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REVIEW ARTICLE

Emergency Neurological Life Support: Acute Non-Traumatic Weakness

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Abstract Acute non-traumatic weakness may be life-threatening if it involves respiratory muscles or is associated with dysautonomia. Most patients presenting with an acute muscle weakness have a worsening neurologic disorder that requires a rapid, systematic approach, and detailed neurologic localization of the findings. In many patients, urgent laboratory tests are needed and may involve neuroimaging. Because acute weakness is a common presenting sign of neurological emergencies, it was chosen as an Emergency Neurological Life Support protocol. An inclusive list of causes of acute weakness is explored, both by presenting complaint and anatomical location, with an outline of the key features of the history, examination, investigations, and treatment for each diagnosis.

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Introduction

The differential diagnosis of acute non-traumatic weakness ranges from the imminently life-threatening to the trivial. The approach to this problem necessarily comprises synchronous resuscitation with investigations and management tailored to the individual patient.

Assessment of the airway is the initial priority. During resuscitation, consideration should be given to a several other time-critical diagnoses that require specific management. These are discussed in connection with tables that include the main features of the history, examination, investigations, and treatment for each diagnosis. Trauma is neither discussed here nor is weakness that is not acute in onset.

The ENLS suggested algorithm for the initial management of acute weakness is shown in Fig. 1. Suggested items to complete within the first hour of evaluating a patient with acute weakness are shown in Table 1.

Assessing Ventilation and the Need for Urgent Intubation

When breathing becomes compromised in patients with neurological weakness, the usual cause is collapse of the oropharyngeal muscles. Diaphragmatic weakness is another significant cause, the diaphragm being responsible for two thirds of respiratory effort. Poor gas exchange may also occur but is less common.

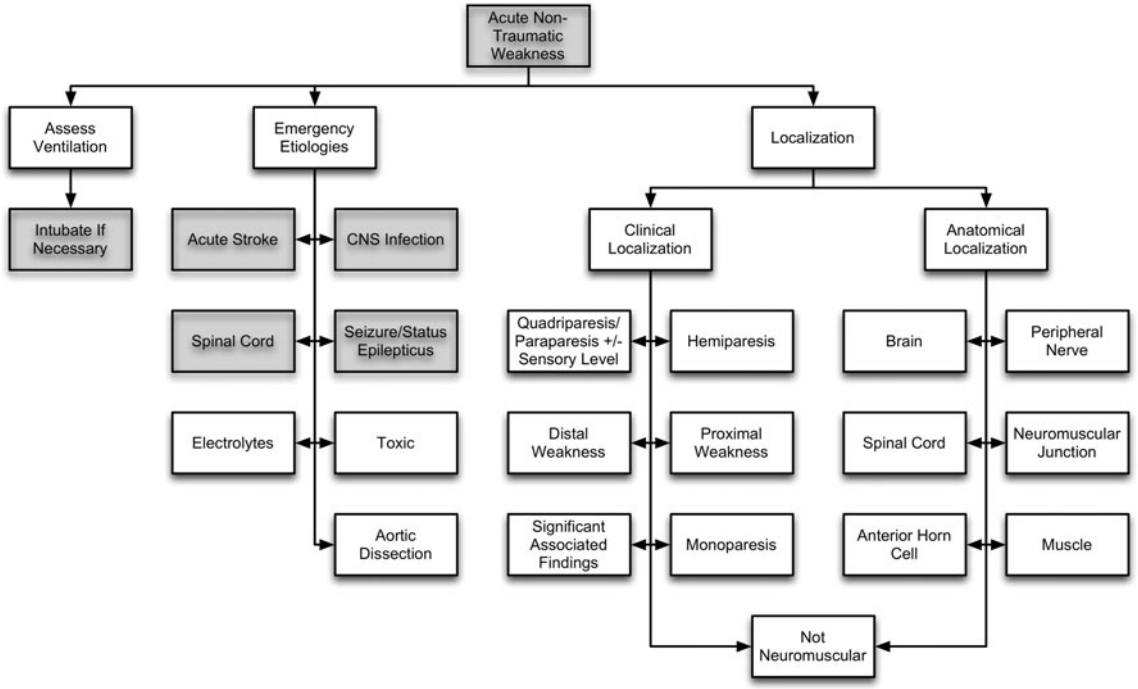

Fig. 1 ENLS acute non-traumatic weakness protocol

Table 1 Acute weakness checklist for the first hour

☐ Assess airway, breathing, and circulation
☐ Characterize the weakness by detailed exam
☐ Build an initial differential diagnosis of the causes of weakness
☐ Consider emergency causes
☐ Labs: glucose, electrolytes, Ca, Mg, PO_4, BUN/Cr, LFTs, and coags
☐ Special labs: TFTs, CK, ESR
☐ Relevant imaging

When there is uncertainty regarding the respiratory status and the direction of its trajectory, it is generally safer to intubate the patient prior to transport, if that is anticipated. If the airway is protected, and respiratory failure is due to the lower respiratory apparatus such as the intercostal muscles or the diaphragm, a trial of non-invasive ventilation may be considered—but not in a rapidly deteriorating patient (e.g., Guillain–Barré syndrome). Also, see the *Airway*, *Ventilation*, and *Sedation* protocol.

In the setting of acute weakness:

- Consider oropharyngeal weakness, which increases the risk of aspiration and prevents clearance of secretions.
- Consider pulmonary function tests to quantify neuromuscular respiratory insufficiency.
- Continue to regularly assess the patient as his or her clinical condition may deteriorate rapidly.

Table 2 Factors to consider in the decision to intubate [1, 2]

General
Increasing generalized muscle weakness
Dysphagia
Dysphonia
Dyspnea on exertion and at rest
Subjective
Rapid shallow breathing
Tachycardia
Weak cough
Interrupted speech (gasping for air)
Use of accessory muscles
Abdominal paradoxical breathing
Orthopnea
Weakness of trapezius and neck muscles: inability to lift head from bed
Inability to perform single-breath count: count from 1 to 10 in single exhalation (roughly equal to FVC <1.0 L)
Cough after swallowing
Objective
Decreased level of consciousness (have a lower threshold to control the airway if patient requires transfer or movement to unmonitored areas)
Hypoxemia
Vital capacity <1 L or 20 mL/kg, or 50 % decrease in VC in a day
Maximum inspiratory pressure >-30 cm H_2O
Maximum expiratory pressure <40 cm H_2O
Hypercarbia (a late finding)

Table 3 Special considerations for intubation [3]

Rapid sequence induction/intubation is advised
Avoid use of succinylcholine if there is evidence of underlying progressive neuromuscular disease (e.g., Guillain–Barre, chronic muscular weakness, or prolonged immobility). Consider 1.0–1.4 mg/kg rocuronium as an alternative [4]. Succinylcholine will be relatively ineffective to achieve muscle relaxation in myasthenia gravis. Either a higher dose (approximately 2.5 times standard dose) of succinylcholine can be used or half-dose of non-depolarizing agents (rocuronium 0.5–0.6 mg/kg)
Consider non-invasive ventilation as a temporizing measure in a neurologically stable patient with a neuromuscular condition expected to have rapid resolution (e.g., myasthenia gravis exacerbation)
Prepare atropine/glycopyrrolate, fluids, and vasopressors if there is evidence of autonomic instability
See the *Airway*, *Ventilation*, and *Sedation* protocol for additional information

Table 2 outlines factors to consider when deciding on whether to intubate. No single parameter independently predicts the need for intubation; rather, the constellation of signs and symptoms with a temporal trend should be considered. Certain salient points that are specific to intubation of patients presenting with weakness are listed in Table 3.

