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Neurology Survival Kit 2017 Mini Series

Session One: Spinal or neuromuscular problem?

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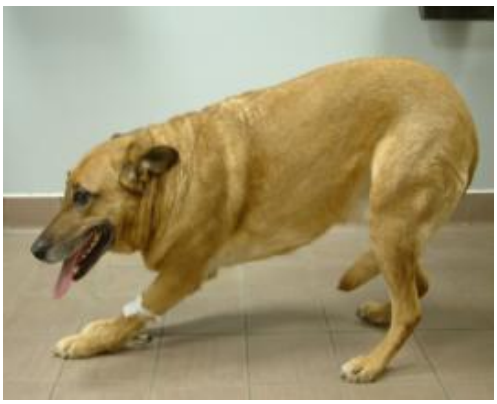


IS IT SPINAL OR NEUROMUSCULAR?

Spinal diseases are important causes of disability in dogs and represent a high proportion of the caseload in a neurology referral centre. One of the main difficulty remains in many cases for the clinician to recognise the origin of the disorder as being the spinal cord and to eliminate other origin of abnormal gait such as cerebral or neuromuscular disorder. The spinal column is made up of bony vertebrae (seven cervical, thirteen thoracic, seven lumbar, three sacral and variable number of caudal vertebrae). Through these vertebrae runs a canal (vertebral canal) inside which the spinal cord is protected. The intervertebral disc is a cartilaginous pad between two adjacent vertebrae and lies beneath the spinal cord. The discs give the spine flexibility and act as shock absorbers. The spinal cord is made of fibers (neuronal processes) linking the brain and the rest of the body including the limbs, anus, bladder and tail. These fibers carry a wide variety of information about movement of the limbs or tail (motor function), control of the bladder or anal function, ability to recognize the position of the body in space and coordination of movement (functions called *proprioception*).

Investigations of spinal cord disease require a very accurate clinical neurolocalisation.

The spinal cord is divided into functional segments (eight cervical, thirteen thoracic, seven lumbar, three sacral and variable number of caudal). These segments contain the cell bodies of the lower motor neuron (LMN). The segments C6 – T2 and L4 – S3 contain the cell bodies of the LMN innervating the thoracic and pelvic limbs. Lesion at the level of these intumescence results in LMN signs in the corresponding limb(s). Some spinal cord segments lie in the vertebra of the same annotation while others do not. Neurological lesion localisation refers to spinal cord segments.

Two broad categories of diseases can affect the spinal cord function: compressive and non-compressive diseases: While disc disease is the most common cause of spinal cord dysfunction in dogs, neoplastic and inflammatory diseases (in particular the dry form of FIP) represent more than half of the underlying causes of spinal cord disease in this species.

WHAT ARE YOU TRYING TO ACHIEVE?

The aims of the neurological evaluation of any companion animal are to answer the following questions:

1. Do the clinical signs observed refer to a nervous system lesion?
2. What is the location of this lesion within the nervous system?
3. What are the main types of disease process that can explain the clinical signs?
4. How severe is the problem?

The first two questions are answered by performing a general physical and neurological examination and aim to determine the anatomical diagnosis (location and distribution of the lesion within the

nervous system). The third question is answered by compiling the information on the patient signalment and history of the problem with the anatomic diagnosis to determine the differential diagnosis. Disease severity helps to determine prognosis of the differential diagnoses. Diagnostic tests are then carried out to investigate the differential diagnosis. The choice and interpretation of these tests must rely on a clear knowledge of the anatomical diagnosis and the expected disease processes.

DO THE CLINICAL SIGNS REFER TO A NERVOUS SYSTEM LESION?

A number of non-neurological conditions may mimic a nervous system lesion. Orthopaedic problems, cardiorespiratory diseases or metabolic disturbances, to name a few, can easily mimic some common neurological presentations such as gait abnormality, neuromuscular weakness or collapse. Furthermore, some inflammatory, infectious or neoplastic diseases of the nervous may also affect other body system. A detailed clinical examination should therefore be performed before embarking on the neurological examination. Orthopaedic examination and evaluation of femoral pulses are particularly important when evaluating a cat with abnormal gait. Ophthalmic (and in particular retinal) examination can be particularly useful when evaluating a cat suspected of neurological form of feline infectious peritonitis, lymphoma, systemic arterial hypertension or Toxoplasmosis.

WHY SHOULD YOU ATTEMPT TO LOCALISE THE PROBLEM?

The purpose of the neurologic examination is to determine the neurologic abnormalities and based on that, the location of the lesion or lesions responsible for causing these abnormalities. The location is the anatomic diagnosis. Narrowing down to which part(s) of the nervous system may be affected can undeniably present a number of advantages.

