming a diagnosis. The muscle selected for biopsy should be mildly weak, preferably MRC grade 4. If the muscle is too weak (i.e., MRC grade 3 or less), the tissue typically has end-stage damage and it is often impossible to distinguish certain myopathic disorders from severe neurogenic atrophy. In patients with little, if any, weakness on examination, needle EMG can be helpful in selecting the muscle to biopsy. However, it is important to biopsy the contralateral muscle in order to avoid artifact from needle EMG. The best muscle to biopsy is the biceps brachii, if it is affected. Alternative muscles are the deltoid or quadriceps muscle. The gastrocnemius muscle should be avoided because there can be neurogenic changes related to an asymptomatic radiculopathy which may make diagnosis of a myopathy difficult.

The muscle specimen is routinely analyzed by light and EM. In addition, biochemical assays for various enzyme deficiencies (e.g., glycogen and lipid storage diseases), Western blot for specific protein abnormalities (e.g., dystrophin), and DNA analysis for genetic mutations (e.g., mitochondrial myopathies) can be performed on the biopsy specimen. Amyloid deposition can be detected with Congo red or crystal violet staining. Various immune staining techniques are employed for the diagnosis of specific muscular dystrophies (e.g., dystrophin staining for Duchenne and Becker muscular dystrophy, merosin staining

for congenital muscular dystrophy, sarcoglycan stains for limb-girdle muscular dystrophies, emerin stain for Emery-Dreifuss muscular dystrophy). Immune staining is also useful in the early diagnosis and in understanding the pathogenesis of the different inflammatory myopathies and vasculitis (e.g., stains for complement, membrane attack complex, immunoglobulins, human leukocyte antigens, and cell markers). Electron microscopy is used for detailed evaluation of the ultrastructural components of muscle fibers.

### Nerve Biopsies

As noted above, nerve biopsies are usually reserved for patients suspected of having amyloidosis or vasculitis. The author only biopsies a nerve if it is abnormal on NCS. The sural nerve is biopsied because it is a pure sensory nerve and a biopsy will not result in loss of motor function. In patients suspected of having vasculitis, a combination of biopsying the superficial peroneal nerve (pure sensory) and the underlying peroneus brevis muscle (the biopsies can be obtained from a single small incision) increases the diagnostic yield. Tissue can be analyzed by frozen section and paraffin section to assess the supporting structures for evidence of vasculitis or amyloid deposition. Semi-thin plastic sections and EM are used to assess the morphology of the nerve fibers and to distinguish axonopathies from myelinopathies. Teased fiber preparations better assess the pathological process of individual nerve fibers.

### Skin Biopsies

There has been an increase in literature on the utility of skin biopsies in patients with peripheral neuropathy. Following a punch biopsy of the skin in the distal lower extremity, immunological staining can be used to measure the density of small unmyelinated fibers. The density of these nerve fibers is reduced in patients with small fiber neuropathies in which NCSs and routine nerve biopsies are often normal. This technique may allow for an objective measurement in patients with mainly subjective symptoms. The ease of the technique and ability to perform a number of repeat skin biopsies allows clinicians the ability to better define the natural history of various small fiber neuropathies and to monitor response of the neuropathy to various therapies.

*The author has nothing to disclose.*

## RECOMMENDED READING

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# Evaluating the Patient With Focal Neuropathy With Needle Electromyography

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## STEPS OF THE NEEDLE ELECTROMYOGRAPHY EXAMINATION

There are four general distinct steps of the needle electromyography (EMG) examination for each muscle in the evaluation of focal neuropathies: (1) evaluation of insertional activity; (2) search for abnormal spontaneous activity; (3) examination of motor unit potentials; and (4) assessment of recruitment. The abnormal waveforms are reviewed in a recent publication.[2]

## INSERTIONAL ACTIVITY

Insertional activity is examined by moving the needle through the muscle briefly and observing the crispness, size, and duration of the electrical potentials produced. These potentials are mechanically evoked injury potentials due to the advancement of the needle. After a brief, small movement of the needle, insertional activity will usually persist no more than 300 ms. However, this duration is dependent upon individual technique; hence practicing evaluation of insertional activity at slow sweep speeds (e.g., 100 ms/div) is useful.

Insertional activity may be decreased or prolonged in duration. Decreased insertional activity signifies that the usual degree of electrical activity is not elicited; i.e., one does not observe a crisp, loud response when moving the needle. Decreased insertional activity can result from not being in muscle or being in a muscle which has fewer viable fibers than normal. Muscles which have become atrophied, replaced by fat, or fibrotic will show reduced insertional activity. Muscles that have become necrotic due to a compartment syndrome or other causes of prolonged ischemia will also have reduced insertional activity and prognosis for recovery of function will be poor. Muscles that have become electrically silent, such as during attacks of periodic paralysis, will also show reduced insertional activity.

Increased insertional activity is generally considered as prolonged muscle membrane activity lasting more than 300 ms after the needle movement stops. An example would be a brief, non-sustained run of positive sharp waves after needle movement. As an isolated finding, prolonged or increased insertional activity is a "soft" finding. No diagnosis can usually be made solely on the basis of this abnormality. It may be seen in some asymptomatic

individuals, known as the syndrome of diffusely abnormal increased insertional activity, an autosomally dominant inherited syndrome without any clear associated symptomatology.

## SPONTANEOUS ACTIVITY

Spontaneous activity consists of electrical discharges that are seen without needle movement or voluntary contraction. These are usually sought after each needle movement when the needle is stationary.

Fibrillation potentials represent abnormal spontaneous single muscle fiber discharges. While fibrillation potentials are essentially always abnormal, they are a non-specific finding. They represent abnormal muscle membrane irritability, which can occur in many entities. Fibrillation potentials are often seen in denervated muscles and may be associated with myopathies. It is common in inflammatory myopathies, but almost any myopathy except for possibly chronic steroid myopathy or the thyroid myopathies, may produce fibrillation potentials. Direct muscle trauma, intramuscular injections, and intramuscular bleeding have all been noted to produce immediate and chronic fibrillations. Neuromuscular junction disorders, particularly presynaptic disorders (e.g., botulism) or occasionally severe postsynaptic defects (e.g., myasthenia gravis) may produce fibrillation potentials. Upper motor neuron lesions, such as stroke and spinal cord injury, have also been shown to produce fibrillation potentials. These are usually seen early after onset of the lesion (usually during the period of flaccid tone) and can be confusing when one is trying to diagnose a peripheral nerve lesion superimposed upon an upper motor neuron disorder. Fibrillation potentials, as well as positive sharp waves, are usually graded on a subjective, qualitative scheme. Usually this ranges from 1+ to 4+, with 1+ representing a reproducibly observed fibrillation in an isolated area and 4+ representing sustained fibrillation potentials, often obscuring the baseline, throughout the muscle. This is an ordinal scale, meaning that as numbers increase the findings are worse. However, it is not an interval or ratio scale, i.e., 4+ is not twice as bad as 2+ or four times as bad as 1+.

Positive sharp waves can be thought of in much the same way as fibrillation potentials. They also represent abnormal single muscle fiber discharges, although they are often evoked by needle movement. Positive sharp waves are thought to have the same pathophysiology as fibrillation potentials and can be graded using the same scheme.

Complex repetitive discharges (CRDs), formerly known as bizarre high-frequency discharges, represent groups of muscle fibers firing in near synchrony. It is believed that there is one pacer cell and nearby muscle fibers are activated via ephaptic transmission (activation by local current, without a synapse). They are usually seen in chronic neuropathic or myopathic conditions, however, they are occasionally seen acutely in inflammatory myopathies. When seen in isolation CRDs are a nonspecific, but usually abnormal, finding similar in diagnostic consequences to positive sharp waves and fibrillations.

Fasciculation potentials represent spontaneous discharges of all or part of a single motor unit. As opposed to a fibrillation potential (where just a single muscle fiber fires), a fasciculation potential involves multiple muscle fibers of the motor unit. Fasciculations produce enough muscle contraction that they can be seen through the skin. Fasciculation potentials are often generated at the anterior horn cell, as in motor neuron diseases, but they may also be generated ectopically distally along the axon, possibly even in intramuscular axons.

Fasciculation potentials can be seen in a variety of neuromuscular disorders. They can be "benign" fasciculations which occur in otherwise healthy individuals in whom there are no other associated signs, symptoms, or electrophysiologic abnormalities. They are often seen in healthy people who are stressed, tired, lack sleep, or who are sensitive to chemicals in the diet (e.g., caffeine). Benign fasciculations are seen in individuals who have no other electrophysiologic findings. In contrast, motor neuron disease is typically expected to show fibrillation potentials, positive sharp waves, and abnormal motor unit potentials in association with fasciculations. In other words, the best way to tell "bad" fasciculations from "benign" fasciculations is by the company they keep. In addition to motor neuron disease and the syndrome of benign fasciculations, fasciculation potentials can be seen in chronic radiculopathies, peripheral polyneuropathies, thyrotoxicosis, and overdosage of anticholinesterase medications.

## MOTOR UNIT ANALYSIS

A great deal of information can be obtained from analysis of voluntarily activated motor unit action potentials (MUAPs). Usually, this information is more specific for neuropathic or myopathic changes than is assessment of spontaneous activity at rest (Figure 1).

Theoretically, in neuropathic conditions where there has been partial denervation and reinnervation, one will see changes representative of the underlying process of axonal sprouting. Within days after partial denervation, intramuscular axons that remain unaffected will send sprouts, usually emanating from distal nodes of Ranvier, to reinnervate nearby denervated muscle fibers. These sprouts are initially not well myelinated and conduct slowly. Consequently in the early phases of reinnervation, MUAPs will have increased polyphasicity and duration.[4] This is the direct result of temporal dispersion in these newly formed sprouts and poor synchronization of muscle fiber discharges. As these sprouts mature, synchronization of muscle fiber discharges improve, and the polyphasicity is somewhat reduced. The final

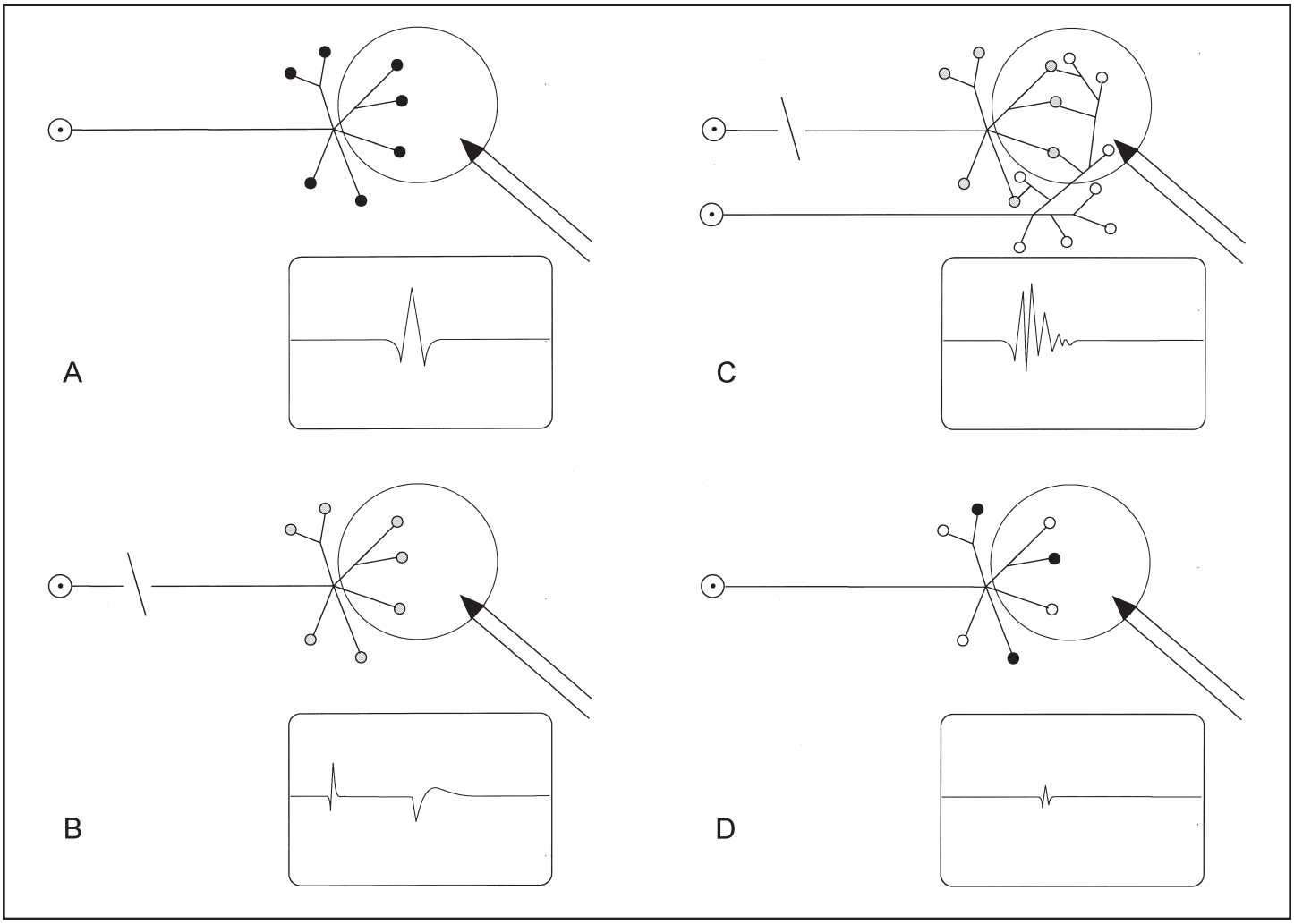


**Figure 1** A: The normal motor unit action potential (MUAP). A needle electrode records from muscle fibers within the recording area of the needle. B: After denervation, single muscle fibers spontaneously discharge, producing fibrillations (or positive sharp waves). C: When reinnervation by axon sprouting has occurred, the newly formed sprouts will conduct slowly producing temporal dispersion (i.e., prolonged MUAP duration) and polyphasicity in the MUAP. The higher density of muscle fibers within the recording area of the needle belonging to the enlarging second motor unit results in an increased amplitude MUAP. D: In the case of myopathies, there is loss of motor unit territory and consequent reduction in the size and duration of individual motor unit action potentials.

status of reinnervated MUAPs is that they are typically high in amplitude, long in duration, and sometimes polyphasic. The increase in amplitude is a result of the increased density of muscle fibers belonging to the same motor unit within the recording area of the tip of the EMG needle.

