# Electrodiagnostic Evaluation of Myopathies

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**KEYWORDS**

• Electromyography • Muscle biopsy • Muscle membrane irritability
• Motor unit action potential • Recruitment

**KEY POINTS**

- Electrodiagnostic studies are an extension of the physical examination.
- In the appropriate clinical setting, they are an important tool in the evaluation of patients with suspected myopathies.
- Electrodiagnostic patterns may help recognize the underlying pathophysiologic process and help direct further testing.

## INTRODUCTION

The evaluation of patients suspected of having a myopathy begins with a thorough history and clinical examination. This process leads to the elaboration of a clinical impression, based on symptoms, progression, family history, and examination findings. Further diagnostic tests are then ordered using a hypothesis-driven approach to add laboratory evidence in support of or against the clinical suspicion. Electrodiagnostic (EDX) studies, in this respect, are an extension of the physical examination and may help establish the diagnosis of myopathy.

EDX studies, however, are not always needed to diagnose a myopathy. This is particularly true in the pediatric and, occasionally, the adult population. Oftentimes, patients with inherited myopathies present with characteristic phenotypes, and, possibly, a positive family history. In these cases, it is reasonable to proceed directly to genetic testing. In addition, at times, the diagnosis ultimately requires a muscle biopsy, regardless of the EDX study results. Therefore, if clinical suspicion for a myopathy is high, generally corroborated by elevated creatine kinase (CK) levels, it is often

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Phys Med Rehabil Clin N Am 24 (2013) 193–207
http://dx.doi.org/10.1016/j.pmr.2012.08.017 **pmr.theclinics.com**
1047-9651/13/$ – see front matter 

reasonable to skip or limit the extent of the EDX studies. Finally, EDX studies may be normal in selected muscle diseases (certain endocrine, metabolic, congenital, and mitochondrial myopathies). Thus, in the appropriate clinical context, normal EDX studies do not necessarily rule out the presence of a myopathy.

EDX studies are most useful to diagnose a myopathy when further data are needed to exclude alternative diagnoses, confirm the presence of a muscle disease, and narrow down the differential. The role of EDX studies is summarized in **Box 1**. First of all, the results of nerve conduction studies (NCSs) and electromyography (EMG) are used to exclude neuromuscular conditions that may mimic a myopathy (such as motor neuron disease and neuromuscular junction disorders or, occasionally, motor neuropathies). Second, EMG is often able to confirm the diagnosis of a muscle disorder, when motor units with characteristic morphology and recruitment pattern are identified (**Figs. 1** and **2**). In such cases, EMG may also add diagnostic information relating to the location, type, and severity of the underlying process. For example, the presence of abnormal spontaneous activity may help narrow down the differential among different myopathic processes (**Box 2**). Finally, EMG may be useful in identifying target muscles for biopsy. This is particularly helpful when the only clinically weak muscles are not easily accessible for biopsy (such as the gluteal muscles, the hip flexors, or the paraspinals). The yield of a muscle biopsy increases when a weak (Medical Research Council grade 4 of 5), but not end-stage, muscle is biopsied. EMG analysis allows the evaluation of multiple sites and the identification of affected muscles that are not weak on neurologic examination.

## ELECTRODIAGNOSTIC APPROACH

A practical EDX approach for patients with suspected myopathy is outlined in **Box 3** (adapted from other sources).[1,2]

### *Nerve Conduction Studies*

The authors usually perform routine NCSs first, expecting sensory NCSs to be normal in myopathies, unless there is a coexistent neuropathy. Motor NCSs are also generally normal, because routine motor NCSs assess distal muscles that are preserved in most myopathic processes. Exceptions in this respect are distal

**Box 1**
**Role of electrodiagnostic studies in the diagnosis of myopathies**

1. Exclude neuromuscular conditions that may mimic a myopathy
   a. Motor neuron disease
   b. Motor neuropathies
   c. Neuromuscular junction disorders
2. Provide EMG evidence of the presence of a myopathy (although EMG may be normal in the presence of selected myopathic processes)
3. Characterize the myopathy
   a. Location (proximal, distal, symmetric, or asymmetric)
   b. Presence/absence of abnormal spontaneous activity
   c. Severity
4. Identify target muscles for biopsy