From a diagnostic point of view, the differential diagnosis is entirely dependent on the anatomic diagnosis. Aside for determining which part of the nervous system is affected, localising the lesion also involve determining if the problem is focal, multifocal (i.e., affecting multiple parts of the nervous system) or diffuse (i.e., affecting globally and symmetrically one or more parts of the nervous system). Such information can then be used to narrow down even further the differential list (see section how to establish a differential diagnosis list).

Furthermore, a number of disease processes may only be diagnosed by exclusion of other causes mimicking a similar clinical history and presentation. This process of exclusion implies evaluating the correct part of the nervous system to confidently rule-out these mimics. Failure to localise the lesion, the interpretation of any diagnostic test results can end up a very challenging task for the clinician in the face of negative findings (as seen with some vascular or degenerative disease of the central nervous system) or findings that do not match the clinical history.

Finally, running a limited number of investigations aimed at narrowing down the differential list to a specific part of the nervous system can only result in less cost for the owners and less time spent to reach a diagnosis for the clinician.

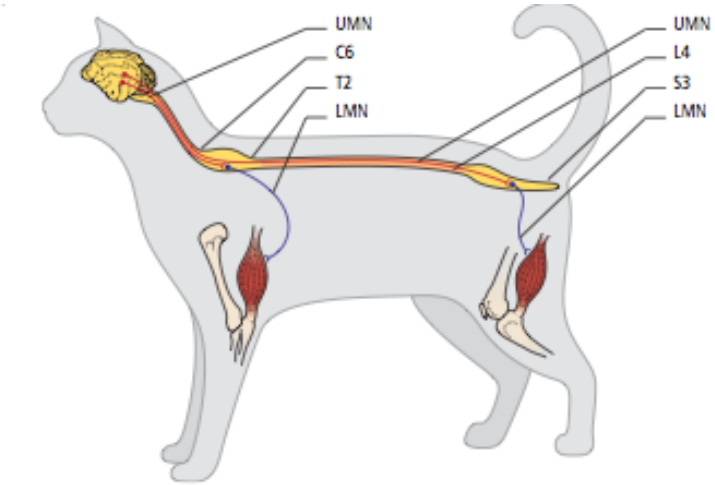
WHAT ARE THE PRINCIPLES OF LESION LOCALISATIONS?

Before rushing into the specifics of the neurological examination, attention should be focused on what questions are aimed to be answered:

1- Is there any neurological abnormality detected?
2- Which part(s) of the nervous system may be involved to explain these abnormalities?
3- Is the lesion localisation focal, multifocal or diffuse?

The first question does not require any detailed knowledge of neuroanatomy or neuroanatomic pathways. By simple observation and testing a number of reflexes and responses (see section hands-on and hands-off approach), the clinician should be able to determine if the cat is neurologically sound or not.

The neurological examination aims to test the integrity of these various components of the nervous system and, if present, detect any functional deficit. Normal findings are as important as the abnormal ones in localising the lesion. Neurological abnormalities detected on examination should be listed and added to the list of abnormal findings collected from the history. Each of these abnormal findings should then be correlated to a specific region or to specific pathways within the peripheral and/or central nervous system. Attempts should then be made to explain all the abnormal findings by a single lesion within one of the following regions of the nervous system: focal forebrain – brainstem – cerebellum - [C1 – C5 spinal cord segments] – [C6 – T2 spinal cord segments] – [T3 – L3 spinal cord segments] - [L4 – L6 spinal cord segments] – [L7 – S3 spinal cord segments], peripheral nerve - neuromuscular junction - muscle. Lesions within these regions of the nervous system result in predictable and specific neurological signs. Note that in localizing a lesion, it is not necessary that all the clinical signs referable to one location or syndrome be present. If a single lesion cannot explain all the listed abnormal findings, the lesion localisation is considered as multifocal or diffuse.



NEUROANATOMICAL BASIS OF THE PARETIC DOG OR CAT

A normal gait requires intact function of the brainstem, cerebellum, spinal cord and sensory and motor peripheral nerves, neuromuscular junction and muscles. The cerebrum's contribution to the gait is less important in cats compared to primates. Evaluation of the gait should be done with the aim of determining if the cat is *ataxic* (uncoordinated), *paretic* (weak) or *lame* (from either neuromuscular disease or an orthopaedic disorder) and which limb(s) are involved. *Ataxia* is defined as an uncoordinated gait and can arise from a peripheral nerve or spinal cord lesion (general proprioceptive ataxia), a vestibular lesion (vestibular ataxia or a cerebellar lesion (cerebellar ataxia).

