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THE WEAK CAT

Practical approach and common neurological differentials

Weakness – is it neurological or non-neurological in origin?

Weakness, or paresis, is defined as a deficiency in a patient's ability to support weight or generate a normal gait. In the weak cat, it is critical first to determine whether the weakness is due to a systemic illness, cardiovascular disease, orthopedic disease or neurological disease (Table 1). Weak cats often are reluctant to move and it may be challenging to differentiate among these four possibilities. As such, all cats presented for weakness should undergo a thorough general physical

examination with a careful cardiopulmonary and orthopedic evaluation, a complete blood count, biochemistry profile and urinalysis.

TABLE 1 Common causes of feline weakness that may be confused with neurological disease

Orthopedic	Cardiovascular	Systemic
Polyarthritis	Arrhythmia	Hypoglycemia
Appendicular fracture(s)	Reduced cardiac output	Diabetic ketoacidosis
Degenerative joint disease	Hypotension	Anemia

Neurological examination of the weak cat

The purpose of the neurological examination is to determine if neurological deficits are present and, based upon detectable abnormalities, to localize the lesion(s) in the central (CNS) or peripheral nervous systems. The integration of a systematic neurological examination into the routine physical examination of weak cats will help the clinician to determine whether or not the weakness is neurological in origin and to regularly make accurate neuroanatomic diagnoses.

The specifics of the neurological examination in cats are presented in a separate article in this special issue,¹ and are also the subject of an authoritative text.² In this review, the discussion focuses on key components of the neurological examination that may be particularly helpful in localizing neurological weakness in the cat.



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Practical relevance Weakness is recognized somewhat infrequently in cats, but is an important manifestation of neurological disease. The clinician must perform a complete neurological examination to determine the neuroanatomic basis for the weakness. As for all species, the neuroanatomic diagnosis allows the clinician to generate an appropriate differential diagnosis, to design a diagnostic plan, to prognosticate, and ultimately to develop a treatment plan.

Clinical challenges The cause(s) of neurological weakness in the cat may be difficult to determine without access to advanced imaging modalities, cerebrospinal fluid analysis or electrodiagnostics. However, an accurate neuroanatomic diagnosis allows the clinician to pursue preliminary anomalous (vertebral anomalies), metabolic (eg, diabetes mellitus, electrolyte abnormalities) and neoplastic differentials via blood work, vertebral column and thoracic radiography, and abdominal ultrasound. Subsequently, referral to a specialty veterinary hospital may be warranted to pursue advanced neurodiagnostics.

Audience This review provides a framework for generating a neuroanatomic and differential diagnosis in the weak cat. It also discusses the pathogenesis and clinical signs associated with the most common neurological differentials for feline paresis. As such, it is aimed at both primary health care and specialty veterinarians.

Patient group The neurological conditions discussed in this review cause weakness in cats of all age groups.



MULTIMEDIA

Nine video recordings showing cats with various manifestations of weakness are included in the online version of this article
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TABLE 2 Neurological examination findings that distinguish between LMN and UMN paresis		
	LMN paresis	UMN paresis
Mentation	Unaffected	Unaffected
Gait and posture	Short and choppy gait, crouched posture	Long-strided, spastic gait accompanied by general proprioceptive ataxia
Spinal nerve reflexes	Decreased	Normal to exaggerated
Muscle tone	Decreased	Increased
Postural reactions	Normal to delayed	Delayed
LMN = lower motor neuron, UMN = upper motor neuron		


As part of the routine neurological examination, the clinician should evaluate mentation (or ‘sensorium’; ie, state of consciousness and awareness), gait and posture, postural reactions, spinal nerve reflexes and muscle tone, and the cranial nerves (Table 2). In cats, the order in which these components of the neurological examination are performed is determined by the degree of patient cooperation. If the cat is resting quietly in its cage, it may be preferable to perform the cranial nerve examination first. If the cat is excited or apprehensive, it may be more practical to evaluate gait and postural reactions before performing the cranial nerve evaluation.

❖ **Mentation** The owner is the best judge of their cat’s mentation and behavior. Change in mentation typically is due to brainstem or cerebral lesions in the ascending reticular activating system and/or limbic system. Unless peracute (eg, feline ischemic encephalopathy/CNS cuterebriasis), prosencephalic (cerebrothalamic) disturbances do not cause weakness. Therefore, a tetraparetic cat that is dull, stuporose or comatose is more likely to have a mid- to caudal brainstem lesion than a cerebrothalamic lesion.

❖ **Gait and posture** The cat’s gait should be evaluated on a non-slippery surface, assess-

Key differences between LMN and UMN paresis

- ❖ A short and choppy gait is seen with LMN paresis, versus a long-strided, spastic gait and general proprioceptive ataxia with UMN paresis
- ❖ Spinal nerve reflexes and muscle tone typically are decreased with LMN paresis, and normal to exaggerated with UMN paresis
- ❖ Postural reactions typically are delayed with UMN paresis and may be normal to delayed with LMN paresis



ing carefully for strength and coordination. The cat’s posture should be assessed while both standing and walking (Fig 1). Key postural changes that may be present in the weak cat involve the position of the head and neck, angle of the hock, and tail position; trembling may also be present.

❖ **Spinal nerve reflexes and muscle tone** The most reliable spinal nerve reflexes are the withdrawal flexor reflexes of the thoracic and pelvic limbs, and the patellar reflex of the pelvic limbs. As described elsewhere in this special issue, reflexes require functional peripheral nerve(s) innervating a specific muscle group (eg, femoral nerve for patellar reflex of the quadriceps muscle) and the spinal cord segments (eg, L4–L6 for femoral nerve) with which the peripheral nerve(s) connect.¹ In cats with neuromuscular paresis caused by lesions of the LMN system, spinal nerve reflexes and muscle tone typically are reduced to absent. With UMN paresis caused by lesions cranial to the intumescences, the spinal nerve reflexes and muscle tone typically are normal to exaggerated.