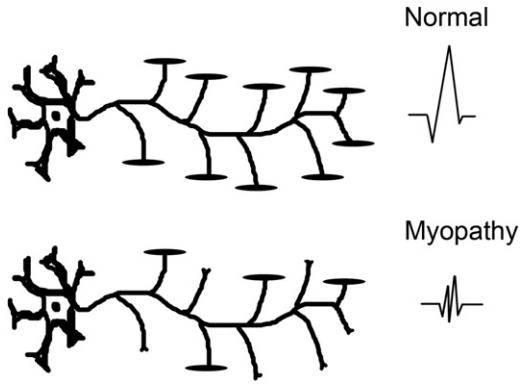


**Fig. 1.** Physiologic model of motor units in myopathies. The pathologic process in myopathies results in dysfunction and dropout of individual muscle fibers located randomly within the motor unit. Motor neurons and motor axons are not affected. As a result, each MUAP is generated by fewer motor fibers. MUAPs become polyphasic, short in duration, and low in amplitude.

myopathies (which preferentially affect distal muscles), the myopathy of intensive care (which is often generalized and may be associated with a polyneuropathy), or severe cases of myopathies that start proximally but then extend to involve distal muscles in the end-stage. If motor NCSs are affected, CMAP amplitudes are expected to be reduced, with preserved distal latencies and conduction velocities, reflecting muscle damage in the face of normal nerve function. The motor NCSs of a myopathy affecting distal muscles may be similar to the ones seen in motor neuron disorders and presynaptic neuromuscular junction transmission disorders. The former are differentiated from a myopathy based on clinical history and needle EMG findings. The latter are ruled out with additional studies (discussed later).

The authors usually perform at least one motor and one sensory conduction study from one upper extremity and one lower extremity (eg, ulnar motor, ulnar sensory, tibial, and sural NCSs).

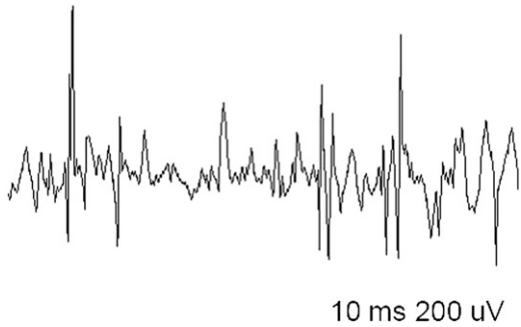


**Fig. 2.** Morphology and recruitment pattern of MUAPs in myopathies. Myopathies are characterized by the presence of polyphasic, short-duration, low-amplitude MUAPs. Because each small motor unit is able to generate only a reduced amount of force compared with normal, with little muscle contraction, many MUAPs are recruited.

**Box 2**
**Myopathies associated with muscle membrane irritability/myotonic discharges on EMG**

1. Inflammatory myopathies (often)
   a. Polymyositis
   b. Dermatomyositis
   c. Inclusion body myositis (IBM)
   d. Immune-mediated necrotizing myopathy (with or without association with cholesterol-lowering agents)
2. Toxic/necrotic myopathies (often)
   a. Cholesterol-lowering agent myopathies (eg, statin myopathies)
   b. Critical illness myopathy
   c. Chloroquine/hydroxychloroquine
   d. Amiodarone
   e. Colchicine
3. Muscular dystrophies, including the distal muscular dystrophies/myopathies, hereditary inclusion body myopathies, and the myofibrillar myopathies
4. Congenital myopathies (some)
   a. Nemaline rod myopathy
   b. Centronuclear/myotubular myopathy
   c. Central core myopathy
   d. Multicore/minicore myopathy
5. Myopathies associated with selected infectious agents
   a. HIV and human T-lymphotropic virus 1–associated myositis
   b. Trichinosis
   c. Toxoplasmosis
6. Metabolic myopathies (some)
   a. GDS II (acid alpha-glucosidase deficiency or Pompe disease)
   b. GSD III (debrancher enzyme deficiency)
   c. GSD IV (branching enzyme deficiency)
   d. Lipid storage myopathies
7. Myotonic disorders
   a. Myotonic dystrophy type 1 (DM1) and myotonic dystrophy type 2 (DM2)
   b. Myotonia congenita, paramyotonia congenita (PMC), potassium-aggravated myotonias
   c. Hyperkalemic periodic paralysis

Depending on the differential diagnosis and the patient comorbidities, additional studies may be needed. Neuromuscular junction disorders generally present with fatigable proximal more than distal muscle weakness. In these circumstances, repetitive nerve stimulation studies of at least one distal and one proximal muscle should be performed. If the amplitudes of the CMAPs are reduced, it is necessary to rule out a presynaptic neuromuscular junction disorder, such as Lambert-Eaton myasthenic

