Chapter 12
Approach to Weakness in the ICU

12.1 Introduction

Weakness in the intensive care unit (ICU) is a critical symptom with a broad differential diagnosis. It can manifest as generalized weakness due to systemic illness or as focal neurological deficits indicative of significant underlying pathology. Weakness may be episodic or persistent, and distinguishing between these patterns is crucial for early diagnostic considerations. Episodic weakness can result from causes such as electrolyte imbalances, periodic paralyses, or myasthenia gravis, while persistent weakness may indicate ongoing neuromuscular or systemic issues.

Proper evaluation and management are vital to improve patient outcomes. This chapter outlines a systematic approach for assessing and managing weakness in ICU patients, integrating clinical assessment, diagnostic testing, and tailored therapeutic strategies. We will explore various etiologies, including central and peripheral causes, neuromuscular junction disorders like myasthenia gravis and Lambert-Eaton syndrome, metabolic myopathies such as mitochondrial disorders, and ICU-acquired conditions like critical illness polyneuropathy (CIP) and critical illness myopathy (CIM) [1, 2]. [Ref. Algorithm 12.1].

12.2 Patient History and Physical Examination

History

Document Onset, Pattern, and Progression

- Onset and Evolution: Understanding when the weakness began, its pattern (episodic vs. persistent), and how it has evolved provides clues about its etiology. Acute onset might suggest a stroke or acute inflammatory demyelinating

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polyradiculoneuropathy (AIDP), whereas a gradual onset could indicate a metabolic disorder or progressive neuromuscular disease (Table 12.1).

- Associated Symptoms: Inquire about symptoms such as fatigue, muscle pain, sensory changes, autonomic symptoms, or fluctuations in weakness.

Table 12.1 Causes of episodic generalized weakness

Electrolyte disturbances	Electrolyte imbalances: Low potassium levels (hypokalemia) High potassium levels (hyperkalemia) Low sodium levels (hyponatremia) High sodium levels (hypernatremia) Low phosphate levels (hypophosphatemia) High calcium levels (hypercalcemia) Low magnesium levels (hypomagnesemia) High magnesium levels (hypermagnesemia)
Neuromuscular junction disorders	Autoimmune conditions: Myasthenia gravis Lambert-Eaton myasthenic syndrome
	Toxin-mediated blockade: Botulism Exposure to certain pesticides (organophosphate poisoning)
	N,M: Medications like aminoglycoside antibiotics affecting neuromuscular transmission
Muscle ion channel disorders (channelopathies)	Periodic paralysis syndromes: Hypokalemic periodic paralysis Hyperkalemic periodic paralysis Andersen-Tawil syndrome
	Other channelopathies: Paramyotonia congenita Congenital myotonia
Central nervous system events	Transient ischemic attacks (TIAs): Brief episodes of neurological dysfunction due to temporary cerebral ischemia
	Migraine with aura: Neurological symptoms preceding headache, including weakness
	Multiple sclerosis relapses: Demyelinating events causing transient neurological deficits
	Seizure activity: Postictal weakness (Todd's paralysis) following a seizure

(continued)

Table 12.1 (continued)

Metabolic and endocrine disorders	Hypoglycemia Hypothyroidism Hyperthyroidism Hyperparathyroidism Addison's disease Acute intermittent porphyria Severe cases leading to muscle weakness
Toxic and drug-related causes	Substance abuse: Alcohol-induced hypoglycemia or electrolyte disturbances
	Medication side effects: Corticosteroid-induced myopathy Statin-associated muscle symptoms
	Environmental exposures: Heavy metal poisoning (e.g., lead, arsenic)
Psychogenic and functional disorders	Functional neurological symptom disorder (conversion disorder): Neurological symptoms not explained by medical Conditions
	Psychological factors: Anxiety or panic attacks leading to subjective weakness
	Chronic fatigue syndrome/myalgic encephalomyelitis: Persistent fatigue with episodes of worsened weakness
Others	Sleep disorders: Sleep paralysis causing transient inability to move upon Waking
	Periodic hypokalemic paralysis associated with thyrotoxicosis: Often seen in Asian populations with hyperthyroidism
	Neurological conditions: Narcolepsy with cataplexy causing sudden muscle weakness triggered by emotions

Medical and Surgical History

- Previous Conditions: Prior neurological disorders, endocrine dysfunctions, or autoimmune diseases.
- Recent Infections: Can suggest Guillain-Barré syndrome (GBS) or post-infectious myelitis [3].
- Surgeries and ICU Stays: Recent surgery or prolonged immobilization might hint at ICU-acquired weakness or postoperative complications.