❖ **Postural reactions** In addition to requiring normal peripheral nerve(s) (sensory and LMN), postural reactions depend on ascending pathways in the spinal cord that deliver sensory information to the brainstem, cerebellum and cerebrum, and descending UMN pathways that terminate on the spinal cord intumescences (ie, spinal cord segments C6–T2 and L4–S3). Therefore, postural reactions test the integrity of almost the

entire peripheral nervous system and CNS. In the authors’ experience, hopping and placing responses are the most useful postural reactions in cats to reveal subtle abnormalities in strength and proprioception. When interpreted outside the context of the neurological examination as a whole, postural reactions are of limited value for lesion localization. However, they may provide key localizing

information when considered in the light of the entire examination.



FIG 1 Pelvic limb UMN paresis. Note the increased muscle tone, knuckling and crossing over of the pelvic limbs

Although neurological paresis is recognized somewhat infrequently in cats, it is important for the practitioner to become proficient at localizing neurological lesions to the central and/or peripheral nervous systems.



Neurological weakness: LMN paresis versus UMN paresis

In neurological patients, paresis may result from a lesion in the lower motor neuron (LMN)/neuromuscular system and/or upper motor neuron (UMN) system (see box, right).

LMN paresis

The LMN/neuromuscular unit is comprised of the neuronal cell body in the ventral gray column of the spinal cord, the peripheral nerve, the neuromuscular junction, and the muscle. Lesions anywhere along this pathway may produce clinical signs indistinguishable from one another (Fig 2).

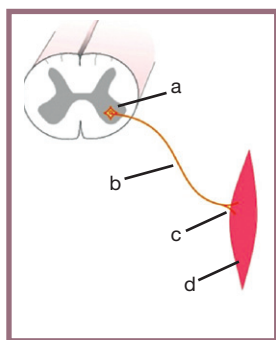


FIG 2 The LMN/neuromuscular unit is comprised of the neuronal cell body (a), peripheral nerve (b), neuromuscular junction (c) and muscle (d). Lesions anywhere along this pathway may lead to LMN paresis

The LMN/neuromuscular unit may be affected focally (eg, a spinal cord lesion affecting LMN cell bodies) or diffusely (eg, a polyneuropathy affecting multiple peripheral nerves). Ambulatory cats with LMN weakness may differ widely in terms of their ability to support weight. Thoracic or pelvic limbs (or both thoracic and pelvic limbs in cats with diffuse neuromuscular disease) may be affected. A cat with a mild to moderate, diffuse neuromuscular disease may be ambulatory with a 'short and choppy', stilted gait (see video 1, doi:10.1016/j.jfms.2009.03.005).

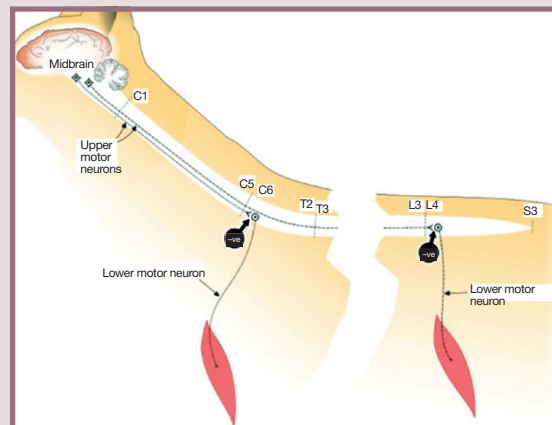
With sciatic nerve (tibial branch) deficits, cats typically walk with a plantigrade posture in the pelvic limbs (see video 2, doi:10.1016/j.jfms.2009.03.005). Cats with neuromuscular disease also may advance both pelvic limbs simultaneously in a 'bunny-hopping' fashion (this also may occur with orthopedic and spinal cord disorders). Spinal reflexes and muscle tone typically are reduced with lesions of the LMN/neuromuscular unit. A cat with a severe neuromuscular disease may be tetraplegic with reduced to absent muscle tone and spinal nerve reflexes. Neuromuscular tetraparesis must be differentiated from UMN tetraparesis occurring secondarily to brainstem or spinal cord disease (see box on page 376).

UMN paresis

The key components of the UMN system for gait generation in cats include neuronal cell bodies located in the mid- to caudal brainstem

Relationship between UMN and LMNs

The cell bodies of the key UMN responsible for gait generation in the cat are located in the mid- to caudal brainstem. The axons from these UMN descend the spinal cord to facilitate the LMNs responsible for the voluntary and reflexive



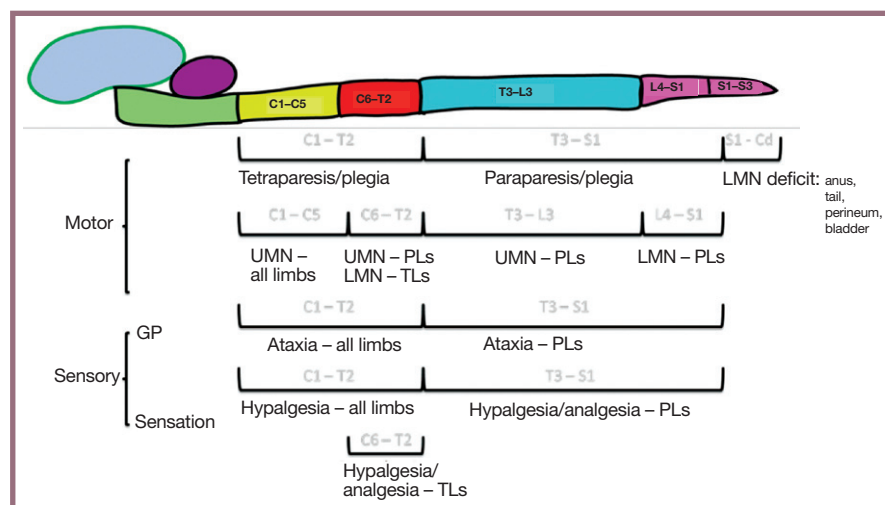
movements of the limbs. Loss of this facilitation leads to UMN paresis.

