

Clinical Approach to the Weak Patient in the Intensive Care Unit

Upinder K Dhand MD

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Motor weakness in a patient in the intensive care unit (ICU) may be related to (1) pre-existing neuromuscular disorder that leads to ICU admission, (2) new-onset or previously undiagnosed neurological disorder, or (3) complications of non-neuromuscular critical illness. Neuromuscular syndromes related to ICU treatment consist of critical illness polyneuropathy, critical illness myopathy, and prolonged neuromuscular blockade, and are now recognized as a frequent cause of newly acquired weakness in ICU patients. Clinical features include quadriplegia, muscle wasting, and difficulty weaning from the ventilator. Evaluation of these patients is based on knowledge of

clinical setting and predisposing factors, focused neurological examination, detailed electrophysiological investigation, serum creatine kinase level, other laboratory studies as needed, and histological examination of muscle biopsy. If a central nervous system (brain or spinal cord) lesion is suspected, neuroimaging studies are required. In addition to conventional nerve conduction and needle electromyography, phrenic nerve conduction, diaphragm electromyography, blink reflex, and (recently) the technique of direct muscle stimulation have been employed. Critical illness polyneuropathy is an axonal motor and sensory neuropathy that often follows sepsis and multiorgan failure. Risk factors for critical illness myopathy are corticosteroids and neuromuscular blocking drugs, acute respiratory illness, and organ transplant. Three subtypes (acute necrotizing myopathy, thick myosin filament loss myopathy, and type II fiber atrophy) are recognized. Major differential diagnoses of critical illness related paralysis are incidental Guillain-Barré syndrome and unmasked myasthenia gravis. Rarely, atypical presentation of amyotrophic lateral sclerosis, polymyositis or other myopathies, and precipitation of porphyria or rhabdomyolysis due to drugs used in the ICU have been described. Recently a poliomyelitis-like flaccid paralysis due to West Nile virus infection was reported. A subgroup of patients with myasthenia gravis with muscle-specific tyrosine kinase antibody is noted to present as respiratory crisis. Muscle biopsy in ICU paralysis syndromes may be helpful in arriving at a specific diagnosis or to classify the type of critical illness myopathy. Nerve biopsy is only rarely indicated. *Key words: critical illness polyneuropathy, critical illness myopathy, electrodiagnosis, flaccid quadriplegia, Guillain-Barré syndrome, intensive care, myasthenia gravis, neuromuscular disorders.* [Respir Care 2006;51(9):1024–1040. © 2006 Daedalus Enterprises]

Introduction

Historically, neuromuscular disorders such as poliomyelitis, Guillain-Barré syndrome, myasthenia gravis, and amyotrophic lateral sclerosis (ALS) have been among the commonest causes of generalized and respiratory muscle weakness that require admission to the intensive care unit (ICU).^{1–3} Management of these patients with acute severe neuromuscular weakness in the modern ICU has led to substantial improvement in mortality and morbidity from these disorders.⁴ However, there has been increasing awareness of new onset neuromuscular weakness in patients with non-neurological critical illness. In 1984, Bolton et al⁵ described severe polyneuropathy in 5 patients with critical illness, who had developed flaccid weakness of extremities and could not be weaned from the ventilator as their critical illness stabilized. They characterized it as axonal motor and sensory neuropathy and distinguished it from acute neuropathy of Guillain-Barré syndrome.⁶ About that time, acute quadriplegic myopathy was also reported in

ICU patients, especially those with status asthmaticus who had received neuromuscular junction blocking agents and corticosteroids.⁷ Experience from various centers all over the world in the last 2 decades has established neuromuscular weakness as an important complication of critical illness in the ICU.^{8–13} Three relatively distinct syndromes (critical illness polyneuropathy [CIP], critical illness myopathy [CIM], and prolonged neuromuscular blockade) have been recognized.^{5,8,10,14–19}

Recent literature has substantially contributed to our understanding of the pathophysiology and risk factors of these syndromes, but it has also generated controversy regarding the relative incidence, causative mechanisms, nosological description, and mode and extent of clinical investigations.^{20–24} Clinically, the difficulties stem from the fact that examination of ICU patients is often unreliable, laboratory findings of the ICU-related syndromes may overlap, and different syndromes may coexist in the same patient.^{8,22,25} Despite these limitations, the aim of clinical assessment of an ICU patient with generalized weakness is to distinguish critical illness related complications from other neurological causes, and to define the specific nature of neuromuscular weakness due to critical illness.

Understanding the Causes of Weakness in ICU Patients

Causes of generalized weakness in the ICU setting may be considered in the context of (1) pre-existing versus new-onset weakness, and (2) localization of the disease

Upinder K Dhand MD is affiliated with the Department of Neurology, University of Missouri, Columbia, Missouri.

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Correspondence: Upinder K Dhand MD, Department of Neurology, University of Missouri, 1 Hospital Drive, M178, Columbia MO 65212. E-mail: dhandu@health.missouri.edu.

CLINICAL APPROACH TO THE WEAK PATIENT IN THE INTENSIVE CARE UNIT

Table 1. Classification of Neurological Causes of Motor Weakness in Intensive Care Unit Patients

Localization	Pre-existing	Previously Undiagnosed/New-Onset	Critical Illness Related
Spinal cord	Trauma	Acute ischemia	Not described
	Infarction	Epidural abscess	
	Transverse myelitis	Acute transverse myelitis	
Anterior horn cell	Amyotrophic lateral sclerosis	Amyotrophic lateral sclerosis	Hopkins syndrome
	Poliomyelitis (West Nile virus)	(predominant diaphragm weakness) West Nile virus poliomyelitis	
Peripheral nerve	Guillain-Barré syndrome	Incidental Guillain-Barré syndrome	Critical illness polyneuropathy
	Chronic inflammatory demyelinating polyneuropathy	Porphyria, vasculitis, toxic, compressive	
Neuromuscular junction	Myasthenia gravis	Unmasked myasthenia gravis	Prolonged neuromuscular blockade
	Lambert-Eaton syndrome	Atypical myasthenia gravis (predominant respiratory weakness, muscle-specific tyrosine kinase antibody)	
	Botulism	Toxic	
Muscle	Muscular dystrophy	Rhabdomyolysis	Critical illness myopathy
	Polymyositis	Toxic myopathies	
	Periodic paralysis	Polymyositis	
	Metabolic/congenital	Myotonic dystrophy	
	Mitochondrial	Adult-onset acid maltase deficiency	
		Pyomyositis	
		Hypokalemic	
		Hypophosphatemic	

process within the nervous system. Various pre-existing neurological disorders, such as Guillain-Barré syndrome, myasthenia gravis, ALS, spinal cord injury, and myopathies that lead to ICU admission are well known.^{2,26-28} New onset generalized extremity and/or respiratory muscle weakness may be further divided into previously undiagnosed/newly acquired neurological disorders, and critical illness related disorders. Some examples of neurological disorders that may occur after admission to ICU are Guillain-Barré syndrome following infective illness or surgery, spinal cord infarct after aortic surgery, and muscle weakness due to severe electrolyte disorder.

In addition, certain disorders may be unmasked (eg, myasthenia gravis) or precipitated (eg, rhabdomyolysis) by infection or medications used in the ICU.²⁸⁻³⁰ Finally, patients with rapidly progressive weakness and respiratory compromise (Guillain-Barré syndrome, acute transverse myelitis) may get admitted to ICU before there is enough time to establish the diagnosis, or patients with unusual presentation of isolated/predominant respiratory muscle weakness (ALS, myotonic muscular dystrophy) may remain unrecognized for a considerable time after admission to the ICU.²⁶⁻²⁸

However, neuromuscular disorders as a consequence of critical illness are now recognized as the most important cause of newly acquired weakness in the ICU. Occurrence of CIP, CIM, or a combination of the two is reported in 30-50% of

patients with critical illness. A study of 92 patients with neuromuscular weakness in an ICU reported CIM in 42%, CIP in 12%, demyelinating neuropathy in 13%, motor neuron disease in 7%, neuromuscular junction disorders in 3%, and other neuropathies in 13% of those patients.³¹

Another approach, which is very relevant to clinical assessment, is to classify the causes of weakness in an ICU patient according to central (intracranial) nervous system, spinal cord, and peripheral (neuromuscular) lesions. Neuromuscular disorders are, in turn, best understood as affecting different parts of the motor unit. By definition, the motor unit consists of the anterior horn cell body, its axon, terminal nerve endings, and the number of muscle fibers that it innervates.³² It is helpful to divide neuromuscular disorders based on involvement of components of the motor unit: the anterior horn cell, peripheral nerve, neuromuscular junction, and muscle. Table 1 summarizes the pre-existing and new onset causes of weakness in relation to site of involvement. The neuromuscular complications of critical illness, as noted, also affect all the components of the motor unit.