Emergency Etiologies

In the initial assessment, a few conditions must be considered first. These are all time-critical emergencies that require resuscitation and rapid, safe neuroimaging to achieve a diagnosis and expedite treatment.

Acute ischemic stroke, typically presenting with hemiparesis or hemiplegia, is probably the most important emergency etiology to diagnose, since specific time-sensitive treatments are available. While it cannot be clinically discerned whether the acute stroke is ischemic or hemorrhagic, acute stroke teams (if available) should be notified immediately, or acute transfer to a primary or comprehensive stroke center should be considered if stroke treatments are not available locally. Rapid imaging and establishing the time of onset are imperative in gaging this urgency.

Acute onset of paraplegia or quadriplegia (tetraplegia) may indicate acute *spinal cord compression*, which is an emergency. Spinal cord compression may be traumatic or non-traumatic. Non-traumatic spinal cord injury may occur from compression (e.g., epidural abscess, hematoma, expanding tumor), spinal cord infarct, or acute demyelination. See Tables 6 and 7 for further details. Acute spinal cord injury may be the first manifestation of an underlying disorder (e.g., aortic dissection, acute leukemia) (Table 11).

Table 4 Significant associated findings

Associated findings	Diagnosis to consider
Acute tetraplegia, facial muscles paralyzed except eyes, clear sensorium	Locked-in syndrome (also consider residual neuromuscular blockade) (Table 20)
Fatigable weakness in eyelids and extra-ocular muscles with variable weakness elsewhere and no sensory symptoms	Myasthenia gravis (Table 13)
History of animal bite, descending paralysis, and possible coagulopathy, rhabdomyolysis, and shock	Envenomation (Table 10)
Severe, refractory hypertension with headache and transient, migratory neurological non-focal deficits	Hypertensive encephalopathy (Table 12)
Ascending paralysis following upper respiratory mild viral illness/infection	Guillain–Barre syndrome (Table 21)
Descending symmetrical paralysis with a clear sensorium and no fever	Botulism (Table 22)
Weakness with prominent cholinergic signs and symptoms	Organophosphate toxicity (Table 9)
Heavy metal exposure, prominent gastrointestinal symptoms, then multi-organ failure	Heavy metal toxicity (Table 23)
Episodic proximal weakness with family history	Periodic paralysis (Table 24)
Heliotrope rash with proximal weakness	Dermatomyositis (Table 25)
Abdominal pain, proximal weakness, psychiatric symptoms, red urine	Acute intermittent porphyria (Table 26)
Tick bite followed by ascending paralysis	Tick paralysis (Table 27)

In the acute phase, a flaccid paralysis below the level of *traumatic spine injury* is seen, and a sensory level will localize the involved segment. Certain cord injury syndromes have their own features. For example, acute cauda equina syndrome may present with lower limb weakness, prominent back pain, sciatica, perineal hypesthesia, bowel and bladder dysfunction, and decreased lower limb reflexes.

A postictal patient or a patient in *status epilepticus* can also present with weakness. Typically, there is little confusion about the diagnosis in a post-ictal patient. However, both post-ictal state and non-convulsive status epilepticus should be considered in the patient with acute weakness, particularly when a collateral history is not available.

In addition, acute generalized weakness may occur due to *meningitis* or *encephalitis* or an acute electrolyte disorder, most notably hypokalemia, hyperkalemia, or hypermagnesemia

Table 5 Physical exam findings for each anatomic localization of weakness

Localization	Pattern of weakness	Sensory loss	Reflexes	Acute etiologies
Cerebral cortex, brainstem, or spinal cord	Distal > proximal, extensors > flexors, hemiparesis or single limb	May be present depending on whether sensory tracts or cortex are involved	Elevated however, reflexes may be decreased initially but later increase	*Acute stroke*, *subarachnoid hemorrhage*, seizure, hypertensive encephalopathy
Spinal cord	Distal > proximal, extensors > flexors, paraparesis, quadriparesis, rarely hemiparesis	May be present depending on whether sensory tracts are involved; loss of sensation below a certain spinal level is diagnostic	Elevated however, reflexes may be decreased initially but later increase	Epidural abscess, tumor, spinal cord infarct
Anterior horn cell	Proximal and distal, fasciculations are prominent	Absent	Decreased if muscle bulk is severely decreased; increased in ALS	ALS, polio
Peripheral nerve	In the distribution of the nerve, or diffusely present as stocking/glove weakness	Present	Decreased	Guillain–Barre syndrome, vasculitis
Neuromuscular junction	First in eye muscles, neck extensors, pharynx, diaphragm, followed by more generalized weakness	Absent	Normal, decreased if muscle is paralyzed	Botulism, tick bite, organophosphate
Muscle	Proximal	Absent	Normal unless muscle severely weak	Rhabdomyolysis

Table 6 Spinal cord infarction [5]

History
Acute tetraparesis or paraparesis with a sensory level corresponding with level of cord infarct
No historical suspicion of trauma or infection
60 % of patients present with pain that localizes to the level of injury
May be associated with aortic surgery or procedures such as celiac ganglion ablation
Risk factors: female sex, atrial fibrillation with no anticoagulation, hypertension, hypercholesterolemia, type II diabetes, smoking, hypercoagulable states
Examination
Anterior spinal artery syndrome is most common: loss of motor function and pain/temperature sensation, with relative sparing of proprioception and vibratory sense below the level of lesion
Initially presents with a flaccid paralysis and loss of deep tendon reflexes
Usually bilateral weakness, occasionally unilateral
Posterior spinal artery syndrome: loss of proprioception and vibratory sense below the level of the injury and total anesthesia at the level of injury; weakness usually mild/transient
Other variants possible
Investigations
MRI is diagnostic, showing an ischemic lesion defined as a well-demarcated T2-weighted hyperintensity matching an arterial territory of the cord
Spinal angiogram recommended if vascular malformation suggested from MRI
Other investigations are as for *ischemic stroke*, i.e., pro-thrombotic and vasculitis screen, toxicology screen, echocardiography, duplex ultrasonography of the cervical arteries, chest X-ray, electrocardiography, 24-h Holter electrocardiography
Treatment
Supportive treatment only
Corticosteroids are currently not recommended, as the current literature indicates minimal benefits outweighed by the risks of this treatment
Consider anti-platelet agents in patients with underlying vascular risk factors or co-morbid vascular disease to prevent more secondary atherothrombotic events

(Table 35). Marked hyperglycemia may present with an acute hemiplegia, but the majority of electrolyte disorders result in symmetric involvement. Hypoglycemia must be excluded early, but it should be noted that most of these patients are confused or have a decreased level of consciousness. Other causes that must be considered include magnesium and phosphate abnormalities.

