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Weakness: A Systematic Approach To Acute, Non-traumatic, Neurologic And Neuromuscular Causes

December 2002
Volume 4, Number 12

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CME Objectives

Upon completing this article, you should be able to:
1. describe an algorithmic, systematic approach to the patient presenting with weakness;
2. discuss the essential elements of the history and examination for diagnosing etiologies of acute weakness;
3. list neuromuscular causes of acute respiratory failure and autonomic instability syndromes; and
4. discuss specific diseases that are characteristic of different neuroanatomic categories of weakness.

Date of original release: December 1, 2002.
Date of most recent review: November 8, 2002.
See "Physician CME Information" on back page.

The chief complaint box on the chart says it all: "Weak and tingling, desires second opinion." To compound your dilemma, an emergency medicine physician across town who saw the patient earlier in the day told her that she was just "anxious." The patient says she is anxious because her legs are "buckling." You hope that your neurologic examination will provide some obvious findings, since neuro never was your forte. Pinprick sensation is normal. Maybe she is "a little weak," but she doesn't seem to be making much of an effort. You have trouble "getting reflexes," but you have trouble interpreting the reflex exam on lots of your patients. By the time you finish examining the patient, your stomach feels as weak as the patient's knees. She probably is just anxious, and you are certain that no diagnostic test or fancy neurologic examination will prove otherwise….But maybe an MRI of the brain or spinal cord or a scan of something would help.

WEAKNESS possibly represents the quintessential nonspecific ED complaint. Simply elucidating what a patient means by "weakness" can be challenging. Perhaps the only more vexing complaint than weakness is the combination of weakness and its equally frustrating companion—"dizziness." (See also the March 2001 issue of *Emergency Medicine Practice*, "The Dizzy Patient: An Evidence-Based Diagnosis And Treatment Strategy.") Having a systematic approach greatly reduces the angst associated with this common ED complaint.

The emergency physician must quickly identify potentially unstable patients, in particular those with impending respiratory failure or circulatory collapse. Such patients would include, for instance, a hemiplegic stroke victim with a middle cerebral artery thrombus, a young adult with an acute myelopathy from a large central disc herniation, or a patient on the verge of

life-threatening ventilatory insufficiency from Guillain-Barré syndrome.

This article focuses on non-traumatic neurologic and neuromuscular causes of acute weakness due to pathology of one of the neuroanatomic subunits listed in **Table 1**. Lesions occurring in any one of these subunits, from the cerebral hemispheres to the innervated muscle(s), can lead to weakness. This article does not cover primary medical conditions in which weakness is a component (e.g., adrenal insufficiency, hypothyroidism) and non-categorical causes of weakness, such as fibromyalgia or chronic fatigue syndrome.

While recognizing the exact lesion may not always be possible, a focus on the neuroanatomic subunits will narrow the search for pathology. Certainly, if an emergency physician is going to convince a radiologist that an emergent MRI is warranted, it will help to know whether the neuropathology is confined to the lower spine or the cerebral cortex.

Critical Appraisal Of The Literature

Despite the prevalence of the complaint, there is a paucity of Class I literature relating to the general evaluation of weakness. Professional organizations such as the American College of Radiology (ACR) provide consensus opinions to help direct appropriate radiographic testing (e.g., ACR Appropriateness Criteria™ for Myelopathy, Class III). Other guidelines dictate specific diagnostic or surgical criteria for specific diagnoses that can cause weakness (e.g., Carpal Tunnel Syndrome by the American Society of Plastic Surgeons, Class III). The algorithms are largely consensus statements based on Class II or Class III evidence.

Definitions And Anatomical Subunits

True *weakness* is medically defined as an inability to carry out a desired movement with normal force because of a reduction in strength of the muscles.[1] Patients often use the word "weak" when a physician might use "malaise." The terms *malaise* and *listlessness* are most appropriately reserved for the perceived weakness that accompanies a broad spectrum of illnesses, from a benign viral process to congestive heart failure. Indeed, most patients who present to the ED with the complaint of weakness will ultimately have such a systemic (non-neurologic) illness. Alternatively, *fatigue* can be distinguished from the more indiscriminate term weakness, when diminution of strength with repetitive actions occurs. In its purest sense, fatigable weakness should be considered pathognomonic for a neuromuscular junction (NMJ) process. However, patients are more likely to describe fatigue with a more generalized medical condition, such as

Table 1. Causes Of Weakness Grouped By Anatomic Subunit.

Central (upper motor neuron)

Cerebrum
- Stroke
- Space-occupying/structural lesion
  - Left (dominant) cerebral hemispheric process
  - Right (nondominant) cerebral hemispheric process

Subcortex/Brainstem
- Stroke
- Space-occupying/structural lesion
  - Lacunar syndromes
  - Midbrain/brainstem syndromes

Spinal cord
- Acute transverse myelitis (infectious or inflammatory)
- Spinal cord infarct
- Spinal epidural or subdural hemorrhage
- Central intervertebral disc herniation
- Tumors (metastatic or primary)
- Multiple sclerosis

Peripheral (lower motor neuron)

Anterior horn
- Amyotrophic lateral sclerosis*
- Poliomyelitis*

Spinal nerve root
- Intervertebral disc herniation

Polyneuropathies
- Guillain-Barré syndrome*†
- Ciguatoxin (ciguatera poisoning)*†
- Tetrodotoxin poisoning (puffer fish poisoning)*
- Saxitoxin (paralytic shellfish poisoning)*
- Porphyria*
- Lead or other heavy metal poisoning*
- Alcohol- or drug-induced
- Diabetic

Plexopathies
- Brachial
- Lumbar

Peripheral neuropathies
- Nerve compression syndromes

Neuromuscular junction disorders
- Myasthenia gravis*
- Lambert-Eaton myasthenic syndrome*†
- Botulism*
- Tick paralysis*
- Organophosphate poisoning*

Myopathies
- Inflammatory (polymyositis)*
- Electrolyte-induced*
- Alcohol- or drug-induced
- Muscular dystrophy*
- Endocrine-related*

Nonphysiologic/Noncategorical
- Conversion disorder
- Malingering
- Chronic fatigue syndrome
- Anxiety disorders
- Fibromyalgia

*Neuromuscular cause of acute respiratory failure
†Frequently associated with autonomic dysfunction

worsening congestive heart failure.

When dealing with consultants, specific nomenclature will demonstrate an emergency medicine practitioner's competency in evaluating weakness. While plegia, paresis, and paralysis are often used interchangeably, *paresis* by definition implies partial or incomplete paralysis, while *plegia* and *paralysis* should be reserved for total loss of contractility. *Quadriplegia* or *tetraplegia* involves all four limbs and implies pathology of the cervical cord, while *paraplegia* (both lower limbs) can be due to thoracic or lumbar spinal cord disease. *Hemiplegia* refers to an upper and lower limb on the same side, while *monoplegia* refers to one limb.

A *myelopathy* involves a lesion of the spinal cord, while a *myopathy* is a disease in which the muscle is affected. Similarly confusing, a *spinal nerve* refers to the nerves exiting the anterior horn of the spinal cord, vs. the *peripheral nerves,* which are "downstream" to the spinal nerves in the peripheral nervous system (e.g., median or femoral nerves). *Radiculopathy* denotes pathology to the spinal nerve, while a *mononeuropathy* implies involvement of any one nerve. *Polyneuropathies* involve many nerves and can include both spinal and peripheral nerves. A *myotome* designates a group of muscles that have a common innervation from the same segment of the spinal cord and thus from the same nerve root. Most muscles belong to more than one myotome, because they typically are innervated by two or more adjacent cord segments and nerve roots. *Bulbar* specifically refers to the tongue, jaw, face, and larynx. Symptomatic dysfunction of the bulbar musculature is an important feature of NMJ processes and will manifest as dysphonia, dysphagia, dysarthria, and difficulty handling secretions.

Neuroanatomic Subunits

Impulses flow from the cerebrum out to the muscle, with stepwise compartmentalization of the anatomical subunits in between. (See Table 1 on page 2.) Because lesions involving the motor areas of the cerebral hemispheres can result in weakness (particularly unilateral), it is important to identify deficits unique to the cerebral cortex. These include dysfunction in language (*aphasias,* e.g., expressive aphasia—inability to name an object), receptive abilities (*agnosias,* e.g., anosognosia—lack of awareness of a profound neurologic deficit), and complex cerebral motor abilities (*apraxias,* e.g., inability to button a shirt in the absence of limiting sensory or motor impairment). Particularly, aphasias must be distinguished from *dysarthrias* (inability to form or produce understandable speech), since aphasias come from dominant cerebral hemispheric lesions, while dysarthrias can be due to a brainstem lesion or another process affecting motor control to peripheral speech organs. *Neglect* (inattention) is also a sign referable to the cerebral hemisphere—in this case, the nondominant cerebral hemisphere, resulting in unawareness of hemispace contralateral to the involved side. The presence of any such cortical findings will exclude a lesion deeper in the brain or in the brainstem.

Processes involving the internal capsule and brainstem can result in weakness, while unintentional movements usually characterize abnormalities of the basal ganglia. More peripherally, the spinal nerves emanate from the anterior horn of the spinal cord, which marks the anatomical beginning of the lower motor neuron (LMN). This neuroanatomic distinction is clinically important, since the distinction between upper motor neuron (UMN) vs. LMN signs (discussed later) is critical to localize a lesion.

Epidemiology

While weakness is a commonly encountered ED complaint, true neuromuscular processes are infrequent, with the exception of strokes and spinal or peripheral nerve entrapment syndromes.[2] Guillain-Barré syndrome (GBS) has become the leading nontraumatic, non-stroke cause of acute flaccid paralysis in Western countries, with an incidence of 0.75-2.0 cases per 100,000 people.[3] Myasthenia gravis (MG) is the most common cause of neuromuscular transmission disease, with a prevalence of 14.2 cases per 100,000 people.[4] Botulism occurs much less frequently, with only slightly over 2000 total U.S. cases reported to the Centers for Disease Control and Prevention (CDC) from 1973 through 1996.[5] Recent reports suggest that West Nile virus can also cause a flaccid paralysis.[6,7]

Differential Diagnosis

The differential diagnosis of weakness is extremely broad, including neurologic, cardiovascular, infectious, toxic, traumatic, autoimmune, metabolic, neoplastic, and congenital processes. Often malaise is secondary to a primary problem such as worsening heart failure or an infection. When a neurologic or neuromuscular problem is suspected, adhere to the algorithmic approach outlined in this article to capture the right "neurologic neighborhood" (see Table 1). Once there, awareness and exclusion of potentially life-threatening or morbidity-producing processes is critical, since in some cases, progression to respiratory failure can occur over hours.

Prehospital Care

Consistent with the prehospital priorities of any emergency condition, medics should support airway, breathing, and circulatory stability as needed. Importantly, in the setting of hypertension and unilateral weakness, blood pressure reduction should generally be avoided. In the setting of a cerebrovascular emergency, a sudden drop in mean arterial pressure may decrease perfusion to the brain and cause neurologic deterioration. Some prehospital systems screen for stroke, which allows receiving hospitals to activate "Code Stroke" protocols.

Emergency Department Evaluation

General Approach

Most patients complaining of weakness will require a

thorough history and physical examination to sort out this nonspecific complaint. The history should include a description of the distribution, time course, and clinical features associated with the weakness. (See **Table 2**.) Begin by categorizing the patient's weakness as either unilateral or bilateral. Once this is established, follow the Clinical Pathways on page 14 (for unilateral weakness) and page 15 (for bilateral weakness) to establish the anatomic lesion. Importantly, sometimes a psychiatric state or nonclassifiable cause of weakness will be suspected. In those instances, as long as potentially rapidly deteriorating conditions are excluded (see Table 1 on page 2), the patient can be referred to a specialist or primary care provider for further evaluation.

Stabilizing Management

The immediate life threats from acute neuromuscular weakness include inability to protect or maintain the airway, respiratory failure from thoracic and diaphragmatic muscle weakness, and circulatory collapse from autonomic instability. Clinical evaluation begins with assessment of the airway and respiratory function. To establish adequacy of the airway and its protective reflexes, assess phonation and the ability to handle secretions. The most important clinical findings associated with neuromuscular respiratory failure are rapid, shallow breathing, the recruitment of accessory muscles, and paradoxical movement of the abdomen during the respiratory cycle ("belly breathing"). The easiest parameter to recognize is tachypnea. Patients with progressive generalized neuromuscular weakness commonly begin to lose tidal volume before upper airway weakness develops, resulting in an increased respiratory rate.[8] Because of the intact ventilatory drive and increased rate of breathing, the pCO_2 may remain normal or low until the tidal volume becomes dangerously low. Equally insensitive may be a relatively normal pulse oximetry reading, for much the same reason. *Therefore, for patients suspected of having GBS, MG, or some other potentially rapidly deteriorating cause of acute weakness, selected pulmonary function tests are often needed to aid in intubation decisions.* Specifically, obtain a forced vital capacity (FVC), negative inspiratory force (NIF), or peak expiratory force. Either an FVC of less than 10-12 cc/kg or an NIF of less than 20 cmH_2O may indicate the need for intubation.[8] Importantly, an experienced respiratory technician needs to verify that the FVC and NIF are not artificially low due to inability to form a tight seal around the mouthpiece of the spirometer from weakness of the orbicularis oris muscle.