Typically, a state of 'disinhibition' predominates with lesions that interrupt the descending UMN. Clinically, this is evident as exaggerated muscle tone and spinal reflexes, and a spastic gait in the ambulatory patient. Lesions in the LMN/neuromuscular unit (cell body, peripheral nerve, neuromuscular junction or muscle) lead to reduced muscle tone and spinal reflexes, and a short-strided gait in the ambulatory patient.

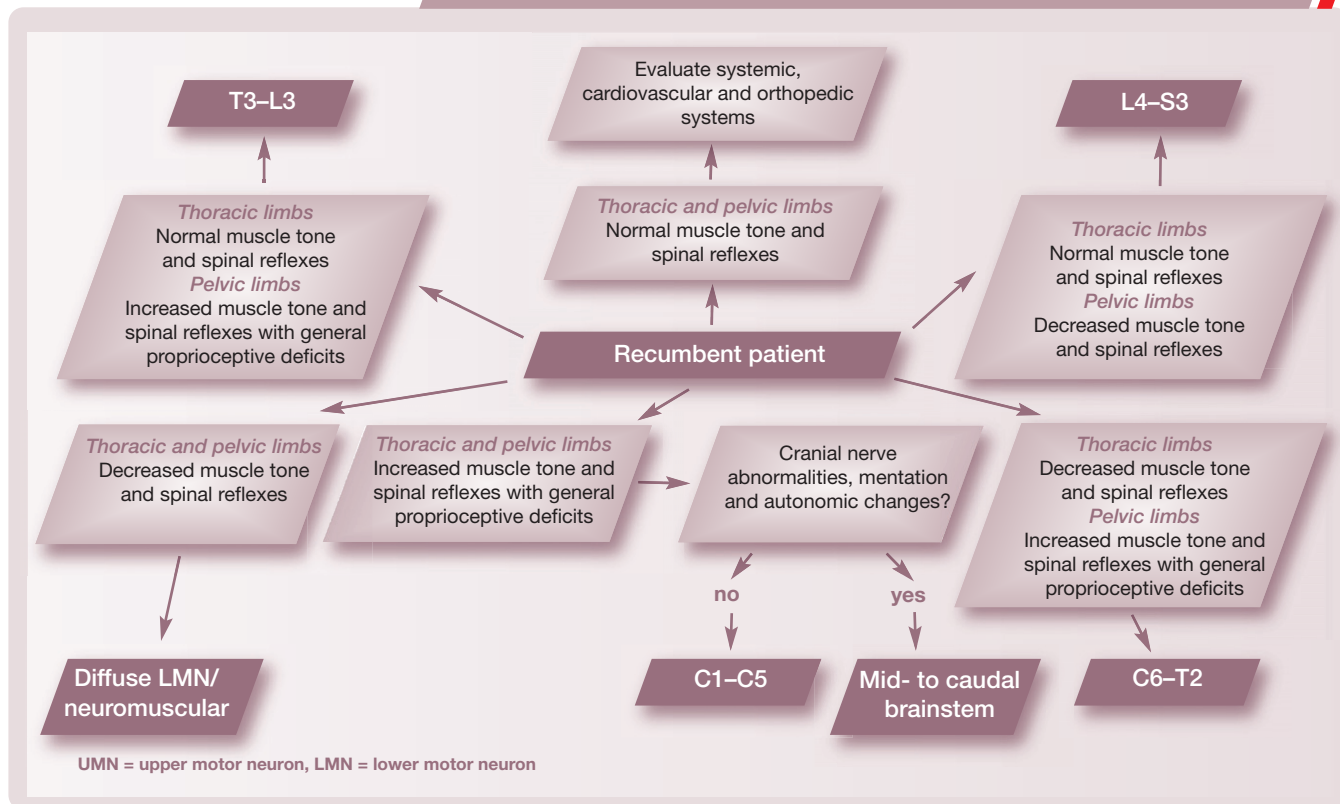
that descend the spinal cord (rubrospinal, reticulospinal and vestibulospinal tracts) and synapse on the LMN cell bodies described above. The descending UMN axons act both to facilitate and inhibit the LMN cell bodies upon which they synapse. Mid- to caudal brainstem or spinal cord lesions interrupting the descending UMN axons result in a lack of facilitation and disinhibition of LMN activity, evidenced as paresis, and increased muscle tone and spinal reflexes, respectively.

Mid- to caudal brainstem and spinal cord lesions disrupting the UMN pathways may result in considerable variability in a cat's ability to generate a gait. Depending on the location of the lesion, thoracic and/or pelvic limbs may be affected with UMN or LMN signs (Fig 3).

FIG 3 Neuroanatomic localization for spinal cord lesions. GP = general proprioception, TLs = thoracic limbs, PLs = pelvic limbs. Adapted from de Lahunta and Glass (2009)²



Neuroanatomic localization for the recumbent cat



Ambulatory patients with UMN paresis typically walk with a long-strided, spastic gait that is accompanied by general proprioceptive ataxia (see video 3, [doi:10.1016/j.jfms.2009.03.005](https://doi.org/10.1016/j.jfms.2009.03.005)). The simultaneous ataxia occurs because the majority of the key UMN pathways (eg, rubrospinal, reticulospinal tracts) that function in gait generation are adjacent anatomically to the general proprioceptive pathways (spinocerebellar tracts, fasciculus gracilis and cuneatus) (Fig 4).