Clinical Assessment

Onset of weakness in ICU patients may not be appreciated in the presence of severe underlying systemic ill-

ness, sedation, and encephalopathy. It is often brought to attention because of flaccidity and wasting of extremities or difficulty in weaning the patient from mechanical ventilation. Evaluation of such a patient requires a systematic approach and consideration of special aspects of the ICU environment.

Limitations of Neurological Examination in the ICU

It is often difficult to elicit patients' cooperation because of inability to communicate, poor attention, sedation, and fatigability. Muscle strength testing may be inadequate and sensory examination not reliable. Acute motor deficits due to central nervous system (upper motor neuron) injury may cause hypotonia and hyporeflexia similar to lower motor-neuron lesions, and clinical differentiation between central and peripheral causes becomes difficult.³³ Also, neuromuscular and central nervous system (CNS) involvement may be coincidental. Knowledge of clinical background or setting in which the weakness evolves is an important guide to differential diagnosis

Clinical Setting of Motor Weakness

Preceding or underlying illness and its treatment in the ICU may have bearing on the nature of motor weakness. CIP often follows sepsis, systemic inflammatory response syndrome, and multiorgan failure,^{5,9,34} whereas CIM often occurs in the setting of treatment with intravenous corticosteroids and nondepolarizing neuromuscular blocking agents.^{7,16,35,36} Patients with asthma, pneumonia, organ transplant, and renal failure seem to be predisposed to development of CIM.^{36,37} Guillain-Barré syndrome may follow an antecedent infective illness, surgery, or trauma for which the patient may have been initially admitted to the ICU.³ Neuromuscular blocking agents and aminoglycosides may unmask latent myasthenia gravis. Similarly, drugs, infection, or trauma may precipitate rhabdomyolysis.^{30,38} The list of medications received by the patient in the ICU should always be checked (Table 2).

Neurological Examination

Central Nervous System Lesions

It is useful to proceed systematically to exclude CNS (intracranial) causes of weakness. These may coexist with neuromuscular disorders or be solely responsible for neurological impairment. Three major features point toward CNS involvement: asymmetric neurologic signs (right or left cerebral hemisphere), altered mental status (encephalopathy), and cranial nerve palsies (brain stem). Appropriate imaging (computed tomography, magnetic resonance imaging) and electroencephalogram usually provide the

Table 2 Drugs Associated With Neuromuscular Weakness in the Intensive Care Unit

Peripheral Nerve
Cancer chemotherapy
Amiodarone
Metronidazole
Neuromuscular Junction
Nondepolarizing neuromuscular blocking agents (vecuronium, pancuronium)
Aminoglycosides, clindamycin, polymyxin-B
Beta blockers
Calcium-channel blockers
Procainamide
Phenytoin, fosphenytoin
Hypermagnesemia
Muscle
Corticosteroids
Colchicine
Amiodarone
Procainamide
Penicillamine
Cholesterol-lowering drugs
Zidovudine

diagnosis. Important CNS processes to be considered for generalized weakness are brain stem infarct, hemorrhage, or central pontine myelinolysis, which may result in "locked-in" syndrome. Various neuromuscular disorders with generalized extremity, bulbar, and ocular involvement (eg, Guillain-Barré syndrome, myasthenia gravis, and botulism) can also mimic "locked-in" syndrome, and should be considered in the differential diagnosis if neuroimaging studies are negative. Rarely, patients with fulminant Guillain-Barré syndrome have had complete motor and sensory paralysis and absent brain stem reflexes, giving the appearance of brain death. In such patients with suspected brain death, when no cause of brain stem syndrome was detected, further investigation showed normal electroencephalogram, presence of visual evoked potentials, or preserved oculocardiac response, which refuted the diagnosis of brain death.^{39,40} CSF and electromyography studies led to diagnosis of Guillain-Barré syndrome, and some of these patients were successfully treated.

Spinal Cord Lesions

History of trauma in a patient with quadriplegia or paraplegia strongly favors traumatic spinal cord injury. However, many spinal cord lesions, such as acute transverse myelitis, epidural abscess, and spinal cord infarct, may present as pre-existing or new onset causes of generalized weakness in ICU patients. In the presence of flaccid weakness due to spinal shock, upper versus lower motor neuron paralysis cannot be distinguished. Presence of sensory level

on trunk, Babinski sign, flexor spasms, loss of anal reflex, loss of sphincter control, and arms weaker than legs are some useful signs of spinal cord involvement.^{33,38} Any suspicion of a spinal cord lesion should lead to radiologic investigation. Magnetic resonance imaging of the spine is the most useful procedure.

Neuromuscular Disorders

The main clinical features of neuromuscular diseases are weakness and wasting of extremities, hypotonia, and hyporeflexia/areflexia, with or without respiratory and/or cranial musculature involvement. It is customary to localize neuromuscular disorders to different parts of the motor unit (ie, anterior horn cell, peripheral nerve, neuromuscular junction, or skeletal muscle). Diseases of the anterior horn cell, neuromuscular junction, and muscle produce pure motor syndromes, whereas most peripheral nerve disorders have sensory and motor findings. Clinical distinction among these categories may be obscured in the ICU setting because of difficulty in eliciting signs, overlapping features, and simultaneous occurrence of more than one syndrome.^{23,33,41,42}

Some helpful clinical signs are asymmetric weakness and fasciculations (ALS, viral poliomyelitis); paresthesia, sensory deficits, and distal symmetric weakness (peripheral neuropathy); cranial nerve palsies and dysautonomia (Guillain-Barré syndrome); and combination of ptosis and weakness of eye closure (myasthenia gravis, prolonged neuromuscular junction blockade).^{28,35,38} Further investigation with biochemical studies, nerve conduction and needle electromyography (EMG), and muscle biopsy are often necessary to arrive at a definitive diagnosis.

Laboratory Evaluation

Serum creatine kinase is elevated in primary muscle disease. The highest levels ($\geq 10,000$ international units) are seen with acute necrotizing myopathy, acute polymyositis, and rhabdomyolysis.⁴³ In CIM, creatine kinase may be 10–100-fold higher than normal, peak early in illness (around 3–4 days), and tend to normalize beyond 10 days.^{28,44} Of note, creatine kinase may be elevated following trauma to muscle or after needle EMG examination. The investigations are tailored to the clinical differential diagnosis; for example, serum electrolytes for hypocalcemia, hypophosphatemia, and hypermagnesemia; immunological studies for vasculitides; and human immunodeficiency virus antibody testing and cerebrospinal fluid (CSF) examination for Guillain-Barré syndrome.

Electrophysiological Studies

Ever since the initial description of CIP, standard EMG and nerve conduction techniques have been employed

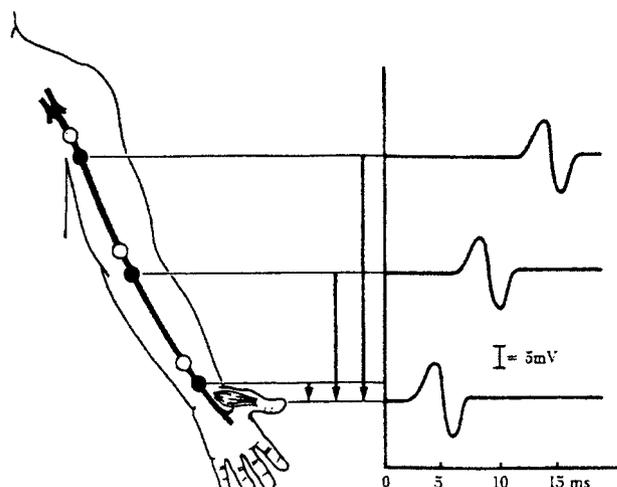


Fig. 1. Motor-nerve-conduction study. The median nerve is stimulated at the wrist, elbow, and axilla, and the recording is made from the thenar muscle. The compound muscle-action potential shows longer latency with increasing distance along the nerve. The motor-nerve conduction velocity is calculated by dividing the distance between 2 stimulation points by the difference in latency. The amplitude of the compound muscle-action potential is measured from baseline to negative peak. (From Reference 47, with permission.)

widely to identify and classify neuromuscular disorders in the ICU setting.^{5,9,19–22,26,34,41,45} Some studies specifically analyzed the data on ICU patients referred for electrophysiological investigations, whereas others prospectively evaluated the pattern of electrophysiological abnormality.^{12,31} Experience in the last 2 decades has established the role of EMG and nerve conduction study (1) to confirm the presence of neuromuscular disorder, (2) to distinguish between primary muscle, nerve, and neuromuscular junction involvement, thus narrowing the differential diagnosis, and (3) at times, to arrive at a specific diagnosis for the given clinical picture. At the same time, methodological difficulties in the ICU, complexity of interpretation of findings, and patient discomfort pose considerable challenges.^{2,8,10,16,21–23,42,46} The technical aspects and basis of interpretation of conventional nerve conduction and needle EMG, and other special techniques relevant to the ICU setting, are discussed.