Finally, specific drugs may cause acute weakness. For example, acute weakness may be caused by a lingering neuromuscular blocker administered during transport or intubation. Acute weakness is also a prominent feature of certain envenomations and organophosphate toxicity, though the latter is rare in the developed world (see Tables 9, 10).

Table 7 Transverse myelitis [6]

History
The development of isolated spinal cord dysfunction over hours or days in patients in whom there is no evidence of a compressive lesion
Segmental spinal cord injury caused by acute inflammation, usually thoracic cord
50 % have preceding infection, often viral
Can occur in multiple sclerosis
Symptoms usually develop over hours
Present with weakness and sensory disturbance below the level of the lesion
Back pain with bladder and bowel dysfunction is common
Examination
Evidence of myelopathy, with weakness and sensory symptoms that correspond to a specific dermatomal and myotomal level
Increased or decreased sensation with paresthesia may be present
Investigations
MRI is diagnostic; however, negative MRI does not exclude diagnosis
Treatment
Many patients are treated with IV methylprednisolone, IVIG, or plasma exchange

Table 8 Hypoglycemia (BGL $<$ 3 mmol/L) [7]

History
Diabetes
Insulin regimen
Oral hypoglycemics
Alcohol
Sepsis
Liver disease
Any cause of hypocortisolemia
Examination
Generalized non-specific weakness
Many forms of focal neurological deficit possible, which may mimic stroke
Tremor, palpitations, anxiety, sweating, hunger, and paresthesia
Dysphoria
Seizures
Decreased consciousness
Investigations
Blood glucose level (more accurate from venous or arterial blood rather than capillary and measured in a blood gas analyzer)
CT head
Treatment
20 mL IV 50 % dextrose
Repeat if necessary
Oral carbohydrate if patient safe to swallow
Alternatively, 1 mg glucagon IM or IV

Table 9 Organophosphate toxicity [8, 9]

History
Insecticide exposure (e.g., malathion, parathion, diazinon, fenthion, dichlorvos, chlorpyrifos, ethion)
Nerve gas exposure (e.g., sarin, VX, soman, tabun)
Ophthalmic agents (e.g., echothiophate, isoflurophate)
Anti-helminthics (trichlorfon)
Examination
Fasciculations with paralysis
Bronchospasm, bradycardia, miosis, lacrimation, salivation, bronchorrhea, urination, emesis, and diarrhea
At 48–72 h, neck flexion weakness, decreased deep tendon reflexes, cranial nerve abnormalities, proximal muscle weakness, and respiratory insufficiency may develop
At 1–3 weeks, ascending flaccid paralysis may develop (delayed neuropathy)
Investigations
RBC acetyl cholinesterase (if available) for severity and to guide oxime therapy
Treatment [9]
Remove contaminated clothes
100 % oxygen
Intubation (no succinylcholine)
Atropine 1.2 mg IV stat, then double the dose every 5 min until bronchospasm and secretions are controlled; an infusion may be required, and glycopyrrolate is an alternative
Pralidoxime 2 g IV over 15 min, then as an infusion
Diazepam to prevent seizures

Table 10 Envenomation [10, 11]

History
Snake bite [11]
Scorpion sting (*C. exilicauda* and *C. suffusus*)
Marine envenomation (mainly Australia):
Stonefish
Blue-ringed octopus
Ingestion of puffer fish (prepared as delicacy in Japan: fugu)
Examination
Snake bites [11]
Cardiovascular: hypotension, shock, arrest
Neurological: paralysis-ptosis, diplopia, bulbar palsy, dysarthria; progression to respiratory muscle paralysis; desaturation is a late sign
Coagulopathy: decreased GCS due to intracranial hemorrhage, bleeding from bite site, ecchymoses, bleeding gums, hemarthroses
Rhabdomyolysis: tender muscles
Bite site: bleeding and necrosis; do not remove the pressure immobilization bandage to examine the bite site
Scorpion sting
Cranial nerve and somatic skeletal neuromuscular dysfunction, with pain and paresthesia
Blue-ringed octopus and puffer fish envenomation

Table 10 continued

Descending symmetrical flaccid paralysis with clear sensorium, nausea and vomiting, blurred vision, ataxia, respiratory failure; symptoms delayed if ingested
Stonefish envenomation
Weakness in the affected limb, severe pain, shock
Investigations
All envenomations: serial pulmonary function tests if descending paralysis; other investigations as clinically indicated
Snake bite: FBC, EUC, LFTs, CK, whole blood clotting time, coagulation screen, D-dimer, fibrinogen levels, urinalysis for blood (myoglobin), head CT if decreased GCS; if envenomation suspected on the basis of clinical findings and pathology, use venom detection kit for bite swab and urine to determine appropriate anti-venom
Treatment
Pressure immobilization bandage
Anti-venom, preferably specific
Supportive care with early intubation for paralysis

Table 11 Aortic dissection [12–14]

History
Severe, sharp or "tearing" posterior chest or back pain
Anterior chest pain
Chest pain may be associated with an acute neurological deficit
Neurological features may include hemiplegia, monoplegia, and paraplegia
History of hypertension is common
Examination
One-third experience neurological deficits [13]
May present with only neurological manifestations in 10 % of Type A dissections
Acute aortic regurgitation may be present (31.6 %) [12]
Weak or absent pulse (15.1 %) (carotid, brachial, or femoral) [12]
Other features may include acute myocardial infarction, cardiac tamponade, hemothorax, hypotension, pain, abdominal pain, back or flank pain, renal failure, or Horner's syndrome
If hypotensive, look for evidence of tamponade, cardiogenic shock, and blood loss
Investigations
FBC, group, and save
ECG to exclude myocardial infarction (may be associated if coronary arteries occluded)
CXR for widened mediastinum and hemothorax
Bedside transesophageal echocardiogram (transthoracic if transesophageal not available)
CT aortogram
CT head
Treatment
Reduce systolic BP to 100–120 mmHg and heart rate to 60–80 bpm with an IV beta-blocker; consider a nitroprusside infusion; avoid hydralazine
Type A: urgent surgery
Type B: initial medical management, though 20 % still require surgery; consider surgery if patient demonstrates progression of dissection, intractable pain, organ malperfusion, or extra-aortic blood

Localization

To form a workable and realistic list of differential diagnoses, the etiology may be considered either in terms of the clinical presentation or by the anatomical location of the lesion.

Clinical Localization

Accurately defining the presenting complaint helps generate a focused differential diagnosis. A good clinical history is essential, as the examination may be difficult or unreliable in the obtunded or confused patient. However, it should be possible to elicit whether the deficit is unilateral or bilateral, which anatomical region is affected, and whether there is a sensory deficit.