**Box 3**
**Suggested EDX protocol for the assessment of a suspected myopathy**

1. Routine NCSs
   a. At least one motor and one sensory conduction study from one upper extremity and one lower extremity (eg, ulnar motor, ulnar sensory, tibial, or sural)

Comments

- If there is a clinical history of fatigability, consider repetitive nerve stimulation studies of at least one distal and one proximal muscle to evaluate for neuromuscular junction disorders.
- If the amplitudes of the compound muscle action potentials (CMAPs) are reduced, exercise the muscle maximally for 10 seconds, then repeat a single supramaximal stimulation. A significant (>100% of baseline) increment in CMAP amplitude is suggestive of a presynaptic neuromuscular junction disorder.
- If there is clinical suspicion for a myotonic disorder, consider performing short and long exercise tests.

2. EMG
   a. At least one proximal and one distal muscle from one upper extremity (eg, deltoid, biceps, extensor digitorum communis, or first dorsal interosseous)
   b. At least one proximal and one distal muscle from one lower extremity (eg, iliopsoas, vastus lateralis, tibialis anterior, or gastrocnemius)
   c. Thoracic paraspinals

Comments

- The number and location of muscles studied depends on the pattern of weakness.
- It is best to study muscles that are clinically weak.
- If both sides are affected equally, perform EDX on the dominant side. Muscle biopsy then is performed on the nondominant side.
- It is best to study muscles that can be easily biopsied on the contralateral side (eg, deltoid, biceps, extensor digitorum communis, or vastus lateralis).
- If results of routine EMG are indeterminate, consider quantitative MUAP analysis.

syndrome. This can be generally accomplished by exercising the muscle maximally for 10 seconds and repeating a single supramaximal stimulation. A significant increment in CMAP amplitude is suggestive of a presynaptic neuromuscular junction disorder (**Fig. 3**). The cutoff for significant CMAP increase has traditionally been considered greater than 100% of baseline, although recent studies suggest that a cutoff of 60% may provide better sensitivity without sacrificing specificity in the appropriate clinical setting.[3] Finally, if there is clinical suspicion for a channelopathy, short and long exercise tests may be considered to help narrow down the differential and direct genetic testing (discussed later and by Fournier and colleagues[4,5]).

### *Electromyography*

Needle EMG examination is the most informative part of the EDX study in myopathic disorders.[6,7] It can confirm the presence of a myopathy, narrow down the differential, and identify an appropriate biopsy site. The number and location of muscles studied depends on the pattern of weakness. At a minimum, the authors recommend studying one proximal and one distal muscle from one upper extremity and from one lower extremity as well as the thoracic paraspinals. This may be sufficient when there is

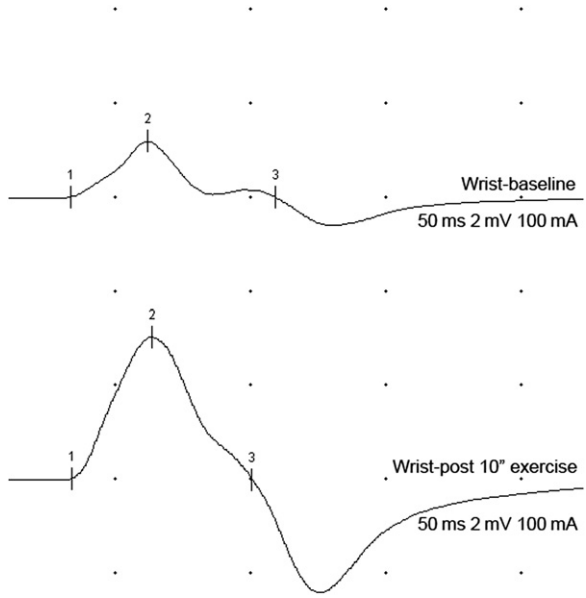


**Fig. 3.** Incremental response to brief exercise in Lambert-Eaton myasthenic syndrome. The upper trace shows the baseline ulnar-abductor digiti minimi CMAP stimulating at the wrist. Baseline CMAP amplitude was reduced compared with normal (1.2 mV). The lower trace shows the ulnar CMAP stimulating at the wrist immediately after 10 seconds of isometrically resisted finger abduction. The amplitude of the ulnar CMAP post 10 seconds of exercise was 3 mV.