Conventional Motor and Sensory Nerve Conduction

These techniques are standard, reproducible, and widely used. Percutaneous stimulation and surface recording electrodes are employed.^{47,48} Motor response is elicited by supramaximal electrical stimulation of an extremity nerve, with recording from an appropriate distal muscle innervated by that nerve (Fig. 1). The compound muscle action potential (CMAP) is the summated response of all stimulated muscle fibers within that muscle. Stimulation at 2

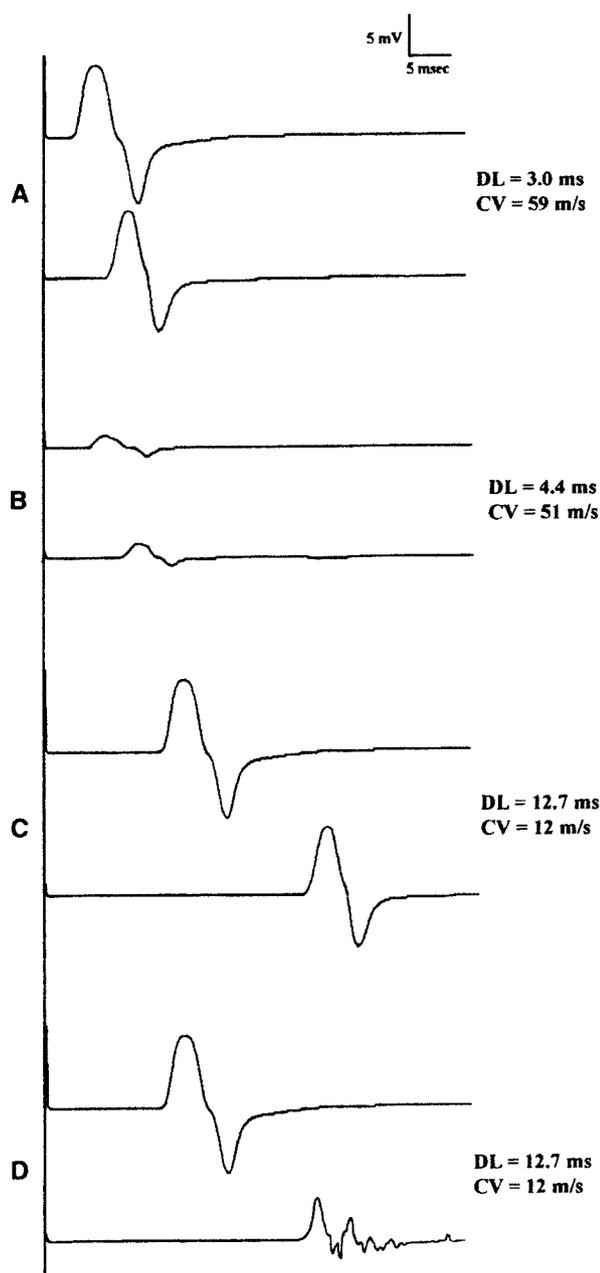


Fig. 2. Patterns of motor nerve conduction abnormality. A: Normal conduction velocity and compound muscle action potential (CMAP) amplitude. B: Normal conduction velocity with reduced CMAP amplitude, which suggests axonal neuropathy or axonal loss. C: Markedly slow conduction with normal CMAP amplitude, consistent with demyelinating neuropathy. D: Slow conduction with reduced amplitude and temporal dispersion of CMAP on proximal stimulation, which signifies conduction block and focal demyelination. DL = distal latency. CV = conduction velocity. (From Reference 46, with permission.)

points along the nerve is required to calculate motor nerve conduction velocity in that segment. Distal motor latency alone cannot be used to calculate motor conduction velocity, because it incorporates the delay at the neuromuscular

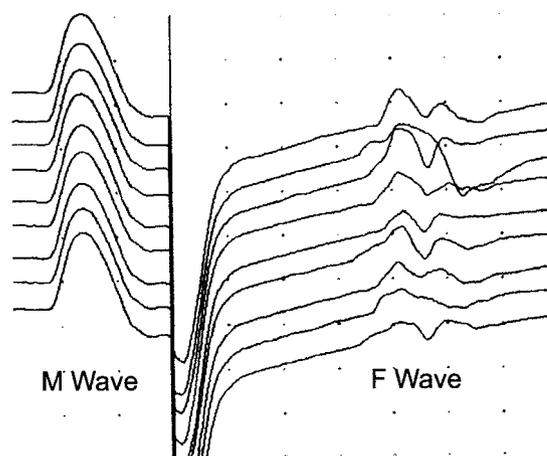


Fig. 3. Recording the F wave in the median nerve, on stimulation at the wrist. The direct motor response (compound muscle action potential or M wave) and late (F wave) responses are shown.

junction. Sensory or mixed nerve action potential is obtained by supramaximal stimulation of a sensory or mixed nerve, with recording electrodes placed along the same nerve, usually 8–14 cm distal or proximal to the stimulating electrode. The distal motor and sensory latencies, motor and sensory conduction velocity, amplitude (onset to negative peak) of CMAP and nerve action potential, and waveforms of these potentials are noted.^{47–49} Abnormality of motor and sensory nerve conduction strongly favors a neuropathic process. In axonal neuropathy, CMAP and nerve action potential amplitude is reduced (corresponding to loss of axons), with normal conduction velocity in surviving axons.^{2,26,33,48} Demyelinating neuropathy is characterized by marked slowing of conduction and/or presence of conduction block indicated by > 50% reduced CMAP amplitude on proximal stimulation of a motor nerve, compared to that on distal stimulation (Fig. 2).^{26,33,46,48,50}

F Wave. Supramaximal stimulation of a motor nerve (eg, median or ulnar nerve at wrist, or peroneal or tibial nerve at ankle) produces an orthodromic volley of impulse distally to the muscle, as well as an antidromic volley that travels proximally along motor axons to the anterior horn cells. A proportion of the anterior horn cells then fire back, and the impulse travels down again to the muscle and is recorded as a late motor response, which is termed an “F wave” (Fig. 3). This represents conduction along the length of the motor nerve, including the proximal segment.⁵¹ In generalized neuropathy, marked slowing or absence of the F wave with relatively normal CMAP is compatible with demyelination.^{52,53} The F wave may be absent or lack persistence if CMAP is markedly reduced due to other causes (eg, motor neuron disease, axonal neuropathy, or advanced myopathy). The F wave is also inhibited in acute CNS lesions, as well as in sedated or unconscious patients.⁵⁴

	Muscle Contraction	EMG Activity	Normal	Neurogenic	Myopathic
I.	None	SA	None		None ±
II.	Mild/Steady	MUP			
III.	Increasing/Full	Recr/IP			

Fig. 4. Needle electromyography (EMG). There are 3 steps to the procedure, and these waveforms show typical EMG patterns. The neurogenic pattern shows the presence of spontaneous activity, large polyphasic motor-unit potentials (MUPs), and a reduced interference pattern. The myopathic pattern shows variable spontaneous activity, small polyphasic MUPs, and a low-amplitude, full interference pattern. SA = spontaneous activity. Recr = recruitment. IP = interference pattern.