If intubation is considered, some authors suggest a non-depolarizing paralytic agent (such as atracurium or rocuronium) as opposed to a depolarizing agent (such as succinylcholine) to avoid hyperkalemia. However, the risk of severe hyperkalemia associated with succinylcholine administration and neurologic injury is largely a case report phenomenon.[9] While neurologic injury may increase potassium release associated with succinylcholine,[10] the risk of severe hyperkalemia appears to begin several days after the inciting event. In acute spinal cord injury, administration of succinylcholine in the ED is not harmful, because the period during which severe hyperkalemia occurs begins at 21 days.[11-15] Processes that are progressive, such as a polyneuropathy like GBS, seem to put the patient at risk of hyperkalemia after seven days.[16] Based on all of the available literature, a conservative estimate would put the initial threat of markedly increased potassium release at three days after complete denervation or seven days after partial denervation

Table 2. Clinical Features That Help Characterize Weakness.

Characteristic	Examples
Distribution	
Proximal	Muscular dystrophies, myopathies, neuromuscular junction disorders
Distal	Polyneuropathies
Generalized	Myopathies
Localized	Radiculopathy, plexopathy, peripheral neuropathy
Time course	
Sudden	Stroke or vascular-related
Acute/subacute	Polyneuropathies, myelopathies, myopathies, neuromuscular junction disorders
Insidious	Myopathies, amyotrophic lateral sclerosis, tumor-related processes, muscular dystrophies
Episodic	Hypokalemic/hyperkalemic periodic paralysis, neuromuscular junction process
Associations	
Aches, tenderness	Myopathy
Aphasia, agnosia, apraxia, neglect	Cortical stroke
Diplopia	Neuromuscular junction disorder, brainstem process
Bulbar symptoms	Neuromuscular junction disorder
Alcoholism	Peripheral neuropathy, myopathy, entrapment neuropathy
Cocaine use	Acute myopathy, stroke
Vomiting/diarrhea, diuretic use	Electrolyte-induced myopathy
Heavy metal exposure	Polyneuropathy
Rash	Dermatomyositis
Tick exposure	Tick paralysis
Recent viral illness	Polyneuropathy, myelopathy
Bladder symptoms	Myelopathy, cauda equina syndrome

(Class II-III).

Autonomic dysfunction can accompany some neuromuscular disorders—most notably GBS (see Table 1 on page 2). Autonomic instability typically manifests as a hyper-sympathetic state and is heralded by a sinus tachycardia.[8] Subsequent abnormalities in heart rate or fluctuating blood pressure can occur. Bradycardia is rare but may require temporary pacing.[8] Importantly, autonomic failure and pulmonary embolism are the major causes of mortality in GBS, although specific referencing data are not available.[8]

History

After determining that a patient's weakness is either unilateral or bilateral, a few key questions will begin to localize the anatomical area of a patient's problem. Key components of the history for someone with *unilateral weakness* include the following:

- Are cortical signs present, such as aphasia, agnosia, apraxia, or neglect?
- Is the face involved?
- Is there a dermatomal or myotomal pattern to the description of weakness distribution?
- Is the description of weakness consistent with involvement of a particular peripheral nerve?
- Is there bowel or bladder involvement?

As a general rule, unilateral facial weakness implies a lesion above the spinal cord, either in the brainstem or cortex (or, in the case of Bell's palsy, a peripheral nerve). For more specific localization between these two, see "Clinical Pathway: Diagnostic Algorithm For Acute Nontraumatic Unilateral Weakness" on page 14. In the case of isolated extremity weakness, knowledge of common radicular and peripheral nerve entrapment syndromes is essential. A localized process (e.g., weakness associated with numbness and tingling of the ring and small finger of one hand) strongly suggests peripheral nerve entrapment (see "Clinical Pathway: Diagnostic Algorithm For Acute Nontraumatic Unilateral Weakness" on page 14 for notable examples), although in some cases distinguishing spinal from peripheral nerve entrapment can be challenging. Similarly, familiarity with key cervical and lumbosacral dermatomes and myotomes (see **Table 3**) will foster recognition of compression of those spinal nerve roots and may help to differentiate spinal root compression from a more peripheral site of compression.

With regard to *bilateral weakness*, the answers to the following historical questions will define the likely site of weakness:

- Is the mental status impaired?
- Which limbs are involved?
- Is a sensory level deficit suggested, or is there any sensory involvement?
- Is there bladder involvement?
- Does the weakness tend to involve primarily proximal or distal muscles?
- Is there a fluctuating pattern to the weakness?
- Are there associated bulbar signs?

A central nervous system (CNS) lesion causing bilateral weakness will usually have accompanying diminished mental status, unless the pathology resides in the spinal cord. Presence of a sensory deficit at or below a sensory level points to a myelopathy, as does any abnormality in bladder function.

The pattern and distribution of weakness will help to narrow the etiology. The proximal motor weakness typically found early in the course of a myopathy may be suggested by difficulty walking up stairs or getting out of a chair if the lower limbs are involved, or difficulty combing or brushing hair with arm involvement. Patients who describe being "weak everywhere" or who have so-called patternless weakness are most likely to be experiencing malaise stemming from either an associated

Table 3. Cervical And Lumbosacral Dermatomes And Myotomes.

Spinal level	Key sensory area for dermatomal testing	Myotome
C5	Radial antecubital fossa	Elbow flexors (biceps*, brachialis, and brachioradialis*)
C6	Thumb	Wrist extensors (extensor carpi radialis longus and brevis)
C7	Middle finger	Elbow extensors (triceps*)
C8	Little finger	Finger flexors* (distal phalanx—flexor digitorum profundus)
T1	Ulnar antecubital fossa	Hand intrinsics (interossei)
L2	Mid-anterior thigh	Hip flexors (iliopsoas)
L3	Medial femoral condyle	Knee extensors* (quadriceps)
L4	Medial malleolus	Ankle dorsiflexors (tibialis anterior)
L5	Dorsal second/third toe web space	Long toe extensors (extensor hallucis longus)
S1	Lateral heel	Ankle plantar flexors* (gastrocnemius, soleus)

* Commonly tested reflexes

medical illness or psychogenic cause. A fatiguing pattern to the weakness, suggested by worsening with repeated activity such as chewing, suggests a neuromuscular junction process. Alternatively, acute attacks of weakness lasting a few hours and then spontaneously resolving should prompt exploration for periodic paralysis due to imbalances in potassium regulation. *Visual symptoms, particularly ptosis or diplopia, and bulbar signs are important to identify, since they are invariably associated with an NMJ process.* Bulbar muscle weakness may manifest as nasal speech, coughing, dysphagia, or dysarthria and will call for careful cranial nerve testing.

Age extremes should prompt consideration of certain processes, such as occult infection or infantile botulism in the very young. In the elderly, consider occult infection, metabolic disorders, a CNS event, or a medication-related process.[17] While various medications can classically lead to certain categories of weakness, such as myopathies from steroids or lipid-lowering agents, carefully scrutinize the impact of all medications in the geriatric population. *In one study of patients with a chief complaint of weakness or dizziness, 20% of those over age 60 had symptoms attributed to prescription medications.*[18]

The time course of symptom onset and progression can help categorize the cause of weakness. When it is abrupt in onset, a stroke or other vascular etiology is suggested. Most other categories of weakness develop over hours to days to weeks.

A few somewhat unusual historical points may provide clues. The complaint of "cold reversal" (cold stimuli being felt as painful and hot) is virtually pathognomonic for ciguatera poisoning.[19,20] Consider multiple sclerosis when a patient describes an electrical or tingling sensation that travels down the spine or into the extremities. This is referred to as Lhermitte's sign (transient sensory symptoms usually precipitated by neck flexion). Although commonly found in multiple sclerosis, a similar complaint can accompany radiculopathies, or more rare entities such as vitamin B_{12} deficiency and Chiari malformation.[1] Another feature suggesting multiple sclerosis includes weakness precipitated by a hot bath. Finally, in a parenteral heroin abuser, consider wound botulism due to contaminated heroin.[21-23]

Physical Examination

The overall physical examination is most helpful for excluding an illness causing malaise, which the patient interprets as weakness. Start with the vital signs. Because occult infection may present as weakness, consider a rectal temperature, since variables such as tachypnea or mouth breathing can yield a falsely low oral temperature.[24-26] Examine the skin for the bronze discoloration of Addison's disease or the heliotropic eyelid rash (a red-purple or violaceous, edematous, macular rash) characteristic of dermatomyositis.[27] If the history suggests a possibility of tick exposure, carefully search for a tick, since removal of the tick is rapidly curative in tick paralysis.[28] Conjunctival pallor suggests anemia, while oral thrush implies immune compromise. Carefully assess the neck for signs of a thyroid abnormality, since thyroid disorders frequently cause weakness.[29,30]

Neurologic Examination

The motor examination is especially helpful in the weak patient. Components of a detailed examination include evaluation of strength, reflexes, fatigability, tone, and fasciculations. Importantly, there is no place for nebulous or uninterpretable documentation of the neurologic examination (e.g., "grossly intact"). For patients with histories highly consistent with spinal or peripheral nerve compression syndromes, an exhaustive neurologic examination is not required.

One critical aspect of localizing a weakness syndrome involves identifying whether upper motor or lower motor neuron signs are present. (See **Table 4**.) UMN disease signs include spasticity, hyperreflexia, and an extensor plantar response (the Babinski reflex) and are lacking in pure peripheral disease, which begins with the spinal nerve root. However, recognize that hyporeflexia and a flaccid paralysis may occur with acute central lesions, with hyperreflexia and spasticity developing later. A common example is the patient with an acute spinal cord injury from trauma. While muscle atrophy and fasciculations also classically help to distinguish LMN from UMN processes, these will rarely be present in patients presenting with acute or subacute weakness, since these typically develop over the long term. It is worthwhile to note that amyotrophic lateral sclerosis presents with both the UMN and LMN features of fasciculations and hyperreflexia.

If weakness is bilateral and signs of LMN disease are present, the major disorders to differentiate are neuropathies, myopathies, and neuromuscular junction disorders.

Table 4. Upper Motor Neuron vs. Lower Motor Neuron Signs.

Clinical test	Upper motor neuron	Lower motor neuron
Reflexes	Hyperreflexia	Hyporeflexia
Muscle tone	Increased/Spastic	Decreased/Flaccid
Fasciculation	None	Present
Atrophy	None	Severe
Babinski sign	Present	Absent

(See **Table 5**.) The key characteristic that distinguishes neuropathies such as GBS is sensory involvement. While myopathies can have associated myalgias, other sensory symptoms should be lacking from these processes. Additionally, neuropathies tend to involve distal muscle groups over proximal muscles, while myopathies are more proximally distributed. Deep tendon reflexes will be decreased in neuropathies but are an unreliable distinguishing feature for myopathies, since they may be present, decreased, or absent. The most distinguishing feature of neuromuscular junction processes is early involvement of the ocular musculature, most often in the form of ptosis and diplopia.

Assessing Strength

The central component of the motor examination in a weak patient will be strength testing. To facilitate interpretation of the examination, employ the standardized motor grading scale agreed on by the Medical Research Council.[31] (See **Table 6**.) Based on historical features, determine if there is a pattern to the weakness. Hemiparesis suggests a hemispheric lesion, while paraparesis is consistent with a spinal cord lesion. If the history suggests a proximal pattern of weakness, such as difficulty walking up stairs or getting out of a chair, seek to distinguish proximal from distal muscle weakness (which will point to a myopathic process vs. a neuropathy). Functional tests include the ability to rise from a squat or out of a chair, or stepping up onto a stool or chair. For isolated extremity weakness suggesting an isolated spinal nerve or peripheral nerve process, rely on testing specific muscle groups. For example, to differentiate an L5 from an S1 radiculopathy due to a herniated disc, test dorsi and plantar flexion of the foot; if an L5 lesion is present, the patient may not be able to walk on his or her heels, while if an S1 lesion is present, the patient will have trouble walking on his or her toes. If a neuromuscular junction process is suspected, oculomotor and bulbar testing is critical. Assess extraocular movements, including the eyelids, masseter muscle strength, facial expression, palatal movement, sternocleidomastoid, and trapezius muscles.

When facial weakness is present, examine the symmetry of forehead skin wrinkles and the strength of forehead muscles to distinguish a Bell's palsy (peripheral 7th cranial nerve dysfunction) from a central process. In Bell's palsy, the forehead will be weak, while with a central process, the forehead will be spared, due to bilateral cortical innervation. Importantly, an isolated "central 7th" lesion, with no other weakness or cortical deficits, is extremely rare, and most often represents a subtle form of Bell's palsy. Weakness of the 9th or 10th cranial nerve can be detected by noting asymmetric movement of the soft palate (uvula is deviated), while weakness of the 12th cranial nerve will lead to the tongue pointing to the weak side. Assessing the symmetry of

Table 5. Distinguishing Features Of Bilateral Peripheral Processes.