Type of ataxia	Neurolocalisation	Clinical signs
Proprioceptive	General proprioceptive pathways - Peripheral nerve - dorsal root - spinal cord - brainstem - cerebral cortex	Abnormal postural reactions with limb paresis
Vestibular	Vestibular apparatus - vestibular nuclei (central) - vestibular portion of CN VIII or vestibular receptors (peripheral)	Head tilt, leaning, falling or rolling to one side, abnormal nystagmus, strabismus, normal (peripheral) or abnormal (central) postural reactions in case of unilateral dysfunction Crouched posture, reluctance to move and wide head excursion in case of bilateral dysfunction

Cerebellar	Cerebellum	Broad-based stance, swaying of the trunk, intention tremors of the head, loss of balance on both sides as well as forward and backward, dysmetric gait, pendular nystagmus, delayed and then exaggerated response to postural reactions testing, ipsilateral menace deficit with normal vision, absence of limb paresis and normal mentation (pure cerebellar disease)

Gait generation requires the interaction between two motor systems: upper motor neuron (UMN) and lower motor neuron (LMN) systems.

The upper motor neuron (UMN) system is the motor system that is confined to the central nervous system (CNS). It is responsible for the initiation and maintenance of normal movements and for the maintenance of tone in the extensor muscles to support the body against gravity. Its cell body lies within the cerebral cortex, basal nuclei, brainstem or spinal cord. It travels through the brain and/or spinal cord white matter and synapses indirectly (via an interneuron) with a LMN to modulate its activity (essentially inhibitory).

The lower motor neuron (LMN) system is the motor system connecting the central nervous system with the muscle to be innervated. Its cell body lies within the ventral horn of the spinal cord grey matter or within the cranial nerve nucleus of the brainstem. Its axon leaves the central nervous system by the ventral nerve roots to join successively a spinal nerve and a peripheral nerve before it synapses with an effector muscle. The LMN is the last neuron in the chain of neurons that produce muscular contraction necessary to maintain posture, support weight and provide the gait (final common pathway to the effector).

The UMN pathways are responsible for stimulating the appropriate LMN that induce the postural and protraction phases of locomotion.

Paresis is defined as a loss of ability to support weight (lower motor neuron disease) or inability to generate a gait (upper motor neuron disease). The term paresis implies that some voluntary movement is still present as compared to paralysis that refers to a more severe paresis with complete (-plegia) loss of voluntary movement. Depending which limbs are affected, the terms paresis/paralysis can be further defined as t*etraparesis/plegia* (all four limbs affected), *paraparesis/plegia* (pelvic limbs affected), m*onoparesis/plegia* (only one limb affected), h*emiparesis/plegia* (limbs on one side affected). Two qualities of paresis can be distinguished: UMN and LMN paresis. *UMN paresis* causes a delay in the onset of protraction, which is the swing phase of the gait. Lesions at many different levels of the CNS can produce the same set of UMN clinical signs. Due to their close anatomic relationship within the caudal brainstem and spinal cord, most gait abnormalities involving the UMN pathways necessary for gait generation also caused some degree of general proprioceptive

(GP) ataxia. From a lesion localisation point of view, upper motor neuron paresis and GP ataxia visible in the gait can occur as a consequence of lesion affecting the brainstem, or spinal cord. Aside for lesion caused by acute disease processes (i.e., infarct, haemorrhage and head trauma), lesion affecting the forebrain cause contralateral paresis that is so mild that it is usually not apparent in the gait. *LMN paresis* affects the gait with lesions in the peripheral nerves, neuromuscular junction and muscles. Motor deficit observed are ipsilateral to the lesion. LMN paresis reflects degrees of difficulty in supporting weight and varies from a short stride to complete inability to support weight, causing collapse of the limb whenever weight is placed on it. Care must also be taken as many cats can have an apparent plantigrade stance (crouched posture) in a hostile environment such as a consultation room. Compared to UMN paresis, disorder of the LMN does not cause ataxia but only paresis.

NEUROLOGICAL EVALUATION OF THE PARETIC DOG OR CAT

The finding of paresis or paralysis in the absence of intracranial signs indicates spinal cord disease or generalized lower motor unit disease. Brainstem injury is unlikely to cause paralysis without obvious additional signs such as altered states of consciousness, vestibular ataxia, cerebellar ataxia, or cranial nerve signs. Aside for lesion caused by acute disease processes (i.e., infarct, haemorrhage and head trauma), lesion affecting the forebrain cause contralateral paresis that is so mild that it is usually not apparent in the gait. The next goal for the clinician is to further localize the problem as diagnostic approaches, differential diagnoses and treatment options differ for each possible disease location.