Needle EMG

Needle EMG is performed with a monopolar or a concentric bipolar needle electrode, in judiciously selected muscles, based on clinical and nerve conduction findings.^{46,55} The standard procedure involves 3 steps (Fig. 4):

1. Spontaneous and insertion activity. Needle electrode insertion into a normal muscle at rest elicits a brief burst of insertion activity but no spontaneous activity other than end-plate noise or spikes if the needle is close to the motor end-plate region. Presence of fibrillation potentials and positive sharp waves indicates denervation or muscle necrosis separating the muscle fibers from their end-plate zone. Fasciculation potentials are seen in anterior horn cell or peripheral nerve disease. Certain abnormalities (eg, myotonic discharges) may provide specific diagnosis.⁵⁵

2. Steady mild voluntary contraction. With slight voluntary activation of the muscle, low threshold, semi-rhythmically firing motor unit potentials (MUPs) are recorded. The duration, amplitude, and number of phases of the MUPs are assessed. In neuropathic lesions with axonal loss, reinnervation of denervated muscle fibers through collateral sprouting of surviving axons results in large polyphasic MUPs. On the other hand, myopathic processes are associated with a reduced number of functional muscle fibers within each motor unit, and therefore MUPs are of small duration and low amplitude.^{32,55-57} Myopathic MUPs also show marked polyphasia due to decreased synchronization of muscle fiber action potentials within the motor unit.

3. Increasing/maximum voluntary contraction. Increasing the force of voluntary contraction increases the firing

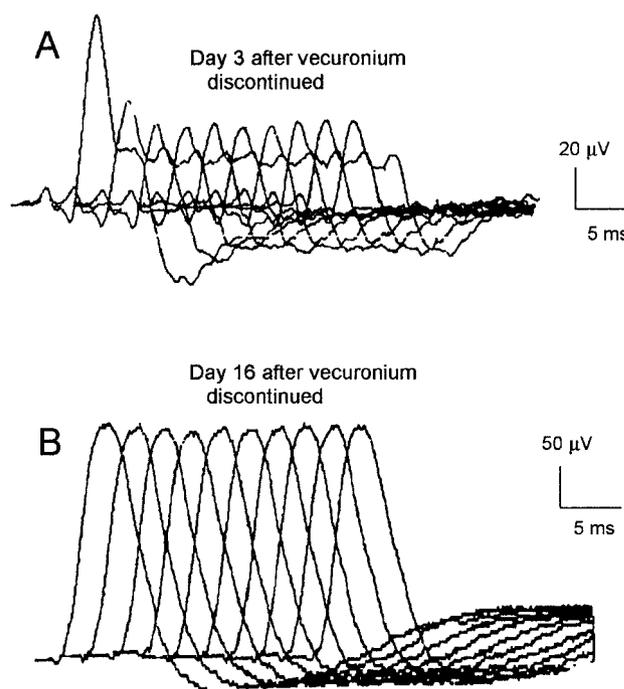


Fig. 5. Repetitive nerve stimulation at a low stimulation rate (2 Hz) in a patient with prolonged neuromuscular junction blockade. A: Decrement response that suggests neuromuscular transmission defect. B: Normal repetitive nerve stimulation response on recovery. (From Reference 26, with permission.)

rate of initial MUPs and produces systematic recruitment of additional MUPs.⁵⁸ Normally, a large number of overlapping MUPs are recorded at maximum effort, which

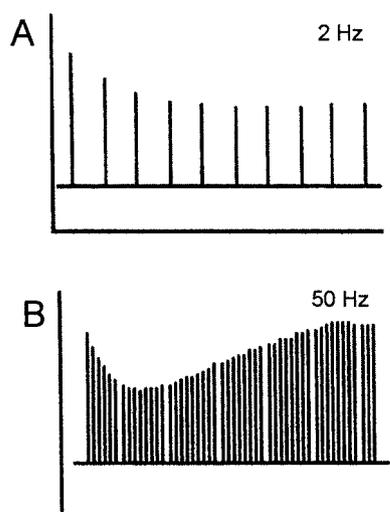


Fig. 6. Repetitive nerve stimulation in a patient with Lambert-Eaton syndrome. A: Decrement response on low (2-Hz) rate of stimulation. B: Increment response on 50 Hz stimulation.

creates what is called an interference pattern. Loss of functional motor units with axonal injury or conduction block produces an incomplete or reduced recruitment/interference pattern. Myopathic diseases have the normal complement of motor units but reduced numbers of functional muscle fibers, which causes a normal interference pattern with reduced amplitude. Recruitment of a large number of MUPs with weak voluntary force (early recruitment) is characteristic of a myopathic pattern.^{46,55}

Neuromuscular Junction Testing

Repetitive Nerve Stimulation. With an electrode setup similar to that used for motor nerve conduction, a train of 10 supramaximal stimuli at 2–3 Hz is applied. A $\geq 10\%$ decrement of CMAP amplitude from first to fourth response is considered significant and indicates compromise of neuromuscular transmission (eg, in myasthenia gravis and neuromuscular junction blockade) (Fig. 5).^{26,46,59} Presynaptic neuromuscular junction disorders (eg, Lambert-Eaton syndrome and botulism) have low baseline CMAP amplitude. An increment response of $> 100\%$ can be elicited following a 10-second exercise of muscle being tested or with fast (20–50 Hz) repetitive stimulation (Fig. 6).⁶⁰

Single-Fiber EMG. The basis of single-fiber EMG is to record a pair of muscle fiber action potentials belonging to the same motor unit. Variability in the interspike interval (termed “jitter”) and absence (blocking) of second potential is observed (Fig. 7). Prolonged jitter and/or blocking characterizes neuromuscular junction dysfunction.^{61,62} Single-fiber EMG is more sensitive than repetitive nerve stimulation; however, it is technically demanding and requires

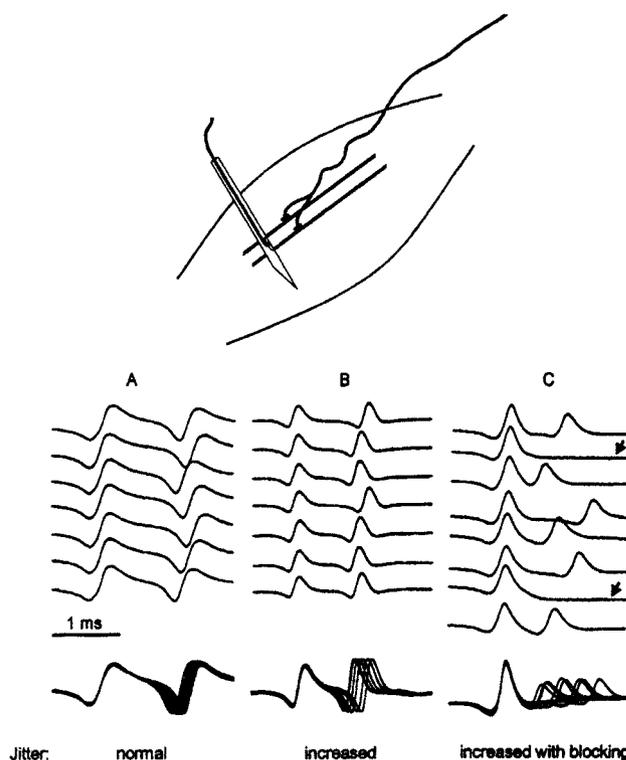


Fig. 7. Single-fiber electromyography and recording of jitter between 2 muscle fiber action potentials of the same motor unit. A: Normal. B: Increased jitter. C: Increased jitter with blocking. Recordings B and C are from a patient with myasthenia gravis. (From Reference 61, with permission.)

special expertise. The procedure can be modified to stimulated single-fiber EMG for patients unable to perform voluntary contraction.⁶³

Train-of-4 Stimulation. Train-of-4 stimulation is a simple bedside procedure, physiologically similar to repetitive nerve stimulation, and is used to monitor nondepolarizing neuromuscular blockade. Typically, the ulnar nerve is stimulated at the wrist (4 impulses at 2 Hz). The patient’s thumb is gently supported in abducted position, and adduction twitch, due to contraction of the adductor pollicis muscle, can be felt.⁶⁴ Normally, all 4 responses are elicited and the nondepolarizing neuromuscular blockade dose is titrated to produce 1 or 2 twitches. Absence of twitches indicates complete blockade (nondepolarizing neuromuscular blockade overdose).⁶⁵ However, whether train-of-4 monitoring has a definitive role in improving recovery time from neuromuscular blockade is controversial.⁶⁶

Respiratory EMG

Phrenic Nerve Conduction. The phrenic nerve conduction study is particularly relevant in patients with suspected respiratory muscle weakness and those who have