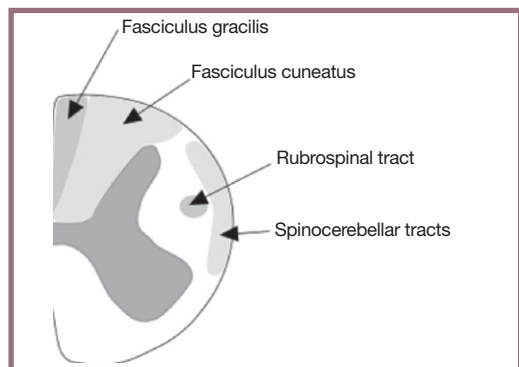


FIG 4 Key descending UMN (rubrospinal tract) and ascending general proprioceptive (spinocerebellar, fasciculus cuneatus and gracilis) pathways. The UMN/general proprioceptive pathways are anatomically adjacent to one another; therefore, with mid- to caudal brainstem and spinal cord lesions, variable degrees of UMN weakness and general proprioceptive ataxia are present simultaneously

Urinary and fecal incontinence

Cats with lesions in the sacral spinal cord segments may show a 'LMN bladder' with urinary incontinence. A LMN bladder is characteristically flaccid and easily expressed. Urine dribbling typically is present and this is due to urethral sphincter incontinence secondary to pudendal nerve dysfunction. Lesions from the caudal brainstem through to spinal cord segment L7 may produce UMN incontinence, characterized by a hypertonic bladder that is difficult to express. Patients often dribble urine, particularly when pressure is applied to the abdomen, because of urinary overflow. Reflex urination typically develops over days to weeks. An UMN bladder often occurs concurrently with severe paraparesis or complete paralysis of the pelvic limbs.

Disorders associated with neuromuscular (LMN) weakness

Neuromuscular disorders are relatively uncommon in cats compared with other neurological diseases (Tables 3 to 5). Neuromuscular signs develop secondarily to lesion(s) anywhere along the LMN/neuromuscular unit (Fig 2); the lesion(s) may be focal or diffuse depending on the nature of the condition.

The various neuromuscular diseases may manifest virtually identically to one another, with signs generally including a short-strided gait (in the ambulatory patient), plantigrade posture in patients with sciatic (tibial branch)

TABLE 3 Feline polyneuropathies

Types	Examples
Inflammatory/infectious	Acute idiopathic polyneuropathies (polyneuritis) Chronic inflammatory demyelinating polyneuropathy Chronic relapsing polyneuropathy Hypertrophic polyneuropathy FeLV or FIV polyneuropathy (rare)
Toxic	Organophosphates (chronic exposure) Heavy metals Vincristine Pyrethrins/pyrethroids
Anomalous	Distal axonopathy of Birman cats Hyperoxaluric neuropathy Neuropathy associated with hyperchylomicronemia Neuropathy associated with sphingomyelinase deficiency
Metabolic	Diabetes mellitus polyneuropathy Hyperthyroid polyneuropathy
Neoplastic	Paraneoplastic polyneuropathy
Nutritional	Tyrosine/phenylalanine deficiency
Common neuropathy is shown in bold FeLV = feline leukemia virus, FIV = feline immunodeficiency virus	

nerve deficits, reduced to absent muscle tone and segmental spinal reflexes, and occasionally cranial nerve deficits and/or megaesophagus.

The work-up for diffuse neuromuscular disease in cats typically includes:

- ❖ A detailed history (exposure to wildlife, parasite control, toxicities, exposure to carrion);
- ❖ Careful physical examination (cardiac and lung auscultation, mucous membrane and pulse evaluation);
- ❖ Complete biochemistry profile (electrolytes, creatine kinase [CK], aspartate

TABLE 4 Feline mononeuropathies

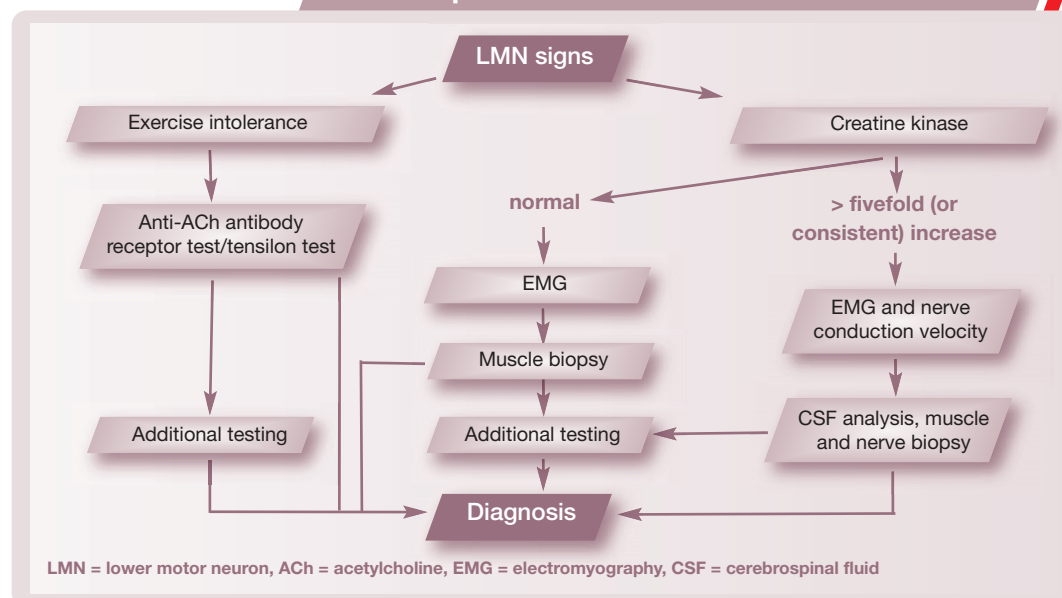
Types	Examples
Vascular	Ischemic neuromyopathy
Inflammatory/infectious	Hypertrophic neuritis Mycobacterial neuritis Idiopathic brachial plexus neuritis
Traumatic	Brachial plexus injury Pelvic fracture Sacrocaudal fracture/luxation Intramuscular injection Bites or blunt trauma
Neoplastic	Lymphosarcoma Peripheral nerve sheath tumor Sarcoma Carcinoma Local extension of soft tissue tumor
Common neuropathies are shown in bold	

aminotransferase [AST]);

- ❖ Thoracic radiography ± abdominal ultrasonography;
- ❖ Tensilon testing (edrophonium chloride challenge test) and anti-acetylcholine receptor antibody testing for acquired myasthenia gravis;
- ❖ Often referral for electrodiagnostics, cerebrospinal fluid analysis, and muscle and nerve biopsies.

In the following discussion, the differentials for focal and diffuse neuromuscular disorders are considered from proximal (disorders affecting the neuronal cell body in the gray matter of the spinal cord) through distal (disorders of the muscle).