STEP 1: Gait evaluation

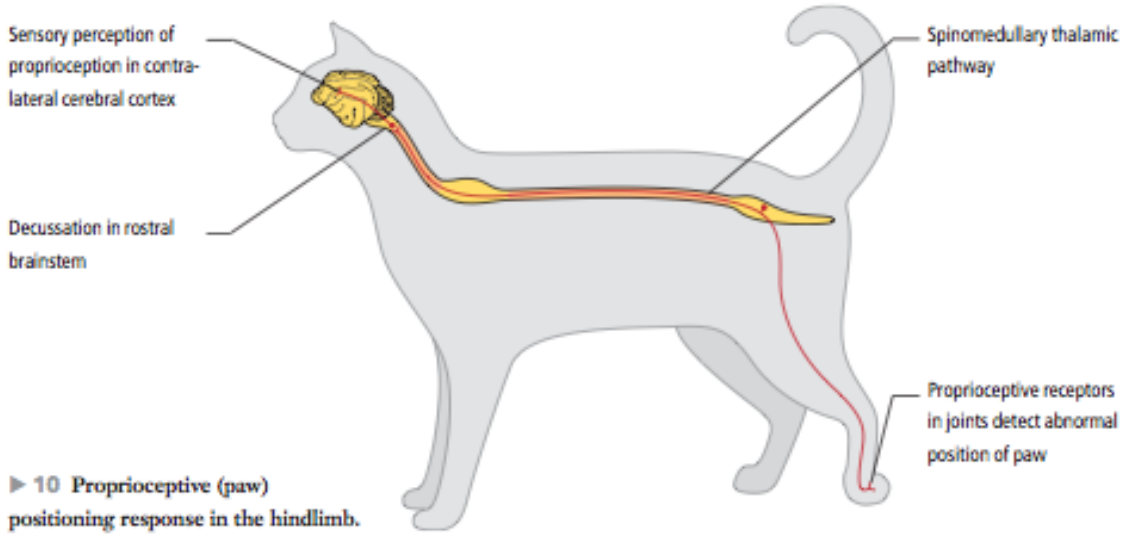
Initial evaluation of an animal with a gait abnormality should be done with the aim of determining if it is ataxic, paretic or lame (from either neuromuscular disease or an orthopedic disorder) and which limb(s) are involved. The locomotor status should be evaluated on a non-slick surface with support if needed. Asymmetry should be assessed and graded. Assessing weakness can be done by describing whether the cat can rise, stand or walk unassisted. Other semi-quantitative descriptors could include how far it can walk without falling, how much support the animal needs to rise or stand, and how much support is needed for purposeful ambulation. Noting the involvement of thoracic limbs is important as some animals with tetraparesis may have marked weakness in the pelvic limbs and minimal weakness in the thoracic limbs.

In ambulatory animals, gait analysis can help differentiate lower motor neuron from upper motor neuron paresis. Lower motor neuron dysfunction typically results in a short-strided gait and decreased ability to support weight. Dysfunction of the descending upper motor neuron system results in a long-strided, reaching and stiff gait. Animals with a caudal cervical lesion are often described as having a “two-engine gait” with a short, choppy gait in the thoracic limbs and a long-strided, floating gait in the pelvic limbs.

STEP 2: Postural reaction testing

Postural reactions should be evaluated in all animals presenting for paresis and paralysis. Each limb should be evaluated and the results noted on the neurological examination form. The aim of postural reaction testing is primarily to detect subtle abnormalities that were equivocal or not obvious on gait evaluation. The results of gait evaluation and postural reaction testing help to identify which limbs are involved. Muscle tone and segmental spinal reflexes are then tested on each abnormal limb to determine if the lesion is UMN or LMN in nature.

Paw position testing can be very difficult to assess in cats. Other postural reaction testing such as the hopping response, weelbarrowing and tactile placing are preferred in this species. If the patient is reluctant to hop, the cat should be held with three limbs restrained and lowered suddenly to the ground surface with the limb to be tested extended. As soon as the paw strikes the ground the cat should be move laterally to force it to hop on that limb.



▶ 10 Proprioceptive (paw) positioning response in the hindlimb.