With a cooperative patient, it should also be possible to establish whether the deficit is symmetrical or asymmetrical, and proximal or distal. Note that it is important to attempt to differentiate between upper motor neuron (UMN) and lower motor neuron (LMN) lesions in the acute setting, though this may be difficult in some situations. In well-established UMN lesions, hyperreflexia (brain and spinal cord), increased tone, and a positive Babinski sign are seen. In comparison, LMN lesions (from the anterior horn cells to the muscles) cause a flaccid, arcflexic weakness and, with time, atrophy and fasciculations. However, in the acute phase, UMN lesions may mimic a LMN lesion: flaccid paralysis, normal or reduced tone, and unreliable reflexes. There is often not enough time for atrophy to be evident, and fasciculations are rarely seen.

Hemiparesis

- *Acute stroke*: *ischemic*, *hemorrhagic*, or *subarachnoid hemorrhage*
- Intracranial mass (Table 18)
- *Meningitis/encephalitis*
- Hypoglycemia/hyperglycemia (Tables 8, 16)
- Postictal Todd's paresis (Table 17)
- Hemiplegic migraine (Table 15)
- Brown–Séquard syndrome (Table 19)

Table 12 Hypertensive encephalopathy [15, 16]

History
Long standing, poorly controlled hypertension
Drug history and poor compliance with anti-hypertensives, especially clonidine
Headaches, confusion, visual disturbances, nausea, and vomiting
Symptoms from other end-organ damage
Examination
Severe, sustained hypertension, with a diastolic BP that is usually >130 mmHg
Transient, migratory neurological non-focal deficits, ranging from nystagmus to weakness, and an altered mental status, ranging from confusion to coma
Fundoscopy may reveal grade IV retinal changes including papilledema, hemorrhage, exudates, and cotton wool spots
Cardiovascular exam findings consistent with severe chronic hypertension
Other causes of weakness, including hemorrhagic stroke, are excluded
Investigations
FBC (microangiopathic hemolytic anemia)
Urea and creatinine, urinalysis (hypertensive nephropathy)
Urine toxicology screen
CT head
Treatment
Invasive BP monitoring
Use a continuous infusion of an IV anti-hypertensive (e.g., sodium nitroprusside, beta-blocker, or calcium channel antagonist)
Lower the diastolic pressure to 100–110 mmHg within 6 h
Aim to reduce initial MAP by no more than 25 %
Avoid lowering BP too much, too quickly, as it may lead to cerebral ischemia

Table 13 Myasthenia gravis [17, 18]

History
History of myasthenia gravis (but may have not been diagnosed)
Acute decompensation may be spontaneous or precipitated by infection, surgery, or tapering of immunosuppression
Drugs may precipitate symptoms, including certain antibiotics, beta-blockers, and magnesium
Excessive treatment with cholinesterase inhibitors may paradoxically cause weakness (see Table 9)
A myasthenic crisis refers specifically to respiratory failure due to acquired autoimmune myasthenia gravis
Examination
85 % of patients have involvement of the eyelids and extra-ocular muscles, resulting in ptosis and/or diplopia [18]
Weak, flaccid facial muscles
Nasal speech with impaired bulbar reflexes
Neck and proximal limb weakness may occur
Respiratory failure occurs in 1 %

Table 13 continued

Respiratory exam may reveal evidence of aspirated secretions or infection
Investigations [18]
Ice pack test (e.g., ice on affected eyelid improves ptosis)
ACh receptor antibody if diagnosis uncertain
Pulmonary function tests
Consider arterial blood gas
Consider CT chest (thymoma may affect breathing)
Treatment
For acute decompensation, admit to ICU
Frequent forced vital capacity measurement
If intubated, withdraw anticholinesterase medications
Plasmapheresis or IV immunoglobulin
High-dose steroids (e.g., 80 mg prednisolone)
Consider other immunosuppressants

Table 14 Non-neuromuscular pathology

Consider
Any severe medical illness can have weakness as a symptom, but generally these will become clinically obvious during the patient's evaluation
Diagnoses of exclusion
Malingering
Conversion disorder
Chronic fatigue syndrome
Anxiety disorders
Fibromyalgia

Table 15 Hemiplegic migraine [19, 20]

History [19]
Typical hemiplegic migraine attacks start in the first or second decade of life and include gradually progressing visual, sensory, motor, aphasic, and often basilar-type symptoms, accompanied by headaches
Most patients also have attacks of migraine with typical aura without weakness
Aura consists of a fully reversible motor weakness
The weakness may resolve before the headache starts or may persist for days
May be preceded by a prodrome of affective symptoms 24–48 h prior to the migraine
May be accompanied by ipsilateral numbness or tingling, with or without a speech disturbance
In familial hemiplegic migraine (FHM), at least one first or second degree relative has had similar episodes
Sporadic hemiplegic migraine is diagnosed when no first or second degree relative has had attacks of hemiplegic migraine
Examination
Neurological exam assessing for other causes of hemiplegia

Table 15 continued

The short time course and full reversibility of deficit are key components
Investigations
Diagnosis of exclusion
CT or MRI to exclude other etiologies
SPECT scan may show hypoperfusion during the aura phase
Genetic testing is available for FHM
Treatment
Early neurologist involvement
Anti-emetics, non-steroidal anti-inflammatory drugs, and non-narcotic pain relievers
Triptans and ergotamine preparations are contraindicated because of their potential vasoconstrictive effects
There is no evidence for anti-platelet agents
Prophylactic treatment may include lamotrigine and acetazolamide

Table 16 Hyperglycemia [21, 22]

History
History of diabetes
Possible precipitating events (e.g., infection, myocardial infarction, surgery, critical illness)
Diabetic regimen and compliance
Neurological symptoms primarily occur when plasma osmolality is >320 mOsmol/L
Neurological symptoms may include hemiparesis, focal motor deficits, decreased consciousness, and seizures
Diabetic ketoacidosis (DKA) usually evolves rapidly, over a 24-h period
Symptoms of hyperosmolar hyperglycemia syndrome (HHS) develop gradually with polyuria, polydipsia, and weight loss for several days before presentation
Examination
Level of consciousness may be reduced
Detailed neurological exam may reveal focal motor and sensory deficits including aphasia, hyperreflexia, hemianopia, and brainstem dysfunction
Other findings associated with HHS include evidence of volume depletion
Patients with DKA may present with hyperventilation and abdominal pain
Investigations
Serum glucose
Plasma osmolality
Serum electrolytes (with anion gap), urea, and creatinine
Complete blood count with differential
Urinalysis, and urine ketones by dipstick
Serum ketones (if urine ketones are present)
Blood gas (if urine ketones or anion gap are present)
Electrocardiogram
CT head to exclude other causes

Table 16 continued

Treatment
Fluid replacement to correct hypervolemia and hyperosmolality
Insulin infusion
Close electrolyte monitoring with potassium, magnesium, and phosphate replacement
Treat precipitant (e.g., sepsis)

Table 17 Postictal Todd's paresis [23, 24]