a high clinical suspicion of myopathy and a patient does not have comorbidities that may affect the needle study (such as a radiculopathy or entrapment neuropathy). Commonly assessed muscles include the deltoid, biceps, triceps, pronator teres, extensor digitorum communis, first dorsal interosseous, gluteal muscles, iliopsoas, vasti, tibialis anterior, and gastrocnemius. Additional muscles may be selected depending on a patient's pattern of weakness and the clinical suspicion. For example, finger flexors are often evaluated in suspected IBM because they tend to be preferentially affected in this condition. Because most myopathies generally involve proximal muscles first, the diagnostic yield increases when more proximal muscles are sampled. The paraspinals are the most proximal muscles that can be examined and may be the only ones with abnormalities in selected myopathies, such as Pompe disease. Instead of cervical or lumbosacral thoracic paraspinals are examined because they are less likely to be affected by unrelated processes, such as nerve root impingement secondary to degenerative spine disease.

The yield of needle EMG increases if clinically weak muscles are studied. EMG is more sensitive than clinical examination and may reveal abnormalities in muscles that, clinically, were believed spared. This is particularly helpful when a decision needs to be made with regards to which muscle to biopsy. Commonly biopsied muscles include the deltoid, biceps, and vasti, and, occasionally, the extensor digitorum communis and tibialis anterior. The gastrocnemius is also easily accessible, but muscle biopsy results may be confounded by the presence of unrelated chronic neurogenic changes secondary to preganglionic neuropathy, which are commonly encountered in asymptomatic individuals. In some patients, the only clinically weak muscles are

not readily accessible for biopsy, such as the hip girdle muscles. In these circumstances, the value of the EMG is to identify suitable targets for biopsy. It is best not to biopsy a muscle where needle EMG has been recently performed in order not to mistake inflammatory changes secondary to needle insertion for true pathologic findings. If both sides are affected equally, the authors perform needle EMG on the dominant side. Muscle biopsy then is performed on the nondominant side, which is generally more comfortable for the patient, especially if an upper extremity is biopsied.

The analysis of spontaneous activity is helpful in narrowing down the differential diagnosis. Muscle membrane irritability, in the form of increased insertional activity, fibrillation potentials, and positive sharp waves (PSWs), is characteristic of certain myopathies but not others (inflammatory and toxic/necrotic processes, muscular dystrophies, and selected congenital and metabolic disorders [see **Box 2**]). Although fibrillation potentials and PSWs are often colloquially referred to as denervating potentials, the authors do not favor this term. Denervation implies the presence of an underlying neurogenic pathophysiologic mechanism. Fibrillation potentials and PSWs may, however, also be present in myopathic disorders when the muscle membrane is irritable due to the presence of inflammation or necrosis. Thus, these myopathies are reported as myopathy with muscle membrane irritability or membrane instability and include inflammatory and toxic/necrotic processes, muscular dystrophies and selected congenital and metabolic disorders.

Occasionally, in chronic myopathies, complex repetitive discharges (CRDs) may be seen. This type of abnormal spontaneous activity is nonspecific and simply speaks to the chronic nature of the underlying process. Alternatively, myotonic discharges yield additional diagnostic information (see **Box 2**). Myotonic discharges, similarly to fibrillations, PSWs and CRDs, are generated at the muscle fiber level. Although their morphology is similar to fibrillations and PSWs, they characteristically wax and wane in both frequency and amplitude. They are typically seen in myotonic disorders, such as DM1 and DM2, myotonia congenita, PMC, potassium-aggravated myotonias, and potassium-sensitive periodic paralysis. In addition, electrical myotonia may be occasionally encountered in selected myopathies that do not present with clinical myotonia, including inflammatory myopathies, metabolic myopathies (eg, Pompe disease), and toxic myopathies (see **Box 2**).

Finally, there are some circumstances when the normal insertional activity generated by needle insertion is decreased. This may occur in chronic end-stage myopathies, when electrically active muscle fibers are replaced by fat or connective tissue, typically in muscular dystrophies or, occasionally, in long-standing inflammatory myopathies. The electromyographer may also feel increased resistance to needle advancement due to the fibrotic nature of the remaining muscle. Decreased insertional activity may also been seen in patients with certain glycogen storage disorders, such as McArdle disease, experiencing a contracture in that muscle or during an episode of severe weakness from periodic paralysis.