Work-up for LMN/neuromuscular disease



The UMN/general proprioceptive pathways are anatomically adjacent to one another. Therefore, with mid- to caudal brainstem and spinal cord lesions, variable degrees of UMN weakness and general proprioceptive ataxia are present simultaneously.



Disorders affecting the LMN cell body

Lower motor neuron paresis occurs when neuronal cell bodies of the cervicothoracic (C6–T2) and/or lumbosacral (L4–S3) intumescence(s) are affected by a lesion (Fig 3). A focal lesion in the cervicothoracic (C6–T2) intumescence will produce LMN signs in the thoracic limbs but UMN signs in the pelvic limbs (Fig 3). Thoracic limb(s) spinal reflexes and muscle tone will be depressed whereas reflexes and tone will be normal to exaggerated in the pelvic limbs. The withdrawal flexor reflex should be interpreted cautiously in the thoracic limbs, as patients with C1–C5 lesions occasionally have reduced thoracic limb reflexes.³ In ambulatory patients with lesions of the cervicothoracic intumescence, the gait will be short and choppy in the thoracic limbs with an accompanying proprioceptive ataxia in the pelvic limbs (see video 4, [doi:10.1016/j.jfms.2009.03.005](https://doi.org/10.1016/j.jfms.2009.03.005)).

Patients with a lesion in the lumbosacral (L4–S3) intumescence will manifest variable LMN signs in the pelvic limbs depending on the location of the lesion. With a lesion of the L4–L6 spinal cord segments, the patellar reflex will be depressed due to a femoral nerve (L4–L6) deficit. The ambulatory patient may be sunken at the stifle, as the quadriceps muscles lack the necessary tone to extend the stifle and allow the patient to bear weight. Cats with L6–S3 lesions typically have reduced withdrawal flexor reflexes in the pelvic limbs due to a sciatic (L6–S1) deficit, reduced tone and atrophy of the caudal thigh muscles, and may have a flaccid LMN bladder and/or anus if the lesion is in the caudal aspect of the lumbar intumescence. Ambulatory patients with L6–S1 lesions may adopt a plantigrade posture.

Motor neuron disease

Inherited motor neuron diseases (also known as spinal muscular atrophy) have been reported sporadically in cats. These disorders result from degeneration of neuronal cell bodies in the spinal cord and brainstem.⁴ Lower motor neuron signs predominate and include progressive tetraparesis through tetraplegia, generalized appendicular muscle atrophy and absent spinal reflexes. Aside from genetic testing of Maine Coon cats, no other ante mortem tests are available to diagnose motor neuron disease.

Sacrocaudal dysgenesis

Sacrocaudal dysgenesis is a congenital condition involving a combination of dysgenesis (or agenesis) of the sacrocaudal vertebrae and spina bifida. In the case of Manx cats, spina bifida occurs in the sacrocaudal vertebrae. Clinical signs typically manifest shortly after birth and are non-progressive in nature. However, cats occasionally show progressive neurological signs due to an accompanying myelodysplasia.⁵ Neurological signs include LMN paresis through flaccid paralysis of the pelvic limbs. Ambulatory cats typically have a plantigrade posture that is accompanied by a bunny-hopping gait. Other signs include LMN urinary and fecal incontinence, and reduced to absent perianal sensation.

Sphingomyelinosis

Sphingomyelinosis (Neimann-Pick disease) comprises a group of storage disorders typified by abnormal accumulation of sphingomyelin in neurons and other cells. Types A, A-variant and C have been reported in cats. Cats with types A and C sphingomyelinosis have neurological deficits that localize predominantly to the cerebellum; however, neurons in the dorsal nerve roots, peripheral ganglia and ventral gray horn of the spinal cord also may be affected.⁴ Therefore, LMN paresis may be present, accompanied by general proprioceptive ataxia because of the spinal cord pathology. The combination of LMN paresis and ataxia is unusual because animals with pure LMN disease typically have normal coordination. The LMN paresis may progress to complete paralysis of the limbs. Spinal nerve reflexes typically are depressed to absent and cats may walk with a plantigrade posture in the pelvic limbs. Additional signs include hepatosplenomegaly, cerebrothalamic signs and vestibular deficits.

Traumatic feline ischemic myelopathy

Traumatic feline ischemic myelopathy is a condition affecting the L2 to caudal spinal cord segments. This problem has been reported in cats with evidence of abdominal trauma (retroperitoneal bleeding, kidney avulsion, peritoneal hemorrhage). Neurological deficits include LMN paralysis of the pelvic limbs and loss of sensation to the pelvic limbs, tail, anus, perineum, and caudal portion of the abdomi-

TABLE 5 Feline myopathies and neuromuscular junctionopathies

Types	Examples
Vascular	Ischemic neuromyopathy
Inflammatory/infectious	Myasthenia gravis (NMJ) Idiopathic polymyositis <i>Toxoplasma</i> polymyositis FIV-associated polymyositis (experimental so far) Autoimmune paraneoplastic polymyositis (associated with malignant tumor)
Toxin	Botulism (NMJ) Tick paralysis (NMJ)
Anomalous	Feline X-linked muscular dystrophy Feline muscular dystrophy due to laminin $\alpha 2$ deficiency Nemaline myopathy Hereditary myopathy of Devon Rex cats Myositis ossificans Glycogen storage diseases Myotonia congenita
Metabolic	Hypokalemic myopathy Hyperthyroid myopathy Hypoadrenocorticism-associated myopathy Glucocorticoid myopathy Hypernatremic polymyopathy
Nutritional	Vitamin E/selenium-responsive myopathy
Common myopathies and junctionopathies are shown in bold NMJ = neuromuscular junctionopathy, FIV = feline immunodeficiency virus	

nal wall. The disorder is thought to result from vehicular trauma that causes spasm of the lumbar and ventral spinal arteries and subsequent ischemia of L2 to caudal spinal cord segments.⁴

Peripheral neuropathies (including mononeuropathies and polyneuropathies)

Peripheral neuropathies occur secondarily to lesion(s) of the nerve root, peripheral nerve (axon) and/or myelin sheath (Tables 3 and 4). Peripheral nerve dysfunction may be associated with a diffuse neuromuscular disorder (ie, polyneuropathy) or may be a focal disorder secondary to trauma or neoplasia (ie, mononeuropathy). The clinical hallmarks of neuropathies are reduced to absent spinal nerve reflexes and muscle tone, LMN paresis to paralysis of limb and/or head muscles, plantigrade posture, and a rapid onset (within 1–2 weeks) of neurogenic muscle atrophy. Chronic neurogenic atrophy may result in severe fibrosis and limited joint movement secondary to contractures. Variable sensory deficits may be present simultaneously because most nerves contain motor and sensory components. Tremors and muscle fasciculations are present occasionally. Although most neuropathies involve spinal nerves, cranial nerve dysfunction may accompany neuropathic disease.