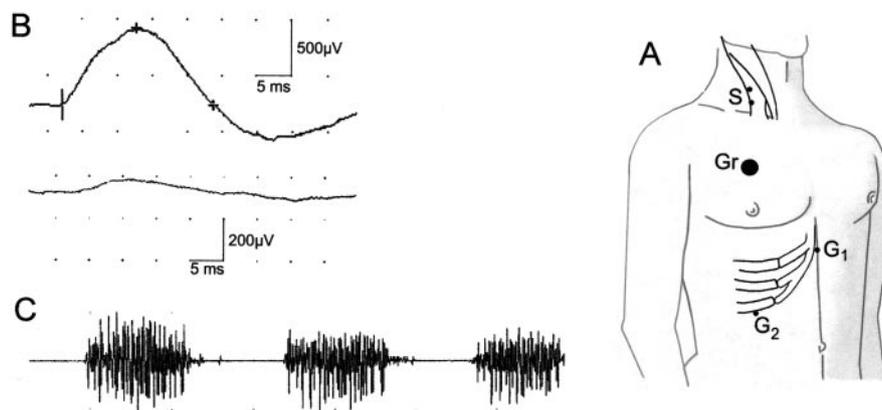


Fig. 8. Phrenic nerve conduction. A: Electrode placement for stimulation (S), ground (Gr), and recording (G₁ and G₂). B: Normal diaphragm compound muscle action potential (CMAP) (top trace) and reduced amplitude of diaphragm CMAP (bottom trace). C: Needle electromyography (EMG) recording from the diaphragm, which shows normal EMG bursts during inspiration.

difficulty weaning from the ventilator. Percutaneous stimulation of the phrenic nerves is performed bilaterally in the supraclavicular fossa, unless precluded by a central line on one or the other side of the neck (Fig. 8). Diaphragm CMAP is recorded with surface disk electrodes placed 16 cm apart, at the xiphoid process and the costal margin.^{67,68} Latency to onset and amplitude of CMAP are noted. Reduced diaphragm CMAP amplitude with near normal phrenic motor latency has been observed in CIP.^{2,68,69} Demyelinating neuropathies (eg, Guillain-Barré syndrome) show markedly prolonged latency and/or reduced amplitude and temporal dispersion of CMAP.^{70,71} A unilateral abnormality often suggests a traumatic or post-operative lesion of the phrenic nerve.^{71,72}

Needle EMG of the Diaphragm. The needle electrode is inserted through any intercostal space, just above the costal margin, between the anterior axillary and medial clavicular lines. Diaphragm activity is identified in the form of bursts of MUPs during inspiration. Spontaneous activity can be assessed during quiet intervals between the bursts.⁶⁸ To evaluate EMG activity of voluntary respiration, intermittent mandatory ventilation is temporarily discontinued under close supervision. Spinal cord (C3-C5) lesions, phrenic nerve injury, and CIP are associated with findings of active denervation.^{68,69,73} Severe chronic obstructive pulmonary disease, ileus, and bleeding diathesis are contraindications for needle EMG of the diaphragm.

Special Techniques

Blink Reflex. Blink reflex may be considered the electrical correlate of the corneal reflex, with the ipsilateral trigeminal nerve as the afferent limb and the bilateral facial nerve as the efferent limb of the reflex arc. Blink reflex has been used in evaluation of peripheral and central lesions of those nerves.

Electrical stimulation of the supraorbital nerve elicits a direct (R₁) ipsilateral response and a delayed (R₂) bilateral simultaneous response from the orbicularis oculi muscles.⁷⁴ Application of the blink reflex in ICU patients with neuromuscular disorders is based on the experience that blink reflex is abnormal in acquired demyelinating neuropathies (eg, Guillain-Barré syndrome and chronic inflammatory demyelinating polyneuropathy) and is unaffected in axonal neuropathies, and thus may help distinguish between Guillain-Barré syndrome and CIP.⁷⁵

Direct Muscle Stimulation. Rich et al²⁰ initially applied the technique of direct muscle stimulation in ICU patients, and they found inexcitability of muscle in patients with acute quadriplegic myopathy. Direct muscle stimulation is performed by placing both stimulating and recording needle electrodes in the muscle distal to the end-plate zone (Fig. 9). A direct muscle-stimulated CMAP is recorded, and then the motor nerve of the muscle is stimulated to obtain a nerve stimulated CMAP with the same recording electrode. In neuropathic lesions (eg, CIP), nerve stimulated CMAP may be reduced or absent, but direct muscle-stimulated CMAP is normal. In contrast, CIM is associated with reduced or absent CMAP on nerve stimulation, as well as on direct muscle stimulation. This observation formed the basis for investigating direct muscle stimulation to distinguish between CIP and CIM. Later studies used the ratio of the nerve-stimulated CMAP to the direct muscle-stimulated CMAP, or the absolute amplitude of the direct muscle-stimulated CMAP, to determine muscle membrane excitability.^{21,22,76} Rich and Pinter⁷⁷ also studied an experimental model of acute quadriplegic myopathy and found that inexcitability of muscle membrane was related to inactivation of sarcolemma Na⁺ channels. The technique has provided a diagnostic method and helped to

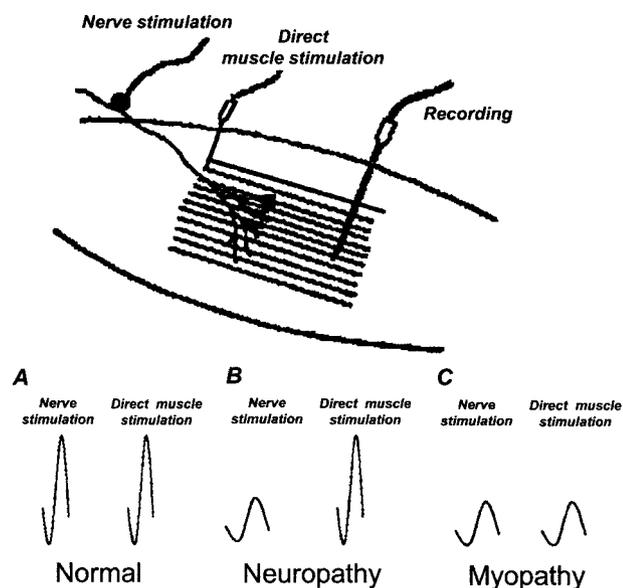


Fig. 9. Direct muscle stimulation. Both the stimulating and recording electrodes are placed in the muscle. A: Potentials on direct muscle and nerve stimulation are obtained. B: Direct muscle potential is normal in nerve lesions. C: Direct muscle potential is absent or reduced in myopathy. (From Reference 25, with permission.)

understand the pathophysiology of CIM. The procedure, however, is technically demanding and has been used only in a few centers so far.

Muscle and Nerve Biopsy

Nerve and muscle histological studies have substantially contributed to our understanding of the wide clinicopathological spectrum of new onset weakness in critically ill patients.^{10,16,18,34,35,78} Various studies on nerve histology (autopsy or surgical pathology) in patients with CIP have confirmed axonal degeneration of motor and sensory nerve fibers without inflammation.^{10,34} Through muscle biopsy studies it became obvious that CIM, as an isolated syndrome or in combination with CIP, may be more common than the neuropathic syndrome. Experience with muscle biopsy has led to definition of various histological subtypes (eg, acute necrotizing myopathy, thick myosin filament loss myopathy [Fig. 10], and type II fiber atrophy).^{10,16,78–80} Many patients have various combinations of these changes. Generally, the role of muscle biopsy in a weak ICU patient is 2-fold: (1) to distinguish a neuropathic from a myogenic process, and (2) to determine the specific etiology, based on morphologic characteristics (eg, polymyositis/dermatomyositis, mitochondrial myopathy, or CIM). Percutaneous punch muscle biopsy or open muscle biopsy can be performed, and the interpretation should be done by experienced individuals. Therefore, the procedure is often carried out for research purposes or when an

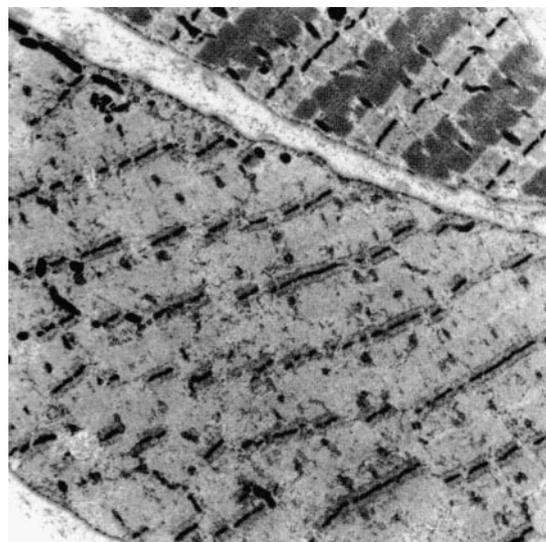


Fig. 10. Electron micrograph from a biceps muscle of an intensive-care patient with quadriplegia, showing thick myosin filament loss. (From Reference 80, with permission.)

underlying neuromuscular disorder is suspected because of an absence of risk factors for CIM or lack of improvement in 3–4 weeks. Nerve biopsy is not indicated in clinical investigations of these patients, unless a specific disorder, such as vasculitic neuropathy, is suspected.

