

Workup of Weakness in the Hospital Setting

Weakness is a common presenting symptom in the hospital setting, often indicating an underlying serious condition that requires a systematic and multidisciplinary evaluation. This guide provides students with a comprehensive framework to evaluate weakness, including neurological, endocrinological, cardiovascular, pulmonary, and rheumatological causes, along with other contributors such as drug use, obstructive sleep apnea (OSA), congestive heart failure (CHF), neuropathies, Guillain-Barré syndrome (GBS), failure to thrive, hypothyroidism, infection/sepsis, and additional etiologies. It includes a stepwise approach, a comparative table across systems with onset clarification, and clinical scenarios for practical application.

Introduction and Pathophysiology

Weakness in the hospital setting can be subjective (perceived fatigue) or objective (measurable motor deficit), and its etiology often spans multiple organ systems. Objective weakness typically results from impaired neuromuscular function, systemic illness, or metabolic derangements affecting muscle performance or energy production.

Neuromuscular: Impaired nerve signaling (e.g., GBS, myasthenia gravis) or muscle dysfunction (e.g., myopathy) reduces motor strength.

Metabolic/Endocrine: Electrolyte imbalances (e.g., hypokalemia), hormonal deficiencies (e.g., hypothyroidism), or energy deficits (e.g., hypoglycemia) impair muscle contraction.

Systemic Inflammation/Infection: Sepsis, critical illness myopathy, or cytokine-mediated fatigue (e.g., in infection, malignancy) cause generalized weakness.

Cardiovascular/Pulmonary: Reduced oxygen delivery (e.g., CHF, COPD) or hypoperfusion (e.g., shock) limits muscle function.

Rheumatologic: Inflammatory myopathies (e.g., polymyositis) or systemic diseases (e.g., SLE) cause muscle inflammation or fatigue.

A systematic workup is essential to identify the underlying cause, as weakness can be a harbinger of life-threatening conditions requiring urgent intervention.

Clinical Presentation

- General Symptoms:
 - **Objective weakness:** Measurable motor deficit (e.g., reduced grip strength, inability to stand).
 - **Fatigue:** Perceived lack of energy, often overlapping with weakness.
 - **Constitutional:** Fever, weight loss, night sweats (infection, malignancy).
- System-Specific Features:
 - **Neurological:** Focal weakness (stroke), symmetric weakness (GBS), sensory loss (neuropathy), ptosis/diplopia (myasthenia gravis), fasciculations (ALS).
 - **Endocrine:** Cold intolerance, weight gain (hypothyroidism), tremor, palpitations (hyperthyroidism), thirst, polyuria (hypercalcemia, diabetes).
 - **Cardiovascular:** Dyspnea, orthopnea, edema (CHF), chest pain, syncope (arrhythmias, shock).
 - **Pulmonary:** Dyspnea, cough, hypoxia (COPD, OSA), respiratory muscle weakness (hypercapnia).
 - **Rheumatologic:** Proximal muscle weakness (polymyositis), joint pain, rash (SLE, dermatomyositis).
 - **Infectious:** Fever, chills, altered mental status (sepsis), localizing signs (e.g., cellulitis, meningitis).
 - **Other:** Failure to thrive (weight loss, malnutrition), drug history (e.g., statins, alcohol), sleep disturbance (OSA).

Stepwise Approach to Evaluation of Weakness

Step 1: History and Physical Exam

- Onset and Pattern:
 - Acute (stroke, GBS, sepsis), subacute (hypothyroidism, drug-induced myopathy), chronic (failure to thrive, ALS). Focal (stroke) vs. symmetric (GBS, myopathy).
- Associated Symptoms:
 - Fever (sepsis), dyspnea (CHF, COPD), neurological deficits (stroke, neuropathy), joint pain (rheumatologic).
- Medical History:
 - Diabetes (neuropathy), thyroid disease, heart failure, COPD, autoimmune disease (SLE), malignancy (paraneoplastic).