Medications

- Drug-Induced Weakness: Certain drugs can induce muscle weakness or neuropathy, such as corticosteroids, neuromuscular blockers, aminoglycoside antibiotics, or chemotherapy agents.
- Exposure to Toxins: Organophosphates, botulinum toxin.

Family History

- Genetic Disorders: Predispositions to neuromuscular disorders, such as muscular dystrophy or hereditary metabolic myopathies.
- Periodic Paralysis: Family history of episodic weakness.

12.3 Examination

Neurological Examination

- Mental Status: Assess for delirium, encephalopathy, or focal neurological deficits.
- Cranial Nerve Function: Determine if there is involvement of cranial nerves, which may suggest central or peripheral etiologies.
- Motor Strength: Evaluate for differences between proximal vs. distal and symmetrical vs. asymmetrical weakness. Use the Medical Research Council (MRC) scale for grading muscle strength [4–6].
- Sensory Function: Loss of sensation may point toward peripheral neuropathy or spinal cord involvement.
- Reflexes: Hyperreflexia can indicate a central cause, while diminished reflexes might suggest a peripheral process.
- Muscle Tone and Bulk: Assess for atrophy, fasciculations, or changes in muscle tone, which could indicate chronic neuromuscular disease or recent immobilization.

Clinical Pearl

- Fluctuating Weakness: Suggests a neuromuscular junction disorder like myasthenia gravis.
- Descending Paralysis: Consider botulism or tick paralysis.
- Symmetrical Distal Weakness with Sensory Loss: Points toward peripheral neuropathy.

12.4 Algorithmic Approach to Weakness

A systematic, stepwise approach is essential for diagnosing the cause of weakness in ICU patients. By integrating clinical findings with diagnostic studies, clinicians can efficiently narrow down potential etiologies.

1. Assess Mental Status and Cranial Nerves
   - Altered mental status or cranial nerve involvement may indicate a central nervous system (CNS) cause.
2. Evaluate Motor and Sensory Function
   - Motor Weakness Pattern: Proximal vs. distal, symmetrical vs. asymmetrical.
   - Sensory Involvement: Presence suggests peripheral neuropathy or spinal cord pathology.
3. Examine Reflexes and Muscle Tone
   - Hyperreflexia and Spasticity: Suggest upper motor neuron (UMN) lesion.
   - Hyporeflexia and Flaccidity: Indicate lower motor neuron (LMN) involvement.
4. Early Neurophysiological Testing
   - EMG and NCS: Critical for differentiating between neuropathies, myopathies, and neuromuscular junction disorders.
5. Imaging Studies
   - MRI/CT: To identify central lesions or structural abnormalities.
6. Laboratory Tests
   - Basic and Specific Tests: To detect metabolic, infectious, or autoimmune causes.

12.5 Determining Central vs. Peripheral Causes (Table 12.2)

Central Causes
Brain Lesions

Table 12.2 Differentiate central vs. peripheral causes

Feature	Central causes	Peripheral causes
Mental status	Altered (encephalopathy)	Normal
Cranial nerves	May be involved (e.g., facial droop)	Usually spared
Weakness pattern	Unilateral, proximal, spasticity	Bilateral, distal, flaccid
Reflexes	Hyperreflexia, Babinski sign	Hyporeflexia, absent reflexes
Sensory loss	Localized (cortical pattern)	Diffuse (glove-and-stocking)
Muscle tone	Increased (spasticity)	Decreased (flaccid)
Fasciculations	Absent	Present (in lower motor neuron diseases)
Muscle atrophy	Rare (early stages)	Common (early onset in neuropathy)

- Stroke: Sudden onset weakness, often unilateral, with UMN signs.
- Tumors: Gradual onset, may present with headaches, seizures.
- Infections: Encephalitis or abscesses causing focal deficits.