Disorders That Cause Neuropathic Weakness

Critical Illness Polyneuropathy

CIP has a rather stereotypical evolution in the ICU. Initial critical illness (eg, sepsis, burn, trauma) is followed by multiorgan failure, septic encephalopathy, difficulty weaning from the ventilator in the absence of cardiopulmonary compromise, and generalized muscle weakness.⁵ Electrophysiological and pathological studies confirm the presence of axonal motor and sensory polyneuropathy in these patients.³⁴ CIP is now recognized as an important and serious complication of sepsis and critical illness.^{6,8–10,13,19,25} Weakness is indicated by the patient's inability to move extremities in response to pain, while strong facial grimacing shows wakeful status. The degree of weakness ranges from moderate paresis with hyporeflexia to severe areflexic quadriplegia. The weakness is predominant distally and in the lower extremities. The cranial nerves are spared, although facial weakness is occasionally reported. Sensory impairment occurs in only 50% of patients, and this may reflect difficulty in performing sensory examination in the ICU. Hyporeflexia/areflexia is common, although muscle stretch reflexes may be normal in about one third of the patients, and at times may be exaggerated if there is concomitant CNS involvement.⁸¹

CLINICAL APPROACH TO THE WEAK PATIENT IN THE INTENSIVE CARE UNIT

Table 3. Clinical Features and Laboratory Findings of Critical-Illness Polyneuropathy, Guillain-Barré Syndrome, and Critical Illness Myopathy

	Findings		
	Critical Illness Polyneuropathy	Guillain-Barré Syndrome	Critical Illness Myopathy
Clinical setting	Sepsis Multiorgan failure Septic encephalopathy	Antecedent viral Surgery <i>Campylobacter jejuni</i> HIV	Neuromuscular blocking drugs Corticosteroids Asthma Organ transplant
Motor weakness	Generalized or distal predominant	Generalized, ascending, areflexia	Generalized or proximal predominant
Cranial nerve palsy	Rare	Common Unilateral/bilateral facial Bulbar	Occasional Ophthalmoparesis, bilateral facial
Dysautonomia	No	Yes	No
Sensory deficit	Distal	Mild, distal	No
Creatine kinase	Normal	Normal	Elevated
Nerve conduction	Reduced CMAP and SNAP amplitude	Marked slowing, conduction block	Reduced CMAP amplitude Normal SNAP amplitude
Needle EMG	Abnormal spontaneous activity common Reduced recruitment Large, polyphasic MUPs	Abnormal spontaneous activity may be seen Reduced recruitment Normal MUPs initially; may be large, polyphasic MUPs later	Mild or no abnormal spontaneous activity (pronounced in necrotizing) Small polyphasic MUPs; early recruitment
Direct muscle stimulation	Normal	Normal	Absent or reduced
Muscle biopsy	Neuropathic changes	Neuropathic changes	Myopathic Thick myosin filament loss Widespread muscle-fiber necrosis in acute necrotizing

HIV = human immunodeficiency virus
 CMAP = compound muscle action potential
 SNAP = sensory nerve action potential
 EMG = electromyography
 MUP = motor unit potential

EMG and nerve-conduction studies show low amplitude of CMAP and nerve action potential, with near normal conduction velocity and the presence of fibrillation and positive sharp wave potentials consistent with axonopathy.^{2,6,12,19,34,42,69} Abnormal phrenic nerve conduction (bilateral reduced or absent diaphragm CMAP) is reported in about 50–80% of patients.^{19,82} Clinical CIP may occur in 30–50% of ICU patients, but prospective electrophysiological studies describe an incidence of 70–80%.^{24,69,82} The occurrence of CIP correlates with duration of ICU stay and severity of sepsis. High mortality (60%) in patients with CIP probably relates to underlying critical illness, but some investigators think that mortality is higher in patients with CIP than in those with comparable Acute Physiology and Chronic Health Evaluation (APACHE III)

score without CIP.⁸³ Follow-up studies showed severe paralysis in 4 of 15 survivors, and impaired quality of life in 11 of 13 survivors. Long-term outcome with moderate-to-severe deficits is variably reported in 30–80% of cases and appears to be much less favorable than Guillain-Barré syndrome or CIM.^{13,84} Clinical and laboratory features that distinguish among these syndromes are outlined in Table 3.

Guillain-Barré Syndrome

Guillain-Barré syndrome is the most common neuromuscular disorder that requires admission to the ICU, as well as the most important differential diagnosis for CIP. Antecedent illness, rapid ascending flaccid paralysis, and

cranial nerve involvement are characteristic features. Elevated CSF protein and electrodiagnostic findings of markedly slow nerve conduction, prolonged or absent F waves, and conduction block (which suggest demyelinating neuropathy) clearly distinguish it from CIP.^{6,33,50} The presence of dysautonomia, abnormal blink reflex, and prolonged phrenic nerve latency are also helpful.^{50,71,75} The axonal variant of Guillain-Barré syndrome (about 5% of cases) may be difficult electrophysiologically to differentiate from CIP. This variant is reported most often in association with *Campylobacter jejuni* infection and GM₁ ganglioside antibody.²⁵ In general, testing for ganglioside antibody levels is not indicated. It is important to distinguish incidental Guillain-Barré syndrome in the ICU (which may follow a medical illness or surgery) from CIP, because specific treatment with intravenous immunoglobulin or plasmapheresis is indicated for Guillain-Barré syndrome.

Other Acute Neuropathies

Occasionally, acute neuropathies due to uncommon causes have been encountered in the ICU setting. Human immunodeficiency virus infection is associated with various clinical forms of peripheral neuropathy and may also present with acute polyneuropathy similar to Guillain-Barré syndrome.³⁸ In the presence of risk factors, human immunodeficiency virus antibody testing is relevant.

Rarely, neuropathy of acute intermittent porphyria may develop in the ICU, because acute attack can be precipitated by medications or infection. It is an acute axonal neuropathy, CSF protein is not elevated, and features such as seizures, arrhythmia, abdominal pain, and psychiatric symptoms may be associated.^{28,38} Toxic neuropathies are unlikely to be encountered in the ICU. Some possibilities are prior cancer chemotherapy (platinum, taxanes, vinca alkaloids, suramin), amiodarone, and metronidazole.³⁸

Peripheral nerve involvement in vasculitis usually presents as subacute onset of mononeuritis multiplex. Widespread involvement may mimic symmetric or asymmetric polyneuropathy.⁸⁵ Involvement of other organs and findings of multifocal axonal neuropathy on EMG are suggestive of the diagnosis. Suspicion of vasculitic neuropathy is an important indication for nerve biopsy.

Compression Neuropathies

ICU patients may be prone to development of focal neuropathies at compression sites (eg, ulnar nerve at elbow, peroneal nerve at fibular head, and radial nerve in spiral groove), due to positioning, weight loss, et cetera. Multiple bilateral focal compressive syndromes may mimic distal polyneuropathy. On electrophysiologic testing, focal slowing of nerve conduction and/or conduction block at common sites of compression, and neurogenic EMG pat-

tern in corresponding muscles, are diagnostic.^{45,47} Compression neuropathies superimposed on CIP have been reported to contribute to long-term deficits.⁸⁶

Acute Poliomyelitis

Poliomyelitis due to poliovirus is no longer prevalent; however, similar acute paralysis may occur due to non-poliovirus infection. Acute, flaccid, and often asymmetric paralysis due to West Nile virus is being increasingly recognized.⁸⁷ Bulbar and respiratory muscles may also be involved. Patients may be admitted to the ICU for altered mental status due to West Nile virus encephalitis or meningitis and later develop flaccid paralysis. Predominantly proximal, asymmetric weakness, preserved reflexes, and normal sensation distinguish West Nile virus paralysis from Guillain-Barré syndrome and CIP. CSF shows increased protein level and lymphocytic pleocytosis, and immunoglobulin M antibody to West Nile virus is detected in serum or CSF. Electrodiagnostic studies show reduced CMAP with normal motor nerve conduction velocity, normal sensory responses, and neurogenic EMG in segmental pattern. Rarely, West Nile virus has been associated with demyelinating neuropathy similar to Guillain-Barré syndrome.⁸⁸