- **Social History:**
 - Alcohol (neuropathy, myopathy), smoking (COPD, malignancy), drug use (e.g., statins, cocaine).
- **Physical Exam:**
 - **Neurological:** Motor strength (MRC scale 0-5), reflexes (hypo- in GBS, hyper- in stroke), sensory loss, cranial nerve exam (e.g., ptosis in myasthenia).
 - **Cardiovascular:** JVD, S3, edema (CHF), murmurs (endocarditis), pulses (hypoperfusion).
 - **Pulmonary:** Crackles, wheezing (COPD, CHF), accessory muscle use (respiratory failure).
 - **Rheumatologic:** Proximal weakness (polymyositis), rash (SLE, dermatomyositis), joint swelling.
 - **General:** Cachexia (failure to thrive), fever (sepsis), lymphadenopathy (malignancy).

Step 2: Initial Labs and Studies

- **CBC:** Anemia (chronic disease, malignancy), leukocytosis/leukopenia (sepsis), eosinophilia (EGPA, drug reaction).
- **CMP:** Electrolytes (hypokalemia, hypercalcemia), BUN/Cr (AKI in sepsis, CHF), glucose (hypoglycemia), LFTs (alcohol, malignancy).
- **Inflammatory Markers:** ESR, CRP (vasculitis, infection, malignancy).
- **Thyroid Function:** TSH, free T4 (hypothyroidism, hyperthyroidism).
- **CK (Creatine Kinase):** Elevated in myopathy (polymyositis, statin-induced).
- **Lactate:** Elevated in sepsis, hypoperfusion (shock, CHF).
- **Blood Cultures:** If sepsis suspected (fever, hypotension).
- **Urinalysis:** Hematuria, proteinuria (vasculitis, SLE).

Step 3: Targeted Workup Based on Suspected Etiology

- **Neurological:**
 - **Stroke:** CT/MRI brain (ischemic/hemorrhagic), carotid ultrasound, EKG (arrhythmias).
 - **GBS:** Lumbar puncture (albuminocytologic dissociation: high protein, normal WBC), EMG/NCS (demyelinating neuropathy).
 - **Myasthenia Gravis:** Anti-AChR antibodies, repetitive nerve stimulation, edrophonium test (if safe).
 - **Neuropathy:** B12, folate, HbA1c (diabetic neuropathy), alcohol history, EMG/NCS.
 - **ALS:** EMG/NCS (fasciculations, denervation), MRI spine (rule out cord compression).

- **Spinal Cord Injury/Compression:** MRI spine (cord edema, compression), neurosurgery consult.
- **Botulism:** History of food exposure, EMG (decremental response), botulinum toxin testing.
- **Multiple Sclerosis (MS):** MRI brain/spine (demyelinating lesions), CSF (oligoclonal bands).
- Endocrine:
 - **Hypothyroidism:** TSH, free T4 (elevated TSH, low T4).
 - **Hypercalcemia:** PTH, 25-OH vitamin D, PTHrP (malignancy).
 - **Adrenal Insufficiency:** AM cortisol, ACTH stimulation test.
- Cardiovascular:
 - **CHF:** BNP, ECHO (reduced EF), chest X-ray (pulmonary edema).
 - **Shock:** Lactate, EKG (arrhythmias), ECHO (hypoperfusion, tamponade).
- Pulmonary:
 - **COPD/OSA:** PFTs (obstructive pattern), ABG (hypercapnia, hypoxia), sleep study (OSA).
 - **Respiratory Failure:** ABG (hypoxemia, hypercapnia), chest X-ray/CT (pneumonia, ARDS).
- Rheumatologic:
 - **Polymyositis/Dermatomyositis:** CK, aldolase, ANA, anti-Jo-1, muscle biopsy.
 - **SLE:** ANA, anti-dsDNA, C3/C4, urinalysis (nephritis).
 - **Vasculitis:** ANCA, ESR/CRP, urinalysis (glomerulonephritis), biopsy (skin, kidney).
- Infectious:
 - **Sepsis:** Blood cultures, lactate, procalcitonin, imaging (e.g., chest X-ray for pneumonia).
 - **Meningitis/Encephalitis:** Lumbar puncture (cell count, glucose, protein, culture), MRI brain.
- Other:
 - **Failure to Thrive:** Nutritional panel (albumin, prealbumin), malignancy workup (e.g., CT chest/abdomen, tumor markers).
 - **Drug Use:** Urine drug screen (cocaine, opioids), statin history (myopathy).
 - **Malignancy/Paraneoplastic:** CT chest/abdomen/pelvis, tumor markers (e.g., CEA, CA 19-9), paraneoplastic antibodies (e.g., anti-Hu).