Myopathic changes in the MUAP result from loss of individual muscle fibers, impairment to muscle fibers, or temporal dispersion of conduction along muscle fibers. In myopathic conditions, the MUAPs are typically small in amplitude and short in duration; fewer muscle fibers from the same motor unit fire within the recording area of the needle electrode.

Polyphasicity as an isolated finding is non-specific and can be over reported and over interpreted. The phases of a motor unit may be counted as the baseline crossings plus one. When MUAPs have more than five phases, they are termed polyphasic potentials. Most normal muscles will have at least 10% polyphasic MUAPs, depending upon the muscle examined and the type of needle electrode used. Increased polyphasicity can be seen in both neuropathic and myopathic conditions, but is not specific for either.

## RECRUITMENT

The assessment of motor unit recruitment has a number of important purposes. Most importantly, it can assess whether reduced strength is due to a reduction in the lower motor neuron pool versus poor central effort. Moreover, in myopathies,

recruitment analysis allows some qualitative assessment for how much force is being provided by each motor unit.

Normal or full recruitment implies the patient can give a full effort with many MUAPs firing at normal rates. Central recruitment implies that there are reduced numbers of motor units firing but that they are firing at a normal or slow speed. This is by far the most common abnormality in recruitment but, in isolation, it is completely non-diagnostic. The central pattern of recruitment can be seen in patients with upper motor neuron lesions, pain, or poor voluntary effort. Reduced and discrete recruitment patterns are pathologically significant and imply there are reduced numbers of motor units firing rapidly; "reduced" recruitment is less severe than "discrete" recruitment (in which there are just a few clearly identifiable motor units firing rapidly with baseline between them). Recruitment is particularly useful in myopathies. In a myopathy each motor unit is weak and it takes more of them firing faster to accomplish a task. Consequently, in a myopathy many MUAPs are activated to provide minimal levels of force.

## USING NEEDLE ELECTROMYOGRAPHY TO DISTINGUISH THE PATHOPHYSIOLOGY OF THE FOCAL NEUROPATHY

Focal traumatic neuropathies can be described using the classification system devised by Seddon.[7,8] *Neurapraxia* is a comparatively mild injury with motor and sensory loss but no evidence of Wallerian degeneration. Focal demyelination and/or ischemia are thought to be the etiologies of the conduction block. Recovery may occur within hours, days, weeks, or up to a few months. *Axonotmesis* is commonly seen in crush injuries. The axons and their myelin sheaths are broken, yet the surrounding stroma (i.e., the endoneurium, perineurium, and epineurium) remains partially or fully intact. Wallerian degeneration occurs, but subsequent axonal regrowth may proceed along the intact endoneurial tubes. Recovery ultimately depends upon the degree of internal disorganization in the nerve as well as the distance to the end organ. Neurotmesis describes a nerve that has been either completely severed or is so markedly disorganized by scar tissue that axonal regrowth is impossible. Examples are sharp injury, some traction injuries, or injection of noxious drugs. Prognosis for spontaneous recovery is extremely poor without surgical intervention.[3] Needle EMG can be used to deduce the type of nerve injury that exists.

### Neurapraxia

In purely neurapraxic lesions the needle EMG examination will show neurogenic changes in recruitment with debatable abnormalities in spontaneous activity. While there is some debate as to whether fibrillation potentials are recorded after a purely neurapraxic lesion, most authors consider fibrillations to represent axon loss. The most apparent change on needle EMG will be

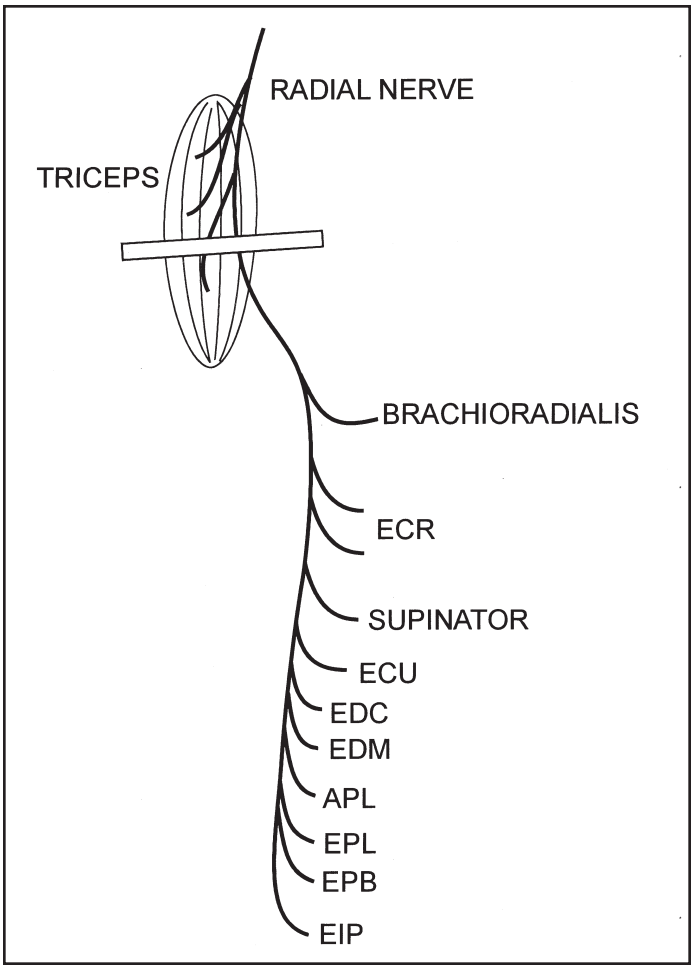


**Figure 2** In the case of muscle trauma accompanying focal peripheral nerve lesions, misleading needle EMG results can be found. In this example of radial neuropathy at the humerus spiral groove, damage to the triceps can create fibrillations and mislead one to a higher level lesion (i.e., above the branch to triceps).

APL = abductor pollicis longus; ECR = extensor carpi radialis; ECU = extensor carpi ulnaris; EDC = extensor digitorum communis; EDM = extensor digiti minimi; EIP = extensor indicis proprius; EPB = extensor pollicis brevis; EPL = extensor pollicis longus.

changes in recruitment. These occur immediately after injury. In complete lesions (i.e., complete conduction block) there will be no MUAPs. In incomplete neurapraxic lesions, there will be reduced numbers of MUAPs firing more rapidly than normal (i.e., reduced or discrete recruitment). Because no axon loss occurs in neurapraxic injuries, there will be no axonal sprouting and no changes in MUAP morphology (e.g., duration, amplitude, or phasicity) anytime after injury.

### Axonotmesis and Neurotmesis

A number of days after an axon loss lesion, needle EMG will demonstrate fibrillation potentials and positive sharp waves. The time between injury and onset of fibrillation potentials will be dependent in part upon the length of distal nerve stump. When

the lesion is distal and the distal stump is short, it takes only 10-14 days for fibrillations to develop. With a proximal lesion and a longer distal stump (e.g., ulnar-innervated hand muscles in a brachial plexopathy), 21-30 days are required for full development of fibrillation potentials and positive sharp waves.

When there are surviving axons after an incomplete axonal injury, remaining MUAPs are initially normal in morphology, but demonstrate reduced or discrete recruitment. Axonal sprouting will be manifested by changes in morphology of existing motor units. Amplitude will increase, duration will become prolonged, and the percentage of polyphasic MUAPs will increase as motor unit territory increases. In complete lesions, the only possible mechanism of recovery is axonal regrowth. The earliest needle EMG finding in this case is the presence of small, polyphasic, often unstable motor unit potentials previously referred to as nascent potentials. Observation of these potentials is dependent upon establishing axon regrowth as well as new neuromuscular junctions and this observation represents the earliest evidence of reinnervation, usually preceding the onset of clinically evident voluntary movement. These potentials represent the earliest definitive evidence of axonal reinnervation in complete lesions.

### Mixed Lesions

When there is a lesion with both axon loss and conduction block, a needle EMG examination can be potentially misleading if interpreted in isolation. If, for example, a lesion results in destruction of 50% of the original axons and conduction block of the other 50%, then needle EMG will demonstrate abundant (e.g., 4+) fibrillation potentials and no voluntary MUAPs. The electrodiagnostic consultant should **not** then conclude that there is a complete axonal lesion, but should instead carefully evaluate the motor nerve conduction studies to determine how much of the lesion is neurapraxic and how much axonotmetic. The important point here is to not take the presence of abundant fibrillations and absent voluntary MUAPs as evidence of complete denervation.[6]

## USING NEEDLE ELECTROMYOGRAPHY FINDINGS FOR LOCALIZATION

Conceptually, if one knows the branching order to various muscles under study, one can determine that the focal neuropathy is between the branches to the most distal normal muscle and the most proximal abnormal muscle. Thus, one can often work down the muscles supplied by a single nerve, find the last normal muscle, and surmise that the lesion is after that branch and before the branch to the first abnormal muscle.

There are, however, a number of potential problems with this approach. First, the branching and innervation for muscles is not necessarily consistent from one person to another. Sunderland[9] has demonstrated a great deal of variability in branching order to muscles in the limbs, variability in the number of branches going to each muscle, and variability in which nerve or nerves supply each muscle. Thus, the typical branching scheme may not apply to the patient under study and consequently the lesion site can be misconstrued.

Second, muscle trauma and associated needle EMG findings can be misleading. As mentioned earlier, direct muscle trauma can result in positive sharp waves and fibrillations for months or longer after injury.[5] Practically speaking, this can result in believing the lesion site is more proximal than it actually is, or errors in diagnosing more than one lesion. For example, in the setting of humeral fracture with radial neuropathy, the triceps frequently demonstrates fibrillation potentials due to direct muscle trauma. However, one could be misled to localize the lesion to the axilla or higher rather than spiral groove, if the triceps findings are not recognized to come from direct muscle injury rather than nerve injury.

Third, the problem of partial lesions can make for misdiagnosis to more distal sites.[10] In partial ulnar nerve lesions at the elbow, for example, the forearm ulnar innervated muscles are often spared.[1] This is thought to be partially due to the sparing of fascicles in the nerve that are preparing to branch to the flexor digitorum profundus and the flexor carpi ulnaris (i.e., they are in a relatively protected position). This finding could lead one to inadvertently localize the lesion distally to the distal forearm or wrist.

*The authors have nothing to disclose.*

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# Evaluating the Patient With Focal Neuropathy With Nerve Conduction Studies

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## COMPOUND NERVE ACTION POTENTIALS AND SENSORY/MIXED CONDUCTION STUDIES

Compound nerve action potentials (CNAPs) or sensory nerve action potentials (SNAPs) are typically recorded by electrically stimulating a peripheral nerve and recording the response a known distance away. Stimulation of a nerve usually activates the nerve in both directions from the point of stimulation. Two main recording techniques are used. "Orthodromic" recording indicates propagation along the nerve that proceeds in a physiologic direction (e.g., stimulating a digital sensory nerve and recording from the wrist). "Antidromic" recording indicates propagation in a nonphysiologic direction (e.g., stimulation of the median nerve at the wrist and recording from a digital nerve). Speed of conduction is the same in either direction.

The clinician makes two measures of CNAPs or SNAPs, (Figure 1):

- speed of conduction (latency or velocity)
- size of the response (amplitude)

Traditionally, the speed of conduction for CNAPs or SNAPs has been measured with latencies; i.e., the time between onset of stimulation and either the onset or the peak of the potential. Peak latency is easier to measure, particularly when the potential is small or the baseline is noisy. Onset latency, while more difficult to measure, does have the physiologic significance of representing arrival of the fastest conducting nerve fibers.

Conduction velocity (CV in m/s) for CNAPs can be derived by dividing the distance (d in mm) between the stimulation site and the active (G1) electrode by the onset latency (t in ms):

$$CV = d/t$$

Latency and conduction velocity can be affected by a number of physiologic and pathologic factors. In healthy control subjects, slowed conduction can be a result of low temperatures or normal aging. Pathologically, demyelination produces slowing. Conditions which result in loss of axons, particularly faster conducting axons, also produce a slowing of nerve conduction or a prolongation of latency.