Amyotrophic Lateral Sclerosis

Previously undiagnosed patients with ALS may present with acute ventilatory failure due to isolated or predominant respiratory muscle weakness.^{31,89} They fail to wean from the ventilator and show signs of limb wasting, generalized fasciculations, and brisk reflexes. Diagnosis is confirmed by electrodiagnostic studies, which reveal widespread active denervation, chronic reinnervation, and fasciculation potentials. Lacomis et al recognized 5 patients with ALS among 92 ICU patients referred for electrophysiological study.³¹

Hopkins Syndrome

In 1974, Hopkins⁹⁰ reported a polio-like syndrome in children following acute asthma. About 30 patients have been reported since then.⁹¹ There is acute flaccid monoparesis or, at times, paraparesis. Marked atrophy and persistent deficits are noted on follow-up. EMG is consistent with motor neuron involvement, and muscle biopsy shows grouped atrophy. Recently, the disorder was reported in adults as well. The etiology is not known; however, increased CSF protein and lymphocytic pleocytosis, and occasional improvement after intravenous immunoglobulin therapy, may point to an immune or inflammatory process.⁹²

Disorders That Cause Myopathic Weakness

Critical Illness Myopathy

A syndrome of acute myopathy in a patient with asthma who received neuromuscular blocking agents and corticosteroids was documented in the 1970s.⁷ Primary muscle involvement in ICU patients initially remained under-recognized, but there has been increasing interest in and multimodal investigations of ICU paralysis syndromes, which have indicated that CIM may be the commonest newly acquired neuromuscular disorder in the ICU.^{8,16,21,22,31,35} Predisposing factors are acute asthma, exacerbation of chronic obstructive pulmonary disease, organ transplant, acute respiratory distress syndrome, sepsis, and use of high doses of corticosteroids and neuromuscular-blocking agents. Patients develop symmetric diffuse weakness of all extremities, muscle wasting, hyporeflexia, and failure to wean from the ventilator. The major differential diagnosis is from CIP and, rarely, other acute myopathies (rhabdomyolysis, acute polymyositis, electrolyte disorders). The clinical setting, preserved reflexes, normal sensory examination, ophthalmoparesis, and facial weakness may favor the possibility of CIM; however, there are no definitive clinical findings to distinguish CIM from CIP, and the examination in the ICU may be unreliable.^{18,33,78}

Elevated serum creatine kinase in acute weakness is an important diagnostic feature, especially in the early part of the illness. Typical EMG features include low amplitude, short duration and polyphasic MUPs, with good recruitment pattern despite pronounced weakness. CMAP amplitude is reduced and sensory potentials are normal. Fibrillation and positive sharp wave potentials, which are usually indicative of axonal injury, also occur in necrotizing myopathies. There are many caveats to interpreting electrophysiological studies in the ICU. Assessment of voluntary EMG may be difficult when the patient cannot activate motor units due to severe weakness, sensory potentials may be technically difficult to elicit, and reduced CMAP with normal motor nerve conduction is seen in CIP as well as CIM. It is therefore not surprising that many investigators have pointed out the difficulties in distinguishing between the 2 neuromuscular syndromes.^{10,21,22,25,42} The newer technique of direct muscle stimulation demonstrates muscle membrane inexcitability in CIM.²⁰ The ratio of nerve-stimulated CMAP to direct muscle-stimulated CMAP is reduced in neuropathic lesions and is closer to 1.0 in CIM.²¹ Recent studies show that combining direct muscle stimulation with routine studies is useful in proper classification of neuromuscular weakness in the ICU; however, the technique is not routinely applicable as yet.^{22,76}

Muscle biopsy shows varying severity of myopathic changes, in contrast to grouped atrophy in neuropathy, but, being an invasive procedure, it is not routinely employed

for clinical diagnosis. Histopathological studies show varying degrees of muscle fiber necrosis, most prominently in acute necrotizing myopathy, without inflammatory cells. Thick myosin filament loss is a distinctive abnormality in CIM (see Fig. 10). Predominant type II muscle fiber atrophy has been termed cachectic myopathy.⁷⁸ Stibler et al⁹³ noted decreased myosin/actin ratio in percutaneously obtained muscle biopsies of CIM patients, and suggested that it may be useful for rapid diagnosis. For clinical purposes, the combination of predisposing events, clinical findings, and electrophysiological investigation allows a reasonable diagnosis of CIP or CIM (see Table 3). Muscle biopsy is considered if other causes of myopathy (eg, polymyositis) are suspected. Most of the advanced techniques are relevant for research purposes.

Rhabdomyolysis

Trauma, sepsis, and various medications (see Table 2) can precipitate acute rhabdomyolysis in ICU patients. Muscle pain, swelling, predominant proximal or generalized weakness, and markedly raised serum creatine kinase are noted. Myoglobinuria, acute renal failure, and other systemic complications are present.^{28,43}

Other Causes of Myopathy

Several primary muscle diseases may present with initial manifestations of respiratory compromise (eg, polymyositis, mitochondrial myopathy, and acid maltase deficiency). Patients with myotonic muscular dystrophy or congenital myopathies may decompensate after general anesthesia. Such patients are emergently admitted to ICU, and the underlying muscle disease may be suspected and evaluated only later during the ICU stay.^{38,94} Muscle biopsy is diagnostic and needs to be considered if a patient in whom CIM is suspected does not show improvement over a few weeks.

Disorders of Neuromuscular Transmission

Prolonged Neuromuscular Junction Blockade

Patients treated with high doses of nondepolarizing neuromuscular blocking agents such as vecuronium and pancuronium may have persistent weakness and fail weaning from the ventilator, even after the blocking drugs have been discontinued.^{14,15} This prolonged blockade may last from several hours to weeks. Patients with renal failure, hepatic dysfunction, acidosis, or hypermagnesemia are more prone to this complication. Examination shows generalized weakness, normal or reduced reflexes, and normal sensation. Bilateral ptosis, and facial and jaw muscle weakness may be present.^{26,33} Electrophysiological features are

reduced CMAP amplitude and decrementing response on 2–3 Hz repetitive nerve stimulation. The physiologic abnormality reverses on clinical recovery.^{26,38} Patients with uncomplicated prolonged neuromuscular blockade recover completely, usually in 1–2 weeks. The condition may coexist with CIP or CIM and has been reported to progress to CIM on sequential studies. Recognition of prolonged neuromuscular blockade has led to more judicious use of neuromuscular blocking drugs in the ICU.⁶⁵

Myasthenia Gravis

Patients with myasthenia gravis typically require admission to the ICU for myasthenic crisis or cholinergic crisis. Several factors, such as infection, electrolyte disorder and drugs used in the ICU (see Table 2), may unmask latent myasthenia gravis. Rarely, respiratory failure may be the presenting feature in myasthenia gravis. Clinically, ptosis, ophthalmoparesis, and facial and bulbar weakness are common, in addition to generalized weakness. Diagnosis is based on positive edrophonium test, decrementing response on repetitive nerve stimulation, and presence of serum acetylcholine receptor antibody. Abnormal jitter on single-fiber EMG is a very sensitive diagnostic test, but is not routinely employed. Between 85% and 90% of patients with generalized myasthenia gravis are seropositive for acetylcholine receptor antibody. Among the seronegative patients, a subgroup with antibody to muscle-specific tyrosine kinase has been identified.⁹⁵ These patients with myasthenia gravis have certain atypical features, including prominent neck extensor, facial and respiratory muscle weakness, and poor response to acetylcholine-esterase inhibitors. Respiratory crisis may be a presenting feature, so in a patient with suspected generalized myasthenia gravis who is seronegative for acetylcholine receptor antibody, serum assay for muscle-specific tyrosine kinase antibody should be considered.

Other Neuromuscular Junction Disorders

Lambert-Eaton Syndrome. This is a presynaptic neuromuscular transmission disorder due to calcium channel antibodies, which impair acetylcholine release from the nerve terminal. It is usually associated with small-cell lung cancer but may also occur as an idiopathic autoimmune disorder. Reduced CMAP on nerve conduction and incrementing response on high frequency repetitive nerve stimulation are characteristic. Similar to myasthenia gravis, patients with Lambert-Eaton syndrome may also present with previously unrecognized or unmasked weakness in the ICU.^{28,29}

Botulism. Generalized weakness and cranial nerve involvement in botulism may resemble Guillain-Barré syn-

drome, but paralysis is often described as descending, and deep tendon reflexes may be preserved.³⁸ Blurred vision and dilated pupils due to paralysis of accommodation are noted. This is also a presynaptic disorder, and electrophysiologic findings of reduced CMAP and increment on tetanic stimulation are observed.