Analysis of motor unit action potential (MUAP) morphology and recruitment pattern is the key element of needle EMG that helps establish the diagnosis of a myopathy. In myopathic processes, there is dropout or dysfunction of individual muscle fibers (see **Fig. 1**). Thus, the size of the motor unit decreases. The number of available motor units does not change because the pathologic process occurs distal to the motor axons. This results in the emergence of short, small, polyphasic MUAPs (see **Figs. 1** and **2**). Sometimes, this combination of findings is referred to as myopathic unit. The authors discourage the use of this term because similar MUAPs may be occasionally found in neurogenic and neuromuscular junction disorders and, therefore, do not always imply a primary muscle disease. Most notably, they may be

seen in early reinnervation after severe denervation (nascent motor units) when each motor unit is composed of only few fibers that have successfully reinnervated. More rarely, they may be seen in neuromuscular junction disorders when there is significant block resulting in functional dropout of individual muscle fibers within each motor unit.

When analyzing MUAP morphology, 3 parameters are evaluated: duration, amplitude, and number of phases. In myopathies, MUAP duration and amplitude both decrease, whereas the number of phases increases; hence MUAPs are brief, small, and polyphasic (see **Figs. 1** and **2**). The most important of these parameters is MUAP duration. The decrease in MUAP duration most closely reflects the decrease in the total number of muscle fibers per motor unit, including those that are located at a distance from the recording electrode. Acoustically, this corresponds to a crisp, high-pitch sound. To diagnose a myopathy, however, many MUAPs should be analyzed per muscle and the results compared with what is normally expected for that particular muscle. There is a range of MUAP duration, influenced by age (MUAP duration increases with age) and muscle studied (eg, some small facial muscles normally have much smaller MUAPs than big limb muscles). Mean MUAP duration is reduced in myopathies, although some of the MUAPs may still be normal.

Occasionally, the results of qualitative needle EMG are indeterminate. This may occur when there are only subtle MUAP changes. In such cases, if there is a high clinical suspicion of an underlying myopathy, quantitative MUAP analysis may be performed to increase the diagnostic yield. This is accomplished using standard EMG equipment. Quantitative data regarding the duration of at least 20 MUAPs are collected. Results are then compared with established age-matched, muscle-specific normative values (for a complete description of quantitative EMG and normative data, see Nandedkar and colleagues[8]).

In a myopathy, these short, small, polyphasic, high-pitch MUAPs display a characteristic early recruitment pattern. Because each motor unit is smaller than normal, it can generate only a small amount of force. Therefore, to produce even a small amount of power, individuals need to recruit many MUAPs that fill the screen early on during muscle contraction (see **Fig. 2**). Only the electromyographer performing the study can adequately identify recruitment as early because how much force is being generated to make such an assessment needs to be known. Importantly, in myopathies, a full interference pattern is seen even in very weak muscles, with many units firing at the same time but producing little power. This is in contrast to weakness secondary to neurogenic processes or central processes. In the former, the interference pattern is not full due to the loss of available motor units. The remaining motor units fire rapidly as a compensatory mechanism creating the pattern of reduced recruitment with rapid firing. In the latter, recruitment is actually normal, but the interference pattern is not full due to lack of activation, with resulting slow firing rate.

The only exception to the pattern of short, small, polyphasic MUAPs with early recruitment (described previously) is cases of end-stage muscle that may occasionally be seen in severe chronic myopathies. If all the muscle fibers of an individual motor unit are lost, there is a reduction in the number of available motor units resulting in reduced recruitment. Some reinnervation and motor unit remodeling may also occur overtime and a mixed population of short and long duration MUAPs may occasionally be seen in severe chronic myopathies, such as IBM, long-standing polymyositis and dermatomyositis, and end-stage muscular dystrophies. Finally, as discussed previously, short, small, polyphasic MUAPs may also be seen in nascent motor units. In these cases, recruitment of such units is reduced, reflecting the reduced number of motor units available due to the underlying neurogenic process.