Spinal Cord Disorders

- Compression: Due to tumors, abscesses, or herniated discs causing weakness below the lesion level.
- Inflammatory Conditions: Transverse myelitis, multiple sclerosis.

Peripheral Causes
Peripheral Neuropathy

- Guillain-Barré Syndrome (GBS): Acute, symmetrical ascending weakness, areflexia, often following infection.
- Diabetic Neuropathy: Chronic distal symmetric polyneuropathy with sensory loss.

Neuromuscular Junction Disorders
Myasthenia Gravis (MG)

- Etiology: Autoimmune antibodies against acetylcholine receptors.
- Clinical Features: Fluctuating weakness, ptosis, diplopia, dysphagia, proximal muscle weakness, worsens with activity.

Diagnostic Tests:

- Acetylcholine Receptor Antibodies: Elevated in most patients.
- Single-Fiber EMG: Shows increased jitter.
- Repetitive Nerve Stimulation: Decremental response.

Treatment Options:

- Acetylcholinesterase Inhibitors: Pyridostigmine.
- Immunosuppressive Therapy: Corticosteroids, azathioprine.
- Plasmapheresis and IVIg: For rapid improvement.
- Thymectomy: Considered in certain cases [7].

Lambert-Eaton Myasthenic Syndrome (LEMS)

- Etiology: Autoimmune antibodies against presynaptic voltage-gated calcium channels.
- Clinical Features: Proximal muscle weakness, autonomic symptoms, hyporeflexia, strength may improve with activity.

Diagnostic Tests:

- Voltage-Gated Calcium Channel Antibodies: Elevated levels.
- EMG: Incremental response on high-frequency stimulation.

Treatment Options:

- 3,4-Diaminopyridine: Enhances acetylcholine release.
- Immunotherapy: Similar to MG.
- Cancer Screening: Often associated with small-cell lung carcinoma [8].

Myopathies

- Critical Illness Myopathy (CIM): Proximal muscle weakness, difficulty weaning from ventilation.
- Metabolic Myopathies: Mitochondrial disorders causing exercise intolerance, muscle pain.

ICU-Acquired Weakness (ICU-AW)
Critical Illness Polyneuropathy (CIP):

- Features: Distal weakness, reduced reflexes, sensory deficits.
- NCS Findings: Reduced amplitude of SNAPs and CMAPs.

Critical Illness Myopathy (CIM):

- Features: Proximal weakness, preserved sensation.
- EMG Findings: Myopathic changes, early recruitment.

Critical Illness Neuromyopathy (CINM):

- Combination: Features of both CIP and CIM.

Management:

- Early Mobilization: Physical therapy initiation.
- Minimizing Sedation: Reduce neuromuscular blockers and corticosteroids.
- Optimizing Glycemic Control: Prevent hyperglycemia-induced nerve damage [4, 5].

Clinical Pearl

- ICU-AW is common in patients with sepsis, multi-organ failure, or prolonged immobilization. Early recognition and intervention can improve outcomes.

12.6 Neurophysiological Studies and Imaging

12.6.1 Neurophysiological Studies

Nerve Conduction Studies (NCS)

- Purpose: Evaluate the integrity and function of peripheral nerves.

Findings:

- Axonal Neuropathies: Reduced amplitude of CMAPs and SNAPs.
- Demyelinating Neuropathies: Prolonged latencies, slowed conduction velocities.

Conditions Diagnosed:

- GBS: Demyelinating patterns.
- CIP: Axonalloss.

Electromyography (EMG)

- Purpose: Differentiate between neuropathic and myopathic processes.