Summary

Complications of critical illness, including CIP, CIM, and prolonged neuromuscular blockade, are now regarded as the major cause of new onset weakness in the ICU setting. These need to be distinguished from other neurological disorders that may begin after admission to the ICU, or when a diagnosis has not been established prior to an emergency admission. The first step in clinical examination is to distinguish CNS lesions, especially brain stem and spinal cord lesions, and to obtain magnetic resonance imaging or computed tomography of the brain or spine, if indicated. Special attention should be paid to patients with “locked-in” syndrome, since this may result from structural brain stem lesions or neuromuscular disorders. Neurological examination in the ICU can be challenging; however, combined clinical and electrophysiological assessment helps delineate anterior horn cell, nerve, muscle, and neuromuscular junction disorders. The nature of the underlying illness and the drugs received in the ICU should be noted. Some of the neurological causes to be considered are new onset Guillain-Barré syndrome, latent myasthenia gravis, predominant respiratory involvement in ALS, rhabdomyolysis, flaccid paralysis associated with West Nile virus, and muscle-specific tyrosine kinase antibody myasthenia gravis presenting with respiratory crisis.

Typical features of CIP include evidence of systemic inflammatory response syndrome and multiorgan dysfunction, followed by generalized or distal weakness, distal sensory deficits, spared cranial nerves, and findings of axonopathy on EMG. CIM often follows use of high doses of neuromuscular blocking drugs and corticosteroids. Generalized or proximal weakness, elevated creatine kinase, and myopathic pattern on EMG are noted. Severe areflexic quadriplegia, markedly elevated creatine kinase, myoglobinuria, and muscle fiber necrosis on muscle biopsy are characteristic of acute necrotizing myopathy. Thick myosin filament loss is another distinct pathological feature of CIM. The technique of direct muscle stimulation has defined inexcitability of muscle membrane as a mechanism of weakness in CIM and has been used by some investigators to distinguish CIM from neuropathic lesions. Muscle biopsy may be used to distinguish between neuropathic versus myopathic lesions, to define type of CIM, and to establish a specific diagnosis when an underlying muscle disease is suspected.

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Discussion

Deem: Which patients should receive muscle biopsy? How do you determine when to do a muscle biopsy?

Upinder Dhand: The main reason for muscle biopsy is to diagnose previously unsuspected underlying muscle disease or to distinguish between ICU-related syndromes. The latter may become more relevant from a research point of view—that is, understanding the relationship of various ICU factors to different neuromuscular syndromes. Most of the time, muscle biopsy is clinically indicated only in selected cases in whom an additional or previously undiagnosed primary muscle disease is suspected.

Deem: Do you use direct muscle stimulation in your hospital?

Upinder Dhand: No, I'm not using that technique. I am aware of only 2 groups doing it: Rich's, at University of Pennsylvania,¹ and Trojaborg's, at Columbia University.²

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Jubran: In what clinical settings do you use needle electrodes to obtain diaphragm EMG? Do you use ultrasound to help guide the measurements? How well do patients tolerate the procedure?

Upinder Dhand: When I'm doing an EMG study in the ICU, and the question is about difficulty in weaning, I test the phrenic nerve conduction and the diaphragm with needle EMG, except when there is an obvious contraindication. For example, in a patient with severe COPD, the lung may be at a much lower level and the procedure could be risky. Or in a patient who has had laparotomy and accessing the diaphragm may be difficult. But usually it's not difficult.

When you put the needle through the intercostal space, you first run into the intercostal muscles, and, incidentally, you can look for denervation in the intercostal muscle itself, and then go on to the diaphragm. The last portion of the diaphragm is actually directly by the thoracic cage, and the pleura is already reflected about an inch or so higher. I think ICU patients probably tolerate the procedure better than other patients, but I do it in my routine laboratory also, in patients with breathing difficulty and neuromuscular weakness. It is fairly well tolerated.

Mehta: We have a really difficult time getting EMGs. It can take months.

So mainly it comes down to suspicion of critical illness polyneuropathy or myopathy. And we've concluded that it really doesn't matter which one it is, because clinically you deal with them in the same way. What do you think?

Upinder Dhand: I think we all are probably learning from experience. As Steve Deem was also saying, these may be considered as one entity. Now you may just call it a neuromuscular syndrome in the ICU setting, and some authors have used the term "critical-illness neuromyopathy." But there is confusion for several reasons. One is that clinical examination and investigations may not clearly distinguish between critical illness neuropathy and myopathy, or the 2 syndromes may coexist. Maybe there is a whole spectrum with neuropathy at one end, myopathy at the other, and overlap in between. The reason I want to differentiate between the two is because of the outcome. The long-term care may be different.

I think critical illness neuropathy probably has more residual deficits and greater chance of mortality, whereas in critical illness myopathy the outcome is probably much better—other than patients who have fulminant, necrotizing myopathy. Moreover, investigations may help identify a different neurological cause. And, finally, I think it is particularly important for

people who are interested in this subject to distinguish between the two, because we are still in the process of understanding these disorders. So I still prefer to investigate.

With regard to getting the EMGs in the ICU, we have a policy that if we get a call for an in-patient EMG, it is done within 24 hours. I don't come at night, but it is within 24 hours.

Mehta: We can't get EEGs within 24 hours!

Hill: You cited a mortality rate of 60% for critical illness polyneuropathy, but I see it as a manifestation of multiple organ system failure, in association with the sepsis syndrome, as in ARDS [acute respiratory distress syndrome], in which mortality is 40% to 50%. But people generally don't die of respiratory failure. Is that the case with critical illness polyneuropathy? Are people dying of multiple organ system failure rather than the neuropathy, per se?

Upinder Dhand: Yes. Various authors have mentioned that the mortal-

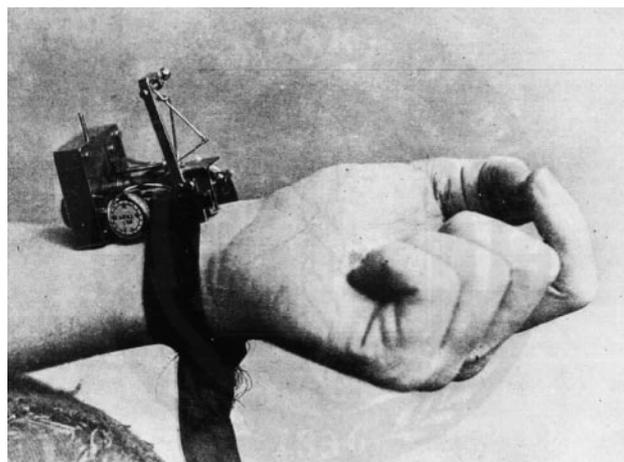
ity is related to the severe underlying illness, so it is not directly the result of critical illness polyneuropathy.

Deem: I'll address that question in my upcoming talk. I have a question about train-of-4 monitoring and neuromuscular blockade in the ICU. At our institution we don't use prolonged neuromuscular blockade nearly as much as we used to, and I don't think we see prolonged neuromuscular blockade as a cause of weakness much any more. I'm interested to know what other people report in that regard. Personally, I don't think train-of-4 monitoring is very useful, because it's technically difficult, like EMG. There's edema, and the nurses aren't very familiar with the technique. I saw an instance where they were having problems and we discovered that the nerve stimulator's battery was dead. I think the best way to prevent prolonged neuromuscular blockade is to not use the drugs, or to use them for short periods of time, and to stop them every day and reassess the patient.

Mehta: I have one more comment related to Herridge's outcomes study with 100 ARDS patients.¹ The most interesting finding was that these patients are not limited by pulmonary function at all. Their pulmonary function within 3, 6, and 12 months was essentially normal. But they're limited by peripheral muscle weakness. And the next phase of Herridge's research program is going to focus on preventive measures for that weakness. A major contributor may be neuromuscular blockers. We use neuromuscular blockers much less frequently than we used to. We don't usually use daily interruption of the blockers, but that's a really good strategy. We're very strict about using train-of-4 monitoring, even when using short-acting agents such as cisatracurium.

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Sphygmograph
Harper's Weekly, New York, March 13, 1897
 Courtesy, National Library of Medicine