## EDX PATTERNS IN SELECTED MYOPATHIES

### *Muscular Dystrophies*

The muscular dystrophies are a group of hereditary, progressive muscle disorders characterized by necrosis of muscle tissue and replacement by connective and fatty tissue.[9] The best-known muscular dystrophies are the dystrophinopathies (Duchenne muscular dystrophy [DMD] and Becker muscular dystrophy [BMD]), which are caused by mutations in the gene encoding the muscle protein dystrophin.[10] EDX testing is of limited utility in the dystrophinopathies, particularly when there is a positive family history. Definitive diagnosis requires genetic testing and, at times, muscle biopsy. EDX testing may be helpful, however, in sporadic cases of DMD and in BMD, which may have a more benign phenotype and a broader differential diagnosis. If needle EMG is performed in a patient with a dystrophinopathy, it typically reveals increased insertional and spontaneous activity in the form of fibrillation potentials and PSWs, along with brief, small, polyphasic MUAPs with early recruitment. In the end stages of the disease, however, when muscle is replaced by connective and fatty tissue, the insertional activity is reduced and a mixed population of short and long duration MUAPs might be appreciated, reflecting the chronicity of the disease process.[11,12]

EDX testing is more helpful in the other muscular dystrophies, in which CK levels may be only mildly elevated and the differential diagnosis is broader. EDX findings again include abnormal spontaneous activity (fibrillation potentials and PSWs) and short, small, polyphasic MUAPs with early recruitment. The pattern of muscle involvement, such as limb girdle versus distal, depends on the specific disease process.

### *Polymyositis/Dermatomyositis*

Polymyositis and dermatomyositis are idiopathic inflammatory myopathies that are characterized on needle EMG by the presence of prominent muscle membrane irritability (fibrillations, PSWs, and even myotonic discharges), especially in proximal muscles.[13,14] MUAPs are small, short, and polyphasic and recruit early. These abnormal features do not distinguish inflammatory myopathies from other myopathies with muscle membrane instability. In long-standing disease, a mixed population of small and long duration MUAPs may be seen (discussed previously).

The degree of abnormal muscle membrane irritability is believed to reflect the ongoing disease activity. Many patients with inflammatory myopathies are treated with high-dose steroids. Some may develop new weakness after a period of symptom improvement on steroids. In these cases, it needs to be determined whether the new weakness is secondary to an increase in disease activity or is attributable to type 2 muscle fiber atrophy, which may occur from disuse or chronic steroid administration. Abnormal spontaneous activity is expected in active myositis, although it is not associated with isolated type 2 muscle fiber atrophy (discussed later).

### *Inclusion Body Myositis*

IBM is an idiopathic inflammatory myopathy that presents generally after the age of 50 years with slowly progressive weakness. The clinical hallmark of IBM is early involvement of the quadriceps, wrist and finger flexors, and ankle dorsiflexors. The clinical diagnosis is often elusive and many patients have been misdiagnosed with other inflammatory myopathies.[15] Unfortunately, patients with IBM do not typically respond to immunosuppressive therapies. EDX studies are nonspecific and may actually provide additional diagnostic confusion. Fibrillations and PSWs are common and, early in the course, are associated with small, short, polyphasic MUAPs. Due to the insidious nature of the myopathic process, however, many patients also exhibit large,

long MUAPs, reflecting the chronicity of the disease.[15,16] Although the morphology of these units may resemble those seen in a chronic neurogenic process, the recruitment pattern in IBM is early pointing toward a myogenic basis. In addition, approximately a third of the patients also demonstrate a mild axonal sensory polyneuropathy on nerve conduction studies.

### *Toxic/Necrotic Myopathies*

Toxic/necrotic myopathies may be induced by several drugs, such as the lipid-lowering agents, or by multifactorial mechanisms, such as in the setting of a critical illness. Asymptomatic CK elevation is common in patients taking lipid-lowering agents. In the absence of symptoms, EMG is often normal. More rarely, these same agents may trigger a toxic myopathy and result in clinical weakness. In these circumstances, fibrillations, PSWs, and even myotonic discharges with early recruitment of short-duration MUAPs become apparent in weak muscles.[17,18]

Patients in an ICU may develop generalized weakness due to critical illness polyneuropathy or myopathy.[19,20] It can be difficult to differentiate between these two conditions and patients can present with a combination of the two. Distal and proximal muscles are both affected. Nerve conduction studies demonstrate low CMAP amplitudes without any evidence of demyelination. Sensory nerve action potential may also be reduced in amplitude if there is a concomitant polyneuropathy or from technical reasons if there is third spacing and edema, which are not uncommon in critically ill patients. Needle EMG shows prominent muscle membrane irritability as well as early recruitment of short-duration MUAPs.