Findings:

- Neuropathic Changes: Fibrillations, positive sharp waves, large-amplitude motor units.
- Myopathic Changes: Small-amplitude, short-duration motor units, early recruitment.

Conditions Diagnosed:

- Myasthenia Gravis: Increased jitter on single-fiber EMG.
- CIM: Myopathic pattern.

Importance of Early Testing

- Guiding Diagnosis and Management: Early EMG and NCS can distinguish between various neuromuscular disorders, enabling prompt and appropriate interventions.

12.6.2 Imaging

MRI/CT Scan of Brain and Spine

- Purpose: Rule out central causes such as stroke, tumors, demyelinating lesions, or spinal cord compression.

Specific MRI Patterns:

- Inflammatory Myopathies: Muscle edema.
- GBS: Nerve root enhancement.
- Compressive Lesions: Epidural abscesses, hematomas.

Ultrasound

- Purpose: Assess muscles and peripheral nerves for structural abnormalities.
- Advantages: Bedside availability, real-time assessment.

Applications:

- Nerve Enlargement: Seen in chronic inflammatory demyelinating polyneuropathy (CIDP).
- Muscle Atrophy: Evaluation in prolonged ICU stays.

Clinical Pearl
- Spinal Imaging is crucial in patients with sudden onset weakness and sensory level to exclude compressive myelopathy, which is a neurosurgical emergency.

12.7 Laboratory Tests

Basic Metabolic Panel
- Electrolyte Imbalances: Hypokalemia, hyperkalemia, hypophosphatemia can cause weakness.
- Renal and Liver Function: Assess for metabolic encephalopathies.

Complete Blood Count (CBC)
- Infection Indicators: Leukocytosis or leukopenia.
- Anemia: Can contribute to fatigue and weakness.

12.7.1 Specific Tests

Creatine Kinase (CK)
- Elevated Levels: Indicate muscle damage, common in myopathies.

Blood Glucose Levels
- Hyperglycemia: Can cause neuropathy.
- Hypoglycemia: Can cause episodic weakness.

Thyroid Function Tests
- Hypothyroidism: Can cause proximal muscle weakness.
- Hyperthyroidism: Associated with thyrotoxic periodic paralysis.

Blood Cultures
- Sepsis Evaluation: In suspected infection-related weakness.

Autoantibodies
- Myasthenia Gravis: Acetylcholine receptor antibodies.
- Lambert-Eaton Syndrome: Voltage-gated calcium channel antibodies.
- Autoimmune Myopathies: ANA, anti-Jo-1 antibodies.

Clinical Pearl
- Electrolyte Corrections: Simple interventions like correcting potassium or phosphate levels can rapidly reverse episodic weakness.

12.8 Management Strategy

12.8.1 Supportive Care

Nutritional Support

- High-Protein Diet: Supports muscle mass and metabolic needs.
- Caloric Adequacy: Prevents catabolism and promotes healing.

Optimizing Physiological Status

- Fluid and Electrolyte Balance: Correct imbalances promptly.
- Oxygenation and Perfusion: Ensure adequate delivery to tissues.
- Glycemic Control: Prevent hyperglycemia-induced complications.

12.8.2 Pulmonary Rehabilitation

Respiratory Muscle Training

- Techniques: Incentive spirometry, inspiratory muscle training.
- Benefits: Improves weaning success from mechanical ventilation.

Noninvasive Ventilation (NIV)

- Indications: Respiratory muscle weakness, COPD exacerbations.
- Advantages: Reduces need for intubation, preserves airway defenses.

Weaning Strategies

- Gradual Reduction: Taper ventilatory support as strength improves.
- Multidisciplinary Approach: Involving respiratory therapists, nurses, physicians.

12.8.3 Physical Therapy and Early Mobilization

Evidence-Based Practice

- Improved Outcomes: Early mobilization reduces ICU stay, mechanical ventilation duration.

Studies:

- Early physiotherapy/occupational therapy led to better functional outcomes.
- ABCDEF Bundle: Incorporates early mobility and minimal sedation.