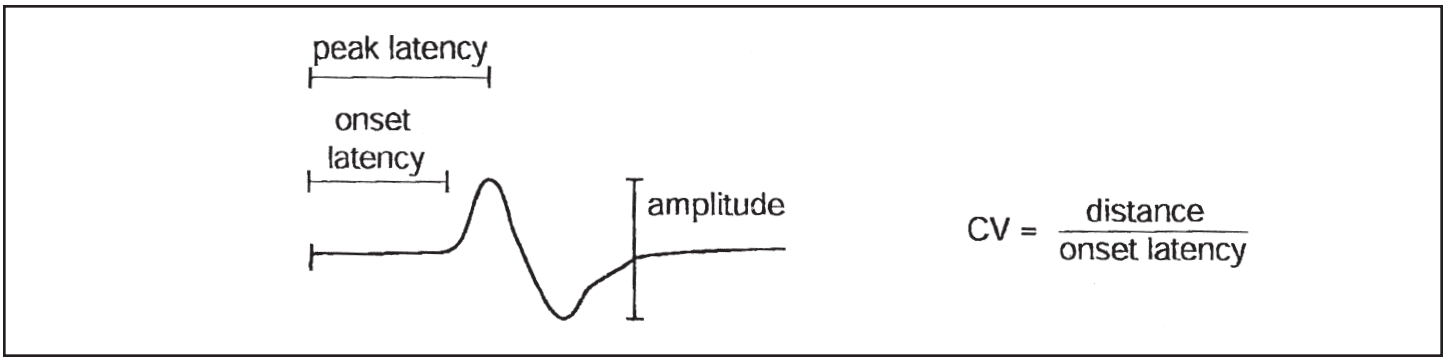


**Figure 1**

Amplitude of the CNAP can be measured from: (1) baseline to peak; (2) peak to peak. In general, the amplitude of the CNAP and SNAP is roughly proportional to the number of axons depolarizing under the active electrode. It can be affected by a number of physiologic and pathologic factors. Cold increases amplitude of the CNAP or SNAP, while aging produces smaller amplitude SNAPs, probably resulting from the gradual loss of large myelinated axons.

Pathologically, the loss of axons will reduce the amplitude of the CNAP. Distal lesions, occurring between the sites of stimulation and recording, will drop the amplitude of the CNAP immediately because conduction cannot traverse the lesion. Proximal lesions (e.g., brachial plexus lesions) which separate sensory axons from their cell bodies (in the dorsal root ganglion) will produce distal axon loss due to axonal (Wallerian) degeneration over time, usually 7-10 days after injury. Thus, a reduced amplitude SNAP could be due to an axonal lesion anywhere distal to the dorsal root ganglion.

## COMPOUND MUSCLE ACTION POTENTIALS AND MOTOR NERVE CONDUCTION STUDIES

Principles of stimulation and recording for motor nerve conduction studies (NCSs) are similar to those used for sensory NCSs with several exceptions. The primary difference is that motor NCSs involve recording a compound muscle action potential (CMAP) over muscle rather than recording directly from nerve. Therefore, the distal latency involves not only conduction along the nerve from the point of stimulation (proceeding at about 50 m/s), but also includes neuromuscular junction transmission time (which takes about 1 ms) and conduction along muscle fibers (about 3 to 5 m/s). While latency from a distal stimulation site can be measured, this cannot be converted into a nerve conduction velocity the same way as it can for the SNAP, because of the additional time for neuromuscular junction transmission and muscle fiber conduction. Therefore, to evaluate conduction velocities, motor nerves are typically stimulated in two places, and the distance between the two stimulation sites is divided by the difference in latency. Neuromuscular junction transmission time and muscle fiber conduction velocity are canceled out in the process (Figure 2).

Many of the same factors affect motor NCSs as affect sensory NCSs. However, there are some important differences. First, because motor neuron cell bodies "live" in the anterior horn of the spinal cord rather than in the dorsal root ganglion, the amplitude of the response is diminished by either anterior horn cell or distal axon damage (i.e., not the dorsal root ganglion). A root lesion proximal to the dorsal root ganglion, for example, would diminish amplitude of the CMAP but not the SNAP. Second, because the recording is from muscle, neuromuscular junction transmission defects or primary myopathies may reduce the amplitude of the CMAP.

## USING NERVE CONDUCTION STUDIES TO DEFINE PATHOPHYSIOLOGY OF THE FOCAL NEUROPATHY

### The Compound Motor Action Potential

#### Neurapraxia

In purely neurapraxic lesions, the CMAP will change immediately after injury, assuming one can stimulate both above and below the site of the lesion (Figure 1). When recording from distal muscles and stimulating distal to the site of the lesion, the CMAP should always be normal because no axonal loss or Wallerian degeneration has occurred. Moving stimulation proximal to the lesion will produce a smaller or absent CMAP, as conduction in some or all fibers is blocked. It should be remembered that amplitudes normally fall with increasing distance between stimulation and recording; hence there is some debate over how much of a drop in amplitude is sufficient to demonstrate conduction block. Amplitude drops exceeding 20% over a 25 cm distance or less are clearly abnormal; smaller changes over smaller distances are likely also suggestive of an abnormality. In addition to conduction block, partial lesions also often demonstrate concomitant slowing across the lesion. This slowing may

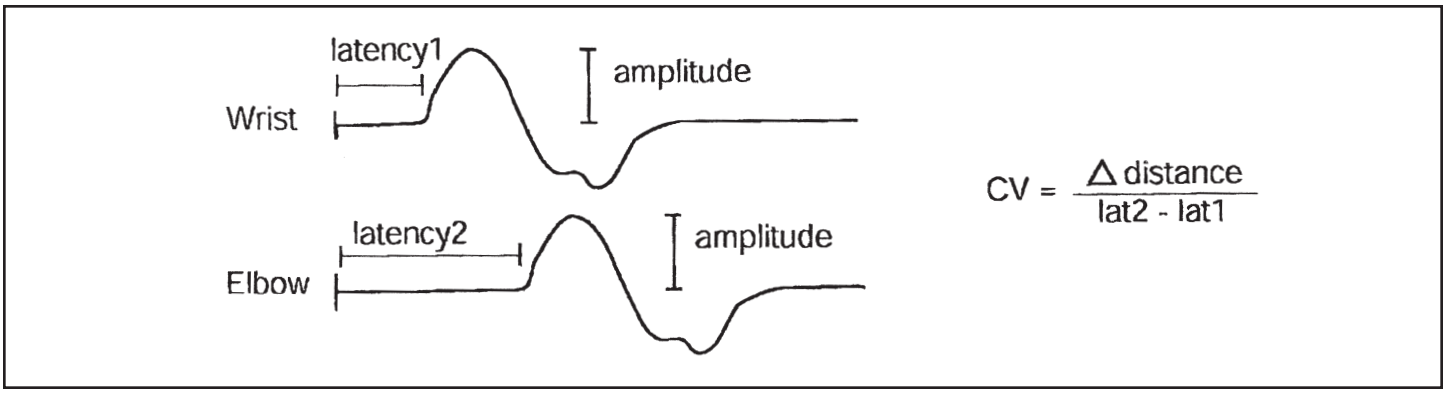


Figure 2

be due to either the loss of faster conducting fibers or demyelination of surviving fibers. All these changes in the CMAP will generally persist until recovery takes place, typically by no more than a few months post-injury. Most importantly, the distal CMAP will never drop in amplitude in purely neurapraxic injuries, because no axon loss or Wallerian degeneration occurs and the distal nerve segment remains normally excitable.

#### Axonotmesis and Neurotmesis

Electrodiagnostically, complete axonotmesis and complete neurotmesis look the same, because the difference between these types of lesions is in the integrity of the supporting structures, which have no electrophysiologic function. Thus, these lesions can be grouped together as axonotmesis for the purpose of this discussion.

Immediately after axonotmesis and for a few days thereafter, the CMAP and motor conduction studies look the same as those seen in a neurapraxic lesion. Nerve segments distal to the lesion remain excitable and demonstrate normal conduction while proximal stimulation results in an absent or small response from distal muscles. Early on, this looks the same as conduction block and can be confused with neurapraxia. Hence, neurapraxia and axontomeis can not be distinguished until sufficient time for Wallerian degeneration in all motor fibers has occurred, typically 9 days post-injury.[2]

As Wallerian degeneration occurs, the amplitude of the CMAP elicited with distal stimulation will fall. This starts at about day 3 and is complete by about day 9.[2] Neuromuscular junction transmission fails before nerve excitability.[3,4] Thus in complete axonotmesis at day 9, one has a very different picture from neurapraxia. There are absent responses both above and below the lesion. Partial axon loss lesions will produce small amplitude motor responses, with the amplitude of the CMAP roughly proportional to the number of surviving axons. One can compare side-to-side CMAP amplitudes to estimate the degree of axon loss, though inherent side-to-side variability of up to 30% to 50% limits the accuracy of the estimate. Using the CMAP amplitude to estimate the degree of surviving axons is also most reliable only early after injury, before axonal sprouting has occurred. Use of this technique later after injury will tend to underestimate the degree of axon loss.

#### Mixed Lesions

Lesions which have a mixture of axon loss and conduction block provide a unique challenge. These are usually determined by carefully examining amplitudes of the CMAP elicited from stimulation both above and below the lesion and by comparing the amplitude with distal stimulation to that obtained from the other side. The percentage of axon loss is best estimated by comparing the CMAP amplitude from distal stimulation with that obtained contralaterally. Of the remaining axons, the percentage with conduction block are best estimated by comparing amplitudes or areas obtained with stimulation distal and proximal to the lesion. Thus if a 1 mV response is obtained with proximal stimulation, a 2 mV response is obtained distally, and a 10 mV response is obtained with distal stimulation contralaterally, one can deduce that probably about 80% of the axons are lost, and of the remaining 20%, half are blocked (neurapraxic) at the lesion site. As mentioned above, this analysis is most useful only in the acute phase, before reinnervation by axonal sprouting occurs.

### Compound or Sensory Nerve Action Potentials

#### Neurapraxia

The SNAP and CNAP will show changes similar to the CMAP after focal nerve injury. In the setting of neurapraxia, there is a focal conduction block at the site of the lesion, with preserved distal amplitude. However, the criteria for establishing conduction block in sensory nerve fibers are substantially different than that for the CMAP. When recording nerve action potentials,

there is normally a greater drop in amplitude over increasing distance between stimulating and recording electrodes, due to temporal dispersion and phase cancellation. Amplitude drops of 50% to 70% over a 25 cm distance are not unexpected and it is less clear just what change in amplitude is abnormal. A large focal change over a small distance is probably significant.[5] Slowing may also accompany partial conduction blocks, as for the CMAP. Responses elicited with stimulation and recording distal to the lesion are normal in pure neurapraxic injuries.

### Axonotmesis and Neurotmesis

Immediately after axonotmesis, the SNAP looks the same as seen in a neurapraxic lesion. Nerve segments distal to the lesion remain excitable and demonstrate normal conduction while proximal stimulation results in an absent or small response. Hence neurapraxia and axonotomeis can not be distinguished until sufficient time for Wallerian degeneration in all sensory fibers has occurred, typically 11 days post-injury.[2] It takes slightly longer for sensory nerve studies to demonstrate loss of amplitude than for motor studies (i.e., 11 days versus 9 days), due to the earlier failure of neuromuscular junction transmission compared to nerve conduction.

## Localization With Nerve Conduction Studies

Localizing peripheral nerve lesions by NCSs usually requires that there be a focal slowing or conduction block as one stimulates above and below the lesion. To see such a change there must either be focal demyelination or ischemia, or the lesion should be so acute that degeneration of the distal stump has not yet occurred. Thus lesions with partial or complete neurapraxia (due to either demyelination or ischemia) can be well localized with motor NCSs, as can acute axonal injuries.

In pure axonotmetic or neurotmetic lesions, it is more difficult if not impossible to localize the lesion using NCSs. In such a case, there will be mild and diffuse slowing in the entire nerve due to loss of the fastest fibers, or there will be no response at all. Conduction across the lesion site will be no slower than across other segments. In addition, provided enough time for Wallerian degeneration has elapsed (i.e., at least 9 days for motor fibers or 11 days for sensory fibers), there will be no change in amplitude as one traverses the site of the lesion. Thus, pure axon loss lesions are not well localized along a nerve by NCSs.

There are some cases in which indirect inferences can be made about the location of purely axonal lesions. For instance, if the ulnar motor response is small or absent and the median motor response is normal, it is implied that an ulnar neuropathy rather than a lower brachial plexus lesion is present. However, in such an instance, the site of pathology along the ulnar nerve may not be well defined.

Another indirect inference that can be made based upon sensory NCSs is placement of the lesion at a pre- versus post-ganglionic location. Lesions that are proximal to the dorsal root ganglion, i.e., at the pre-ganglionic level (proximal root, cauda equina, spinal cord) tend to have normal SNAP amplitudes, even in the setting of reduced or absent sensation.[1,6] This is a particularly bad prognostic sign when seen in the setting of possible root avulsion. On the other hand, lesions occurring distal to the dorsal root ganglion have small or absent SNAPs (when these are recorded in the appropriate distribution). Thus, SNAPs may be useful to differentiate root versus plexus or other pre- versus post-ganglionic locations. A limitation, particularly in partial lesions, is the wide variability in SNAP amplitudes seen in normal individuals. Mixed pre- and post-ganglionic lesions are also potentially difficult to interpret.