History
Follows seizure
More common when seizures prolonged (status epilepticus)
Can last seconds, but often has a duration of hours
Examination
Weakness always present, but wide variation in location, severity, duration, tone reflexes, and sensory involvement
Investigations
To exclude other forms of weakness
Treatment
Supportive

Table 18 Intracranial mass [25, 26]

History
Hemiparesis is uncommon with brain tumors
Other symptoms of brain tumors vary widely from headaches, seizures, nausea, ataxia, and cognitive dysfunction to focal neurological deficits
Manifestations may be subtle, particularly in the early stages
As with other UMN lesions, weakness is generally more pronounced in flexors of lower extremities than in extensors, and more pronounced in extensors than flexors in upper extremities
Transient weakness may represent a postictal state, as in postictal Todd's paresis
Fever, headache, and focal neurological deficit is characteristic of a brain abscess
Examination
Detailed neurological exam may help localize the lesion and create a list of differential diagnoses
Investigations
CT head with and without contrast to identify tumor, exclude other diagnoses, look for associated hemorrhage, and assess for bone or vascular involvement
MRI usually required
Consider functional MRI, perfusion MRI, PET, and SPECT imaging, depending on the situation
Treatment
Involve neurological clinicians

Table 18 continued

Peritumoral vasogenic edema responds to glucocorticoids (dexamethasone IV 10 mg stat then 4 mg IV every 6 h)
Corticosteroid use should be avoided prior to biopsy or surgery if either a primary CNS lymphoma or infectious process is part of the differential diagnosis
Manage raised ICP in the standard step-wise approach
If there is evidence of intra-tumoral hemorrhage, correct any coagulopathy and control BP
Brain abscesses require targeted anti-microbial treatment and sometimes drainage

Table 19 Brown–Séquard syndrome [27, 28]

History
Sudden onset hemiplegia with contralateral loss of pain and temperature
Non-traumatic causes include
Extramedullary spinal neoplasm
Herniated cervical intervertebral disc
Incomplete hemisection causing Brown-Sequard syndrome plus other signs and symptoms is more common than the classical form
Examination
Ipsilateral weakness
Impaired ipsilateral proprioception and vibratory sensation
Contralateral loss of pain and temperature sensation
Investigations
MRI
CT myelography if MRI contraindicated
Treatment
Spinal precautions if from traumatic injury
Surgery with spinal cord decompression
See *Spinal Cord Compression* and *Traumatic Spinal Injury* Protocols

Hemiparesis is acute weakness involving only one side of the body. While acute hemiplegia is most commonly due to an *ischemic stroke*, other differentials must be considered, as management of these differentials vary.

The history and demographic of the patient is likely to narrow the diagnosis, and examination findings provide further clues. A blood glucose level and a non-contrast head computed tomography are part of the initial workup.

Quadriparesis/Paraparesis ± Sensory Level

- *Spinal cord compression*
- Spinal cord infarction (Table 6)
- Transverse myelitis (Table 7)

Table 20 Locked-in syndrome [29, 30]

History
Sudden onset tetraplegia, facial weakness, and frequently loss of horizontal gaze
Most commonly caused by *ischemic stroke*
May be caused by central pontine myelinolysis, *encephalitis*, or tumor
Examination
Flaccid symmetrical tetraparesis
Consciousness preserved, with voluntary vertical eye and eyelid movements possible
Hearing, vision, pupillary reflexes, and sensation all normal
Consciousness may be affected initially but returns to normal
Investigations
CT brain with spiral CT angiography [30]
Consider MRI/MRA
Treatment
See *Acute Stroke* protocol

Table 21 Guillain–Barré syndrome [31–36]

History [34]
Usually follows 2–4 weeks after mild respiratory or gastrointestinal illness
Typically symmetrical ascending paralysis
10 % present with upper limb or facial weakness
Respiratory failure occurs in approximately 10 % and oculomotor weakness in 15 %
Limb paresthesia are common (80 %)
Dysautonomia occurs in 70 %
Examination [34]
Symmetrical ascending paralysis
Absent deep tendon reflexes
Signs of respiratory failure (see Table 3)
Miller Fisher syndrome variant presents with ophthalmoplegia, ataxia, and areflexia
In acute motor axonal neuropathy variant, sensation is preserved and occasionally deep tendon reflexes
Acute motor and sensory axonal neuropathy has more sensory symptoms
Other rarer variants exist [35]
Investigations
CSF analysis: elevated protein, normal cell count
Electromyography
Nerve conduction studies
Glycolipid antibodies may be associated with different subtypes
Treatment
Supportive care
Plasma exchange and IVIG are equivalent in efficacy, and both improve outcome. Choice depends on local availability, patient preference, risk factors, and contraindications
No benefit for corticosteroids [36]

Table 22 Botulism [37–39]

History
Descending symmetrical paralysis with a clear sensorium and no fever
No sensory deficits other than blurred vision
If foodborne, follows ingestion by 12–36 h
Prodromal symptoms include nausea, vomiting, abdominal pain, diarrhea, and dry mouth with sore throat [37]
Wound botulism may follow deep infected regions with the presence of spores
Infantile botulism occurs from 1 week to 1 year in infants who are formula fed and may present with constipation followed by weakness, feeding difficulties, descending or global hypotonia, drooling, anorexia, irritability, and weak cry [38]
Examination
Cranial nerves first affected: fixed dilated pupils (causing blurred vision), diplopia, nystagmus, ptosis, dysphagia, dysarthria, and facial weakness
Flaccid paralysis descends and commonly involves muscles of respiration and may cause bladder and bowel dysfunction
Investigations
Do not delay treatment waiting for tests
Stool, vomit, suspected food and wound cultures looking for C
Botulinum spores serum assay for botulinum toxin
Pulmonary function tests
Treatment [39]
Equine serum heptavalent botulism antitoxin used for children >1 year of age and adults
Human-derived botulism immune globulin used for infants <1 year of age
·Penicillin G (or metronidazole) for wound botulism but not for other forms

Table 23 Heavy metal toxicity [40–42]

History
Peripheral neuropathies may occur within a few hours to days of acute high-dose exposure, especially lead, arsenic, and thallium [42]
Metal toxicities most commonly present with nausea, persistent vomiting, diarrhea, and abdominal pain and often with encephalopathy, cardiomyopathy, dysrhythmias, acute kidney injury, and metabolic acidosis
Examination
Detailed CNS and PNS exam
Lead neuropathy initially affects motor fibers in radial and peroneal distributions
Mees lines (horizontal hypopigmented lines across all nails)
Evidence of anemia and renal or liver failure
Investigations
FBC (anemia) with blood film analysis (looking for basophilic stippling, which is found in lead toxicity or arsenic toxicity but is not specific)
Urea, creatinine, electrolytes, and liver function tests and coagulation studies assessing for renal or liver failure
Serum and urine metal levels (specifically, depending on which metal suspected)
Treatment
Stop further exposure
Consult toxicologist/poison center
Consider polyethylene glycol whole bowel irrigation
Consider chelation therapy in lead intoxication with encephalopathy (e.g., succimer, dimercaprol)