Step 4: Advanced Testing and Specialist Consultation

- Neurology:
 - EMG/NCS, MRI brain/spine, nerve/muscle biopsy if unclear etiology.

- Endocrinology:
 - ACTH, cortisol, aldosterone (adrenal insufficiency), ACTH stimulation test.
- Cardiology:
 - Cardiac cath (ischemia), Holter monitor (arrhythmias).
- Pulmonology:
 - Bronchoscopy (infection, malignancy), sleep study (OSA).
- Rheumatology:
 - Biopsy (skin, muscle, kidney), autoimmune serologies (e.g., anti-Jo-1, ANCA).
- Infectious Disease:
 - Cultures, serologies (e.g., HIV, syphilis), lumbar puncture (meningitis).

Expanded Neurological Causes of Weakness

Stroke:

Cause: Ischemic (thrombotic/embolic) or hemorrhagic; affects corticospinal tracts.

Presentation: Focal weakness (hemiparesis), sensory loss, hyperreflexia, Babinski sign, acute onset.

Pathophysiology: Occlusion (ischemic) or rupture (hemorrhagic) of cerebral vessels causes infarction/bleeding, impairing motor pathways.

Guillain-Barré Syndrome (GBS):

Cause: Post-infectious (e.g., Campylobacter, CMV), autoimmune demyelination of peripheral nerves.

Presentation: Symmetric ascending weakness, areflexia, sensory loss (distal), respiratory failure (20% of cases).

Pathophysiology: Molecular mimicry triggers antibodies against myelin, causing demyelination and conduction block.

Myasthenia Gravis (MG):

Cause: Autoimmune; antibodies against acetylcholine receptor (AChR) or MuSK.

Presentation: Fatigable weakness, ptosis, diplopia, bulbar weakness (dysarthria, dysphagia), worse with activity.

Pathophysiology: Antibodies block AChR at neuromuscular junction, reducing muscle contraction.

Peripheral Neuropathy:

Cause: Diabetic, B12 deficiency, alcohol, chemotherapy (e.g., vincristine), HIV.

Presentation: Distal symmetric weakness, sensory loss (numbness, paresthesias), hyporeflexia, "stocking-glove" pattern.

Pathophysiology: Axonal degeneration or demyelination impairs nerve conduction, affecting distal muscles/sensory nerves.

Amyotrophic Lateral Sclerosis (ALS):

Cause: Degenerative; upper and lower motor neuron involvement, genetic (e.g., SOD1 mutation).

Presentation: Progressive weakness, fasciculations, spasticity (UMN), atrophy (LMN), dysarthria, dysphagia.

Pathophysiology: Motor neuron degeneration in cortex (UMN) and anterior horn (LMN) leads to muscle denervation and atrophy.

Multiple Sclerosis (MS):

Cause: Autoimmune demyelination of CNS, often relapsing-remitting.

Presentation: Episodic weakness, sensory loss, optic neuritis, internuclear ophthalmoplegia, Lhermitte's sign.

Pathophysiology: Inflammatory plaques in white matter disrupt nerve conduction, causing motor/sensory deficits.

Spinal Cord Injury/Compression:

Cause: Trauma, tumor, disc herniation, abscess.

Presentation: Acute/subacute weakness below lesion, sensory loss, hyperreflexia, bowel/bladder dysfunction.

Pathophysiology: Compression or transection of spinal cord interrupts corticospinal tracts, causing paresis.

Botulism:

Cause: Clostridium botulinum toxin, often from canned foods.

Presentation: Descending weakness, diplopia, dysarthria, dysphagia, respiratory failure, normal sensation.

Pathophysiology: Toxin inhibits acetylcholine release at neuromuscular junction, causing flaccid paralysis.

Poliomyelitis/Post-Polio Syndrome:

Cause: Poliovirus (historical), residual weakness in survivors.

Presentation: Asymmetric weakness, atrophy, fasciculations (post-polio: new weakness years later).

Pathophysiology: Virus destroys anterior horn cells, causing LMN weakness; post-polio involves progressive neuronal loss.

Lambert-Eaton Myasthenic Syndrome (LEMS):

Cause: Paraneoplastic (often SCLC), antibodies against presynaptic VGCC.