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# Evaluating the Patient With Peripheral Neuropathy

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## INTRODUCTION

The evaluation of patients with suspected polyneuropathy (subsequently referred to as "neuropathy") is relatively straightforward, and consists of a combination of clinical, electrophysiologic, and laboratory studies. Evaluation of suspected neuropathy is among the most frequent investigations performed in the electromyography (EMG) laboratory. The electrodiagnostic (EDX) examination includes sensory and motor nerve conduction studies (NCSs), evaluation of late responses, and needle EMG. In clinically appropriate situations, autonomic testing should be performed to assess involvement of the parasympathetic and sympathetic fibers. Clinicians use the EDX evaluation as an extension of their neurologic examination to confirm clinical findings, localize abnormalities, and identify the underlying pathophysiology. A well-designed electrophysiological evaluation of a patient with neuropathy focuses the differential diagnosis, directs the subsequent laboratory evaluation, and often suggests a specific diagnosis or class of disorders.

This outline emphasizes a general approach to the evaluation of neuropathy and was initially prepared for EDX consultants. Primary care physicians also can use the outline with no experience in electrodiagnostic medicine, as a guide to interpretation and evaluation of EDX reports on their patients. In most instances, adherence to the classification presented will suggest a specific diagnosis or reduce the differential diagnosis, and at times suggest an unsuspected systemic disorder. Exceptions exist to the rules outlined in this manuscript, but they form the basis of clinical experience and education.

## WHAT TO EXPECT FROM THE ELECTRODIAGNOSTIC MEDICINE CONSULTANT

The EDX consultant plays an important role in the evaluation of suspected peripheral disorders, and the referring physician should expect more information from the consultant than a remark that a neuropathy is or is not present. It is not sufficient simply to confirm the presence of abnormality or to conclude that the findings are in keeping with a neuropathy without suggesting possible etiologies. The EDX consultant is a neuromuscular specialist with extensive experience in the evaluation and treatment of patients with neuropathy, who should use the clinical and electrophysiologic information to aid the referring physician to focus on a group of disorders or a specific diagnosis. Features of the clinical examination particularly important to the evaluation of neuropathy are shown in Table 1.

Routine NCSs of motor and sensory nerves primarily test large myelinated fibers. By nature of the fibers they assess, NCSs do not evaluate the integrity or function of small myelinated or unmyelinated fibers. Almost all patients with neuropathy demonstrate large fiber dysfunction, thus making the EDX examination a powerful clinical tool for evaluating suspected neuropathy. Few findings are diagnostic of a specific disorder, but a comprehensive EDX examination is a sensitive indicator of mild peripheral nerve dysfunction. Important questions addressed by the EDX study are summarized in Table 2. Because the information obtained is only useful when collected in a systematic and organized manner, there are some components of the EDX examination that a referring physician can monitor, as

a checklist, to determine the quality of the EDX evaluation (Table 3).

While clinical skills are important for documenting the distribution and magnitude of abnormality at the bedside, the EDX consultant carries the evaluation further by helping to identify the underlying pathophysiology. This additional information will focus the differential diagnosis to a smaller number of possible conditions so that appropriate and cost-wise laboratory investigations can be ordered. One of the most important tasks of the EDX consultant is to distinguish axonal loss lesions from lesions characterized by uniform or multifocal demyelination. Identification of multifocal demyelination on NCS testing raises awareness for a large group of acquired demyelinating neuropathies that may not have been considered prior to performance of the electrophysiologic testing. This group of neuropathies is frequently treatable and may be associated with systemic illness. In some cases, neuropathies can be detected and classified electrodiagnostically before the systemic disorder or causative agent (occupational, metabolic, or pharmacologic) is discovered. Good examples of this are paraneoplastic sensory neuropathy, mild cases of hereditary motor sensory neuropathy type I (HMSN I) (i.e., Charcot-Marie-Tooth [CMT] disease), neuropathies associated with monoclonal proteins, and early cases of diabetic neuropathy.

The EDX consultant also assists the referring physician by excluding disorders that mimic neuropathy but are difficult to distinguish clinically. An important example is the identification of an abnormality on needle examination of paraspinal muscles. Such an abnormality is characteristic of a radiculopathy or anterior horn cell (AHC) disorder, and is not recorded in a neuropathy unless another pathologic process is present. The EDX consultant also helps to distinguish a diffuse symmetric neuropathy from a confluent mononeuritis multiplex. While clinically difficult, the discovery of a mononeuritis multiplex and vasculitis could have crucial therapeutic implications for the patient. Other conditions that mimic neuropathy but can be differentiated using NCSs and needle EMG are distal myopathies, motor neuron disorders, neuromuscular junction disorders, and myelopathies.

## THE ELECTRODIAGNOSTIC EXAMINATION

### Nerve Conduction Studies

Sensory and motor responses (sensory nerve action potentials [SNAPs] and compound muscle action potentials [CMAPs]) are recorded using surface electrodes and percutaneous electrical stimulation (Figures 1 and 2). Amplitudes and latencies are usually measured using electronic cursors, and conduction velocities are calculated based upon the distances and time differences

**Table 1** Features of the clinical examination important in the evaluation of suspected neuropathy

| |
|---|
| **General Information** |
| Onset and temporal profile of motor, sensory, and autonomic complaints |
| Type and distribution of paresthesia, hyperesthesia and hyperpathia |
| Distribution of weakness |
| Industrial and medical history for toxin or drug exposures |
| Family history, especially bony deformities such as pes cavus or hammer toe |
| Social habits including recreational drug use |
| Antecedent illness or symptoms of underlying disease (particularly diabetes) |
| **Clinical Examination (anticipated in most neuropathies)** |
| General |
| Findings most prominent in distal lower extremities |
| Relative symmetry |
| Associated findings such as ataxia, tremor, bony deformities (pes cavus or hammer toes, scoliosis) |
| Palpate peripheral nerves (tenderness, paresthesia, hypertrophy) |
| Motor (emphasis upon distal muscles) |
| Intrinsic hand muscles, finger and wrist extensors |
| Toe extensors and foot dorsiflexors |
| Sensory (greater in feet than in hands) |
| Demonstrate distal to proximal sensory loss gradient |
| Identify involved modalities |
| Large fiber: vibration, light-touch, touch-pressure (common); joint position sensation (JPS) when severe |
| Small fiber: temperature, pin-pain, deep pain |
| Discriminative sensations less helpful in peripheral disorders |
| Absence of sensory level on the trunk |
| Vibratory loss to iliac crest and prominent JPS loss suggests spinal cord lesion |
| Reflexes |
| Achilles reflexes usually absent |
| Diffusely hypoactive reflexes not necessarily abnormal |
| Absence of pathologic reflexes (e.g., Babinski response) |
| Autonomic nervous system |
| Postural hypotension |
| Sluggish pupillary reaction to light |
| Abnormality of sweating |
| Bowel, bladder, or sexual dysfunction |
| Vasomotor changes in the feet more than hands |

**Table 2** Expectations for the electrodiagnostic evaluation of neuropathy

| |
|---|
| Document evidence of a peripheral abnormality |
| Detect presence |
| Document location (diffuse, focal, multifocal) |
| Identify peripheral modalities involved |
| Sensory fibers |
| Motor fibers |
| Autonomic fibers |
| Identify the predominant pathophysiology |
| Axonal loss lesions |
| Uniform demyelination |
| Multifocal demyelination with partial or complete conduction block |
| Conduction slowing suggestive of membranopathy |
| Combination of above |
| Establish temporal profile when possible (acute, subacute, chronic, old, ongoing) |
| Exclude accompanying or alternative disorders |
| Determine prognosis |

**Table 3** Checklist: Evaluating the electrodiagnostic report

| |
|---|
| Clinical findings consistent with your evaluation? |
| Limb temperatures monitored and recorded? |
| Cool limbs warmed (31°C-32°C minimum)? |
| Sites of recording and stimulation noted for each nerve tested? |
| Individual measures reported? |
| Sensory studies (amp, DL, CV) |
| Motor studies (amp, DL, CV, F-wave latency) |
| Needle examination (insertional activity, fibrillation potentials, positive sharp waves, MUAP recruitment, amp, and % poly) |
| Presence or absence of partial or complete conduction block, temporal dispersion described? |
| Normal values provided? |
| Design and comprehensiveness of the EDX study sufficient to: |
| Document the problem? |
| Exclude alternative explanations (avoid errors of omission)? |
| Appropriated negative findings described? |
| Interpretation consistent with clinical findings? |

amp = amplitude; DL = distal latency; CV = conduction velocity; MUAP = motor unit action potential; % poly = percent polyphasic MUAPs

between stimulation sites. Amplitude measurements of sensory nerves reflect the number of intact sensory fibers, whereas the amplitude of the motor response or CMAP measures the number and integrity of functioning motor nerve and muscle fibers. Latency and conduction velocity measurements reflect transmission time in the largest myelinated nerve fibers. Conduction over an entire motor nerve can be evaluated by F-wave latency (Figure 3). F-wave measurements accentuate mild generalized slowing because of the long conduction distances (stimulation site to spinal cord and back). Most normal values are age-dependent and some vary according to patient size. Limb temperature probably is the largest source of variability that is important in the evaluation of neuropathy. Its measurement is not infrequently skipped or not reported in a busy EMG laboratory, thus leading to errors and a major source of misinterpretation. Cooling increases distal latency, decreases conduction velocity, and increases amplitude, a combination of findings atypical for any pathologic process. In most patients a one degree Centigrade drop in temperature leads to a decrease of conduction velocity of 2 m/s and a similar prolongation of distal latency.

### Needle Electromyography

The needle EMG examination evaluates insertional activity, positive sharp waves and fibrillation potentials, other activity at rest such as fasciculations, myotonia, and complex repetitive discharges, and volitional motor unit action potential recruitment, size, and configuration. The role of the needle EMG examination in evaluating neuropathy is limited but important. It is a sensitive indicator of denervation and reinnervation (chronic and old), and helps to define the distribution of axon loss, especially in muscles not tested by commonly-performed NCSs (e.g., paraspinal muscles, cranial nerve innervated muscles, and muscles innervated by the brachial and lumbosacral plexi).

### Electrodiagnostic Examination in Suspected Neuropathy

The EDX evaluation is designed to test nerves suspected to be abnormal based upon the patient's history and findings. Initial impressions are confirmed or altered, and the study is modified to accept or reject additional considerations until a final diagnosis is achieved. Protocols for evaluating neuropathy are straightforward (Table 4). When the neuropathy is mild, the study is directed toward the most susceptible sites, such as the distal leg and foot. When the neuropathy is suspected to be severe, evaluation of less involved sites provides more useful information than severely affected areas of the body. Because absent responses impart no information about the presence or absence of demyelination, responses recorded from proximal nerves in the legs and arms can provide data on whether the primary pathologic process is axon loss or demyelination. Bilateral studies are performed on some nerves to evaluate for symmetry of

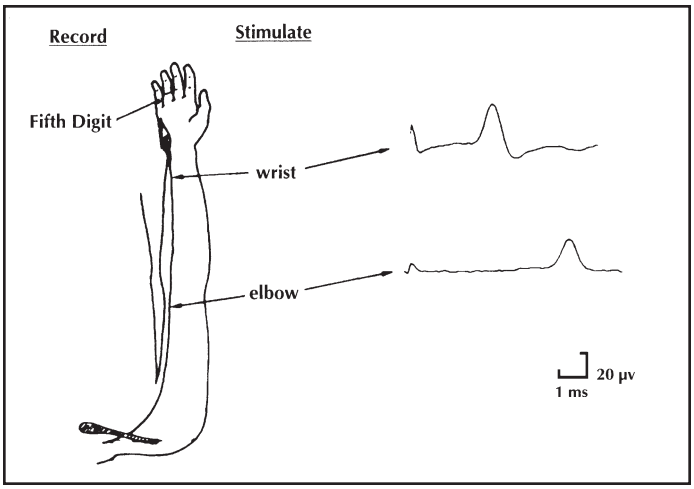


**Figure 1** Representative sensory nerve conduction study. Sensory nerve action potentials recorded from the fifth digit following ulnar nerve stimulation at the wrist and elbow. Calibration: 1 ms and 20 µV. (Reproduced with permission from Albers JW, Leonard JA Jr. Nerve conduction and electromyography. In: Crockard A, Hayward R, Hoff JT, editors. Neurosurgery: the scientific basis of clinical practice, 2nd edition. Oxford, England: Blackwell Scientific Publications Ltd; 1992. Vol 2, p 735-757, chap 44.)