Sedation Management

- Minimizing Sedatives: Reduces delirium, facilitates participation in therapy.
- Protocols: Daily sedation interruption, sedation scales.

12.8.4 Immunotherapies

Guillain-Barré Syndrome (GBS)

- IVIg and Plasmapheresis: Reduce autoimmune attack on nerves.
- Early Initiation: Improves recovery time [3, 9–11].

Myasthenia Gravis (MG)

- Acetylcholinesterase Inhibitors: Symptomatic relief.
- Immunosuppressive Therapy: Corticosteroids, azathioprine.
- Plasmapheresis and IVIg: For myasthenic crisis.
- Thymectomy: Surgical option in certain patients.

12.8.5 Targeted Treatments

Metabolic Disorders

- Supplementation: Correct deficiencies (e.g., thiamine in Wernicke's encephalopathy).
- Dietary Modifications: For mitochondrial disorders.

Infections

- Antimicrobial Therapy: Based on culture and sensitivity.

Clinical Pearl

- Early Immunotherapy in autoimmune neuromuscular disorders can significantly improve outcomes and reduce morbidity.

12.9 Risk Factor Minimization

12.9.1 Preventative Measures

Physical Therapy

- Early Mobilization: Prevents deconditioning, reduces ICU-acquired weakness.
- Customized Programs: Tailored to patient's condition and tolerance.

Sedation Management

- Minimizing Neuromuscular Blockers: Avoid prolonged use to prevent CIM.
- Sedation Protocols: Use the lowest effective dose.

Nutritional Support

- Adequate Intake: Prevents muscle wasting.
- High-Protein Diets: Supports muscle repair.

Clinical Pearl

- Interdisciplinary Approach: Collaboration among healthcare professionals enhances patient recovery and reduces complications.

12.10 Stepwise Diagnostic Pathway

A structured approach ensures efficient identification of the underlying cause of weakness.

12.10.1 Initial Assessment

- Detailed Clinical History: Onset, pattern, progression, associated symptoms.
- Basic Laboratory Tests: Electrolytes, glucose, CBC, renal and liver function tests.

12.10.2 Focused Examination

- Neurological Examination: Localize the lesion and assess severity.

12.10.3 Initial Diagnostics

Episodic Weakness:

- Electrolyte Evaluation: Correct imbalances.
- ECG: Rule out cardiac arrhythmias.
- Persistent Weakness.
- Neurophysiological Studies: EMG and NCS to differentiate disorders.

12.10.4 Advanced Diagnostics

- Autoimmune Testing: Antibody panels for MG, LEMS, autoimmune myopathies.
- Imaging: MRI of brain and spine for central causes.
- Lumbar Puncture: CSF analysis in suspected GBS.

12.10.5 Tailored Diagnostics

- Muscle Biopsy: In metabolic or inflammatory myopathies.
- Genetic Testing: For hereditary neuromuscular disorders.

Medical Research Council (MRC) Scale for Muscle Strength Assessment
The MRC scale is a standardized tool for evaluating muscle strength in ICU patients, assessing six muscle groups bilaterally. Each muscle group is graded from 0 (no contraction) to 5 (normal strength), with a total score ranging from 0 to 60.

Muscle Groups Assessed
- Shoulder abductors.
- Elbow flexors.
- Wrist extensors.
- Hipflexors.
- Knee extensors.
- Foot dorsiflexors.

Each muscle group is examined on both the left and right sides, and a score is assigned based on the following scale:

MRC Scoring Guide
- Grade 5: Full strength, normal muscle function.
- Grade 4: Movement against gravity and resistance.
- Grade 3: Movement against gravity only.
- Grade 2: Movement of the limb without overcoming gravity.
- Grade 1: Visible muscle contraction without any limb movement.
- Grade 0: No visible contraction.