Table 24 Periodic paralysis (PP) [43]

History
Episodes of flaccid muscle weakness occurring at irregular intervals with normal strength between episodes
Usually hereditary, therefore family history is important
Various types of periodic paralysis exist, including
Hyperkalemic PP
Hypokalemic PP
Paramyotonia congenita
Thyrotoxic PP
Andersen–Tawil syndrome
Seek precipitants (e.g., post exercise, fasting, cold alcohol, stress, and duration of episode)
Examination
All forms usually exhibit
Interictal lid lag and eyelid myotonia
Normal sensation
Fixed proximal weakness
Diminished reflexes during episode
Differentiating findings include perioral and limb paresthesias, myotonia between attacks, pseudo-hypertrophy of muscles, and findings of thyrotoxicosis
Investigations
Serum potassium (although not always low in “hypokalemic” PP)
Elevated creatine kinase
Potassium: creatinine ratio
Blood gas analysis for evidence of concomitant metabolic acidosis or alkalosis
ECG
Consider EMG and nerve conduction studies
Treatment
Hyperkalemic PP (milder) usually responds to high carbohydrate food; thiazide or acetazolamide for prophylaxis
For hypokalemic PP (more severe weakness), potassium supplementation (e.g., 40–60 mmol KCl orally, IV if severe weakness); acetazolamide for prophylaxis
Paramyotonia congenita: weakness mild, no specific treatment
Thyrotoxic PP: beta-blockers; treat thyrotoxicosis
Andersen–Tawil syndrome: acetazolamide as prophylaxis for PP

Table 25 Dermatomyositis [44]

History
May present with skin and/or muscle involvement
Proximal muscle weakness: muscle fatigue or weakness when climbing stairs, walking, rising from a sitting position, combing hair, or reaching for items above shoulders
Characteristic rash
Systemic symptoms include arthralgia, arthritis, dyspnea, dysphagia, arrhythmia, and dysphonia
Examination
Heliotrope rash (blue-purple discoloration on the upper eyelids)
Raised, violaceous, scaly eruption on the knuckles (Gottron's papules)
Proximal symmetrical muscle weakness
Muscle pain and tenderness may be present
Sensation is normal, and tendon reflexes are preserved
Joint swelling (particularly of the hand) occasionally occurs in some patients with dermatomyositis
May be signs of underlying malignancy (present in 20–25 %)
Investigations
Elevated CK, aldolase, lactate dehydrogenase, or alanine aminotransferase
Auto-antibody serology not useful for acute diagnosis
Skin biopsy
Muscle biopsy: inflammation, perifascicular atrophy
Treatment
Corticosteroids: prednisone (0.5–2 mg/kg/day) up to a dose of 60 mg/day initially
Consider immunosuppressive or cytotoxic steroid sparing agents
Consider IVIG if refractory

Table 26 Acute porphyria [45]

History
Rare disorder presenting with abdominal pain and psychiatric symptoms
Pain may begin in chest or back and move to abdomen
Gastrointestinal symptoms are common (e.g., vomiting, diarrhea, constipation)
Acute weakness may occur early or late
Seizures possible
Use of certain medications known to exacerbate
Examination
Muscle weakness usually begins proximally and more often in upper limbs
Symmetrical hypotonic, hyporeflexic flaccid paralysis
Up to 20 % suffer respiratory muscle paralysis
No rash unlike other forms of porphyria
Tachycardia and hypertension may be present
Investigations
Sodium: hyponatremia
Urine color: dark/reddish
Urine analysis: increased porphobilinogen
Treatment
IV hemin
Manage hyponatremia appropriately
Consider anti-epileptic drugs
Supportive management

Table 27 Tick paralysis [46, 47]

History
Typically presents with unsteady gait followed by an ascending symmetrical flaccid paralysis 2–6 days post-tick attachment
Sensory symptoms include paresthesias and hypoesthesia in limbs and face
Anorexia, lethargy, drowsiness, and confusion may precede weakness
Ataxia may be only symptom
Examination
Tick found attached to patient
Ascending symmetrical flaccid paralysis
Hypotonic, hyporeflexic
Progresses to affect all cranial nerves including pupillary dilatation
Potential respiratory muscle compromise
Sensory function is generally preserved other than mild paresthesias and hypoesthesis
No fever
Investigations
Locate tick
EMG shows reduced amplitude of compound muscle action potentials
No abnormalities seen with repetitive nerve stimulation studies
Labs, CSF analysis, MRI all typically normal
Treatment
Paralyze tick with insecticide and remove with forceps
Supportive care

Quadriparesis/paraparesis is symmetrical weakness of either all four limbs (quadriparesis) or legs (paraparesis), characteristically with a sensory level. Non-traumatic spinal cord injury may occur from *compression* (e.g., epidural abscess, hematoma, expanding tumor, prolapsed intervertebral disc), ischemia, or inflammation (transverse myelitis).

In the acute phase, a flaccid paralysis below the level of cord injury is typically seen, with an accompanying corresponding sensory level, although there is considerable variation. Neurologic examination should localize the lesion in patients with acute paraplegia or quadriplegia. Sensory abnormalities localize in the vertical plane (cervical, lumbar, or sacral) and, when combined with other

Table 28 Acute myopathy [43, 48]

History
Metabolic causes: periodic paralyses, hypo and hyperkalemia, hypophosphatemia (Table 36)
Inflammatory causes: polymyositis, dermatomyositis, rhabdomyolysis, infectious causes
Toxic etiologies: alcohol, corticosteroids, statins, retroviral agents, colchicine, cocaine, heroin
Endocrine causes: Addison's disease, Cushing's disease, hypo or hyperthyroidism, hyperparathyroidism
Typically presents with symmetric proximal muscle weakness, malaise, and fatigue
No sensory complaints except occasional myalgia
In rhabdomyolysis, dark colored urine and/or fever may be present
Examination
Symmetric proximal muscle weakness
No sensory disturbance other than myalgia
Dark urine in rhabdomyolysis
Fever may be present in rhabdomyolysis, polymyositis, and infectious causes
Other findings specifically associated with associated endocrinopathies may be present
Investigations
CK with isoenzymes (may not correlate with clinical condition)
Electrolytes, calcium, magnesium
Serum urea, creatinine, and electrolytes
Complete blood count
Erythrocyte sedimentation rate
Aspartate aminotransferase
Urinalysis: myoglobinuria
Specific workup for individual endocrinopathies
Consider EMG, nerve conduction velocity testing, and muscle biopsy
Treatment
Remove or treat any precipitant
Safely correct electrolyte abnormalities
Vigorous hydration for rhabdomyolysis

Table 29 Lambert–Eaton myasthenic syndrome (LEMS) [48–50]