	Neuropathy	Myopathy	Neuromuscular junction
Distribution of weakness	Distal > proximal	Proximal > distal	Diffuse (ocular, bulbar, and respiratory)
Reflexes	Decreased	Normal to decreased	Normal
Sensory involvement	+	-	-
Atrophy	±	±	-
Fatigue	±	±	+
Serum CPK	Normal	Normal to increased	Normal

Table 6. Standardized Motor Examination Rating Scale.

Score	Response
0	Total paralysis
1	Palpable or visible contraction
2	Active movement through full range of motion with gravity eliminated
3	Active movement through full range of motion against gravity
4	Active movement through full range of motion against resistance (but weak)
5	Normal

Source: Medical Research Council. Aids to the investigation of peripheral nerves. London: Crown Publishing; 1976.

Table 7. Tendon Reflex Rating Scale.

Scale	Tendon reflex amplitude
0	Absent with reinforcement
1	Present but decreased in amplitude and velocity from the normal range and elicited with reinforcement
2	Normal amplitude and velocity without reinforcement
3	Increased in amplitude and/or velocity with spread to adjacent site
4	Increased in amplitude and/or velocity with spread to adjacent site and duplication of the jerk or clonus

shoulder shrug will identify unilateral 11th cranial nerve weakness.

Assessing Reflexes

Reflex findings also aid in lesion localization. (See Table 3 on page 5.) Tendon jerks are conventionally graded on a scale from zero to 4, with zero representing absent jerks and 4 representing hyperactivity with clonus. (See **Table 7** on page 7.)

If a lesion involves a cerebral hemisphere, anticipate asymmetry between the sides, with hyperreflexia on the affected side. The presence of symmetrical hyperreflexia and extensor plantar responses indicates an interruption of the corticospinal tracts bilaterally. This usually means a spinal cord lesion, but it could be the result of bilateral hemisphere disease or a brainstem process. If nerve root compression is suspected from the history, unilateral *lack* of a given lower extremity reflex can help localize the lesion. For example, loss of one ankle jerk indicates a lesion of the S1 nerve root. Alternatively, symmetrical absence of ankle jerks and decreased knee jerks indicate a neuropathy.

The *Babinski sign* is a UMN lesion finding and exists when the great toe dorsiflexes and the other toes fan out when the sole of the foot is stroked.[32] (A less sophisticated, but equally unambiguous, way to refer to the presence of the Babinski sign is the phrase "up-going toe.") Describe the response of the great toe as either flexor or extensor (e.g., extensor plantar response). It is important to distinguish a Babinski sign from simple withdrawal of the great toe, which will be the response of many normal patients who are ticklish.

A few other maneuvers will help the emergency medicine practitioner localize the lesion (and impress the neurologist). A positive *Hoffman sign* consists of reflex flexion of the fingers, most easily seen in the thumb, and is a UMN sign. Test this reflex by holding the patient's middle finger between your second and third fingers, and flick the patient's distal phalanx downward with your thumb. Recognize that the presence of a Hoffman sign alone does not imply pathology. As with any individual feature of the neurologic examination, it must be interpreted in the context of other tendon jerks and signs of a UMN lesion. Clonus represents the repetitive contraction of a muscle or muscle group and is most easily elicited at the ankle. While clonus is another UMN sign, one or two beats of reflex clonus can be obtained at the ankle in many normal individuals. Test for clonus with the patient in the supine position and hold the patient's leg flexed at the knee. While maintaining this position, rapidly dorsiflex the foot and hold it in the dorsiflexed position. In a patient with a severe myelopathy, sustained clonus can be maintained virtually indefinitely as long as upward pressure is maintained on the foot. Finally, absence of the so-called cutaneous reflexes (the *cremasteric reflex* and *anal wink*) can help localize lesions. The cremasteric reflex (T12-L1) is elicited in the male by stroking the proximal inner thigh with a pointed instrument (or tongue blade) and observing the scrotal sac. A normal reflex involves a retraction of the scrotum. (Testicular torsion will also cause loss of the cremasteric reflex, but rarely will such a patient present with acute weakness.) The anal wink (S2-S4) is elicited by stroking the skin around the anal sphincter and watching it contract. Absence of either reflex is abnormal. Depending on the other neurologic examination findings present, spinal shock or damage of the lumbosacral cord or roots will be the cause.

Fatigability

The phenomenon of fatigability with initially normal strength is a specific characteristic of disorders of the NMJ.[33] In cases where the history identifies the bulbar or eye findings characteristic of an NMJ process, perform repetitive or sustained oculomotor muscle testing to provoke ptosis or diplopia.

Assessing Tone

Because muscle tone must be subjectively assessed with the patient relaxed and because non-neuromuscular

Cost- And Time-Effective Strategies For Acute Weakness

1. Maximize neuroanatomic localization by the history and, in particular, the examination.

A good neurologic examination is worth a thousand MRIs, especially when the MRI is of the brain and the pathology is in the neuromuscular junction! Since a great deal of emergency medicine involves neurologic problems, it is imperative for emergnecy physicians to be comfortable with basic neuroanatomic localization and pathologic conditions that affect each subunit. Equally important is the ability to perform a neurologic examination that will aid in localizing pathology.

Avoid neuroimaging studies when weakness is highly consistent with peripheral nerve dysfunction.

2. Rely on observation or close follow-up rather than shotgun testing for cases in which the examination is unimpressive.

Patients with early Guillain-Barré syndrome may still have reflexes present and will have normal cerebrospinal fluid. No serological testing will help elucidate this diagnosis. Rather than performing extensive serological testing or a lumbar puncture, rely on the progression of the patient's features. In a reliable patient, this may not even necessitate admission to the hospital, as long as close follow-up is absolutely guaranteed. ▲

processes, such as bone or joint abnormalities, may confound testing, assessing tone may be challenging for the emergency medicine practitioner. Evaluate the LMN sign of *flaccidity* by looking for a difference from one side to the other if unilateral weakness exists.[1,34] For the upper extremity, shake the forearm and observe the floppiness of the movements of the hand at the wrist. Alternatively, with the arms raised overhead, compare the degree of flexion or limpness of the wrist on each side. To test for flaccidity in the lower extremities, rapidly flex the thigh after instructing the supine patient to let the leg flop or relax. In a patient with normal tone, the heel may transiently slightly come off the bed and then drag along the top of the bed as the thigh is flexed. The heel of the flaccid leg will drag across the bed from the very beginning. Alternatively, the spastic leg will jerk upward and the heel may never fall back to the bed. This maneuver can be particularly helpful in distinguishing psychogenic paraplegia from an acute spinal cord emergency. To assess hypertonic *spasticity*, which is a UMN sign, examine the biceps and adductors of the thigh. For example, with the patient lying down, hypertonicity in the adductors of the thigh can be felt by rapidly rotating the thigh back and forth. For the arm, rapidly flex and extend the elbow to feel a catch or interruption of extension at the elbow. Recognize, however, that rigidity (vs. spasticity) can also cause increased tone, but this will almost always indicate extrapyramidal dysfunction. Spasticity differs from rigidity in that it selectively increases the tone in the flexor muscles of the arm and the extensors of the leg, whereas rigidity affects flexors and extensors equally.[1] In particular, the "cogwheel rigidity" seen in Parkinsonism can be confused with spasticity. This term refers to resistance that stops and starts in a quick repetitive sequence as the extremity is passively moved through a range of motion. The severe muscle rigidity seen with neuroleptic malignant syndrome (classically referred to as "lead pipe rigidity") is an unmistakable finding.

Fasciculations

Since "muscle twitching" may be encountered as an ED complaint, some points regarding fasciculations are worth noting. *Fasciculations* are an LMN sign caused by disorders of the anterior horn cell or spinal nerve root compression, although they typically develop later in the LMN disease process. They are commonly experienced as a benign phenomenon in the absence of any disorder of the LMN.[35] Importantly, benign fasciculations can generally be differentiated from fasciculations due to LMN processes by several features.[1] They have a predilection for males, increase with age, and have a propensity to involve certain muscle groups, particularly the calves and thighs. When they occur in the arm muscles, they tend to be seen as a repetitive twitch in the same muscle fascicle, and they do not display associated weakness or atrophy. Alternatively, anterior horn or nerve root disease causes random twitches in many parts of the muscle.

Assessing Gait

Walking is one of the most important components of any neurologic examination, and in the case of weakness, gait testing will aid in distinguishing UMN from LMN lesions.[1] Spasticity caused by a bilateral UMN lesion will result in stiff, jerky movements of the legs, or if the lesion is unilateral, the spastic leg will be circumducted (a revolving around movement). Alternatively, distal weakness from an LMN lesion will produce a floppy foot or feet that slap(s) on the floor and must be lifted high to prevent the toe from dragging and tripping the patient ("foot drop").

Assessing Sensation

While the presence, pattern, or absence of sensory symptoms and signs can be helpful in confirming the neuroanatomic level producing weakness, the subjective nature of sensory findings can make interpretation daunting. Classically, a cortical lesion causes relatively mild hemisensory loss, which affects touch and proprioception more than pain. The patient may simply describe this as the arm or leg "feeling funny." More specifically, sensory impairment known to require cortical processing, such as stereognosis and graphesthesia, will localize a lesion to the contralateral sensory cortex. *Stereognosis* relies on light touch and position sense and is tested by placing an object in a patient's hand and having him or her identify it with eyes closed. *Graphesthesia* is tested by tracing a number or letter on the surface of the skin, usually the palm, and asking the patient to name the number or letter.

A spinal cord lesion will often affect sensation on both sides of the body, with the upper level of the sensory loss defining the lesion level. In contrast, cervical central cord lesions most commonly produce a "cape" sensory loss over the shoulders that affects pain and temperature sensations, but spares vibration and proprioception (so-called "dissociated" sensory loss). Lesions of the conus medullaris or cauda equina produce loss of sensation in the perineum. To test for vibratory sensation, a beeper set on the vibrate mode can be used in place of a tuning fork, but don't expect this substitution to detect subtle deficits. An absence of sensory symptoms in the setting of suspected neuromuscular disease, other than muscle aches, suggests that the weakness is due to a myopathy or NMJ process.

Sorting Out Psychogenic Causes Of Weakness

A common pattern of feigned weakness is a sudden collapse of the limb after an initial, often normal effort ("giveaway weakness"). Typically this results in a phasic, ratchet-like collapse as the muscle is tested, most commonly the biceps. Another contrived pattern may be exhibited when the shoulder is abducted and then pushed downward by the examiner. The malingering patient will bend his trunk to that side, giving the impression that his arm is being pushed downward, when in fact the relationship with the trunk remains the same. In unilateral lower-extremity weakness, testing for

Hoover's sign can be helpful. With the patient lying supine, judge the effort put forth in the lower extremities by placing one hand between the heel and the examining table while testing the ability of the patient to raise the other leg off the table. Normally, with full effort the heel on the table is forced downward to support the raising of the opposite leg. With feigned weakness in one leg, when full effort is used to raise the "good leg," normal downward pressure will be felt from the feigned "weak" leg. Alternatively, when the feigned "weak" leg is supposed to be raised, very little if any pressure will be felt under the opposite leg with presumably normal strength.

When evaluating a weak upper extremity, pay close attention to the response when testing for "pronator drift." A true weak arm will pronate (and sometimes flex) when drifting downward, since supination is most affected by weakness. An arm that drifts or drops downward with no pronation indicates malingering. To distinguish psychogenic paralysis of an arm, observe the movement of the arm when shaking the patient's shoulders. A truly paralyzed arm that is held limply at the side will flail from side to side when the patient's shoulders are shaken back and forth. If, instead, the arm is observed to remain tightly held against the body, it has normal strength and tone.

Hysterical paraplegia can be distinguished from a true spinal cord emergency in several ways. It may initially be suspected if the patient reacts remarkably calmly about their severe deficit (so-called *"la belle indifference"*). On observation, the patient may display ease in rolling over and moving in bed, with confirmation on examination by the presence of normal reflexes. If a patient feigning "weak legs" can be convinced to undergo gait testing, suspect nonorganic weakness if the patient displays a markedly exaggerated effort to take a step. The malingerer may display extraordinary strength and coordination in a contrived effort to create an impressively abnormal gait. Despite these tests and patterns that may indicate a psychogenic cause of the patient's weakness, diagnosing a patient with "malingering" or "psychosomatic disorder" in the ED is fraught with pitfalls. Unless you are absolutely certain of this diagnosis, it is prudent not to label the patient with a psychogenic disorder. Instead, ensure follow-up to confirm the absence of serious pathology.