Presentation: Proximal weakness (improves with activity), hyporeflexia, autonomic dysfunction (dry mouth).

Pathophysiology: Reduced acetylcholine release due to VGCC antibodies, often improves with repetitive use.

Table: Causes of Weakness by System, Onset, Differentiation, and Treatment

System	Cause	Onset	History/ Exam Findings	Diagnostic Studies	Treatment
Neurological	Stroke	Acute (hours)	Focal weakness, sensory loss, hyperreflexia, Babinski	CT/MRI brain, carotid US, EKG	tPA (ischemic, <4.5h), aspirin 325 mg PO, neuro consult
Neurological	GBS	Acute (days- weeks)	Symmetric ascending weakness, areflexia, post- infectious	CSF (high protein, normal WBC), EMG/NCS (demyelination)	IVIG 0.4 g/kg/day x 5 days, respiratory support

System	Cause	Onset	History/ Exam Findings	Diagnostic Studies	Treatment
Neurological	Myasthenia Gravis	Subacute (weeks)	Fatigable weakness, ptosis, diplopia, bulbar symptoms	Anti-AChR Abs, repetitive nerve stimulation	Pyridostigmine 60 mg PO q4h, IVIG, steroids
Neurological	Peripheral Neuropathy	Chronic (months-years)	Distal weakness, sensory loss, "stocking-glove"	B12, HbA1c, EMG/NCS	Treat cause (B12 1000 µg IM, glycemic control), gabapentin 300 mg PO TID
Neurological	ALS	Chronic (months-years)	UMN/LMN signs, fasciculations, progressive	EMG/NCS (denervation), MRI spine	Riluzole 50 mg PO BID, supportive (PT, respiratory support)
Neurological	MS	Subacute/Chronic (episodic)	Episodic weakness, sensory loss, optic neuritis	MRI brain/spine (lesions), CSF (oligoclonal bands)	Methylprednisolone 1 g IV daily x 3-5 days, natalizumab
Neurological	Spinal Cord Injury	Acute (hours)	Weakness below lesion, sensory loss, hyperreflexia	MRI spine (cord edema, compression)	Surgical decompression, steroids (controversial), rehab
Neurological	Botulism	Acute (hours-days)	Descending weakness, diplopia, dysarthria, normal sensation	EMG (decremental response), toxin testing	Antitoxin, supportive (ventilation if respiratory failure)
Neurological	LEMS	Subacute (weeks-months)	Proximal weakness (improves with use), hyporeflexia	Anti-VGCC Abs, EMG (incremental response)	3,4-DAP 10 mg PO QID, pyridostigmine, treat cancer
Endocrine	Hypothyroidism	Subacute/Chronic (months)	Fatigue, cold intolerance, proximal weakness	TSH ↑, free T4 ↓	Levothyroxine 1.6 µg/kg/day PO (IV if myxedema coma)
Endocrine	Hyperthyroidism	Subacute (weeks-months)	Tremor, weight loss, proximal weakness	TSH ↓, free T4 ↑	Methimazole 20 mg PO daily, beta-blockers (propranolol)
Endocrine	Adrenal Insufficiency	Acute/Subacute (days-weeks)	Weakness, hypotension, hyperkalemia	AM cortisol ↓, ACTH stimulation test	Hydrocortisone 100 mg IV q8h, fluids