History
In 40 % of patients with LEMS, cancer (commonly small cell lung cancer) is present
Progressive proximal lower limb weakness (e.g., difficulty standing from sitting)
Ptosis, diplopia, and dysarthria as cranial nerves become involved, (less commonly than in myasthenia gravis)
Autonomic dysfunction with dry mouth
Exacerbated by heat or fever and certain drugs
Examination [49]
Proximal muscle weakness, lower limbs more than upper
Depressed tendon reflexes, post-tetanic potentiation, and autonomic changes
Sensation preserved
Ptosis or diplopia (usually mild) in 25 %
Respiratory failure rare
Investigations
Voltage gated calcium channel antibodies
AChR antibodies
Repetitive nerve stimulation: characteristic findings
EMG: characteristic findings
Look for malignancy with imaging, consider bronchoscopy
Treatment [50]
Confirm diagnosis and distinguish from myasthenia gravis before starting treatment
Supportive treatment in interim
Treat underlying malignancy if it is found
When confirmed, consider 3,4-diaminopyridine, IVIG, or plasma exchange

Table 30 Diabetic lumbosacral radiculoplexus neuropathy [51, 52]

History
Diabetes mellitus with proximal weakness in the quadriceps, hip adductors, and iliopsoas muscles
Asymmetrical pain in the hip, buttock, or thigh
Often occurs in conjunction with significant recent weight loss
Associated with poor glycemic control
Patients without distal symmetrical polyneuropathy most often have sudden, unilateral onset
Occasionally the initial presenting feature of diabetes mellitus
Examination
Proximal lower limb muscle weakness and wasting
Minimal sensory loss is observed
Knee-jerk reflex is absent, with commonly preserved ankle jerks
Ankle jerks may also be absent, with underlying distal symmetrical polyneuropathy
Investigations
Fasting blood glucose and HbA1C
Imaging of lumbo-sacral spine to exclude other causes
EMG and nerve conduction studies
Treatment
Optimize glycemic control
Physical and occupational therapy

long tract signs, point to localization in the horizontal plane (extradural, intradural, or intramedullary). Key sensory levels (T4 nipple, T10 navel) should be used. Spinal cord infarction and transverse myelitis may cause acute cord injury without cord compression; these are outlined in the Tables 6 and 7.

Table 31 Vasculitic neuropathy [53, 54]

History
May be part of systemic vasculitis or a non-systemic vasculitic neuropathy
Asymmetric or multifocal painful sensorimotor neuropathy is most common presentation
May present as mononeuritis multiplex or a sensorimotor neuropathy, which may or may not be symmetric
Typically sensory symptoms of pain, burning, or paresthesias precede weakness of muscles supplied by the affected nerve
Sensory symptoms virtually always present
Constitutional symptoms, including weight loss, anorexia, fatigue, arthralgias, myalgias, and fevers, occur in approximately two-thirds of patients
Examination
Detailed neurological exam reveals a flaccid asymmetric paresis with sensory abnormalities in variable distributions
Lower limbs are more commonly involved than upper limbs
Distal involvement is more frequent than proximal
Cranial nerve involvement occurs in 8 % of patients, typically involving the facial nerve
Proximal symmetric polyneuropathy is least frequent presentation
Investigations
Vasculitic screen, including erythrocyte sedimentation rate, anti-nuclear antibodies, extractable nuclear antigens, rheumatoid factor, anti-neutrophil cytoplasmic antibodies, hepatic enzymes, renal function tests, serum complement serum immunoelectrophoresis (or immunofixation) and quantitative immunoglobulins, cryoglobulins, Hepatitis B antigen and antibody, Hepatitis C antigen, and CBC (anemia)
Nerve conduction studies and EMG
Nerve and muscle biopsy
Treatment
Consider combination therapy with steroids and cyclophosphamide in liaison with treating neurologist
Manage neuropathic pain with agents such as gabapentin, amitriptyline, nortriptyline, or carbamazepine

Table 32 Toxin-induced peripheral neuropathy [55]

History
Many drugs and industrial chemicals may cause distal axonopathy
Drugs include alcohol, amiodarone, chloramphenicol, disulfiram, isoniazid, lithium, metronidazole, nitrofurantoin, nitrous oxide, thalidomide, vincristine, and thallium. Dose, duration of exposure and host factors affect outcome
Presentation is often with pain, paresthesiae, and hypoesthesia in the feet, with distal weakness and gait disturbance
Autonomic dysfunction may be present
Examination
Sensory changes in glove and stocking distribution
Distal weakness progressing proximally
Hyporeflexia, symmetrical loss of ankle jerks first
May be evidence of CNS involvement
Investigations
EMG
Nerve conduction study
Serum levels for suspected toxin
Consider nerve and muscle biopsies
Treatment
Prevent ongoing exposure
Supportive care

Table 33 Nerve compression syndromes [56, 57]

History
History of acute or prolonged neural pressure causing a radiculopathy, plexopathy, or peripheral neuropathy
History depends on the region involved
Pain and paresthesias typically precede hypoesthesia and weakness/atrophy
Common specific examples include median nerve at wrist, ulnar nerve at elbow and wrist, radial nerve in proximal forearm, scapular nerve, lateral femoral cutaneous nerve, common peroneal nerve, tibial nerve, and lower brachial plexus
May be caused by pregnancy, obesity, or systemic conditions (e.g., hypothyroidism)
Nerve root weakness from a prolapsed intervertebral disc produces symptoms in the affected dermatome and myotome
Examination
Reduced strength in the muscles supplied by the affected nerve
Flaccid, hypotonic, hyporeflexic paralysis
Wasting and atrophy if chronic
Sensory symptoms include pain, paresthesias, and hypoesthesia
Skin changes include dry, thin, hairless skin; ridged, thickened, cracked nails; and recurrent skin ulceration
Investigations
Nerve conduction studies
MRI
Consider EMG
Treatment
Treat or remove precipitants
Surgery if conservative management fails

Proximal Weakness

- Acute myopathy (Table 28)
- Guillain–Barré syndrome (Table 21)
- Acute diabetic lumbosacral radiculoplexus neuropathy (DLRN) (Table 30)
- Myasthenia gravis (Table 13)
- Acute West Nile virus associated paralysis
- Lambert–Eaton myasthenic syndrome (LEMS) (Table 29)

Proximal weakness is weakness predominantly affecting the hip or shoulder girdle musculature. Acute proximal

Table 34 Acute poliomyelitis [58]

History
Typically occurs in unvaccinated patients from an area with endemic polio (Afghanistan, India, Nigeria, Pakistan, Angola, Chad, and Democratic Republic of the Congo)
However, may rarely occur after receiving live attenuated vaccine
Only a minority of infections (<5 %) experience paralytic poliomyelitis
Flaccid asymmetric weakness and muscle atrophy, lower limbs more than upper limbs
Incubation period 4 days–5 weeks
Severe muscle pain and spasms are followed by weakness
Bulbar symptoms are more common in adults
Transient acute urinary retention in 50 %
Examination
Asymmetric proximal weakness is typically present, with more involvement of lumbar than cervical segments
Sensation is preserved
Deep tendon reflexes are diminished or absent
Atrophy of muscle may be detected three weeks after onset of paralysis, which becomes maximal at 12–15 weeks and remains permanent
Cranial nerves may also be affected uni- or bi-laterally
Investigations
Elevated WBC
CSF: pleocytosis, mildly elevated protein with normal glucose
Viral studies for throat swab, stool, blood, and CSF
MRI may show localization of inflammation to the spinal cord anterior horns
EMG
Treatment
Supportive care