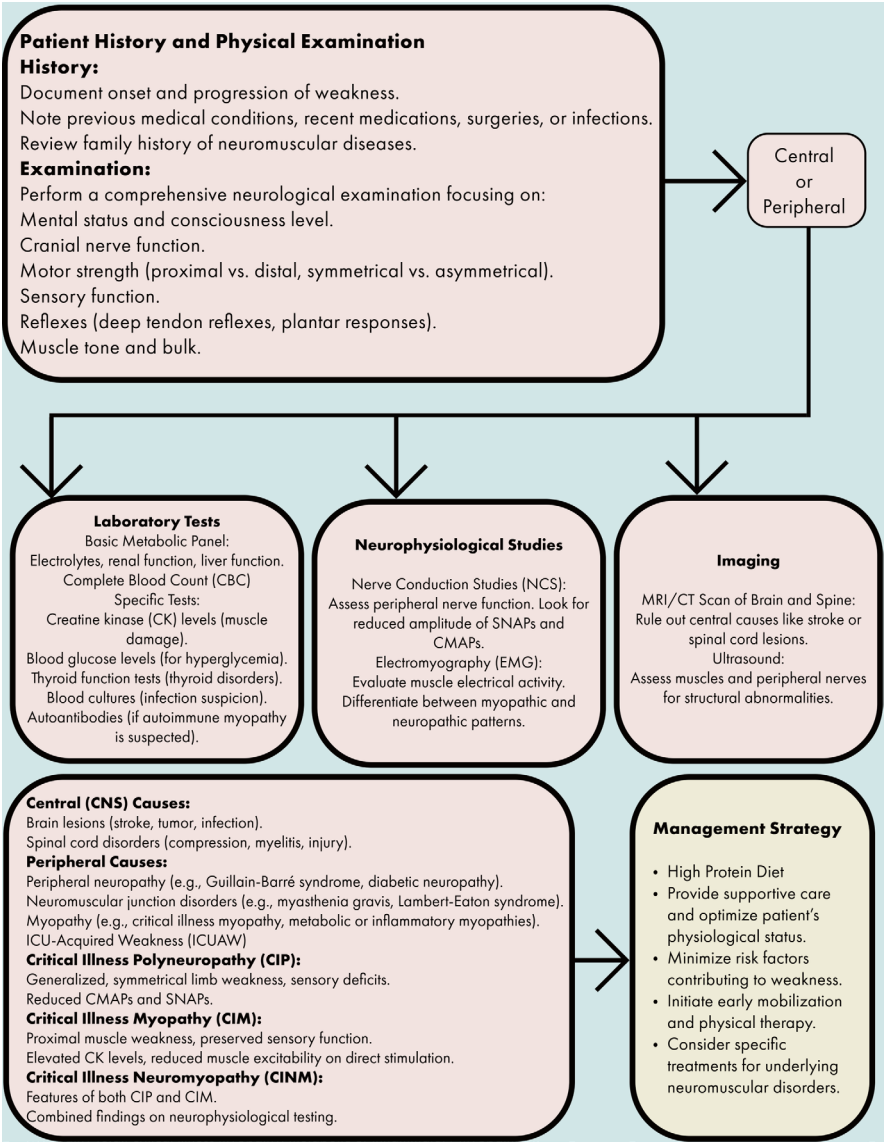
At the Bedside
1. Evaluate muscle strength bilaterally for each of the six muscle groups listed above.
2. Assign a score from 0 to 5 based on the patient's ability to move against gravity and resistance.
3. Sum the total MRC score out of 60. A score close to 60 indicates normal strength, while lower scores suggest varying degrees of muscle weakness.
4. Interpretation:
    - Score < 48: This indicates significant muscle weakness and may suggest critical illness-related myopathy.
    - Score ≤ 36: Suggests severe weakness, often seen in conditions like ICU-acquired weakness (ICUAW).

This bedside assessment helps in identifying and monitoring muscle strength, aiding in treatment decisions and rehabilitation planning for ICU patients.

12.11 Conclusion

Managing weakness in the ICU involves a comprehensive approach that integrates detailed clinical assessment, diagnostic testing, and individualized therapeutic strategies. Early identification and intervention are key to mitigating the impacts of ICU-acquired weakness and other neuromuscular complications.

Algorithm 12.1: Approach to weakness in the ICU



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