Brachial plexus injury

A focal lesion such as a brachial plexus injury typically results from trauma. Brachial plexus injuries are associated with LMN paresis through complete paralysis of the affected limb due to focal demyelination, axonopathy, or complete avulsion or tearing of the nerves. If the radial nerve is involved with the brachial plexus injury, the cat will have a dropped elbow due to lack of tone in the triceps muscles and an inability to extend the elbow (see video 5, [doi:10.1016/j.jfms.2009.03.005](https://doi.org/10.1016/j.jfms.2009.03.005)).

Autonomous sensory zones should be evaluated to help localize the extent of the avulsion; typically there are mild to severe sensory deficits accompanying the LMN dysfunction in the affected limb.² A guarded to fair prognosis is given to cats that have mild sensory deficits. Cats that lack sensation to the affected limb have a poor prognosis.

Diabetes mellitus

A peripheral neuropathy may accompany uncontrolled diabetes mellitus in the cat. Patients typically have a plantigrade posture in the tarsi due to a tibial neuropathy (see video 2, [doi:10.1016/j.jfms.2009.03.005](https://doi.org/10.1016/j.jfms.2009.03.005)). Pelvic limb withdrawal flexor reflexes typically are reduced. Thoracic limb paresis is present less commonly. Diabetic ketoacidosis, a complicated form of diabetes mellitus, may be associated with moderate to severe weakness in cats due to a peripheral neuropathy.

Neuromuscular junctionopathies

Disorders of the neuromuscular junction are typically due to ineffective release of acetylcholine (ACh) into the neuromuscular junction or ineffective binding of ACh to the post-synaptic ACh receptor (Table 5). Some neuromuscular junctionopathies present very similarly to myopathies, whereas others mimic polyneuropathies.

Botulism

Botulism is associated with ineffective release of ACh from the pre-synaptic membrane. The paresis is caused by the *Clostridium botulinum* toxin (type C toxin most commonly in small animals) which binds to SNARE proteins (synaptobrevin, syntaxin and SNAP-25) in the pre-synaptic membrane, preventing normal transport of ACh vesicles to the surface of the pre-synaptic membrane. *Clostridium botulinum* and its toxins may be present in carrion or occasionally may be introduced through a puncture wound. Cats may manifest diffuse neuromuscular signs as soon as a few hours after ingestion. Unlike patients with tick paralysis (see later), cranial nerve deficits (facial nerve paresis, dysphagia) are common in cats with botulism.

Myasthenia gravis

Myasthenia gravis may be a congenital disorder but more commonly is an acquired, immune-mediated disease that is associated with autoantibodies directed against the patient's ACh receptors on the post-synaptic membrane. The autoantibodies block binding of ACh to its receptor, which results in neuromuscular paresis. A presumptive diagnosis may be made with a positive response to acetylcholinesterase inhibitors (edrophonium chloride, neostigmine). The demonstration of anti-ACh antibodies in the serum provides a definitive diagnosis; however, cases occasionally are seronegative. Abyssinians and Somali cats are overrepresented for this condition.

There are three clinical syndromes associated with myasthenia gravis – namely, focal, generalized and fulminating forms. In the focal form, cats may present with esophageal weakness, dysphagia, fatigable palpebral reflexes, and voice changes. The generalized form is associated with diffuse neuromuscular paresis, often typified by exercise intolerance. Postural abnormalities may be seen, including low head and neck carriage, and trembling while standing. In the fulminating form (see video 6, [doi:10.1016/j.jfms.2009.03.005](https://doi.org/10.1016/j.jfms.2009.03.005)), which carries an extremely guarded prognosis, cats typically are recumbent and may need respiratory support via oxygen supplementation or mechanical ventilation. However, even with severe disease, clinical signs may resolve with pyridostigmine bromide (Mestinon) therapy and occasionally immunosuppression (see video 7, [doi:10.1016/j.jfms.2009.03.005](https://doi.org/10.1016/j.jfms.2009.03.005)). Myasthenia gravis may be associated with polymyositis, polyneuritis or thymic neoplasia.

Tick paralysis

A flaccid, ascending neuromuscular disorder may be caused by a neurotoxin that is introduced into the bloodstream by certain species of ticks. Ticks must be attached for 24–48 h for a sufficient amount of neurotoxin to enter the bloodstream. The tick neurotoxin prevents pre-synaptic release of ACh into the neuromuscular junction, resulting in diffuse neuromuscular paresis. Compared with dogs, cats appear to be relatively resistant to tick paralysis. In North America, the wood ticks *Dermacentor variabilis* and *Dermacentor andersoni* are incriminated most commonly. When sufficient toxin is introduced, cats manifest neuromuscular paresis within 3–7 days of tick attachment. Once the tick is removed, neuromuscular weakness begins to resolve within 1–3 days.

Myopathies

Myopathies are disorders of the muscle that may be degenerative, metabolic, inflammatory, idiopathic or vascular in origin (Table 5).

Many inherited myopathies are breed-specific, and some have a predilection for males, such as the X-linked dystrophin deficiency. Myopathies tend to have a bilaterally symmetrical distribution with preservation of reflexes and pain perception. Affected cats may manifest generalized weakness and sometimes develop a palmigrade and/or plantigrade stance, exercise intolerance, fatigue, a stiff, stilted gait, and, often, ventroflexion of the head and neck.