### *Steroid Myopathy*

Steroid myopathy manifests as proximal muscle weakness and atrophy, affecting the leg more than the arms. The needle EMG is typically normal.[21] On histopathology, steroid myopathy is characterized by type 2B muscle fiber atrophy, which explains the paucity of findings on EDX testing. The evaluation of MUAP morphology on needle EMG is limited to the analysis of type 1 fibers, which, based on the size principle of recruitment, are the first recruited fibers. Because type 2 fibers are preferentially affected in steroid myopathy, the abnormal MUAPs they generate are not detectable because these are obscured by their initially recruited type I counterparts.

### *Pompe Disease*

Pompe disease (GSD II or acid alpha-glucosidase deficiency) is a metabolic myopathy caused by deficiency of a lysosomal enzyme, which is important in carbohydrate metabolism causing muscle weakness. It may present in a classic severe infantile form or have a later childhood or adult onset. The diagnosis of the adult-onset form may be elusive because CK levels may be normal and the pattern of weakness (generally proximal) may be confused with several other myopathies. There can be a predilection for involvement of the muscles of ventilation, with dyspnea the presenting symptom in some patients. Recognition of this disease is important because infusion of the recombinant enzyme is available. Characteristically, needle EMG in Pompe disease is irritable.[22] Abundant spontaneous activity may be present in proximal muscles and may include not only fibrillations and PSWs but also CRDs and myotonic discharges. These findings, however, in mild cases, may be limited to the paraspinal muscles.

### *Dystrophic Myotonias and Nondystrophic Myotonias*

Myotonic disorders include the myotonic dystrophies and the nondystrophic myotonias. The former, DM1 and DM2 (or proximal myotonic myopathy), are characterized by dystrophy of the muscle tissue, progressive weakness, and clinical myotonia. Most patients with DM1 and DM2 exhibit electrical myotonia, although myotonia may not necessarily be present in every muscle.[23] The distribution of electrical myotonia is predominantly distal in both the arms and legs in DM1. In DM2, electrical myotonia is seen distally in the arms, but it often affects both the proximal and distal leg muscles.[23] Finally, classic waxing-waning discharges (true electrical myotonia) predominate in DM1. Alternatively, in DM2, a less specific waning pattern (ie, spontaneous discharges that only wane in frequency or amplitude, or pseudomyotonia) is more common, making the electrodiagnosis of DM2 more challenging.[23]

The nondystrophic myotonias are caused by mutations in different ion channels (hence, the alternative name, channelopathies) and manifest with various phenotypes (stiffness, myotonia, and episodes of transient weakness in variable combinations) without dystrophic changes in the muscle tissue.[24] Needle EMG may identify myotonic discharges in myotonia congenita, PMC, potassium-aggravated myotonias, and, at times, hyperkalemic periodic paralysis. Clinical and electrical myotonia are absent in hypokalemic periodic paralysis. Nerve conduction studies play an important role in differentiating among these disorders because specific patterns may be recognized on short and long exercise tests helping to direct genetic testing.

The short and long exercise tests are variations of standard motor nerve conduction studies.[5,6] They are typically performed on the ulnar nerve, recording from the abductor digiti minimi. The CMAP amplitude is measured 3 to 5 times before exercise to ensure a stable baseline. For the short exercise test, the patient is instructed to isometrically activate the selected muscle for 10 seconds. This is followed by serial assessment of the CMAP amplitude immediately after exercise and then every 10 seconds for 1 minute. A normal response includes a transient 5% to 10% increase in CMAP amplitude immediately after exercise with normalization within 10 seconds. Typically, 3 subsequent trials are performed. The same protocol may also be repeated after limb cooling, particularly if PMC is suspected (discussed later).

**Box 4**
**Myopathies that may have a normal EMG**

1. Type II muscle atrophy
   a. Steroid myopathy
   b. Disuse myopathy
2. Some mitochondrial myopathies
3. Some congenital myopathies
4. Metabolic myopathies with dynamic[a] phenotype if not performed during acute exacerbations
   a. GSD V (McArdle disease or myophosphorylase deficiency)
   b. GDS VII (phosphofructokinase deficiency)
   c. Carnitine palmityltransferase II deficiency

[a] Here, metabolic myopathies are referred to as having a dynamic phenotype when they are associated with exercise-induced symptoms (exertional myalgias, cramps, and myoglobinuria) as the dominant clinical features.