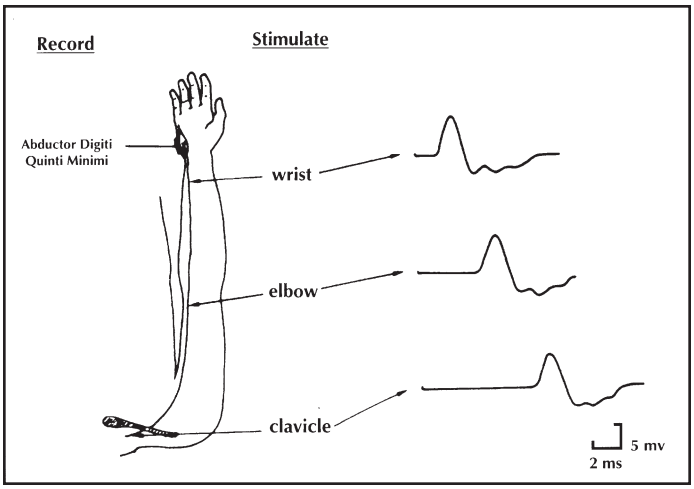


**Figure 2** Representative motor nerve conduction study. Compound muscle action potentials recorded from hypothenar muscles following ulnar nerve stimulation at the wrist, elbow, and clavicle. Calibration: 2 ms and 5 mV. (Modified and reproduced with permission from Albers JW, Leonard JA Jr. Nerve conduction and electromyography. In: Crockard A, Hayward R, Hoff JT, editors. Neurosurgery: the scientific basis of clinical practice, 2nd edition. Oxford, England: Blackwell Scientific Pub-lications Ltd; 1992. Vol 2, p 735-757, chap 44.)

the neuropathy and to eliminate the possibility of a superimposed multifocal process such as mononeuritis multiplex.

The initial goal of nerve conduction testing is to determine whether sensory or motor axons are involved. Lesions proximal to the dorsal root ganglia produce abnormalities detected on the sensory examination (often in a radicular pattern), but all sensory nerve conduction parameters such as amplitude and distal latency remain normal in nerves subserving the areas of sensory loss. Abnormal sensory amplitudes imply peripheral involvement distal to the dorsal root ganglion either in the plexus, peripheral nerve, or digital nerves. Weakness and atrophy in combination with low motor amplitudes reflect abnormality of the lower motor neuron, but cannot localize the lesion more precisely. Additional evaluation is required to place the abnormality at the level of the motor neuron, nerve root, axon, neuromuscular junction, or muscle.

The second goal in performing NCSs to assess a neuropathy is to identify whether the primary pathophysiology is axonal degeneration or demyelination. Axonal degeneration results whenever the cell body (neuronopathy) or axon (axonopathy) is affected. Axon loss lesions give rise to reduced amplitudes (sen-

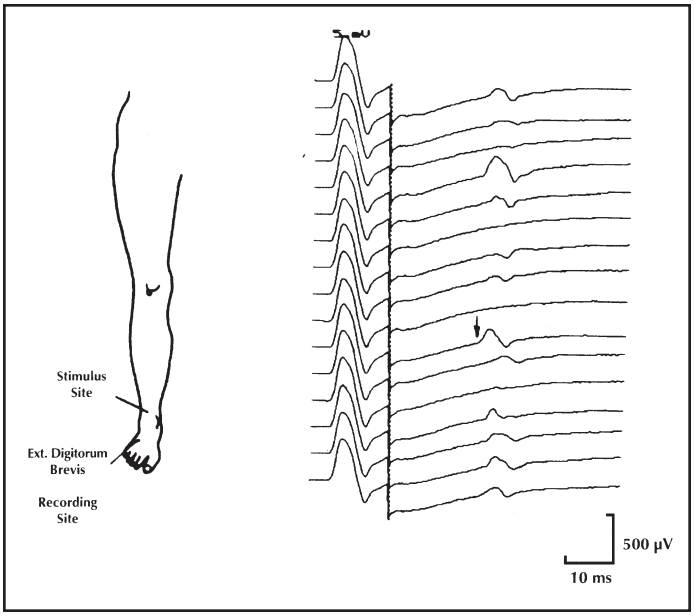


**Figure 3** Representative F waves following antidromic peroneal nerve stimulation. (Reproduced with permission from Albers JW, Leonard JA Jr. Nerve conduction and electromyography. In: Crockard A, Hayward R, Hoff JT, editors. Neuro-surgery: the scientific basis of clinical practice, 2nd edition. Oxford, England: Blackwell Scientific Publications Ltd, 1992. Vol 2, p 735-757, chap 44.)

sory or motor), yet little or no changes to the distal latency or conduction velocity. Amplitudes are reduced proportional to the amount of axonal loss, but conduction along intact axons is only reduced to the extent that large myelinated axons are lost. On needle EMG, voluntary motor unit recruitment decreases and increased insertional activity, fibrillation potentials, and positive waves appear in response to hypersensitivity to acetylcholine and proliferation and migration of extrajunctional acetylcholine receptors. Some denervated muscle fibers become reinnervated by collateral sprouts from surviving axons, producing large motor units. A reduction in the CMAPs does not always imply damage to the AHC or peripheral motor nerve. CMAPs can be reduced when muscle fibers are lost due to a myopathic process or local trauma. In the latter two conditions, the motor distal latency and conduction velocity will be normal.

Conduction slowing results from several processes, including loss of large axons, demyelination (hereditary or acquired), and altered sodium channels at the nodes of Ranvier. The amount of slowing after selective loss of large axons is relatively mild, whereas primary demyelination typically produces substantial slowing, depending on the severity and distribution of the demyelination. Demyelination does not alter muscle membrane excitability, but most demyelinating neuropathies are associated with some superimposed axonal degeneration. When conduction slowing is identified, the EDX consultant first must determine whether an inherited or an acquired disorder exists. Hereditary disorders typically produce uniform involvement of the myelin sheath, uniform slowing in all fibers, and uniform slowing in all segments of the nerve both proximally and distally. Slowing of conduction velocity is recorded in the setting of relatively preserved amplitudes and in the absence of abnormal temporal dispersion or conduction block. Acquired demyelinating neuropathies produce abnormalities on nerve conduction testing which are characteristically multifocal and nonuniform. Greater involvement of some fibers and fiber segments compared to others leads to long-duration CMAPs with partial conduction block and differential slowing because of transmission failure along some axons. Abnormal dispersion of the CMAP and/or conduction block is observed when proximal sites are stimulated and the waveforms compared to those recorded on distal stimulation (Figure 4). Markedly different waveform morphologies can be observed when the motor nerve is stimulated at multiple sites.

### Interpretation

Interpreting EDX data is usually not difficult, but it requires an organized approach, a knowledge of normal reference values for the laboratory, a thorough understanding of peripheral nerve

**Table 4** Proposed electrodiagnostic studies in evaluating neuropathy

| |
|---|
| Strategy differs depending upon severity of the suspected neuropathy |
| Test most involved site if mild or moderate |
| Test least involved site if severe |
| Peroneal motor nerve (extensor digitorum brevis muscle); If no response: |
| Tibial motor nerve (abductor hallucis muscle) |
| If no peroneal or tibial responses are recorded, study: |
| Peroneal motor nerve, recording from the anterior tibial muscle |
| Ulnar motor nerve (abductor digit minimi muscle) |
| Median motor nerve (abductor pollicis brevis muscle) |
| Sural sensory nerve (ankle) |
| Median sensory nerve (index finger) |
| Test additional nerves if findings equivocal (e.g., radial sensory, musculocutaneous) |
| Definite abnormalities should result in testing of: |
| Opposite extremity |
| Evaluation of suspected superimposed focal or multifocal process |

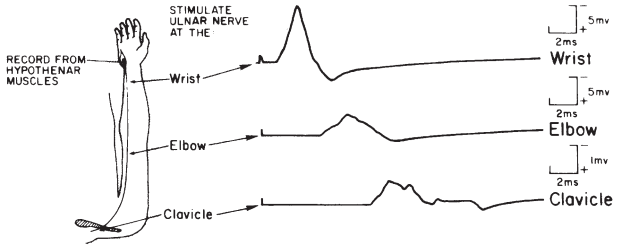


**Figure 4** Compound muscle action potentials recorded from hypothenar muscles following ulnar nerve stimulation at distal and proximal sites. Responses from patient with an acquired demyelinating neuropathy, demonstrating abnormal temporal dispersion with partial conduction block, increased duration, and decreased conduction velocity. (Reproduced with permission from Albers JW, Kelly JJ Jr. Acquired inflammatory demyelinating polyneuropathies: clinical and electrodiagnostic features. Muscle Nerve 1989;12:508-513.)

anatomy, and an appreciation of technical variables that affect the recording and results of the testing procedures. Several nerve conduction "pearls" must be kept in mind when evaluating patients with neuropathy. The most important is recognition that sensory responses remain normal in disorders affecting the nerve roots because lesions proximal to the dorsal root ganglia do not interfere with the sensory evoked response. In nerve root lesions, the dorsal root ganglion remains intact, thus preserving distal sensory metabolism and elicitable SNAPs. Therefore, the combination of profound sensory loss, areflexia, and normal sensory responses is inconsistent with a diagnosis of neuropathy. This constellation is suggestive of a nerve root process. Second, sensory responses are abnormal in any disorder producing an interruption of axon conduction between the dorsal root ganglion and the distal nerve. Abnormal sensory responses will be recorded in a generalized neuropathy, a plexus lesion, or isolated mononeuropathy. Third, a single abnormal sensory response is insufficient to diagnose neuropathy. An absent sural response is not necessarily diagnostic of any abnormality, particularly in older or obese patients, in whom sural responses are sometimes difficult to record. Conversely, a normal sural response virtually excludes a clinically significant neuropathy because the sural response disappears whenever a relatively small proportion of axons are damaged. Exceptions occur in early acute Guillain-Barré syndrome (GBS) and in small fiber neuropathy.

## NEUROPATHY CLASSIFICATION BASED UPON ELECTRODIAGNOSTIC FINDINGS

The peripheral nerve responds in a limited number of ways to a pathologic insult. Those include axon degeneration, demyelination, and metabolic changes that alter nerve conduction. The classification of peripheral neuropathy that follows is based upon the limited number of ways that peripheral nerve responds to disease and separates peripheral disorders into broad categories based upon the presence or absence of sensory abnormalities, motor abnormalities, and conduction slowing.

### Motor or Motor Greater Than Sensory Axonal Loss

Many of the presumably "idiopathic neuropathies" referred to tertiary medical centers are found to be hereditary. The axonal form of CMT disease is known as hereditary motor sensory neuropathy type II (HMSN II), and it is the prototype of axonal motor greater than sensory neuropathy (Table 5). This autosomal dominant disorder is characterized by progressive distal weakness and sensory loss beginning in the third or fourth decade. Distal atrophy may be severe, producing an inverted champagne bottle appearance to the legs, in association with pes cavus, hammer toes, hyporeflexia, and mild sensory loss. On nerve conduction testing, motor amplitudes are reduced in the setting of normal or minimally slowed conduction velocities.

**Table 5** Motor or motor greater than sensory, axonal loss

| |
|---|
| Axonal form of Charcot-Marie-Tooth disease (hereditary motor sensory neuropathy type II) |
| Dapsone toxicity |
| Disulfiram toxicity |
| Acute motor axonal neuropathy |
| Acute motor sensory axonal neuropathy |
| Hyperinsulinism |
| Nitrofurantoin toxicity |
| Organophosphate poisoning |
| Porphyria |
| Paraneoplastic motor neuropathy (lymphoma or carcinoma) |
| Vincristine toxicity |

Sensory responses are absent in about 50% of patients with HMSN II. When present, differentiating HMSN II from a familial progressive muscular atrophy can be difficult. As expected, the needle examination demonstrates neurogenic changes which have a distal predilection (increased insertional activity, positive sharp waves and fibrillation potentials, and reduced recruitment of chronic denervated motor units).

The hepatic porphyrias include acute intermittent porphyria, hereditary coproporphyria, and variegate porphyria; all demonstrate overproduction of porphyrin precursors and porphyrins. Clinical abnormalities include the triad of abdominal pain, psychosis, and neuropathy. Porphyric neuropathy resembles GBS with its subacute onset of weakness, areflexia, dysautonomia, and elevated cerebrospinal fluid (CSF) protein. Mental status changes, asymmetry, proximal weakness initially, and biochemical evidence of abnormal porphyrin metabolism help to distinguish the two conditions. Expected nerve conduction abnormalities include reduced CMAP amplitudes, essentially normal conduction velocities, fibrillation potentials, and decreased MUAP recruitment. Sensory responses occasionally are spared.

Other axonal motor greater than sensory neuropathies include acute motor axonal neuropathy (AMAN), the axonal form of GBS, as well as a variety of toxic and drug-induced neuropathies and the remote effect motor neuropathy associated with lymphoma or carcinoma. Vincristine toxicity typically produces a chronic axonal sensorimotor neuropathy, but occasionally results in rapidly progressive weakness with little increase in sensory involvement, resembling a "pure motor" neuropathy or neuronopathy. Vincristine prescription can be particularly problematic in a patient with a previously existing polyneuropathy such

as one of the hereditary motor and sensory neuropathies. In this clinical setting, the resultant superimposed neuropathy can be rapid in onset and severe leading to quadriplegia.

### Motor Greater Than Sensory Uniform Conduction Slowing

Charcot-Marie-Tooth disease type I (HMSN I), is characterized by uniform demyelination pathologically and nerve conduction slowing electrophysiologically (Table 6). It represents the prototype of a uniformly demyelinating neuropathy. This dominantly inherited hypertrophic neuropathy presents in early adult life with distal weakness, areflexia, and foot deformities. Other clinical findings include palpably enlarged nerves, hammer toes and pes cavus, abnormal vibratory sensation in the toes, and hyporeflexia. Conduction velocities are markedly reduced, often as low as 25 m/s or less.