Autonomic Nervous System Dysfunction

Among the most obvious impairments of sympathetic innervation is Horner's syndrome, which consists of ipsilateral ptosis (lid droop), miosis (small reactive pupil), and anhidrosis (lack of sweating) of the face. Interruption of descending preganglionic sympathetic fibers in the brainstem or spinal cord can lead to Horner's syndrome. More peripherally, since postganglionic sympathetic fibers course along the carotid arteries, an internal carotid artery dissection can produce an ipsilateral partial Horner's syndrome (without anhidrosis). The miosis and ptosis occur because of a compressive effect of the expanding intramural hematoma from the internal carotid artery dissection on the sympathetic fibers. Facial anhidrosis is not present because the facial sweat glands are innervated by the sympathetic plexus surrounding the external carotid artery.

Like sympathetic disruption, parasympathetic disruption can occur from one of several lesions. If a midbrain lesion impacts the third nerve nucleus or nerve, it can disturb the parasympathetic pupillomotor fibers, resulting in paralysis of the pupillary sphincter, producing pupillary dilatation. If an acute transverse spinal cord lesion exists, autonomic dysfunction, especially loss of sweating, can provide clues to the level of the lesion, since sweating will be lost below the lesion. To detect this, slightly rub the dorsal surface of the forefinger along the skin, starting below the expected level of the lesion, and stroke upward.[1] The finger will slide easily over the smooth, dry skin below the lesion, but stick momentarily as it meets the normal moist skin at the upper border of the lesion.

Diagnostic Testing

The extent of diagnostic testing performed in the ED on a weak patient can vary dramatically, depending on the differential diagnoses and pace of deterioration. Certainly, a potentially septic patient with no obvious source of infection will undergo extensive diagnostic testing, whereas patients with peripheral nerve entrapment syndromes may undergo no diagnostic testing. For any diffusely weak patient, it may be reasonable to perform a hemoglobin measurement and perhaps electrolyte panel testing. Beyond those baseline tests, a focused differential diagnosis will dictate selected testing.

While an almost reflexive tendency to order calcium, magnesium, and phosphate may exist, refrain from such a "shotgun" approach unless renal insufficiency, malignancy, diuretic use, volume depletion, mineralocorticoid deficiency, or other predisposing conditions are present or suspected.[36] While some believe an ECG is a reasonable screening tool if an abnormal potassium or calcium level is suspected,[37,38] other data suggest it is not reliable.[39]

While both pulse oximetry and arterial blood gas analysis provide a reasonable index of oxygenation, they are insensitive in identifying patients with significant neuromuscular disease. A baseline chest radiograph may provide useful diagnostic information when a malignancy is suspected. Such circumstances would include a brachial plexopathy when Pancoast syndrome is suspected or to explore for small-cell lung cancer in a patient with Lambert Eaton syndrome (discussed later).[40,41] Since the total serum creatine phosphokinase level is a sensitive marker for muscle damage, perform it as a screening test if an acute myopathy is considered. On occasion, thyroid function tests or serum cortisol levels may be clinically indicated, but leave esoteric testing to a rheumatologic or neurologic consultant, since most of these will not impact the ED disposition.

Cerebrospinal fluid (CSF) analysis may help diagnose GBS or myelitis. In GBS, the CSF typically reveals

elevated protein without pleocytosis, whereas with myelitis, CSF analysis reveals a pleocytosis, with a normal glucose, and normal or slightly elevated protein.[42] A process such as an inflammatory demyelinating peripheral neuropathy from HIV may yield a lymphocytic pleocytosis.[43]

Neuroradiologic testing depends on the location of the suspected lesion. If a cortical process is assumed, obtain a nonenhanced head CT. While this study can appear normal in the early stages of ischemic stroke , it will identify acute hemorrhage, mass lesions, and cerebral edema.[44] If an intracranial tumor or infection is suspected, a contrast head CT may be indicated. Subcortical lesions, such as those in the brainstem, are best imaged via magnetic resonance imaging (MRI), since this portion of the brain is poorly visualized on head CT. MRI, while difficult to obtain on an emergent basis, is the imaging modality of choice if a spinal cord or nerve root process is suspected.[44] If MRI is unavailable or the patient has contraindication to MRI, consider CT scanning with myelography, since it has comparable effectiveness to MRI in diagnosing many myelopathic processes.[45]

An Algorithmic Approach To Acute Non-traumatic Weakness

Unilateral Weakness

Cortical Findings

The initial question to explore in a patient complaining of unilateral weakness is whether or not the limb(s) and the lower face on the *same side* are involved. If so, the lesion resides in the contralateral cerebral hemisphere. To further pinpoint the lesion, evaluate for cortical signs, such as aphasia, neglect, apraxia, a gaze preference, or a visual field deficit. Aphasia usually corresponds to a left hemispheric stroke, since the left cerebral hemisphere is "dominant" (controls language function) in the majority of both right-handed and left-handed individuals. Left-sided neglect or "hemi-inattention" is a cortically mediated deficit, which usually results from a right hemispheric stroke. This usually impressive phenomenon will result in the practitioner being totally ignored if the clinician is conducting the clinical evaluation from the patient's left side. While patients may experience right-sided neglect with left hemispheric lesions, detecting neglect in this case is more challenging, due to the frequently superimposed aphasia.

When one of the command centers for conjugate gaze located in either frontal lobe is damaged, the unopposed action of the other will cause deviation of the eyes to the side of the lesion and away from the hemiplegia (the patient "looks to the lesion"). The other important cortical eye finding is a contralateral homonomous hemianopia (losing the right half or left half of the vision in both eyes), which will occur with a lesion anywhere along in the hemispheric visual pathways. Cortical sensory loss will accompany the hemiplegia if the sensory cortex, located across the Rolandic fissure, is involved. Rarely, a cortical infarction can cause pure motor hemiparesis, with no cortical findings other than hemiparesis.[46]

Lacunar Syndromes

Lesions in the subcortical cerebral hemisphere, namely deep hypertensive hemorrhages and ischemic lacunar strokes, can cause weakness. Importantly, these will lack the previously mentioned features restricted to the cortex. (See **Table 8**.) Lacunar infarcts involve much less total area than large vessel strokes, but they can result in impressively extensive weakness. These small, deep cerebral infarcts are almost exclusively due to disease of the perforating vessels, caused by hypertension, and account for about one-quarter of strokes.[47] Several nonischemic lesions have also been associated with each of the classically described lacunar syndromes, including hemorrhage and tumor.[48-51]

Brainstem Processes

The hallmark of weakness syndromes referable to the brainstem is "crossed" findings (ipsilateral cranial nerve weakness and contralateral hemiparesis). This occurs with lesions to cranial nerve nuclei or their tracts and corticospinal tracts before their decussation. The cranial nerve dysfunction and pattern of involvement will help to further refine lesion location within the brainstem. Dysfunction of cranial nerves III and IV suggests a midbrain lesion; VI and VII, the pons; and IX-XII, the medulla. Most frequently, this will be due to a vertebrobasilar or so-called "posterior circulation" stroke. (See **Table 9** on page 12.)

Table 8. Lacunar Syndromes With Weakness As A Feature.

Name	Clinical findings	Usual location
Pure motor stroke	Paralysis of the face, arm, and leg on one side; no sensory signs, visual field defect, aphasia, apraxia, or agnosia	Posterior limb of the internal capsule or in the pons
Ataxic hemiparesis	Weakness of the lower limb associated with striking dysmetria of the arm and leg on the same side	Corona radiata and the anterior limb of the internal capsule
Sensorimotor stroke	Hemiparesis or hemiplegia with ipsilateral sensory impairment	Thalamus and adjacent internal capsule
Dysarthria (clumsy hand syndrome)	Facial weakness, severe dysarthria, and dysphagia, with mild hand weakness and clumsiness	Corona radiata and the anterior limb of the internal capsule

Brown-Séquard Syndrome

Most myelopathies present with bilateral weakness, even if their distribution is patchy. The main exception to this is the *Brown-Séquard syndrome*, in which hemisection or hemi-involvement of the spinal cord results in ipsilateral hemiplegia or monoplegia, ipsilateral loss of vibration and proprioception, and contralateral loss of pain and temperature below the level of the lesion. While this typically has a penetrating traumatic etiology, idiopathic cases from pre-existing dural defects have been reported.[52-55]

Radiculopathies

Continuing from the central nervous system to the peripheral nervous system, the next processes to consider are *radiculopathies*, a term that refers to any diseased condition of the spinal roots. These syndromes typically present with pain in a dermatomal distribution, with demonstrable weakness on examination less frequently identified.[56] Cervical and lumbosacral dermatomes and myotomes are the only ones worthwhile remembering, since most spinal nerve compression syndromes usually involve one of those levels.[57]

Plexopathies

The best clue in diagnosing a plexopathy (a lesion of a nerve plexus, such as the brachial or lumbar plexus) is identifying a motor and sensory deficit in a limb that involves more than one spinal or peripheral nerve. Some of these cases are due to trauma, but many result from radiation or malignancies.[58,59] LMN signs are more prominent than sensory findings.

Peripheral Nerve Processes

Peripheral nerve injuries most typically involve *neurapraxias*, which imply temporary insult to the nerve that resolves after the source of compression is relieved. Compression of peripheral nerves occurs in locations where the nerve passageway is narrow, such as around joints where the nerve slides back and forth with flexion and extension.

Entrapment of the median nerve within the carpal tunnel, or carpal tunnel syndrome, is the most common of all peripheral nerve compression syndromes.[60] On history, distribution of symptoms to the radial part of the hand and nocturnal exacerbation of symptoms correlate most strongly with carpal tunnel syndrome.[61] While Tinel's sign (percussion directly over the median nerve at the wrist) is often recommended to help diagnose carpal tunnel syndrome, two reviews have concluded that it is not useful for this purpose.[62,63] Phalen's test, which increases nerve stretch or compression by sustained wrist flexion, has greater sensitivity and specificity than Tinel's sign, but it still has little diagnostic value.[63] *More sensitive and specific tests include testing thumb adduction and the hand elevation test.*[63,64] To perform the hand elevation test, have the patient elevate both hands above the head and maintain that position until they feel paresthesia or numbness in the distribution of the median nerve. Importantly, since the nerve branch to the thenar eminence arises before the carpal tunnel, the patient should have no symptoms over this area. The test is considered positive if symptoms occur within two minutes. To test thumb adduction, instruct the patient to raise his or her thumb perpendicular to the palm as the examiner applies downward pressure on the distal phalanx. This maneuver reliably isolates strength of the abductor pollicis brevis, which is innervated only by the median nerve. Oral steroids are more effective than nonsteroidal anti-inflammatory drugs or diuretics for patients who opt for conservative treatment.[65]

While the ulnar nerve can get compressed at the shoulder, elbow, or wrist, the so-called cubital tunnel syndrome is the most common compressive neuropathy involving the ulnar nerve.[66] This tunnel exists where the nerve passes from the medial aspect of the upper arm, through a narrow passage behind the medial epicondyle of the distal humerus, and into the forearm. Anyone who has ever hit his or her "funny bone" has experienced this usually fleeting neuropraxia.

Every ED physician should be familiar with the "Saturday night palsy," from compression of the radial nerve at the axilla or along the humerus.[67] This usually occurs in an intoxicated patient, as a result of falling asleep in a chair with the involved arm hanging over the back of the seat. Because the resulting wrist drop will impair grip mechanics and weaken grip strength, it is important to consider this entity when a patient complains of weakness in one hand. By passively extending the patient's wrist, the emergency physician can distinguish a radial nerve neuropraxia from a more central process. Grip strength will improve or return to normal with passive wrist extension when a "Saturday night palsy" is present.

Table 9. Notable Midbrain And Brainstem Syndromes Causing Weakness.

Location	Eponym	Ipsilateral	Contralateral
Midbrain	Weber	3rd nerve palsy	Hemiparesis
Pons	Millard-Gubler	Facial palsy	Hemiparesis
Pons	Foville's	Facial paresis, abducens palsy	Hemiparesis
Pons	Locked-in	Quadriparesis with paralysis of horizontal eye movements and jaw, face, and bulbar muscles; consciousness and vertical eye movement preserved	

Peroneal nerve neuropathies are the most common peripheral nerve compression syndromes involving the lower limb.[68] The common peroneal nerve is most frequently irritated from compression when crossing the legs at the knee, while the deep peroneal nerve is most frequently compressed in women from the straps of high-heeled shoes that compress the nerve anteriorly at the level of the lower shin. In either case the patient will complain of a foot drop.