Table 35 Hypermagnesemia [59]

History
Typically follows excessive magnesium administration in context of renal impairment
More likely when supranormal magnesium levels targeted (e.g., in management of pre-eclampsia)
Lethargy and confusion are most common neurologic manifestations
As concentrations rise, generalized weakness develops, which progresses to involve muscles of respiration resulting in respiratory failure
Examination
Hyporeflexia: early loss of deep tendon reflexes often precedes other signs
Flaccid tetraparesis involving all muscle groups
Lethargy, confusion
Investigations
Serum magnesium levels
Treatment
Cease magnesium administration

Table 35 continued

IV calcium gluconate or chloride if symptoms severe
IV fluids
Consider dialysis

Table 36 Hypophosphatemia [60–62]

History
Hypophosphatemia may occur with
Intracellular shift: re-feeding syndrome, respiratory alkalosis, diabetic ketoacidosis, rapidly growing malignancies, osmotic diuresis, certain drugs including diuretics, malabsorption, renal tubular acidosis
Increased urinary excretion: primary or secondary hyperparathyroidism, osmotic diuresis (e.g., hyperosmolar hyperglycemic syndrome), diuretics, renal tubular acidosis, transplanted kidneys, congenital defects, or Fanconi syndrome)
Decreased intestinal absorption: diarrhea, malabsorption syndromes, phosphate binders (e.g., aluminum hydroxide)
Decreased dietary intake: anorexia nervosa or chronic alcoholism
Weakness may present as a painful proximal myopathy
Other neurological symptoms may include changes in mental function, seizures, and neuropathies
Other features may include arrhythmias, skeletal muscle weakness, respiratory failure, rhabdomyolysis, leukocyte dysfunction, sepsis, and sudden death
Examination
Proximal muscle weakness is common, though any muscle group may be involved, alone or in combination, ranging from ophthalmoplegia to proximal myopathy to dysphagia or ileus
Muscle pain is common
Weakness may be so profound as to mimic Guillain–Barre syndrome [60, 62]
Confusion, seizures, and coma may occur
Impaired cardiac contractility may occur, leading to generalized signs of myocardial depression
Investigations
Serum phosphate
Hypomagnesemia is commonly associated
Hypercalcemia if hyperparathyroidism
Urea, creatinine, other electrolytes
Rhabdomyolysis screen
Treatment
Correct precipitant
Replace total body phosphate with careful IV sodium or potassium phosphate

weakness classically presents with difficulty rising from a chair or brushing hair. The most common cause is myopathy. Less common causes include LEMS (Table 29) and myasthenia gravis. DLRN may be the presenting feature of diabetes mellitus and is also important to

Table 37 Acute weakness communication with assessment and referral

☐ Cause of weakness if known; differential diagnosis if not known
☐ Airway status and any respiratory issues
☐ Salient history and exam findings
☐ Relevant labs and imaging (if done)
☐ Treatments provided

consider. While poliomyelitis is very rare in western countries, it remains endemic elsewhere (Table 34). West Nile virus, with similar semiology as acute poliomyelitis, is more common in the United States and Europe.

Distal Weakness

- Vasculitic neuropathy (Table 31)
- Toxin induced peripheral neuropathy (Table 32)
- Nerve compression syndromes (Table 33)

Distal weakness is weakness mainly affecting the extremities. It is typically caused by peripheral neuropathies that often present along with sensory symptoms. Distal weakness affects the hands and feet, causing the patient to drop objects or develop gait disturbance due to foot drop. The pattern of weakness and history are of great significance. Of the many types of peripheral neuropathy, vasculitic and toxin induced are the most likely to produce an acute weakness. It may also be produced by local nerve compression syndromes (e.g., carpal tunnel syndrome that predominantly affects peripheries, causing both sensory and motor symptoms).

Monoparesis

- *Acute stroke*
- Intracranial mass (Table 18)
- Postictal Todd's paresis (Table 17)
- Nerve compression syndromes (Table 33)
- Diabetic lumbosacral radiculoplexus neuropathy (Table 30)
- Acute poliomyelitis (Table 34)

Monoparesis refers to paralysis of a single muscle, muscle group, or limb. Acute paralysis involving a single limb may be caused by a central or a peripheral lesion. Historical and examination factors may help to localize the lesion. For example, sudden onset right arm weakness with an associated dysphasia is most likely to result from a central lesion, whereas wrist drop in the right hand, with hypoesthesia on the back of the hand following falling asleep with the arm over the back of a chair, results from a peripheral nerve compression syndrome. Poliomyelitis is rare, but can occur in the unvaccinated.

Significant Associated Findings

Certain constellations of symptoms and signs can make specific, often unusual diagnoses more likely. Table 4 lists some of these, and each is elaborated further in separate tables. Stroke syndromes may also have characteristic patterns which are too numerous and varied to discuss here. However, findings such as aphasia, agnosia, apraxia, and neglect with acute weakness or sensory signs should prompt consideration of *acute stroke*.

Not Neuromuscular

Some disease states may produce symptoms of generalized weakness or fatigue that do not have a neuromuscular basis. These may be medical emergencies in their own right meriting urgent specific treatment (see Table 14).

Anatomical Localization

Understanding the cause of weakness can be aided by localizing anatomically, since diseases are often specific for each anatomic region. The neurological examination greatly aids the localization of weakness by anatomic means. Figure 1 breaks down anatomic regions into the brain and spinal cord, the anterior horn cell, the peripheral nerve, neuromuscular junction (NMJ), and muscle.

Diseases of the brain and spinal cord produce "UMN weakness," meaning disruption of descending motor axons or cell bodies that innervate the LMN (the anterior horn cell, peripheral nerve, and NMJ). After performing a neurological examination, refer to Table 5 to ascribe the appropriate anatomic localization.

The key features to focus on are the presence or the absence of sensory signs (loss of sensory modality) or symptoms (complaints of numbness or tingling). If sensory signs/symptoms are absent, peripheral nerve is eliminated, and central nervous system processes are reduced in likelihood.

Anterior horn cell causes are principally Lou–Gehrig's disease (ALS) and polio, neither of which have acute treatments. Reflexes are helpful to determine among the remaining causes which is most likely to occur. In general, lesions of the brain and spinal cord and the NMJ are the most emergent causes to consider, as there are specific treatments for some of these diseases (*acute stroke* and *spinal cord compression*) or public health concerns (botulism, Table 22).

Ideally, both the anatomic and the clinical localizations will agree with each other and the diagnosis can then be made. Substantial disagreement in localizations should raise concerns over one or both localizations.

Communication

A checklist of items to consider with assessment and referral for affected patients is provided in Table 37.

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