**Table 6** Motor great than sensory uniform conduction slowing

| |
|---|
| Amiodarone |
| Charcot-Marie-Tooth disease type I (hereditary motor sensory neuropathy type I) |
| Cytosine arabinoside (ara-C) |
| Dejerine-Sottas disease (hereditary motor sensory neuropathy type III) |
| Hexacarbons |
| Perhexiline maleate |
| Sodium channel blockers |

In adults, reference values for motor conduction velocity typically exceed 50 m/s in the arms and 40 m/s in the legs. Conduction velocities less than 70% of the lower limit of normal are indicative of demyelination or membranopathy and are inconsistent with axonal loss alone because the approximate conduction velocity of the smallest recordable myelinated axons lay between 70% and 100% of the lower limits of normal. Therefore, an abnormality of the myelin sheath or the membrane must be present to account for the markedly reduced velocities. Pathologically, the distribution of demyelination in HMSN I is uniform throughout the nerve. Thus, conduction velocity slowing is uniform from segment to segment and abnormal temporal dispersion and partial conduction block, hallmarks of acquired multifocal demyelination, are not usually recorded. CMAP amplitudes and morphology remain unchanged between distal and proximal stimulation sites.

Amiodarone use is associated with a slowly progressive motor neuropathy and in some patients prominent conduction slowing often is in the range of 20 to 30 m/s. Abnormal temporal dispersion and partial conduction block are not features of this neuropathy, and slowing is related to preferential loss of the largest myelinated fibers. The motor abnormalities are associated with low-amplitude sensory responses when the neuropathy is severe. In other patients, the EDX features of amiodarone induced neuropathy are those of an axonal loss neuropathy or axonopathy.

Neurotoxins that block sodium channels include tetrodotoxin derived from the puffer fish and saxitoxin whose source is the contaminated shellfish (red tide). Sodium channel blockade impedes the rapidly changing local currents needed to propagate saltatory nerve conduction. The effect of these neurotoxins is similar to that seen with cooling temperature, thereby slowing conduction velocity. Motor amplitudes are reduced, but no abnormal temporal dispersion or partial conduction block is observed.

Several hexacarbon solvents and glues are implicated in causing neuropathy after occupational or recreational exposures. N-hexane and methyl n-butyl ketone are metabolized to 2,5-hexanedione, the likely neurotoxic agent. The neuropathy is characterized by progressive distal sensory loss, reduced or absent reflexes, eventual weakness and atrophy, and sometimes autonomic dysfunction. Patients who voluntarily inhale n-hexane sometime develop a rapidly progressive motor greater than sensory neuropathy. Motor and sensory amplitudes are reduced and conduction slowed, suggestive of primary demyelination; however, in this case, the slowing is due to secondary myelin damage resulting from giant axonal swellings. Positive waves and fibrillation potentials are recorded on needle EMG, as well as reduced recruitment of enlarged motor units, abnormalities expected from axon loss.

### Motor Greater Than Sensory Multifocal Conduction Slowing

Inflammatory demyelinating polyneuropathies are acquired immune diseases that include acute GBS, chronic inflammatory demyelinating polyneuropathy (CIDP), and other chronic dysimmune neuropathies which mimic CIDP (Table 7). Chronic inflammatory demyelinating polyneuropathy is an example of a relatively common, treatable, and reversible neuropathy that was rarely recognized 25 years ago. Because it is frequently associated with an underlying systemic illness (plasma cell dyscrasia, Waldenstrom's macroglobulinemia, gamma heavy chain disease, cryoglobulinemia, lymphoma, systemic lupus erythematous, Castleman's disease, occult malignancy, and human immunodeficiency virus infection), recognition is important. The inflammatory demyelinating neuropathies typically present with progressive weakness, areflexia, decreased sensation, dysautonomia, and elevated CSF protein.

Abnormal temporal dispersion and/or partial conduction block of CMAP responses, slowed nerve conduction velocities, and prolonged distal latencies and F-wave latencies characterize the acquired demyelinating neuropathies (Figure 4). In general,

**Table 7** Motor greater than sensory multifocal conduction slowing

| |
|---|
| Arsenic (acute intoxication) |
| Guillain-Barré syndrome (GBS) |
| Subacute inflammatory demyelinating polyneuropathy |
| Chronic inflammatory demyelinating polyneuropathy |
| Chronic disimmune polyneuropathy |
| Monoclonal gammopathy of undetermined significance |
| Osteosclerotic myeloma |
| Multiple myeloma (substantial proportions are axonal) |
| Systemic lupus erythematous |
| Waldenstrom's macroglobulinemia |
| Gamma heavy chain disease |
| Cryoglobulinemia |
| Castleman's disease |
| Lymphoma |
| Carcinoma |
| Human immunodeficiency virus |
| Multifocal motor neuropathy with conduction block |

undue emphasis and importance should not be placed on mild conduction slowing as it is often observed in axon loss conditions. The electrophysiologic evaluation should be sufficiently extensive, when possible, to include motor nerves with reasonably preserved distal amplitudes. If responses cannot be elicited from motor nerves in the legs and distal upper extremities, the EDX consultant should test proximal motor nerves such as the musculocutaneous and the spinal accessory. In general, conduction velocities less than 70% of the lower limit of normal can be attributed to primary demyelination. In some patients, marked prolongation of distal latencies will be recorded at a time when routine nerve conduction velocities are normal or only slightly slowed. Absent F responses alone may be recorded in the first week of an acute demyelinating neuropathy and may be the earliest finding in GBS. The needle EMG examination has a secondary role in the assessment of demyelinating polyneuropathies and is performed to document the degree of accompanying axon loss, the distribution of denervation, and the duration of the disease. It is a relatively insensitive measure of severity and prognosis. In GBS, the needle examination is usually not performed until the fourth week or later of illness at a time when axon loss, if present, would be recordable.

Acute arsenical neuropathy is one component of a systemic illness characterized by nausea, vomiting, diarrhea, dermatitis, cardiomyopathy, pancytopenia with basophilic stippling, and abnormal liver function tests. The temporal profile of a gastrointestinal illness followed by a rapidly evolving neuropathy suggests the diagnosis of GBS, and acute arsenic poisoning is frequently misdiagnosed as GBS. Mees' lines, a delayed hallmark of severe poisoning, do not appear on the nails until 6 to 8 weeks after exposure and, consequently, are not helpful during the initial phase of the evaluation when recognition of the poisoning and treatment is crucial. As in GBS, CSF protein becomes elevated several weeks after the onset of arsenical neuropathy, but other laboratory abnormalities such as pancytopenia, basophilic stippling of red blood cells, elevated liver function tests, and cardiomegaly suggest a toxic etiology. Determining arsenic in a 24-hour urine collection is often the most sensitive test for confirming the diagnosis. Blood arsenic levels are often normal by the time the diagnosis of arsenic poisoning is considered. Initial EDX studies in acute arsenic poisoning show reduced conduction velocity, increased temporal dispersion, partial conduction block, and low-amplitude or absent sensory responses. Serial studies usually demonstrate a dying-back neuropathy with progressive axonal degeneration, suggesting that the initial electrophysiologic findings probably relate to generalized axonal failure rather than a primary demyelinating process. Clinically, acute arsenic poisoning evolves into a severe, irreversible, chronic motor and sensory polyneuropathy with prominent weakness and neuropathic pain.

### Sensory Axonal Loss (Neuropathy or Neuronopathy)

Sensory symptoms and signs are usually the earliest features of most sensorimotor neuropathies. Much less common are polyneuropathies that begin with a sensory presentation and remain sensory in their manifestation. The most common axonal sensory neuropathies or neuronopathies are listed in Table 8. These disorders typically present subacutely with paresthesias, impaired vibration and joint position sensation, and areflexia. As the diseases progress, patients often develop impaired coordination, involuntary movements, and gait disorders—all features betraying large fiber sensory dysfunction in the limbs.

Pyridoxine (vitamin $B_6$) can produce a neuropathy when deficient in the diet or when taken in excess. Vitamin fanatics occasionally take pyridoxine in "megadoses" to treat a variety of conditions which include premenstrual syndrome, carpal tunnel syndrome, schizophrenia, fibromyalgia, autism, and hyperkinesis. Dose-related neurotoxicity can develop from long-term cumulative exposure or after short-term administration of large doses. Sensory loss may be complete and irreversible, and is sometimes associated with choreoathetoid movements. Cisplatin produces a dose-related sensory neuronopathy indistinguishable from the paraneoplastic sensory neuronopathy associated with small cell lung carcinoma and antineuronal antibodies. In many patients, the unusual electrophysiologic constellation includes normal motor studies and completely absent sensory responses (in the arms and legs). This pattern of abnormalities is atypical for an early sensorimotor neuropathy and is more in keeping

**Table 8** Sensory axonal loss

| | |
|---|---|
| Cisplatin | Pyridoxine toxicity |
| Congenital | Sjögren's syndrome |
| Metronidazole | Styrene poisoning |
| Paraneoplastic sensory neuronopathy | Thalidomide |

with a sensory neuronopathy from pathology in the dorsal root ganglia diffusely.

### Sensory Greater Than Motor Axonal Loss

This classification constitutes the largest number of neuropathies. Many of these sensorimotor neuropathies present with predominantly sensory abnormalities and mild, often subclinical, motor changes (Table 9). The latter are frequently apparent on needle EMG examination only, without clinical evidence of weakness. These neuropathies include most toxic and metabolic neuropathies, nutritional disorders, connective tissues disorders, and some degenerative conditions. Most toxic-metabolic polyneuropathies are characterized by distal axonal degeneration (dying-back) of sensory and motor axons. Most are physiologically similar and cannot be distinguished without laboratory testing. Sensory symptoms and signs predominate with dysesthesias, paresthesias, distal sensory loss, and loss of distal reflexes being the most common clinical presentation. Weakness and atrophy of distal muscles often develop later in the illness. In most patients with a sensorimotor axonal loss neuropathy, sensory amplitudes are abnormal early in the course of disease at a time when sensory distal latencies and conduction velocities are normal or slightly abnormal. Compound muscle action potential amplitudes become abnormal later in the illness, first in distal leg nerves. Conduction velocities, motor distal latencies, and F-wave latencies remain essentially normal unless extensive axon loss ensues which affects the large diameter motor fibers. On needle examination, increased insertional activity, fibrillation potentials, positive waves, and decreased recruitment of reinnervated motor units are seen distally.

Ethyl alcohol is thought to be one of the most common causes of neuropathy in the United States. It is associated with several other neurological disorders that are related either to the direct neurotoxic effects of alcohol or its metabolites, secondary nutritional disorders, genetic predisposition, or a combination of these factors. The role of ethyl alcohol as the toxin that produces neuropathy is controversial because most individuals who consume large amounts of alcohol are also nutritionally compromised. Clinically similar neuropathies to that seen in alcohol abuse occur in vitamin deficiency states (e.g., thiamine and other B vitamins). Many scientists and physicians believe that alcohol-induced neuropathy occurs in the setting of normal nutrition, perhaps because of impaired axonal transport. Paresthesias and painful distal dysesthesias are common early symptoms. The neuropathy is slowly progressive, and distal weakness, unsteady gait, and areflexia commonly appear, often along with dysautonomia.

**Table 9** Sensory greater than motor axonal loss

| | |
|---|---|
| Acromegaly | Amitriptyline |
| Amyloidosis | Chloroquine |
| Chronic illness neuropathy | Colchicine |
| Connective tissue diseases | Ethambutol |
| Rheumatoid arthritis | Gold |
| Periarteritis nodosa | Hydralazine |
| Churg-Strauss vasculitis | Isonicotine hydrazine |
| Degenerative disorders | Lithium |
| Friedreich's ataxia | Metronidazole |
| Olivopontocerebellar | Nitrous oxide |
| Gout | Phenytoin |
| Hypothyroidism | Sulfapyridine |
| Metals | Sulfasalazine |
| Arsenic (chronic) | Statins |
| Gold | Thalidomide |
| Lithium | Thallium |
| Mercury | Vincristine |
| Multiple myeloma | Polycythemia vera |
| Myotonic dystrophy | Sarcoidosis |
| Nutrition | Toxic |
| $B_{12}$ deficiency | Acrylamide |
| Folate deficiency | Carbon disulfide |
| Post-gastrectomy | Ethyl alcohol |
| Thiamine deficiency | Hexacarbons (glue sniffing) |
| Pharmaceuticals | Organophosphorous esters |
| Amiodarone | |

The EDX consultant's role in the evaluation of a sensorimotor axonal loss neuropathy lay in confirming the presence of sensory and motor involvement, documenting the extent and severity of axon loss, eliminating uniform or multifocal demyelination, and testing for any superimposed neuropathic process such as a mononeuropathy, mononeuritis multiplex, or a polyradiculopathy. By combining the EDX results with the clinical findings, the EDX consultant may assist the referring physician in reaching a specific diagnosis. Examples include identifying a painful neuropathy and superimposed bilateral carpal tunnel

syndrome in a patient with amyloidosis, correlating a tremor and neuropathy with lithium or mercury intoxication, noting the preservation of reflexes and abnormal corticospinal tract signs in a patient with vitamin $B_{12}$ deficiency, and detecting the coexistence of neuropathy and myopathy in a patient taking colchicine for a prolonged period of time.