Ischemic thromboembolic neuromyopathy

Aortic thromboembolism leads to an acute 'neuromyopathy' due to ischemia of muscles and peripheral nerves originating from the L4–S3 spinal cord segments. The most common cause of aortic thromboembolism in the cat is hypertrophic cardiomyopathy. Turbulent blood flow in the left atrium produces a thrombus, which is ejected through the aorta and ultimately lodges in a distal artery, most commonly the aortic trifurcation (obstructing the internal and external iliac arteries and the median sacral artery).

The clinical syndrome typically manifests within 24 h and is marked by LMN paresis or flaccid paralysis of the pelvic limbs. Absent femoral pulses, firm, painful muscles and cold extremities often are present. Although LMNs are affected, patellar reflexes may be spared.⁶ Pain sensation in the distal pelvic limbs often is diminished to absent. Less commonly, subclavian or brachial artery thromboembolism occurs, resulting in paresis or paralysis of a thoracic limb (see video 8, [doi:10.1016/j.jfms.2009.03.005](https://doi.org/10.1016/j.jfms.2009.03.005)).⁷

A cat with arterial thromboembolism typically has a poor to grave prognosis. Even if a recovery occurs, the underlying cardiac condition must be addressed or this neuromyopathy is likely to recur.

Hyperthyroidism

Hyperthyroidism is a common feline endocrine disorder that may be associated with generalized neuromuscular weakness. Systemic signs may include hyperactivity, tachycardia, polyuria, polydipsia, polyphagia in the face of weight loss, aggression and a palpable thyroid nodule. Neurological signs include tetraparesis, cervical ventroflexion, inability to jump, and collapse due to neuromuscular weakness.⁸ Occasionally, treatment with methimazole leads to LMN signs associated with acquired myasthenia gravis.⁸

Hypokalemic myopathy

Hypokalemia in cats most commonly results from inadequate dietary formulations or chronic renal disease.⁹ Hypokalemic cats typically manifest a stiff, stilted gait,

In neurological patients, paresis may result from a lesion in the LMN/neuromuscular system, the UMN system, or both.



exercise intolerance, and ventroflexion of the neck (see video 9, doi:10.1016/j.jfms.2009.03.005). Neuromuscular weakness may be episodic and results from strenuous activity.

An autosomal recessive hypokalemic myopathy has been described in 2–6 month old Burmese kittens.¹⁰ Carpal knuckling can be a distinctive clinical feature in Burmese kittens with hypokalemic myopathy and some cats are sunken in the tarsi.¹¹ The condition may resolve spontaneously in affected kittens.

Careful supplementation should correct the myopathy associated with potassium deficiency; however, the primary disorder must be addressed in cats with renal disease.

Metabolic myopathies

Other metabolic disorders that may be associated with generalized weakness in the cat include hypocalcemia, hyponatremia, hypophosphatemia, hypercalcemia and uremic encephalopathy.

Hypocalcemia may lead to a neuromuscular syndrome in cats. The most common causes of hypocalcemia are ethylene glycol toxicity and renal disease. Other causes include primary and secondary hypoparathyroidism, phosphate-containing enemas and post-parturient eclampsia. Clinical signs of hypocalcemia include restlessness, nervousness, muscle spasms, a stiff, stilted gait, tonic-clonic spasms, tetraparesis and seizures.¹¹

Muscular dystrophies

Muscular dystrophy in cats occurs as an inherited disorder secondary to deficiencies in dystrophin (X-linked) or merosin, which are glycoproteins essential for normal muscle development and function. Clinical signs typically become evident in the first few months of life and include diffuse hypertrophy of skeletal muscles, exercise intolerance, a stiff, stilted gait, cervical rigidity, difficulty jumping, protrusion of the tongue, and vomiting and regurgitation.¹² Serum CK and AST are elevated markedly and definitive diagnosis is achieved via muscle biopsy, histopathology and immunohistochemistry. Potential complications of feline muscular dystrophy are insufficient water intake, dehydration, hyperosmolar syndrome, acute renal failure and rhabdomyolysis.¹¹

Disorders associated with UMN and/or LMN weakness

A lesion in the UMN system typically results in increased muscle tone, muscle spasticity, paresis and general proprioceptive ataxia. A lesion in the mid- to caudal brainstem or C1–C5 spinal cord segments creates UMN paresis in the thoracic limbs and pelvic limbs (Fig 3). Occasionally, C1–C5 lesions are associated with reduced withdrawal flexor reflexes in the thoracic limbs.³ As mentioned earlier, in the discussion on LMN weakness, lesions of the cervicothoracic intumescence produce LMN paresis in the thoracic limbs and UMN paresis in the pelvic limbs. Lesions of spinal cord segments T3–L3 spare the thoracic limbs and produce UMN signs exclusively in the pelvic limbs (Fig 3).

Focal disorders affecting the UMN and/or LMN

Focal disorders of the UMN and/or LMN system will produce neurological signs that relate to the location of the lesion in the CNS (Fig 3).

Discospondylitis

Discospondylitis develops occasionally in cats secondarily to bacterial or fungal infection of the vertebral end plates and intervertebral discs.¹³ Neurological signs are caused by spinal cord and/or nerve root compression, abscesses, inflammatory tissue, pathologic fractures and vertebral instability. Discospondylitis may cause UMN or LMN paresis depending on the location of the vertebral lesion.

Hypervitaminosis A (deforming cervical spondylosis)

Adult cats fed whole liver diets or cats oversupplemented with vitamin A may develop hypervitaminosis A.¹⁴ This degenerative disorder is associated with excessive bone formation along the vertebral column and long bones; most commonly, the cervical vertebral column is affected. The patient may develop scoliosis or cervical ventroflexion, and occasionally fusion of the atlantoaxial joint occurs. Palpation of the neck may cause discomfort due to bony compression of the nerve roots. Neurogenic cervical neck muscle atrophy may be evident as well. Cats may show lameness and postural abnormalities due to joint fusion and exostosis in one or multiple limbs, and a 'kangaroo-like' sitting posture has been described. Other signs include an unkempt hair coat (because bony abnormalities preclude normal grooming), depression and emaciation.