System	Cause	Onset	History/ Exam Findings	Diagnostic Studies	Treatment
Endocrine	Hypercalcemia	Acute/ Subacute (days- weeks)	Lethargy, weakness, confusion	Calcium ↑, PTH, PTHrP	IV fluids (NS 200-300 mL/h), zoledronic acid 4 mg IV
Cardiovascular	CHF	Subacute/ Chronic (weeks- months)	Dyspnea, edema, generalized weakness	BNP ↑, ECHO (EF ↓), CXR (edema)	Furosemide 40 mg IV, lisinopril 10 mg PO daily, oxygen
Cardiovascular	Shock	Acute (hours)	Hypotension, tachycardia, weakness	Lactate ↑, ECHO, EKG	Fluids (30 mL/kg), norepinephrine 5-20 µg/min IV
Pulmonary	COPD	Chronic (years)	Dyspnea, wheezing, respiratory muscle weakness	PFTs (obstructive), ABG (hypercapnia)	Bronchodilators, BiPAP, oxygen (SpO2 88-92%)
Pulmonary	OSA	Chronic (years)	Daytime fatigue, snoring, hypoxia	Sleep study (AHI >15), ABG	CPAP, weight loss, oxygen if hypoxic
Rheumatologic	Polymyositis	Subacute (weeks- months)	Proximal weakness, myalgias	CK ↑, anti-Jo-1, muscle biopsy	Prednisone 1 mg/ kg/day PO, methotrexate 15-20 mg PO weekly
Rheumatologic	SLE	Subacute/ Chronic (months)	Fatigue, rash, myalgias, nephritis	ANA +, anti- dsDNA, low C3/ C4	Methylprednisolone 1 g IV x 3 days, hydroxychloroquine 400 mg PO daily
Infectious/ Other	Sepsis	Acute (hours- days)	Fever, hypotension, generalized weakness	Lactate ↑, blood cultures, procalcitonin	Antibiotics (piperacillin- tazobactam + vancomycin), fluids, source control
Infectious/ Other	Failure to Thrive	Chronic (months- years)	Weight loss, cachexia, weakness	Albumin ↓, malignancy workup (CT, tumor markers)	Nutritional support (TPN), treat underlying cause (e.g., cancer)
Infectious/ Other	Drug-Induced (Statins)	Subacute (weeks)	Proximal weakness, myalgias	CK ↑, statin history	Discontinue statin, supportive care, monitor CK

Hospital Management of Weakness

Initial Stabilization:

- **Airway/Breathing:** Oxygen for hypoxia (SpO₂ <90%); intubate if respiratory failure (e.g., GBS, myasthenia crisis, respiratory failure).
- **Circulation:** IV fluids (NS 30 mL/kg bolus) for hypovolemia/shock; vasopressors (e.g., norepinephrine 5-20 µg/min IV) for MAP <65 mmHg.
- **Electrolytes:** Correct hypokalemia (KCl 20-40 mEq IV), hyperkalemia (calcium gluconate 1 g IV, insulin/dextrose), hypoglycemia (D50W 50 mL IV).

Targeted Treatment:

- Neurological:
 - **Stroke:** tPA (if ischemic, <4.5h), aspirin 325 mg PO, neuro consult.
 - **GBS:** IVIG 0.4 g/kg/day IV x 5 days or plasma exchange; respiratory support (intubation if FVC <15 mL/kg).
 - **Myasthenia Crisis:** Pyridostigmine 60 mg PO q4h, IVIG/plasma exchange, steroids (prednisone 1 mg/kg/day PO).
- Endocrine:
 - **Hypothyroidism:** Levothyroxine 1.6 µg/kg/day PO (IV if myxedema coma: 200-400 µg load).
 - **Adrenal Insufficiency:** Hydrocortisone 100 mg IV q8h, fluids.
 - **Hypercalcemia:** IV fluids (NS 200-300 mL/h), zoledronic acid 4 mg IV.
- Cardiovascular:
 - **CHF:** Furosemide 40 mg IV, nitroglycerin 10-50 µg/min IV, oxygen.
 - **Shock:** Fluids, vasopressors, treat underlying cause (e.g., dobutamine for cardiogenic shock).
- Pulmonary:
 - **COPD/OSA:** Bronchodilators (albuterol), NIV (BiPAP) for hypercapnia, oxygen titrated to SpO₂ 88-92%.
 - **Respiratory Failure:** Intubation, mechanical ventilation (low tidal volumes 6 mL/kg).
- Rheumatologic:
 - **Polymyositis:** Prednisone 1 mg/kg/day PO, methotrexate 15-20 mg PO weekly.
 - **SLE:** Methylprednisolone 1 g IV daily x 3 days, hydroxychloroquine 400 mg PO daily.
- Infectious:
 - **Sepsis:** Broad-spectrum antibiotics (e.g., piperacillin-tazobactam 4.5 g IV q6h + vancomycin 15 mg/kg IV q12h), fluids, source control.

- **Meningitis:** Ceftriaxone 2 g IV q12h + vancomycin, steroids (dexamethasone 0.15 mg/kg IV q6h) for bacterial.

Supportive Care:

- **Nutrition:** TPN if prolonged NPO (e.g., GBS, failure to thrive); enteral feeding preferred.
- **Physical Therapy:** Early mobilization to prevent deconditioning (e.g., post-ICU myopathy).
- **Prophylaxis:** DVT (enoxaparin 40 mg SC daily), stress ulcer (pantoprazole 40 mg IV daily).