### Mixed Sensory and Motor Conduction Slowing and Axonal Loss

In early symmetric diabetic neuropathy, sensory symptoms and signs usually predominate over motor complaints (Table 10). Weakness eventually develops usually manifesting initially as toe and ankle dorsiflexion impairment. Neurological signs include decreased vibration and pain sensation in a stocking distribution. Joint position sense may be impaired in a severe neuropathy. Ankle reflexes are usually absent and other reflexes hypoactive. Atrophy and weakness spreads to other distal muscles, later followed by more proximal involvement.

Even asymptomatic, neurologically intact diabetic patients can have nerve conduction abnormalities. Conduction velocities at the lower limit of normal are common. With increasing severity, CMAP amplitudes become reduced and nerve conduction velocities become slower. Abnormal temporal dispersion and partial conduction block to a small degree can be recorded, but are not prominent. Most patients with isolated sensory abnormalities and all patients with generalized sensorimotor diabetic neuropathy have electrophysiologic features reflecting active and chronic denervation distally.

Patients with renal failure independent of diabetes mellitus develop a sensorimotor neuropathy characterized by low-amplitude motor and sensory responses, sometimes in association with pronounced conduction slowing. This is most apparent in patients with end-stage renal disease (ESRD). The magnitude of slowing is greater than expected from axonal loss, and chronic demyelination and remyelination plus membrane changes contribute to the slowing. Although NCSs can play an important role in making the diagnosis of ESRD neuropathy, they are not required or useful to evaluate the effectiveness of dialysis. Determining the adequacy of dialysis is complicated, and the best indicators of effective treatment are clinical, not electrodiagnostic. Dialysis and renal transplantation are generally effective treatments for reversing the neuropathy of ESRD, but EDX improvement is a late finding.

In summary, patients with clinical features of neuropathy can be categorized using NCSs into convenient classifications. The grouping described in this review separates neuropathies into those that are sensory, motor, or both, and into conditions which are predominately axonal loss or demyelinating (uniform or multifocal). In many patients, proper application of the principles outlined in this article can direct the referring physician towards a specific and potentially treatable cause of the neuropathy.

**Table 10** Mixed sensory and motor conduction slowing and axonal loss

| | |
|---|---|
| Diabetes mellitus | End-stage renal disease |

*The author had nothing to disclose.*

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# Evaluating the Patient With Suspected Radiculopathy

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## 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 spondylosis, 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 consultants 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 that informs 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 article.

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 anatomic 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 consultant 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, electromyography (EMG) precisely identified the involved root level 84% of the time.[63] Electromyography 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.[67]

Regarding the cervical nerve roots and the brachial plexus, there are many anatomic variations. Perneczky described an anatomic study of 40 cadavers. 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 consultant 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 neurological and musculoskeletal conditions can produce pain, weakness, and sensory symptoms. In addition to the standard peripheral neurological 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

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

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

ESR = erythrocyte sedimentation rate

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 both plexopathies 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 illiac 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 like a stocking. It is extremely strong laterally where it becomes the illiotibial 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 illiotibial 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. 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.

**Table 2** Common musculoskeletal disorders mimicking lumbosacral radiculopathy

| Condition | Clinical symptoms/signs |
|---|---|
| Fibromyalgia syndrome and polymyalgia rheumatica | As in Table 1 |
| Hip arthritis | Pain in groin, anterior thigh, pain with weight bearing, positive Patrick's test |
| Trochanteric bursitis | Lateral hip pain, pain with palpation on lateral and posterior hip |
| Illiotibial band syndrome | Pain along outer thigh, pain with palpation |
| Knee arthritis | Pain with weight bearing |
| Patellofemoral pain | Anterior knee pain, worsen with prolonged sitting |
| Pes anserinus bursitis | Medial proximal tibia pain, tender to palpation |
| Hamstring tendinitis, chronic strain | Posterior knee and thigh pain, can mimic positive straight leg raise, common in runners |
| Baker's cyst | Posterior knee pain and swelling |
| Plantar fasciitis | Pain in sole of foot, worsened with weight bearing activities, tender to palpation |
| Gastrocnemius-soleus tendinitis, chronic strain | Calf pain, worsened with sports activities, usually limited range of motion compared to asymptomatic limb |

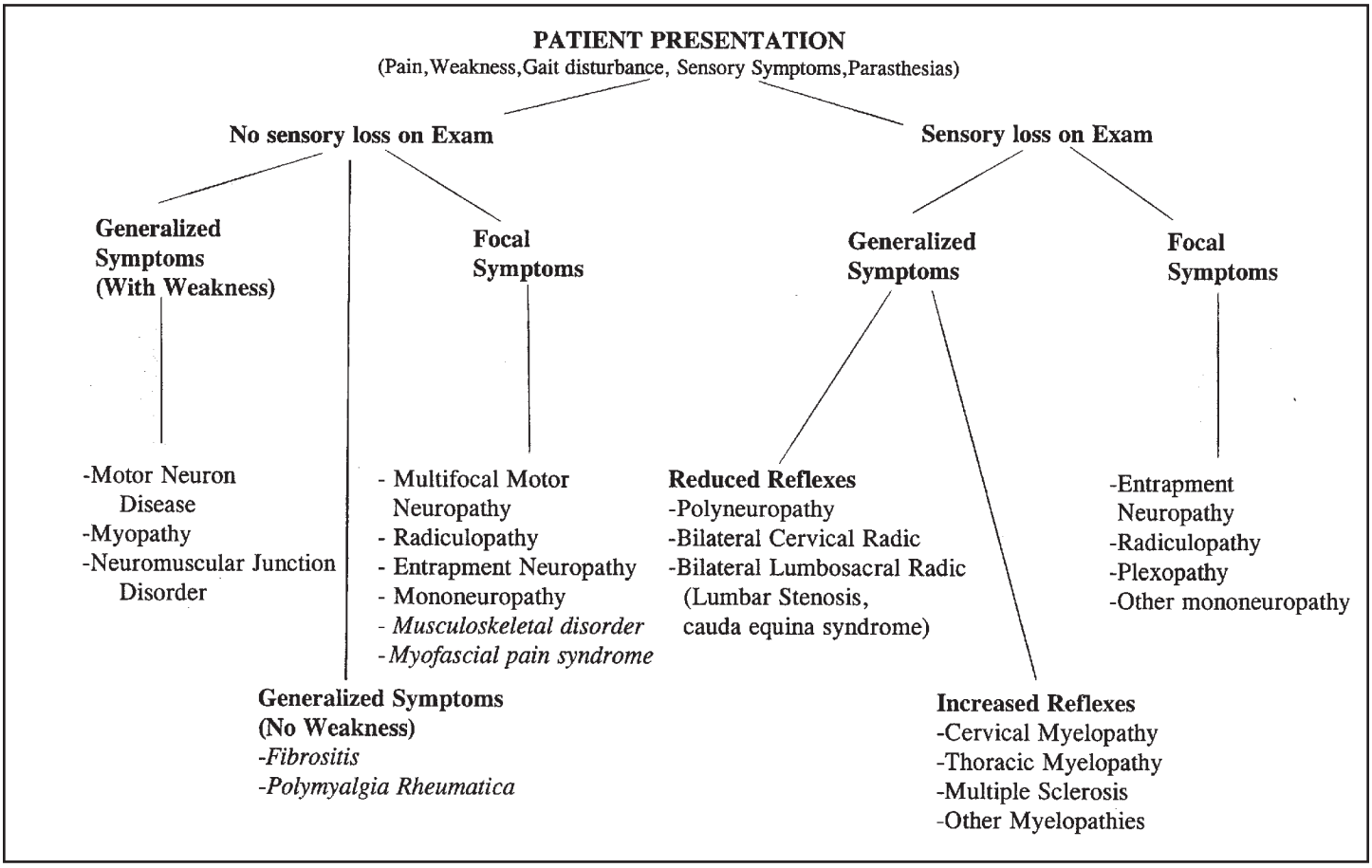


**Figure 1** Algorithmic approach to structuring the EDX examination based upon physical examination signs and the location of the patient's symptoms. Focal symptoms refer to single limb symptoms whereas generalized symptoms are present when the patient complains of symptoms affecting more than one limb.

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 consultant 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.[35,36] 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 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.[35] Weakness in any leg muscle group resulted in about 2.5 times greater chance of identifying a lumbosacral radiculopathy on EMG.[35]

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.[36] Combinations of findings, particularly weakness plus reflex changes, resulted in a nine-fold greater likelihood of cervical radiculopathy.[36]

### AANEM 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.[1] 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.[65] 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 consultant 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 CONDUCTIONS

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.[65] It is a monosynaptic reflex that is an S1 mediated response and can differentiate to some extent 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%.[31,38,40,43,51,65] However, many of these studies suffered from lack of a control group, imprecise inclusion criteria, or small sample sizes.

Marin and colleagues[39] prospectively examined the H reflex and the extensor digitorum brevis reflex in 53 normals, 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 be useful to identify subtle S1 radiculopathy, yet there are a number of shortcomings related to these responses. They can be normal with radiculopathies,[43] and because they are mediated over such a long physiological pathway, they can be abnormal due to polyneuropathy, sciatic neuropathy, or plexopathy.[65] 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[18] 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.[65] 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.[31,52,59]

London and England[41] reported two cases of persons with neurogenic claudication from lumbosacral spinal stenosis. They demonstrated that the F-wave responses could be reversibly changed after 15 minutes of ambulation which provoked symptoms. This suggested an ischemia-induced conduction block in proximal motor neurons. A larger scale study of this type might find a use for F waves in the identification of lumbosacral spinal stenosis and delineate neurogenic from vascular claudication.

### Motor and Sensory Nerve Conduction Studies

Standard motor and sensory NCS may not be helpful in identifying a cervical or lumbosacral radiculopathy, however they should be performed to screen for polyneuropathy and exclude common entrapment neuropathies if the patient's symptoms could be explained by a focal entrapment.

Plexopathies often pose a diagnostic challenge, as they are similar to radiculopathies in symptoms and signs. In order to distinguish plexopathy from radiculopathy, sensory responses which are accessible in a limb should be tested. In plexopathy, they are likely to be reduced in amplitude, whereas in radiculopathy they are generally normal. If substantial axonal loss has occurred at the root level, the CMAP recorded in muscles innervated by that root may be reduced in both plexopathies and radiculopathies. This is usually when severe axonal loss has occurred such as with cauda equina lesions or penetrating trauma that severely injures a nerve root. The distal motor latencies and conduction velocities are usually preserved as they reflect the fastest conducting nerve fibers.[65]

## SOMATOSENSORY EVOKED POTENTIALS, DERMATOMAL SOMATOSENSORY EVOKED POTENTIALS, AND MAGNETIC EVOKED POTENTIALS

The AANEM guidelines recently 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.[1]

Physiological evidence of multiple or single root involvement in lumbosacral spinal stenosis can be documented with DESPs 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.[55] 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.[66] 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.[42] In this group 87% showed gait disturbances, and 82% showed hyperreflexia. Magnetic resonance imaging 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 interosseus 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.[60] 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.[17] 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.[15] 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 ELECTRODIAGNOSTIC TESTING

Electrodiagnostic testing is expensive and uncomfortable for patients, therefore, it is important to understand why it is performed and the expected outcomes. Electrodiagnostic 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.[23]

- 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.[57,58]

## ELECTROMYOGRAPHY AND DIAGNOSTIC SENSITIVITIES

The need for EMG, particularly in relationship to imaging of the spine, has been recently highlighted.[49] 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.[26] 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.[3] 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. Electromyography 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.[49] 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.[7] 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.[44]

In sharp contrast to these findings, Dumitru, Diaz, and King examined the lumbosacral paraspinal muscles and intrinsic foot muscles with monopolar EMG.[15] 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

**Table 3** Selected studies evaluating the sensitivity of EMG relative to various "gold standards." Unless otherwise stated the EMG parameters used in sensitivity calculations were fibrillation potentials.

| STUDY | SAMPLE SIZE | GOLD STANDARD | EMG SENSITIVITY |
|---|---|---|---|
| **LUMBOSACRAL (RADICULOPATHY)** | | | |
| Weber and Albert[63] | 42 | Clinical + Imaging HNP | 60% |
| Nardin and colleagues[45] | 47 | Clinical | 55% |
| Kuruoglu and colleagues[31] | 100 | Clinical | 86% |
| Khatri and colleagues[28] | 95 | Clinical | 64% |
| Tonzola and colleagues[61] | 57 | Clinical | 49% |
| Schoedinger[53] | 100 | Surgically proven | 56% |
| Knutsson[27] | 206 | Surgically proven | 79% |
| Young and colleagues[67] | 100 | Clinical and imaging | 84% * |
| Linden and Berlit[40] | 19 | Myelography and CT | 78% |
| **LUMBOSACRAL (SPINAL STENOSIS)** | | | |
| Hall and colleagues[24] | 68 | Clinical + myelogram | 92% |
| Johnson and colleagues[27] | 64 | Clinical + myelogram | 88% † |
| **CERVICAL (RADICULOPATHY)** | | | |
| Berger and colleagues[2] | 18 | Clinical | 61% |
| Partanen and colleagues[46] | 77 | Intraoperative | 67% |
| Leblhuber and colleagues[38] | 24 | Clinical + myelogram | 67% |
| So and colleagues[56] | 14 | Clinical | 71% |
| Yiannikas and colleagues[66] | 20 | Clinical and/ or radiographic | 50% |
| Tackman and Radu[59] | 20 | Clinical | 95% |
| Hong, Lee, and Lum[25] | 108 | Clinical | 51% |

* Both fibrillations or large motor units >8 mV were considered positive.