Bilateral Weakness

Central/Brainstem Lesions

A CNS lesion causing bilateral weakness will usually present with diminished mental status, unless the pathology resides in the spinal cord. Certainly bilateral, symmetrical, simultaneous lesions of the motor cortex are unlikely, but a lesion in the interhemispheric fissure, such as a parasagittal meningioma, could result in paraparesis simulating a spinal cord lesion. This is because the leg areas on the medial sides of the motor strip of each cerebral cortex face each other in the interhemispheric fissure. Another rarely occurring, but tiny lesion at the decussation of the pyramids *(cruciate paralysis of Bell)* could cause bilateral paralysis of the upper extremities, with no involvement of the lower extremities. However, this usually results from trauma.[69-71] Perhaps the most tragic of all is the "locked-in syndrome," which consists of quadriparesis, mutism, and preserved consciousness.[72] In this case, a pontine lesion causes paralysis of horizontal eye movements and jaw, face, and bulbar muscles, but preserves consciousness and vertical eye movement. In the ED, distinguishing a patient with the locked-in syndrome vs. one who is comatose is critical, since "locked-in" patients historically have a devastating natural course and may be candidates for intra-arterial thrombolytic therapy to recanalize a basilar artery occlusion. Remarkable neurologic recovery has been achieved even up to 12 hours after a patient's symptom onset.[73]

Myelopathies

Nontraumatic myelopathies typically present with bilateral extremity weakness and sensory deficits. Symptoms typically involve the legs, and less commonly include the arms when cervical spinal cord lesions are involved. Bowel and bladder symptoms may appear if the descending pathways that control the urinary and rectal sphincters are interrupted.[74] Impotence or priapism can also occur. Other disturbances in autonomic function can be found below the level of the lesion, such as loss of sweating and trophic skin changes, as well as loss of temperature control and vasomotor instability.

The time course of onset of a myelopathy will help differentiate its cause. Acute disruptions not related to trauma suggest a vascular lesion, while a subacute or chronic time course hints at an inflammatory process. While myelopathies typically present with some degree of signs of UMN disease, the traumatic and vascular processes that produce myelopathy often initially produce a flaccid areflexic paralysis known as *spinal shock*. Within days, the motor syndrome becomes characteristic of a UMN paralysis with hyperreflexia and bilateral extensor plantar responses. While a distinct level to the sensory findings is classically described, a sensory level may not be obvious on examination.

The emergency physician's main job is to recognize a myelopathy and rule out epidural compression syndrome. It is important to realize that significant back pain may not exist with these processes, while pain is virtually always a prominent feature of a radiculopathy.It is not necessary to generate the exhaustive list of lesions that can cause extradural, intradural, extramedullary, or intramedullary lesions. A myelopathy will usually be diagnosed through the history and physical alone and is almost always confirmed by MRI. Importantly, if an epidural compression syndrome is suspected, contact a spine surgeon immediately and begin steroids (dexamethasone 10-100 mg IV), since prognosis depends on the patient's neurologic status at the time of intervention.[75] (See also the February 2000 issue of *Emergency Medicine Practice*, "Back Pain: Cost-Effective Strategies For Distinguishing Between Benign And Life-Threatening Causes.")

Acute transverse myelitis is an acute inflammation of the spinal cord. The classic presentation is acute, symmetric numbness and weakness, with bladder dysfunction.[76] The term transverse is somewhat of a misnomer, since the inflammatory process can be patchy, and functional loss is often incomplete. It usually affects patients 15-40 years of age and is associated with a broad range of precedent or concurrent infections.[77,78] The physical examination reveals paraplegia, usually symmetric, with weakness more profound in the lower extremities. Importantly, significant pain may be absent in patients with myelitis. As with other spinal cord problems, MRI has proven to be the best diagnostic modality for acute transverse myelitis, but there may be a delay of five days between the onset of symptoms and the appearance of lesions on the MRI.[79] CSF analysis reveals a pleocytosis, with a normal glucose, and normal or slightly elevated protein.[42]

Although uncertainty remains as to the beneficial effect of steroids in acute transverse myelitis, this treatment is widely offered to patients in the acute phase.[80] The prognosis with acute transverse myelitis varies, with most recovery achieved within three months of diagnosis,[81] with a direct relationship between initial deficit severity and long-term outcome.[42]

Peripheral Neuropathies

Unlike myopathies and NMJ disorders, neuropathies affect both motor and sensory symptoms. They cause weakness due to the involvement of a large number of nerves. Distal power is reduced most dramatically, since neuropathies most severely affect longer nerves. Deep tendon reflexes are characteristically diminished. *Importantly, the weakness from a peripheral neuropathy is often heralded by paresthesias, and invariably, vibratory sense is lost distally.*

Continued on page 18

Clinical Pathway: Diagnostic Algorithm For Acute Nontraumatic Unilateral Weakness

Limbs and lower face on same side (spastic hemiparesis, upper motor neuron signs)?

YES → **Contralateral cerebral hemisphere** (Class II-III)

NO ↓

Cranial nerve signs ± hemiparesis (ipsilateral face/contralateral body, upper motor neuron signs)?

YES → **Brainstem process** (Class II-III)

NO ↓

Hemiplegia or monoplegia, ipsilateral loss of vibration/proprioception, contralateral loss of pain and temperature (most likely after penetrating trauma)?

YES → **Brown-Séquard syndrome** (Class II-III)

NO ↓

Myotomal weakness (weakness associated with an isolated spinal nerve), dermatomal sensory involving (usually pain)?

YES → **Radiculopathy** (Class II-III)

NO ↓

Nerve plexus syndrome?

YES →

Brachial plexopathy
Shoulder, back, or arm pain, followed by weakness of the arm or shoulder girdle; diminished reflexes **(Class II-III)** **OR**

Lumbar plexopathy
Ipsilateral back pain, followed by progressive leg weakness; sensory findings are absent; deep tendon reflexes may be diminished; bowel and bladder functions are not affected **(Class II-III)**

NO ↓

Peripheral nerve entrapment neuropathy syndrome?

YES →

Examples:

Radial nerve palsy (Saturday night palsy)
Wrist drop and weakness of finger and thumb extension; sensory findings usually minimal **(Class II-III)**

Ulnar nerve entrapment
Weakness of small finger flexion, adduction/abduction of fingers; sensory findings in small and ring fingers **(Class II-III)**

Median nerve compression (carpal tunnel syndrome)
Weakness of thumb adduction; sensory findings in palmar and dorsal surfaces of thumb (sparing thenar eminence), index, and middle fingers **(Class II-III)**

Sciatic nerve compression
Weakness of the anterior tibial and gastrocnemius muscles **(Class II-III)**

Entrapment of the common or deep peroneal nerve
Footdrop; sensory findings in web space between the great and second toes **(Class II-III)**

NO ↓

Consider somatoform disorder (Class II-III)

Cortical signs (altered mental status, associated visual field deficit, gaze preference, aphasia, neglect)?

NO → **Possible lacunar syndrome** (Class II-III)

YES ↓

Combination of:
- right-sided hemiparesis?
- right-sided sensory deficit?
- right visual field deficit?
- left gaze preference?
- aphasia?

YES → **Left (dominant) cerebral hemisphere process** (Class II-III)

NO ↓

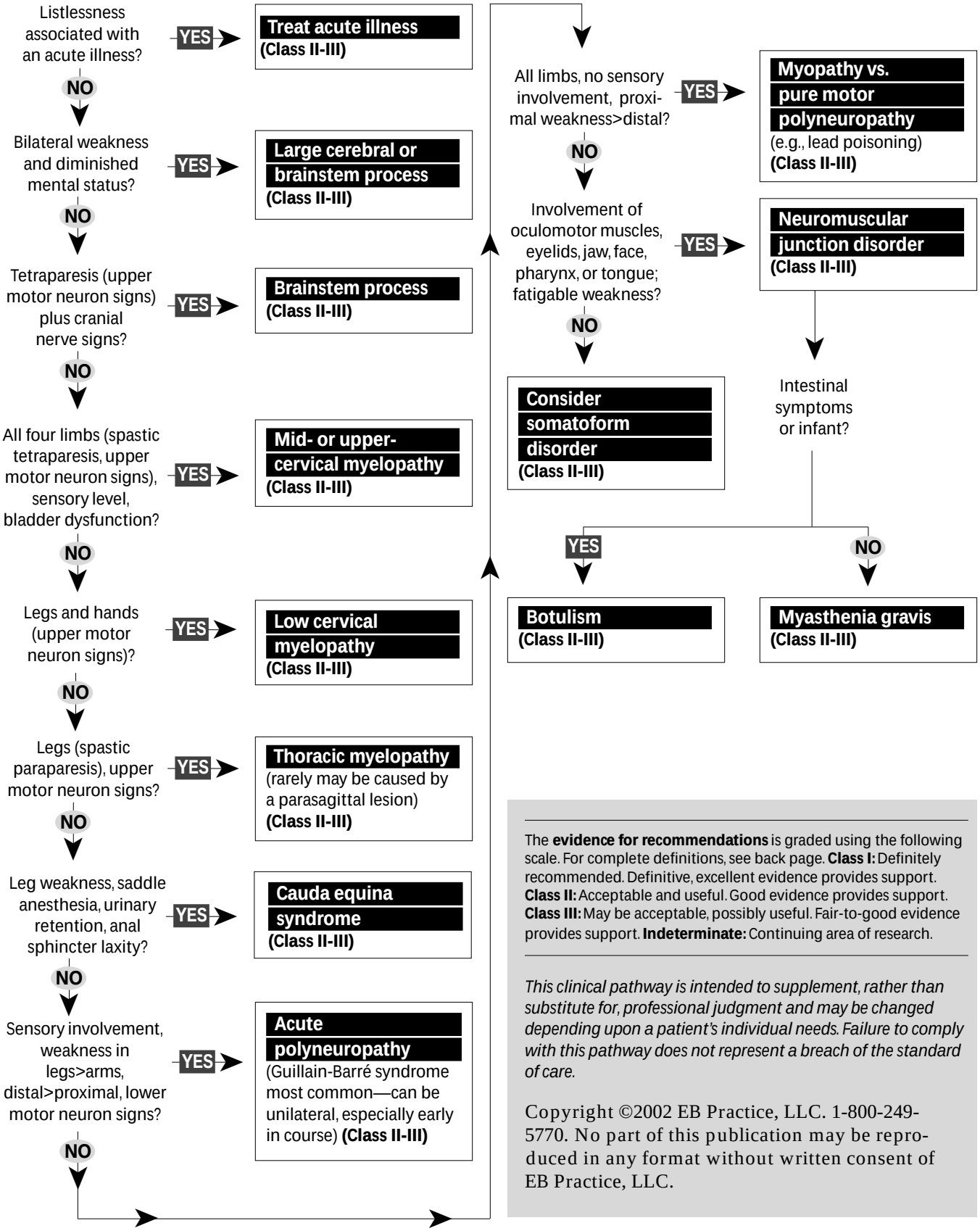
Combination of:
- left-sided hemiparesis?
- left-sided sensory loss?
- left visual field deficit?
- right gaze preference?
- left-sided neglect?

YES → **Right (nondominant) cerebral hemisphere process** (Class II-III)

The **evidence for recommendations** is graded using the following scale. For complete definitions, see back page. **Class I:** Definitely recommended. Definitive, excellent evidence provides support. **Class II:** Acceptable and useful. Good evidence provides support. **Class III:** May be acceptable, possibly useful. Fair-to-good evidence provides support. **Indeterminate:** Continuing area of research.

This clinical pathway is intended to supplement, rather than substitute for, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

Clinical Pathway: Diagnostic Algorithm For Acute Nontraumatic Bilateral Weakness



The **evidence for recommendations** is graded using the following scale. For complete definitions, see back page. **Class I:** Definitely recommended. Definitive, excellent evidence provides support. **Class II:** Acceptable and useful. Good evidence provides support. **Class III:** May be acceptable, possibly useful. Fair-to-good evidence provides support. **Indeterminate:** Continuing area of research.