Key Pearls

- **Presentation:** Focal (stroke) vs. symmetric (GBS, myopathy); systemic symptoms (fever, dyspnea, rash) guide differential.
- **Stepwise Approach:** History/exam → initial labs (CBC, CMP, CK, TSH) → targeted tests (ANCA, EMG, ECHO) → advanced testing (biopsy, MRI).
- **Causes:** Neurological (stroke, GBS, MG), endocrine (hypothyroidism), cardiovascular (CHF), pulmonary (COPD, OSA), rheumatologic (polymyositis, SLE), infectious (sepsis), other (drugs, failure to thrive).
- **Hospital Management:** Stabilize (oxygen, fluids, electrolytes), treat cause (immunosuppression, antibiotics), support (nutrition, PT).
- **Prognosis:** Variable; best for reversible causes (hypothyroidism, sepsis), worse for progressive (ALS, malignancy).

References

UpToDate: "Approach to the Patient with Weakness" (2025). [UpToDate Weakness](#)

AAN: "Guidelines for the Diagnosis of Neuromuscular Disorders" (2024). [AAN Guidelines](#)

ATS: "Management of Respiratory Muscle Weakness" (2023). [ATS Guidelines](#)

NEJM: "Critical Illness Myopathy and Neuropathy" (2024). [NEJM CIM](#)

Case Scenarios

Case 1: A 60-Year-Old Male with Acute Weakness

Presentation: A 60-year-old male presents with 2 days of symmetric leg weakness after a recent diarrheal illness. Exam shows T 37°C, BP 120/80 mmHg, areflexia, 3/5 strength in legs, sensory loss.

Labs/Studies: CSF: Protein 80 mg/dL, WBC 2/μL (albuminocytologic dissociation). EMG/NCS: Demyelinating neuropathy.

Diagnosis: Guillain-Barré Syndrome (GBS) → Acute symmetric weakness, areflexia, post-infectious.

Management: Admit to ICU (respiratory monitoring). Start IVIG 0.4 g/kg/day IV x 5 days. FVC monitoring (30 mL/kg, no decline). Supportive: Enoxaparin 40 mg SC daily (DVT prophylaxis), PT. Monitor for autonomic dysfunction (e.g., arrhythmias). Strength improves to 4/5 at 1 week. Discharge with neurology follow-up.

Case 2: A 55-Year-Old Female with Fatigue and Dyspnea

Presentation: A 55-year-old female with a history of HTN presents with 3 weeks of fatigue, dyspnea, and leg swelling. Exam shows T 37°C, BP 150/90 mmHg, RR 20/min, SpO₂ 92% on room air, JVD, S₃, 2+ edema.

Labs/Studies: BNP 800 pg/mL, Cr 1.5 mg/dL, ECHO: EF 30%, chest X-ray: Pulmonary edema.

Diagnosis: Congestive Heart Failure (CHF) → Subacute weakness, dyspnea, edema, reduced EF.

Management: Admit for CHF exacerbation. Start furosemide 40 mg IV BID, lisinopril 10 mg PO daily, metoprolol succinate 25 mg PO daily. Oxygen to SpO₂ >92%. Monitor daily weights, Cr (improves to 1.2 mg/dL). Weakness improves with diuresis. Discharge with cardiology follow-up.

Case 3: A 40-Year-Old Female with Proximal Weakness

Presentation: A 40-year-old female presents with 1 month of difficulty climbing stairs and rash on her hands. Exam shows T 37.5°C, BP 130/85 mmHg, heliotrope rash, Gottron's papules, 4/5 proximal strength.

Labs/Studies: CK 2000 U/L, anti-Jo-1 positive, muscle biopsy: Inflammatory myopathy.

Diagnosis: Dermatomyositis → Subacute proximal weakness, rash, elevated CK.

Management: Admit for treatment. Start prednisone 1 mg/kg/day PO (60 mg daily). Methotrexate 15 mg PO weekly initiated. Monitor CK (decreases to 500 U/L), strength (improves to 5/5). TMP-SMX 1 DS tab PO daily (PCP prophylaxis). Discharge with rheumatology follow-up.

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