† This study assessed EMG parameters and used quantitative EMG with a unique grading scale not used in clinical practice. Fibrillations were infrequent. This limits the generalizability of this otherwise strong study.

CT = computerized tomography; HNP = herniated nucleus pulposis

positive waves in the lumbar paraspinal muscles. Electrodiagnostic consultants 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,[4,32,33] or amyotrophic lateral sclerosis,[30] and following spinal surgery[54] or lumbar puncture.[7]

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.[19,20,21,22] The "mini PM" score provides a quantitative means of deriving the degree of paraspinal muscle denervation.[19] It distinguishes normal findings from EMG findings in persons with radiculopathy. This novel and quantitative technique may prove to identify 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 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 consultants 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.[10] 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% (Tables 4 and 5). When paraspinal muscles were not part of the screen, eight distal limb muscles recognized 92-95% of radiculopathies. Without paraspinal muscles, the identification rates were consistently lower. If one only considers fibrillations and positive sharp waves in the EMG assessment, identification rates are lower. Six muscle screens including paraspinal muscles yielded consistently high identification rates and studying additional muscles lead to marginal increases in identification. Individual screens useful to the EDX consultant are listed in Tables 4 and 5. In some instances a particular muscle cannot be studied due to wounds, skin grafts, dressings, or infections. In such cases the EDX consultant can use an alternative screen with equally high identification. These findings were consistent with those derived from a large retrospective study.[33]

**Table 4** Five muscle screen identifications of patients with cervical radiculopathies

| MUSCLE SCREEN | NEUROPATHIC ACTIVITY | SPONTANEOUS |
|---|---|---|
| Without Paraspinals | | |
| deltoid, APB, FCU, triceps, PT | 92% | 65% |
| biceps, triceps, EDC, FCR, FDI | 85% | 54% |
| deltoid, triceps, EDC, FDI, FCR | 84% | 58% |
| biceps, triceps, PT, APB, FCU | 91% | 60% |
| **With Paraspinals** | | |
| deltoid, triceps, PT, APB, PSM | 98% | 80% |
| biceps, triceps, EDC, FDI, PSM | 95% | 73% |
| deltoid, EDC, FDI, PSM, FCU | 90% | 73% |
| biceps, FCR, APB PT, PSM | 95% | 77% |

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.[10])

### The Lumbosacral Radiculopathy Screen

A prospective multi-center study was conducted at five institutions by Dillingham and colleagues.[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 confirmable radiculopathies will be missed. A large retrospective study noted similar findings, concluding that five muscles identified most electrodiagnostically confirmable radiculopathies.[37]

Dillingham and Dasher[9] re-analyzed data from a study published by Knutsson almost forty years earlier.[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 4 muscles with 1 being the lumbosacral paraspinal muscle yielded (1) an identification rate

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

| MUSCLE SCREEN | NEUROPATHIC | SPONTANEOUS ACTIVITY |
|---|---|---|
| **Without Paraspinals** | | |
| deltoid, APB, FCU, triceps, PT, FCR | 93% | 66% |
| biceps, triceps, FCU, EDC, FCR, FDI | 87% | 55% |
| deltoid, triceps, EDC, FDI, FCR, PT | 89% | 64% |
| biceps, triceps, EDC, PT, APB, FCU | 94% | 64% |
| **With Paraspinals** | | |
| deltoid, triceps, PT, APB, EDC, PSM | 99% | 83% |
| biceps, triceps, EDC, FDI, FCU, PSM | 96% | 75% |
| deltoid, EDC, FDI, PSM, FCU, triceps | 94% | 77% |
| biceps, FCR, APB, PT, PSM, triceps | 98% | 79% |

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 = lumbosacral paraspinal muscles; PT = pronator teres.

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.[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.[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 non-paraspinal muscles must be examined. Another way to think of this:

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

**Table 6** Four muscle screen identifications of patients with lumbosacral radiculopathies. 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-paraspinal muscles included positive waves, fibrillations, increased polyphasic potentials, neuropathic recruitment, increased insertional activity, CRDs, or large amplitude 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.

| Screen | Neuropathic | Spontaneous Activity |
|---|---|---|
| **Four Muscles Without Paraspinals** | | |
| ATIB, PTIB, MGAS, RFEM | 85% | 75% |
| VMED, TFL, LGAS, PTIB | 75% | 58% |
| VLAT, SHBF, LGAS, ADD | 52% | 35% |
| ADD, TFL, MGAS, PTIB | 80% | 67% |
| **Four Muscles With Paraspinals** | | |
| ATIB, PTIB, MGAS, PSM | 97% | 90% |
| VMED, LGAS, PTIB, PSM | 91% | 81% |
| VLAT, TFL, LGAS, PSM | 88% | 77% |
| ADD, MGAS, PTIB, PSM | 94% | 86% |

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.[10])

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.

## 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.[24] 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.[24]

## LIMITATIONS OF THE NEEDLE ELECTROMYOGRAPHY SCREEN

These cervical and lumbosacral muscle screens should not substitute for a clinical evaluation and differential diagnosis formulation by the EDX consultant. 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 set of muscles are studied. 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 consultant 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

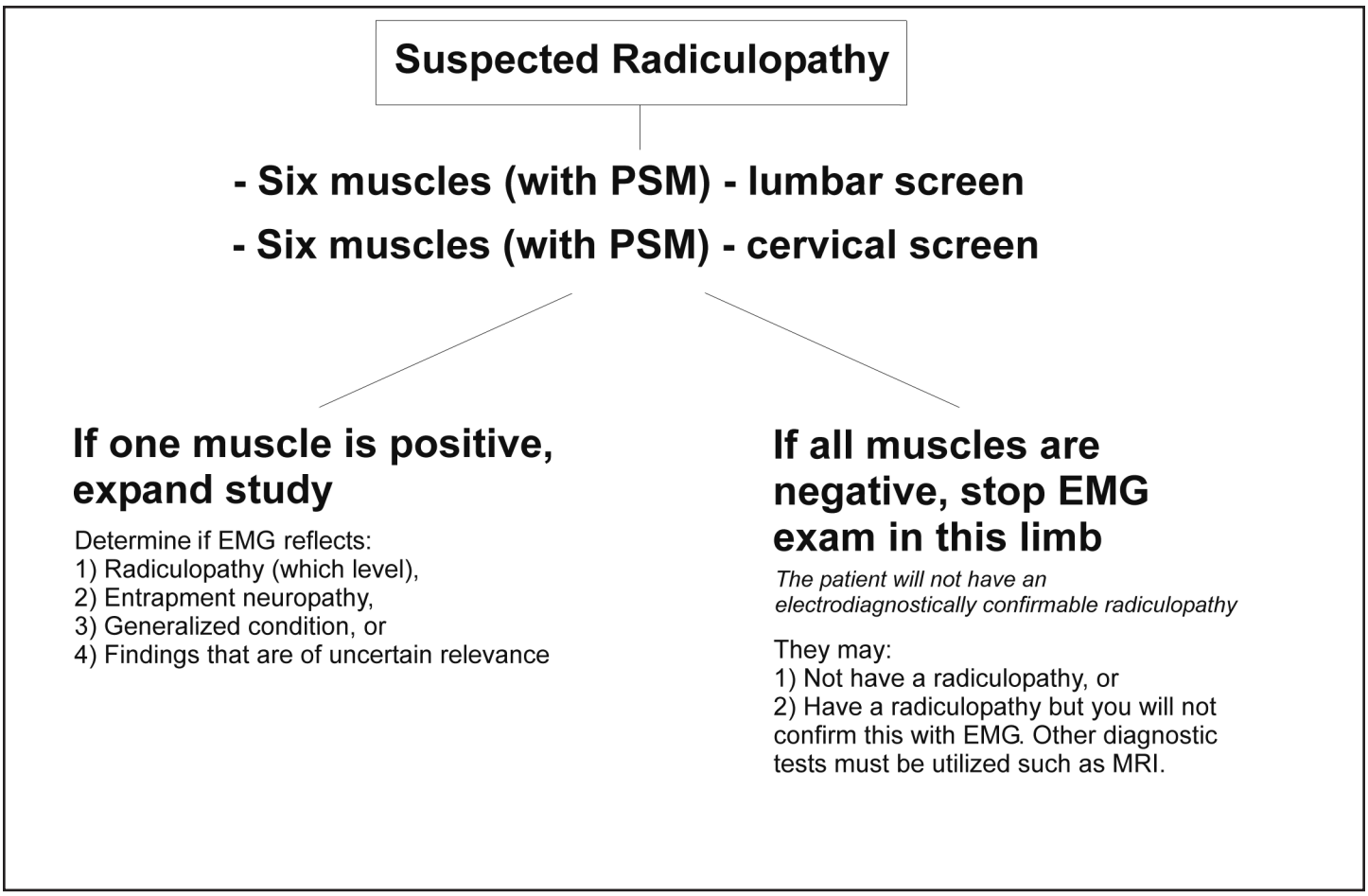


**Figure 2** Implications of an electromyography (EMG) screening evaluation.

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

| Screen | Neuropathic | Spontaneous Activity |
|---|---|---|
| **Five Muscles Without Paraspinals** | | |
| ATIB, PTIB, MGAS, RFEM, SHBF | 88% | 77% |
| VMED, TFL, LGAS, PTIB, ADD | 76% | 59% |
| VLAT, SHBF, LGAS, ADD, TFL | 68% | 50% |
| ADD, TFL, MGAS, PTIB, ATIB | 86% | 78% |
| **Five Muscles With Paraspinals** | | |
| ATIB, PTIB, MGAS, PSM, VMED | 98% | 91% |
| VMED, LGAS, PTIB, PSM, SHBF | 97% | 84% |
| VLAT, TFL, LGAS, PSM, ATIB | 97% | 86% |
| ADD, MGAS, PTIB, PSM, VLAT | 94% | 86% |

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.

neuron disease. It is incumbent upon the EDX consultant to formulate a differential diagnosis and methodically evaluate for the diagnostic possibilities, further refining the examination as data are acquired.

## SYMPTOM DURATION AND THE PROBABILITY OF FIBRILLATIONS

In the past, a well-defined temporal course of events was thought to occur with radiculopathies despite the absence of studies supporting such a relationship between symptom duration and the probability of spontaneous activity in a muscle. It was a commonly held notion that in acute lumbosacral radiculopathies, the paraspinal muscles denervated first followed by distal muscles, and that later reinnervation started with paraspinal muscles and then with distal muscles. This paradigm was recently challenged by a series of investigations.[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.

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

| Screen | Neuropathic | Spontaneous Activity |
|---|---|---|
| **Six Muscles Without Paraspinals** | | |
| ATIB, PTIB, MGAS, RFEM, SHBF, LGAS | 89% | 78% |
| VMED, TFL, LGAS, PTIB, ADD, MGAS | 83% | 70% |
| VLAT, SHBF, LGAS, ADD, TFL, PTIB | 79% | 62% |
| ADD, TFL, MGAS, PTIB, ATIB, LGAS | 88% | 79% |
| **Six Muscles With Paraspinals** | | |
| ATIB, PTIB, MGAS, PSM, VMED, TFL | 99% | 93% |
| VMED, LGAS, PTIB, PSM, SHBF, MGAS | 99% | 87% |
| VLAT, TFL, LGAS, PSM, ATIB, SHBF | 98% | 87% |
| ADD, MGAS, PTIB, PSM, VLAT, SHBF | 99% | 89% |
| VMED, ATIB, PTIB, PSM, SHBF, MGAS | 100% | 92% |
| VMED, TFL, LGAS, PSM, ATIB, PTIB | 99% | 91% |
| ADD, MGAS, PTIB, PSM, ATIB, SHBF | 100% | 93% |

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.

The findings from these investigations underscored the fact that the pathophysiological processes involved with cervical and lumbosacral radiculopathies are complex.[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 consultant 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, chemical 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.[62] 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.[57] Spengler and colleagues confirmed and underscored these previous findings regarding objective methods to assess the probability of surgical success preoperatively.[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.

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[64] showed that surgery for a herniated nucleus pulposis causing sciatica was more effective at pain control at one 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.[8,27,40,61] In fact, on follow-up MRI studies, lumbosacral disc herniations and disc fragments resolve in 76% of patients.[40]

The outcomes for cervical radiculopathy are generally good in the absence of myelopathy.[8,23,61]

Saal, Saal, and Yurth demonstrated that persons with cervical disc herniations have a similar favorable clinical course as persons with lumbosacral radiculopathy.[61] 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 consultant 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. EDX findings must be interpreted relative to the patient's clinical presentation, and the consultant should tailor the EDX study to the clinical situation. EMG complements spinal imaging and often raises other diagnostic possibilities in addition to confirming clinical suspicians.

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