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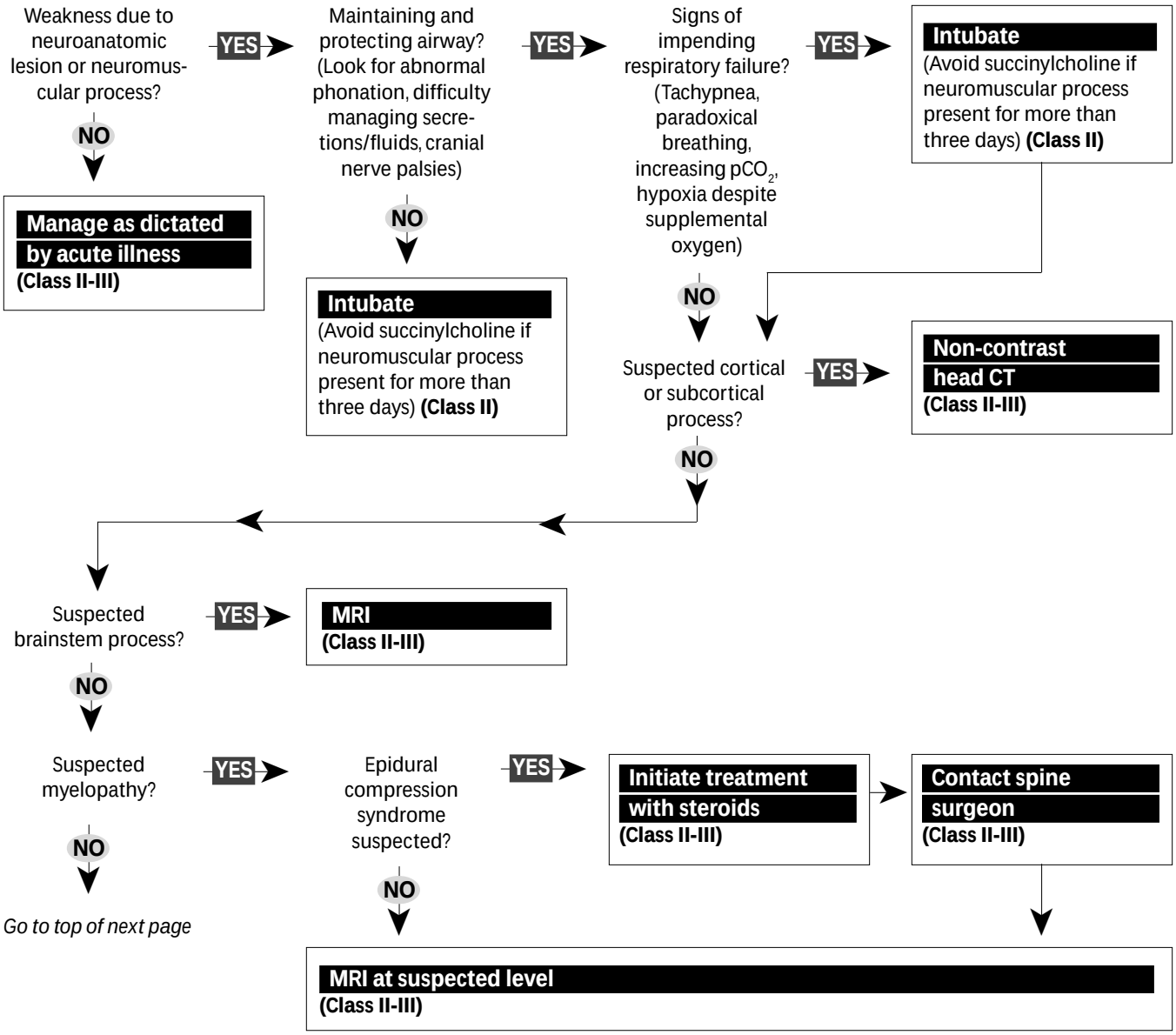
Clinical Pathway: Management And Diagnostic Testing Algorithm For Nontraumatic Weakness



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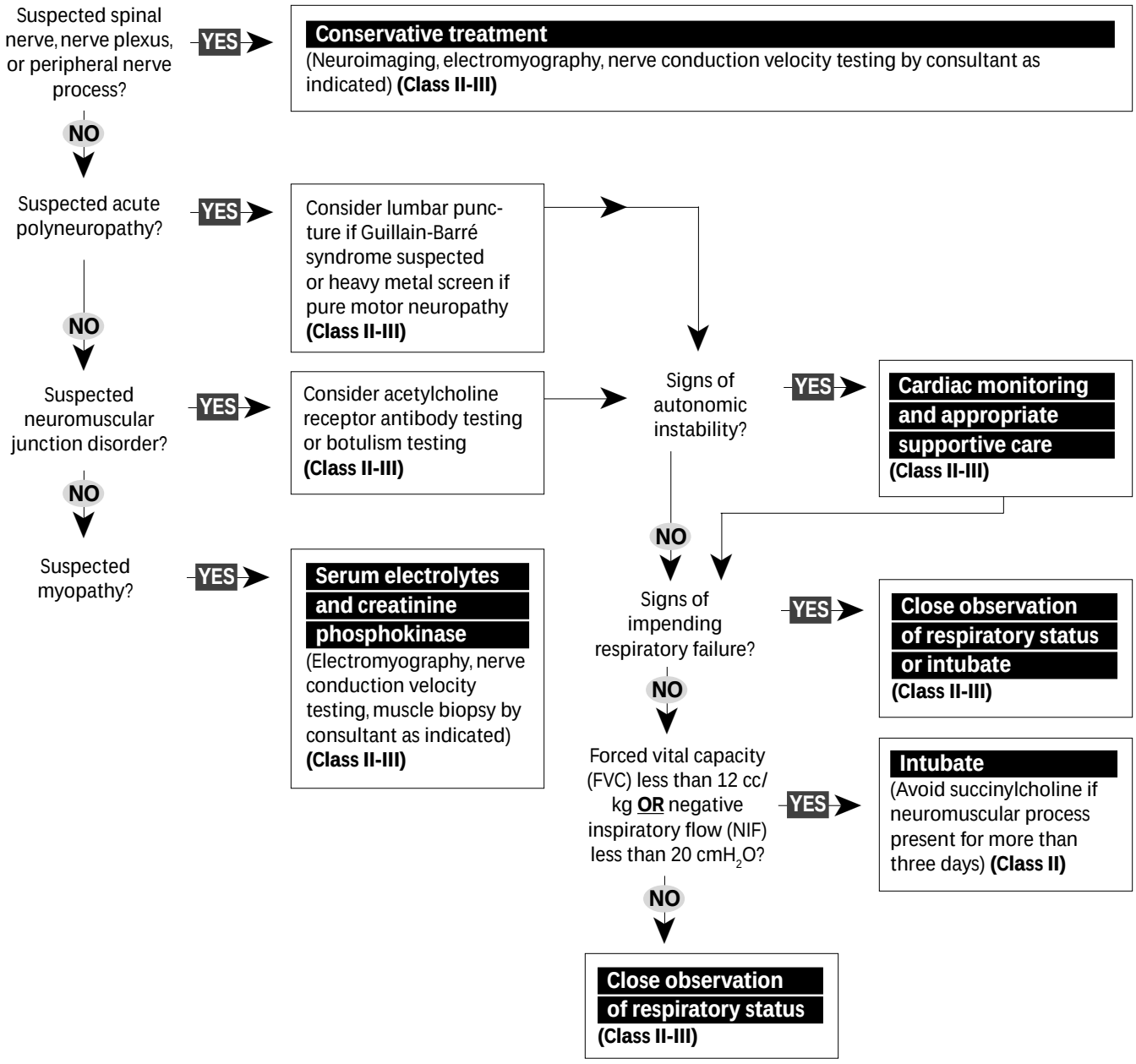
This clinical pathway is intended to supplement, rather than substitute for, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

Clinical Pathway: Management And Diagnostic Testing Algorithm For Nontraumatic Weakness (continued)



The **evidence for recommendations** is graded using the following scale. For complete definitions, see back page. **Class I:** Definitely recommended. Definitive, excellent evidence provides support. **Class II:** Acceptable and useful. Good evidence provides support. **Class III:** May be acceptable, possibly useful. Fair-to-good evidence provides support. **Indeterminate:** Continuing area of research.

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Continued from page 13

Guillain-Barré Syndrome

GBS is the most common acute motor polyneuropathy, possibly due to a post-infectious phenomenon.[3] The classic presentation of GBS is one of bilateral ascending motor paralysis that progresses over days to weeks. GBS can present unilaterally, and proximal muscle weakness may occur or even predominate.[82] Weakness develops acutely (within days) or subacutely (up to 4 weeks). *Deep tendon reflexes are almost always absent in the involved extremities, so the presence of normal reflexes virtually rules out the diagnosis.* Conversely, the patient with lower-extremity weakness and absent reflexes should be considered to have GBS until proven otherwise. Overall, weakness progresses to involve the cranial nerves in up to 50% of cases.[83] Rarely, it may involve the cranial nerves and descend, most notably in the form of the Miller-Fischer variant of GBS, which classically consists of the triad of ataxia, areflexia, and ophthalmoplegia.[84]

The diagnosis of GBS is based on the patient's clinical presentation. Lumbar puncture, which can be deferred to the admitting physician or performed by the ED physician, is recommended in the acute phase. However, absence of elevated CSF protein does not rule out GBS. The major reason to examine the CSF is to preclude other diagnoses causing an inflammatory demyelinating peripheral neuropathy, such as HIV, which may yield a lymphocytic pleocytosis.[43] In GBS, the CSF typically reveals elevated protein without pleocytosis, but this finding may not be found until the second week of the illness.[8]

While the clinical course is usually favorable, with most cases showing complete recovery, one-year outcomes are poor in about 15% of cases.[85-87] *The most feared complication from GBS is respiratory failure from muscle weakness,* which develops in up to 30% of the patients.[85,88-90] While inherently unpredictable, the course of patients with GBS can, to some extent, be predicted on the basis of clinical information and simple bedside tests of respiratory function. In one study, the need for mechanical ventilation was associated with rapid disease progression, bulbar dysfunction, bilateral facial weakness, or autonomic instability (unexplained blood pressure or heart rate fluctuations or significant bowel or bladder dysfunction).[90] Other factors associated with progression to respiratory failure include significantly abnormal pulmonary function tests on initial or serial exams.

Since GBS is probably caused by autoimmune factors, plasma exchange is used to treat GBS. The role of this therapy has been verified by two large randomized trials, and a Cochrane systematic review concluded that plasmapheresis hastens recovery.[91-93] While pooled

Ten Pitfalls To Avoid

1. "His motor strength was 'grossly intact' when I saw him. I even documented that on my chart."

Ambiguous documentation such as this is never appropriate in the chart of any patient, especially one complaining of weakness. Use the standardized rating scale endorsed by the Medical Research Council to grade and document strength, and do so in an unambiguous way. Tailor the examination and documentation to the complaint. For a patient complaining of isolated right upper-extremity weakness, that may mean documenting "5/5 strength in R elbow flexors/extensors, wrist extensors, finger flexors, and hand intrinsics" instead of "5/5 RUE."

2. "Her main complaint was the scalp wound she sustained after she fell. She didn't even tell me she was weak."

Falling or gait instability are frequent signs of weakness. Any patient who presents to the ED after a fall that is not obviously due to some environmental factor needs to have the reason for their fall explored.

3. "Her only complaint was tingling, and I often have trouble interpreting hyporeflexia on my physical examination. How was I supposed to know she would wind up on a ventilator the next day?"

Guillain-Barré syndrome is frequently heralded by paresthesias. While there is a broad range of normal for the reflex examination, if there is any question of hyporeflexia in a patient complaining of paresthesias and/or weakness, consider an acute polyneuropathy. If no weakness is found on examination but reflexes are diminished, the patient may be discharged home with explicit instructions about returning should weakness or difficulty in breathing develop.

4. "His pulse ox was 99%, so I admitted him to a non-monitored bed and told the neurologist he could see him in the morning."

Unfortunately, when the nurse went on rounds in the morning, the patient was found dead in bed. Any patient diagnosed with a neuromuscular process that leads to respiratory failure should be appropriately monitored. Pulse oximetry may reveal nothing about respiratory insufficiency until it's too late—get PFTs.

5. "The radiologist on call said an emergent MRI of the spine was not warranted. He convinced me to sit on the patient until the morning when a spine surgeon could come in and corroborate my exam findings."

A patient identified to have an epidural compression

Continued on page 19

gamma globulin may be useful if given in the first two weeks of the disease, no adequate trials have determined its effectiveness. There is no evidence that steroids are beneficial, but if a patient with GBS needs corticosteroid treatment for another reason, it is probably safe.

Ciguatera Toxin

Ciguatoxin poisoning is the most common foodborne illness caused by a chemical toxin reported to the CDC.[94] While it is endemic throughout the India-Pacific and Caribbean regions, it has also been reported from more northern portions of the United States.[95,96] The responsible agent is a heat-resistant toxin produced by a marine dinoflagellate that attaches to algae and is passed up the food chain through larger and larger fish. Unlike the other major fish toxin, tetrodotoxin, ciguatoxin is carried by a number of different species of fish that cannot be identified as toxic by any outward appearance. The action of ciguatoxin relates primarily to its effects on the sodium channel.[97]

The clinical symptoms of ciguatoxin poisoning fall broadly into four categories: gastrointestinal, neuropathic, cardiovascular, and a diffuse pain syndrome. Importantly, the particular polyneuropathic feature of "cold reversal" (cold stimuli being felt as painful and hot) is considered almost pathognomonic for ciguatoxin poisoning.[19,20] Symptoms of toxicity usually begin 3-5 hours after the ingestion of contaminated food, but they can be delayed by several days. As with other polyneuropathies, perioral and distal paresthesias usually initiate the toxic syndrome, followed by weakness, myalgias, dizziness, and dry mouth. Ptosis, dilated pupils, photophobia, and even transient blindness are among the neuro-ophthalmologic findings.[98] Clinical morbidity usually relates to respiratory compromise, hypotension, and generalized weakness.