**Box 5**
**Myopathies that may have a normal CK level**

A normal or only mildly elevated CK level does not preclude the following diagnoses in the appropriate clinical context:

- Dermatomyositis
- IBM
- Congenital myopathies
- Metabolic myopathies
- Mitochondrial myopathies

More rarely, some of the muscular dystrophies (limb-girdle, facioscapulohumeral, scapuloperoneal, Emery-Dreifuss, and oculopharyngeal and distal) may be present with normal or only mildly elevated CK levels.

The long exercise test involves isometric contraction of the selected muscle for 5 minutes, with periods of brief rest (3 to 4 seconds) every 30 to 45 seconds during the exercise. This is followed by sequential CMAP measurements immediately after exercise, then every minute for the first 5 minutes after exercise, and finally every 5 minutes for approximately 45 minutes. In normal subjects, a transient mild decrease in CMAP amplitude (5%–10%) is observed immediately after exercise, but the CMAP amplitude normalizes within 1 min and remains stable for the remainder of the test.

**Box 6**
**Diagnostic studies used to characterize myopathic processes**

*Often performed to diagnose a myopathy*

1. CK levels
2. Thyrotropin, electrolytes, renal and liver function tests, complete blood count, erythrocyte sedimentation rate, and serum protein electrophoresis/immunofixation
3. Genetic testing (hypothesis-driven, step-wise; avoid panels)
4. NCS/EMG
5. Muscle biopsy (if above are nondiagnostic)

*Used only within the appropriate clinical context, to further characterize a myopathy*

1. ECG and echocardiogram
2. Pulmonary function tests
3. Videofluoroscopic swallow studies
4. Exercise forearm test with measurement of lactate and ammonia.
5. Malignancy work-up (occult malignancies may be associated with inflammatory and necrotizing myopathies)
6. Antinuclear antibody, rheumatoid factor, and antibodies to extractable nuclear antigens (connective tissue disorders may be associated with inflammatory and necrotizing myopathies)
7. Myositis-specific antibodies (especially Jo-1, which may indicate concurrent interstitial lung disease in patients with inflammatory and necrotizing myopathies)

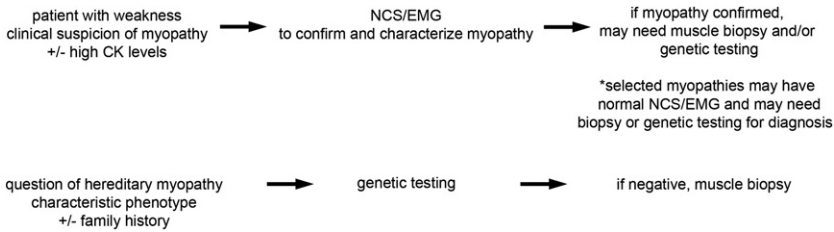


**Fig. 4.** Suggested algorithm to diagnose a myopathic process.

The short exercise test may identify characteristic response patterns in some patients with PMC and myotonia congenital (MC). In PMC, there may be a decrement in the CMAP amplitude compared with baseline that worsens with successive stimuli and trials.

Typically, performing the short exercise test after limb cooling bring out even more marked reductions in CMAP amplitude. In MC, the short exercise test may be normal (usually in the autosomal dominant form) or abnormal (in the autosomal recessive form). The abnormal pattern seen in autosomal recessive MC includes an initial CMAP reduction immediately after exercise that improves with successive stimuli returning to baseline within 1 minute. Such CMAP amplitude reduction is less marked during subsequent trials. The long exercise test is most useful to identify hereditary periodic paralysis. In periodic paralysis, there is an early increase in CMAP amplitude immediately after exercise that is followed by a gradual delayed decrease over a prolonged period of time. The long exercise test is also abnormal in PMC, with early decrease in CMAP amplitude immediately after exercise that may persist for hours. For a more detailed description of these techniques, readers are referred to the seminal articles by Fournier and colleagues.[5,6]

## SUMMARY

In summary, EDX studies may play an important role in the evaluation of patients with suspected myopathies (**Boxes 4** and **5**). Although multiple diagnostic tests are often used to work-up a patient (**Box 6**), they are often expensive and uncomfortable for the patient. Thus, the authors cannot emphasize enough that these tools should be used judiciously in a step-wise, hypothesis-driven fashion. A comprehensive history and physical examination along with pattern recognition are invaluable in directing further testing, so as to avoid unnecessary tests and, most importantly, interpret test results correctly (**Fig. 4**).

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