Intervertebral disc disease

Intervertebral disc disease is an uncommon cause of paresis in cats.¹⁵ It may lead to variable

degrees of LMN paresis or UMN paresis and general proprioceptive ataxia depending on the location of the disc herniation (Fig 3). Typically, intervertebral disc disease is subclinical in cats, but there is an increased prevalence of clinical disease in older and overweight animals. Lumbar discs are affected most commonly and signs range from pain, paresis and ataxia through paralysis and sensory deficits. The authors have diagnosed several cats with lumbosacral intervertebral disc herniations that had a plantigrade posture in the pelvic limbs mimicking a tibial neuropathy.

Lymphosarcoma

Lymphosarcoma is a common neoplastic condition that may occur in cats of any age. Several forms have been reported including mediastinal, multicentric, visceral, gastrointestinal and CNS lymphosarcoma. With the last, a slowly progressive or acute onset of UMN or LMN paresis may be seen, depending on the location of the lesion(s). Lymphosarcoma most commonly affects the spinal segments T3–S2;¹⁶ however, lesions may occur anywhere along the neuraxis. Occasionally, lymphosarcoma will infiltrate peripheral nerves resulting in LMN signs in the affected limbs.

Mucopolysaccharidosis

Mucopolysaccharidosis type 1 (MPS 1) is a lysosomal storage disease of kittens that may cause mild UMN paresis and general proprioceptive deficits.¹⁷ The neurologic deficits localize to the cervical spinal cord due to accumulation of mucopolysaccharides in the neuronal cell bodies of cervical spinal segments and/or fusion of cervicothoracic vertebral bodies. Exaggerated spinal reflexes, general proprioceptive ataxia of the pelvic limbs, cervical pain and decreased cervical range of motion can be seen. Along with the cervical cell bodies, neurons in other parts of the CNS may also be affected. Other signs such as lameness, facial deformities, corneal clouding and bone dysplasia may be present.

Mucopolysaccharidosis type VI (MPS VI) is an autosomal recessive trait in Siamese cats with neurological signs similar to MPS 1. With MPS VI, neurological signs commonly localize to the thoracolumbar spinal column.¹⁸

Tetanus

Tetanus is relatively uncommon in the cat.¹⁹ It is not associated with lesions of the UMN, but is included here because of the hypertonicity associated with the condition. *Clostridium tetani* is a Gram-positive anerobe that is most commonly introduced into the patient via a skin wound. After inoculation, the bacterium produces numerous toxins, in particular tetanospasmin, which affects interneurons (Renshaw cells) in

TABLE 6 Focal and multifocal disorders affecting the UMN and/or LMN

Feline infectious peritonitis
Toxoplasmosis
Rabies
Discospondylitis
Hypervitaminosis A (deforming cervical spondylosis)
Intervertebral disc disease
Lymphosarcoma
Mucopolysaccharidosis

the spinal cord responsible for extensor motor neuron inhibition. More specifically, tetanospasmin blocks pre-synaptic glycine vesicle release from the Renshaw cell (glycine is a normal inhibitory neurotransmitter in the spinal cord), thereby causing extensor rigidity. Depending on toxin load, signs of tetanus may be focal (eg, affecting a single limb) or generalized (affecting multiple limbs and the head).

Multifocal disorders affecting the UMN and/or LMN

There are several multifocal disorders that may produce mixed signs of UMN and LMN paresis in the cat (Table 6). Depending on the location of the lesions, these diseases may be associated with either UMN or LMN paresis, or both (Fig 3).

Feline infectious peritonitis

Feline infectious peritonitis is caused by a pathogenically mutated form of the enteric feline coronavirus (FCoV). The non-pathogenic FCoV typically is spread by the oronasal route through infected feces. Young cats (between 6 months and 2 years) and older cats (> 10 years) are most commonly affected. A non-effusive (brain and eye) form develops in cats that mount a combined humoral and cell-mediated immune response, compared with the effusive form in which cats develop a humoral immune response only.²⁰ Central nervous system signs associated with the non-effusive form reflect the location of the multifocal lesions affecting the brain and/or spinal cord. This condition carries a grave prognosis, and there has been no effective treatment published to date.

Toxoplasmosis

The cat is the definitive host for *Toxoplasma gondii*, a protozoan that is transmitted to cats by ingestion of feces (sporozoites), through vertical transmission (tachyzoites), or by ingestion of organisms in animal tissue (bradyzoites). Although neurological toxoplasmosis is uncommon in cats, *T gondii* may produce a multifocal encephalomyelitis. Concurrent infection with feline immunodeficiency virus has been associated with clinical toxoplasmosis in cats.²¹

Rabies

Rabies should always be among the differentials considered for an unvaccinated, outdoor cat that presents with an acute onset, rapidly progressive neurological condition. The causative agent of rabies is a rhabdovirus, of the genus *Lyssavirus*, that may infect any domestic or wild cat.²² After inoculation, the rabies virus replicates in skeletal muscle, and then moves centripetally from the motor end plates to the peripheral nerves, and from there to the CNS. The virus subsequently travels centrifugally to other parts of the CNS or peripheral nervous system, including the neuromuscular junction, and replicates and concentrates in the salivary glands (permitting transmission by a bite). While a LMN syndrome is common, clinical signs may be profoundly variable.

KEY POINTS

- ❖ **UMN weakness may be caused by diseases that are confined to the spinal cord and mid- to caudal brainstem.**
- ❖ **LMN/neuromuscular weakness may be caused by lesions in the LMN cell body in the ventral gray horn of the spinal cord, ventral nerve root, peripheral nerve, neuromuscular junction, or the muscle itself; these localizations are indistinguishable by physical examination alone.**
- ❖ **There are several disease processes that can cause an UMN weakness, LMN/neuromuscular weakness, or both.**
- ❖ **An accurate neuroanatomic diagnosis allows the clinician to formulate an appropriate differential diagnosis, perform the correct diagnostics, prognosticate, and ultimately to develop a therapeutic plan.**



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