Treatment for ciguatoxin poisoning is primarily supportive. Amitriptyline (25 mg BID) has been advocated for the management of pruritic and dysesthetic symptoms.[99] While IV mannitol has been used since 1988 to treat the symptoms of ciguatoxin poisoning, a recent prospective clinical study of 50 patients with ciguatoxin poisoning concluded that mannitol was not superior to normal saline in relieving symptoms and signs of ciguatoxin poisoning at 24 hours and had more side effects.[100,101]

The other major fish toxin (tetrodotoxin) has been implicated in Haitian "zombies." The toxin, which occurs in puffer fish, causes a paralysis so profound that breathing is undetectable, rendering lifelessness. The zombie victim would then be buried alive, only to stagger from the grave a day later.

Ten Pitfalls To Avoid (continued)

syndrome or signs of a significant myelopathy needs steroids and a stat MRI. When such neuroimaging cannot be obtained, document the reason, institute empiric steroid therapy, and consult immediately.

6. "That woman had so much psychosocial stuff going on, her weakness had to be psychosomatic."

The reason the patient was anxious was because she could no longer climb the steps of her home. Non-categorical or somatoform disorders are a diagnosis of exclusion when evaluating a weak patient. Only after organic causes are excluded should patients be labeled with a somatoform disorder.

7. "The patient was comatose when I saw her."

When the neurologist evaluated the patient 10 hours later, he immediately recognized the patient to be "locked-in." Unfortunately, even though the patient was taken to the catheterization lab at that point, her basilar artery thrombus did not respond to intra-arterial lysis. Although patients with the locked-in syndrome due to a posterior circulation stroke may appear comatose, careful examination will identify that their consciousness is preserved. The only way such a patient may be able to communicate with anyone is via vertical eye movements.

8. "The patient told me his vision was blurred. Lots of patients complain of blurry vision. How was I supposed to know he meant he was experiencing double vision?"

Blurred vision is a complaint that must be differentiated from double vision. If diplopia is described, cranial nerve dysfunction and bulbar signs must be explored to rule out a brainstem stroke or neuromuscular junction process. Do a detailed examination of the extraocular muscles and specifically ask the patient about double vision.

9. "The parents said that their infant was lethargic and not feeding well, but the kid was afebrile. I ruled out sepsis and dehydration. What was the problem?"

A good history is necessary in all cases of acute weakness. In this case, the child had infantile botulism. It was later found out that the parents had been mixing raw honey with their child's formula to "help him out with his bowel movements."

10. "Every geriatric patient I see complains of weakness. Her oral temperature was normal. How was I to know she was uroseptic?"

In an elderly patient, weakness may be the chief complaint for a broad range of diseases. Medical conditions such as congestive heart failure and infection must be explored as potential etiologies to the patient's presentation. ▲

Myopathies

Myopathies result from a primary process in the myocyte, such as muscular dystrophy, or as a manifestation of a systemic disorder, as occurs in the metabolic or inflammatory polymyopathies. Patients with generalized myopathies usually have no sensory disturbance, but inflammatory myopathies may have associated muscle aches or pain. Patients with a myopathy typically have proximal motor weakness initially before the process extends distally. The only prevalent myopathy that presents with greater involvement of distal muscles is myotonic muscular dystrophy, and patients will rarely present to the ED undiagnosed. *Although NMJ processes also affect large proximal muscles, they frequently affect the bulbar musculature, while myopathies do not.* Reflexes may be maintained until weakness is severe; therefore, do not rely on hyporeflexia to help distinguish myopathies from other neuromuscular processes. Additionally, while atrophy is a characteristic finding in a myopathy, it may not be apparent on ED presentation.

Polymyositis/Dermatomyositis

Polymyositis is an inflammatory myopathy affecting individuals over 30 years of age.[102] Patients usually present with slowly progressive proximal muscle weakness, while some also complain of dysphagia and a few progress to respiratory failure. There is no sensory loss and reflexes remain intact.

Dermatomyositis, unlike polymyositis, can affect children and, like polymyositis, affects mostly women.[102] The clinical manifestations of dermatomyositis are similar to those of polymyositis, except for the usual appearance of a violaceous rash, typically over the face and hands. As with other myopathies, the motor examination shows a proximal distribution of weakness, without sensory or reflex abnormalities. The laboratory findings are also similar, with an elevated erythrocyte sedimentation rate and creatine phosphokinase in most instances. Treatment is aimed at immunosuppression via agents like corticosteroids and methotrexate.

Electrolyte-Induced Weakness

While the most significant electrolyte disturbance leading to weakness involves potassium, virtually any electrolytic derangement can cause weakness, including hypophosphatemia, hypocalcemia, hypercalcemia, hyponatremia, hypernatremia, hypomagnesemia, and hypermagnesemia.[103] Acute widespread paralysis and weakness, when seen with disorders of potassium regulation, is known as periodic paralysis and can manifest with either hypokalemia or hyperkalemia.

Hyperkalemic Periodic Paralysis

The hyperkalemic form of periodic paralysis follows an autosomal dominant pattern of inheritance and is less common than the hypokalemic form. Patients first develop symptoms in infancy or early childhood, with frequent attacks generally lasting 1-3 hours.[104] Attacks are often precipitated by cold exposure or after exercise or emotional stress. Importantly, hyperkalemia is not present during many attacks of weakness. The disease is defined by the patient's response to potassium rather than by the absolute potassium level during attacks.[104] Laboratory evaluation frequently reveals slightly elevated serum potassium when patients are not reporting attacks.

Hypokalemic Periodic Paralysis

Hypokalemic periodic paralysis results from either familial periodic paralysis or thyrotoxic periodic paralysis.[105] The weakness that occurs during attacks of paralysis is usually confined to the limbs, although facial and respiratory muscle weakness can occasionally occur. Patients are often unable to walk and at times may be totally quadriplegic. During attacks of severe weakness, patients are hyporeflexic. Patients may have subjective sensory symptoms, but tests of sensation are invariably normal. Cardiac disturbances such as premature ventricular complexes are common. Attacks of weakness typically resolve over 3-4 hours but may occasionally persist for as long as 24 hours if untreated.[106] Once the attack has resolved, patients are again completely normal. While the administration of potassium usually abolishes symptoms, replacement should be used cautiously, since serum potassium can fluctuate after replacement, in some cases causing symptomatic hyperkalemia.

Familial Periodic Paralysis

Attacks of weakness from hypokalemia due to familial periodic paralysis usually occur either while the patient is sleeping at night or when the patient has rested following exercise. Attacks can begin as early as age 3 or 4 but typically have their onset in the second decade. Almost invariably, attacks of familial periodic paralysis begin before age 30.[104] The appearance of typical attacks of hypokalemic weakness in patients after age 30 is usually indicative of either thyrotoxic hypokalemic periodic paralysis or a secondary cause of hypokalemia leading to periodic paralysis.[107]

Thyrotoxic Periodic Paralysis

Thyrotoxic periodic paralysis is a relatively uncommon hypokalemic syndrome compared to familial periodic paralysis. As many as 10% of thyrotoxic Asian males may develop thyrotoxic periodic paralysis, apparently due to autosomal dominant transmission, but Caucasians are rarely affected.[107] Clinically, attacks of thyrotoxic periodic paralysis are invariably associated with hypokalemia and resemble those of familial periodic paralysis. The thyrotoxic state increases Na^+K^+-ATPase activity and causes hypokalemia.[108,109] Since the Na^+K^+-ATPase pump is also activated by insulin and androgens, high-carbohydrate meals or exercise can precipitate hypokalemic periodic paralysis. The diagnosis of thyrotoxicosis is often clinically inapparent but should be suspected when a patient over the age of 30 first develops typical periodic paralysis.[104] Examination during attack-free intervals

often demonstrates proximal weakness from the thyrotoxicosis. Thyrotoxic periodic paralysis is a self-limiting disorder that is ultimately cured by the treatment of the underlying hyperthyroidism.

Heavy Metal Intoxication

Another entity that may present with bilateral weakness without sensory involvement is a pure motor polyneuropathy, such as follows heavy metal intoxication, most notably lead. Lead exposure causes systemic side effects, with abdominal cramps, constipation, and anorexia. While lead toxicity was very common in the past, it is now rare, with most exposures being occupational (lead smelters, lead-acid storage battery manufacturing, scraping or burning lead-based paint from buildings). High-dose lead neuropathy primarily affects motor nerves in a characteristic pattern, with wrist drop more common than foot drop. Recovery of motor function follows removal from the exposure.[110]

Neuromuscular Junction Processes

Myasthenia Gravis

While MG is the most common disease of the neuromuscular junction, overall it is relatively uncommon, with an estimated incidence of 2-5 cases per million.[3,4] MG can present initially in the ED as an acute crisis, but most cases present with the diagnosis already established.[111-113]

MG is a classic antibody-mediated autoimmune disorder caused by antibodies directed against the acetylcholine receptor.[114] The clinical hallmark of MG is pathologic fatigability. The most common presenting symptoms of MG are ocular (ptosis, diplopia), with the disease remaining isolated to these muscles in up to 20% of all patients.[114] Alternatively, patients may present with other bulbar symptoms. Limb weakness, when it occurs, tends to disproportionately involve the upper extremities.[115] The muscle weakness occurs first in transient attacks. It may be precipitated by heat, stress, bright light, surgery, infection, or pregnancy.

The diagnosis of MG in a patient with ocular, bulbar, and limb weakness, which fluctuates throughout the day and improves with rest, is not difficult. The patient with MG has normal pupils, deep tendon reflexes, and sensation. The patient with milder disease or disease limited to a specific muscle group may present a diagnostic dilemma. To make the diagnosis in these more mild forms, perform provocative maneuvers, the simplest being extended gaze testing which leads to fatigue due to repeated muscle contraction. Alternatively, in a patient with ptosis, employ the ice test, which relies on the effect of temperature on myasthenic symptoms, with heat exacerbating weakness and cooling improving the strength in muscles.[116] To perform this test, place an ice pack over the droopy eyelid for two minutes. The test is considered positive for ocular myasthenic weakness when the lid rises by 2 mm or more. This has been shown to occur in myasthenic, but not in non-myasthenic, ptosis.[117] A small, randomized, single-blinded study compared the ice test with resting in myasthenic patients with ptosis.[118] The ice test significantly improved the ptosis to a greater extent than resting. Both were 100% specific for myasthenic weakness, but the ice test was more sensitive (90% vs. 50%). Similar results were reported from a study of bilateral orbital cooling on extraocular motility.[119]

A more invasive and potentially hazardous test that can aid in the ED diagnosis of MG is response to a short-acting anticholinesterase agent (edrophonium). This agent blocks acetylcholine esterase, thereby retaining enough acetylcholine within the synaptic cleft to stimulate the decreased number of postsynaptic binding sites. The edrophonium or Tensilon test is performed by giving incremental intravenous injections of edrophonium chloride.[114] Guidelines recommend the infusion of a 1-2 mg test dose of edrophonium chloride intravenously. The patient is re-examined for a resolution of their weakness, with the reversal of eyelid ptosis being the most specific sign. Edrophonium chloride acts in seconds, with a duration of 5-10 minutes. Be prepared for the rare patient who develops muscle fasciculations, respiratory depression, sinus bradycardia, atrial ventricular block, and rarely, cardiac arrest. Atropine is an effective antidote for these muscarinic effects but will have no effect on skeletal muscle paralysis. If the test dose of edrophonium is tolerated and no definite improvement in strength occurs, another 3-4 mg can be given. If there is still no response, a final 4-5 mg dose is given. False-positive responses to edrophonium chloride have been reported in ALS, Lambert-Eaton myasthenic syndrome, GBS, wound botulism, cavernous sinus lesions, polymyositis, and alcoholic myositis.[114,120]

Patients who present to the ED with MG already established, but with an exacerbation of their weakness, may present a diagnostic challenge. Their weakness may be due to a myasthenic crisis or a cholinergic crisis caused by cholinesterase inhibitor therapy (pyridostigmine and neostigmine). Since most cholinergic crises occur superimposed on an underlying myasthenic crisis, in questionable cases it is best to protect the airway, support ventilation, and withdraw all anticholinergic medications. Although a Tensilon test may help distinguish between myasthenic and cholinergic crises, the interpretation of this maneuver in this situation is complex and best left to an experienced neurologist. Crisis is a temporary exacerbation, regardless of the proximate cause, and the goal is to keep the patient alive until it subsides, usually within two weeks.

As with all neuromuscular processes, the major focus of ED management of MG is ongoing evaluation of the patient's respiratory status. While avoiding certain medications in MG patients is advised, banning the use of all drugs ever reported to be associated with a flare-up of MG would leave very few drugs that myasthenics could take. (See **Table 10** on page 22.) Use bedside spirometry to quantitatively evaluate the extent of respiratory neuromuscular weakness. For MG patients with coexisting respiratory diseases who may have their respiratory symptoms worsened by acetylcholinesterase

inhibitors, consider using inhaled ipratropium bromide to reverse airway resistance, through its bronchodilatory action at the muscarinic blocking receptor. If intubation is necessary, use a nondepolarizing agent instead of succinylcholine.

Plasmapheresis and intravenous immunoglobulin (Ig) therapy can be used to produce a rapid but temporary improvement of severe symptoms, but this will obviously be instituted in the ICU.

Lambert-Eaton myasthenic syndrome is a rare autoimmune neuromuscular and autonomic disorder associated with small-cell lung cancer that presents differently than other NMJ processes.[40] Fatigability is less prominent than with MG, and the distribution of weakness, which affects the limbs and spares the extraocular muscles and eyelids, is also different.[1] Pharyngeal weakness with dysphagia is the only cranial nerve weakness typically encountered, and dry mouth and taste abnormalities are common.[1] Also in contrast to myasthenia gravis, autonomic dysfunction and reflex changes develop.[121]

Botulism

While only about 100 cases of botulism are reported to the CDC each year, it is likely that botulism is underrecognized. It is a potentially life-threatening, neuroparalytic disorder caused by the toxin of *Clostridium botulinum*. The botulinum toxin prevents the release of acetylcholine from nerve endings at the neuromuscular junction. It is the most lethal toxin known to man on a per nanogram basis—it's more than 100,000 times more toxic than sarin gas.[122] Symptom onset usually occurs 18-36 hours after exposure (range, 6 hours to 8 days).[123] Most cases are the result of contaminated canned foods, but cases may also occur as a result of a wound infection, particularly in the parenteral drug abuser.[21,22,124]

The symptoms of classic botulism result from interference with cholinergic neurotransmission and can be grouped into three neuromuscular categories: cranial nerves, autonomic nerves, and the neuromuscular junction. Cranial nerve involvement results in ocular and bulbar findings, while autonomic involvement causes parasympathetic blockade, including constipation and urinary retention. *Adults present with the so-called "four Ds": diplopia, dysarthria, dry mouth, and dysphagia.* Pupils that are fixed and dilated are present in about 50% of the victims.[123] Bilateral weakness results from interference at the NMJ, with upper extremities affected more than the lower, and proximal muscles more affected than those distal.[125] Deep tendon reflexes can be normal, which assists in differentiating the disease from GBS, but they can also be absent or hypoactive. Paresis may become so severe that moving about or even turning in bed is impossible. Often this muscular involvement particularly affects the neck muscles, so that the patient is unable to raise the head or needs to use the hands to turn the head. Although there is no objective sensory involvement in botulism, paresthesias may occur in as many as 14% of cases.[123]

Infantile botulism, which was first reported in 1976, has a peak incidence at 2-4 months and is now the most common form of botulism in the United States.[5] It results from ingestion of the *C. botulinum* spores, with the toxin produced after incubation of the spores in the gut. Honey, usually raw, may be responsible for 15% of the cases of infantile botulism; therefore, the CDC recommends that honey not be given to children younger than 1 year of age.[126] Infant botulism only occurs in children less than 1 year of age. Infants present with poor suck, constipation, listlessness, and lethargy, with generalized lack of muscle tone, most noticeably characterized by a floppy head.[127] As with botulism in adults, cranial nerve defects are common, including ptosis, ophthalmoplegia, and flaccid facies. Treatment is supportive, but the safety and efficacy of a human-derived antitoxin product (human botulism immune globulin) administered to infants with botulism is being determined. As of November 2002, this product is available in the United States solely for the treatment of infant botulism, under an Investigational New Drug protocol. (For information on obtaining human botulism immune globulin, contact the California Department of Health Services at 510-540-2646.)

In wound botulism, gastrointestinal symptoms are absent. In recent years, researchers have increasingly

Table 10. ED Medications That May Have Deleterious Effects In Patients With Myasthenia Gravis.

Local anesthetics
- Lidocaine
- Procaine

Depolarizing and nondepolarizing neuromuscular blocking agents

Antibiotics
- Aminoglycosides
- Tetracyclines
- Sulfonamides
- Penicillins
- Clindamycin
- Macrolides
- Fluoroquinolones

Cardiovascular agents
- Quinidine
- Quinine
- Procainamide
- Beta-blockers
- Calcium-channel blockers

Anticonvulsants
- Phenytoin
- Barbiturates

Corticosteroids

Iodinated contrast

Adapted from: Myasthenia Gravis Foundation of America. Medications and myasthenia gravis. A reference for health care professionals. http://www.myasthenia.org/drugs/reference.htm.

observed the connection between botulism and subcutaneous or intramuscular injection of so-called "black tar" heroin.[21-23] It is believed that in these cases the heroin is contaminated ("cut") with soil containing the *C. botulinum* toxin. Importantly, since the toxin is the culprit, many injection drug user wounds responsible for introducing the toxin show no signs of infection.[22,124,128-130]

While the definitive diagnosis remains the identification of botulinum toxin in the stool or serum, ancillary testing supports the diagnosis, which excludes other neuromuscular processes. This includes documentation of a normal neuroimaging study of the brain, normal CSF, and a negative Tensilon test. The toxin assay is available in only a few reference laboratories, and the results are useful only to confirm the diagnosis later in the patient's course. In cases of suspected foodborne botulism, serum and stool specimens and implicated foods should be tested for the botulism neurotoxin. If wound botulism is suspected, obtain a swab of the wound exudate (for anaerobic culture) and a serum toxin assay.

As with many of the neuromuscular processes discussed, respiratory failure remains the immediate life threat associated with botulism and can develop precipitously, with minimal to no warning. The mainstay of treatment for severe botulism is supportive therapy with mechanical ventilation. Ventilatory support is most commonly needed for 2-8 weeks.[131] Antitoxin is the only specific pharmacologic treatment available for botulism. It acts by neutralizing toxin molecules that are not yet bound to nerve endings. One vial per patient is administered, and it is believed that no additional doses are necessary. Based on a retrospective analysis of 134 cases of type A botulism, early use of antitoxin prevents progression of illness and shortens the duration of ventilatory failure in severe cases of botulism.[132]

In a foodborne outbreak or an intentional poisoning, such as might result from biological terrorism, emergency physicians may be the first to recognize a public health emergency. Promptly inform state and local epidemiologists of all suspected botulism cases, as well as epidemiologists at the CDC, who are available 24 hours a day for clinical consultation and release of antitoxin when appropriate (emergency telephone number, 404-639-2888). (See also the July 2002 issue of *Emergency Medicine Practice*, "Bioterrorism And The Emergency Physician: On The Front Lines.")

Disposition

The most important disposition decision involving neurologic or neuromuscular weakness is ensuring that a patient likely to experience respiratory or cardiovascular instability is admitted to an ICU. Even a patient with no signs of respiratory difficulty in the ED can deteriorate rapidly.[90] In many patients, consultation with a neurologist will aid in determining the most appropriate disposition, especially when the diagnosis remains obscure. For patients discharged home, discharge instructions that are time-specific are imperative when a polyneuropathy such as early GBS cannot be totally excluded. Patients must be advised to return to the ED *immediately* if worsening weakness or difficulty breathing develops, rather than to "see your doctor if symptoms worsen."

Summary

The spectrum of diseases that can result in a complaint of weakness is almost limitless, encompassing both organic disease and psychiatric illness. The challenge is to differentiate acute neurologic, neuromuscular, and organic entities from chronic disease and functional states. Classic presentations of weakness syndromes may be limited to textbooks, but relying on key questions and the preponderance of clinical features will identify the correct neuroanatomic level of disease. Awareness or exclusion of potentially life-threatening or other dangerous processes permits appropriate diagnostic testing and disposition. ▲

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study, will be included in bold type following the reference, where available. In addition, the most informative references cited in the paper, as determined by the authors, will be noted by an asterisk (*) next to the number of the reference.

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Physician CME Questions

81. The most important clinical finding(s) associated with neuromuscular respiratory failure is/are:

a. rapid, shallow breathing.
b. the recruitment of accessory muscles.
c. paradoxical movement of the abdomen during the respiratory cycle.
d. all of the above.

82. In patients in whom Guillain-Barré syndrome, myasthenia gravis, or some other potentially rapidly deteriorating cause of acute weakness is suspected:
a. a normal or low pCO_2 indicates that the patient is in no imminent danger.
b. tachypnea indicates that the patient is in no imminent danger.
c. a normal pulse oximetry reading indicates that the patient is in no imminent danger.
d. additional pulmonary function tests are necessary to determine the need for intubation.

83. Sudden-onset weakness is most likely due to:
a. a stroke or other vascular-related cause.
b. multiple sclerosis.
c. tick paralysis.
d. dermatomyositis.

84. Unilateral facial weakness suggests a lesion above the spinal cord, either in the brainstem, cortex, or peripheral nerve.
a. True
b. False

85. Patients who describe being "weak everywhere" or who have so-called patternless weakness are most likely to be experiencing:
a. a stroke.
b. peripheral nerve entrapment.
c. malaise stemming from an associated medical illness or psychogenic cause.
d. lead poisoning.

86. Visual symptoms—particularly ptosis, diplopia, and bulbar signs—are invariably associated with:
a. a central nervous system disorder.
b. a peripheral nervous system disorder.
c. a neuromuscular junction process.
d. an infectious disease process.

87. Acute weakness in the elderly may be due to:
a. an occult infection.
b. a metabolic disorder.
c. a CNS event.
d. a medication-related process.
e. any of the above.

88. The hallmark of weakness syndromes referable to the brainstem is:
a. "crossed" findings (ipsilateral cranial nerve weakness and contralateral hemiparesis).
b. aphasia, neglect, apraxia, a gaze preference, or a visual field deficit.
c. contralateral homonomous hemianopia.
d. ipsilateral hemiplegia or monoplegia, ipsilateral loss of vibration and proprioception, and contralateral loss of pain and temperature below the level of the lesion.

89. Spasticity, hyperreflexia, and a positive Babinski sign indicate:
a. a lower motor neuron process.
b. an upper motor neuron process.
c. possible neuropathies, myopathies, or neuromuscular junction disorders.
d. malingering.

90. A sudden collapse of a tested limb after an initial normal effort most likely indicates:
a. a lower motor neuron process.
b. an upper motor neuron process.
c. possible neuropathies, myopathies, or neuromuscular junction disorders.
d. malingering.

91. Fasciculations most likely indicate:
a. a lower motor neuron process, or a benign phenomenon.
b. an upper motor neuron process.
c. possible neuropathies, myopathies, or neuromuscular junction disorders.
d. malingering.

92. A CNS lesion causing bilateral weakness will usually present with diminished mental status, unless the pathology resides in the spinal cord.
a. True
b. False

93. In patients with epidural compression syndrome:
a. a spine surgeon should be consulted immediately.
b. steroids (dexamethasone 10-100 mg IV) should be initiated immediately.
c. the prognosis depends on the patient's neurologic status at the time of intervention.
d. all of the above.

94. All of the following are true about patients with Guillain-Barré syndrome *except:*
a. The classic presentation is one of bilateral ascending motor paralysis that progresses over days to weeks.
b. Weakness progresses to involve the cranial nerves in up to 50% of cases.
c. Deep tendon reflexes are almost always absent in the involved extremities, so the presence of normal reflexes virtually rules out the diagnosis.
d. Respiratory failure from muscle weakness almost never develops.

95. Botulism may result from:
a. ingestion of raw honey in infants younger than 1 year.
b. contaminated heroin.
c. a bioterror event.
d. any of the above.

96. Carpal tunnel syndrome:

a. is the least common of all peripheral nerve compression syndromes.
b. is most accurately diagnosed by Tinel's sign.
c. is most accurately diagnosed by Phalen's test.
d. is most accurately diagnosed by a history of distribution of symptoms to the radial part of the hand and nocturnal exacerbation of symptoms, in addition to positive thumb adduction and hand elevation tests.

This test concludes the July through December 2002 semester testing period of *Emergency Medicine Practice*. The answer form for this semester and a return envelope have been included with this issue. Please refer to the instructions printed on the answer form. All paid subscribers are eligible to take this test.

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- Definitely useful
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- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful

Level of Evidence:
- Generally higher levels of evidence
- Non-randomized or retrospective studies: historic, cohort, or case-control studies
- Less robust RCTs
- Results consistently positive

Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate
- Continuing area of research
- No recommendations until further research

Level of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

Significantly modified from: The Emergency Cardiovascular Care Committees of the American Heart Association and representatives from the resuscitation councils of ILCOR: How to Develop Evidence-Based Guidelines for Emergency Cardiac Care: Quality of Evidence and Classes of Recommendations; also: Anonymous. Guidelines for cardiopulmonary resuscitation and emergency cardiac care. Emergency Cardiac Care Committee and Subcommittees, American Heart Association. Part IX. Ensuring effectiveness of community-wide emergency cardiac care. *JAMA* 1992;268(16):2289-2295.

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Publisher: Robert Williford. **Executive Editor**: Heidi Frost.

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Emergency Medicine Practice (ISSN 1524-1971) is published monthly (12 times per year) by EB Practice, LLC, 305 Windlake Court, Alpharetta, GA 30022. Subscription price: $299, U.S. funds. (Call for international shipping prices.)