STEP 3: Evaluation of muscle tone and segmental spinal reflexes

Muscle tone should be assessed by flexing and extending the limb and joints. Although increased resistance is indicative of UMN signs, it can also be seen in fractious, excitable or painful animals, as well as in association with LMN paresis affecting the flexor system. Diminished tone is a hallmark of LMN signs. Although many spinal reflexes are described, the most reliable one in cats are the withdrawal reflex and the patellar reflex. Other spinal reflexes (triceps, biceps, extensor carpal radialis and gastrocnemius) are more difficult to perform and to interpret. The withdrawal reflex is performed with the cat in dorsal recumbence between the thighs of the examiner. A noxious stimulus is applied to the tested limb by pinching the nail bed or digit with the fingers or haemostat. This stimulus causes

a reflex contraction of the flexor muscles and withdrawal of the tested limb. If this withdrawal reflex is absent, individual toes can be tested to detect if specific nerve deficits are present. It should be stressed that the withdrawal reflex in the thoracic or pelvic limbs does not depend on the animal's conscious perception of noxious stimuli (nociceptive function). The withdrawal reflex is a segmental spinal cord reflex that only depends on the function of the local spinal cord segments. The patellar reflex is elicited by hitting the patellar ligament and observing a reflex contraction of the quadriceps muscle and extension of the stifle joint. It is performed again with the cat in dorsal recumbence between the thighs of the examiner. Evaluation of the cat extensor tone on the pelvic limb can also be used as a control in cats with ambiguous patellar reflex as it involves the same neuro-anatomical components (femoral nerve and quadriceps muscle). The patellar reflex evaluates the integrity of spinal cord segments L4 to L6 (and associated nerve roots) as well as the femoral nerve. A weak or absent patellar reflex indicates a lesion of the L4 to L6 spinal cord segments or the femoral nerve.

STEP 4: Evaluation of tail, bladder and anal sphincter

Tail function is evaluated by assessment of voluntary tail movement, tail tone and sensation. Bladder and urethral function are evaluated by assessment of bladder size, resistance to manual expression, and presence of urine dribbling. The bladder is often large, firm and difficult to express with UMN lesions (i.e. lesions cranial to S1 spinal cord segment); while large, flaccid and easily (but incompletely) expressed with LMN lesions. The anal sphincter is evaluated by assessment of anal tone on digital rectal palpation, presence of anal reflex and sensation.

UMN bladder	**LMN bladder**
Lesion cranial to the S1 segment Conscious voiding attempts usually absent Bladder expression difficult Large bladder Perineal tone and reflex present May get overflow incontinence when the bladder becomes over-distended	Lesion caudal to S1 segment Conscious voiding attempts absent Bladder easily expressed Half-full to large flaccid bladder Perineal tone and reflex reduced to absent Frequent urine dribbling

STEP 5: Sensory testing

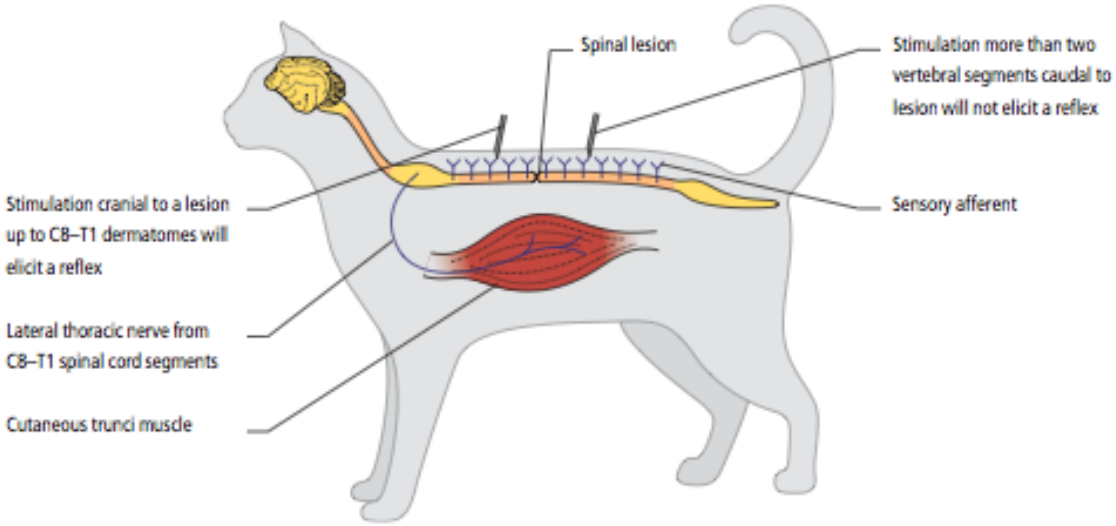
Sensory evaluation is the final component of the neurological examination. Nociception testing is performed with a small hemostat systematically over the surface of the affected limbs. Application of pressure should only be escalated when the initial stimulus fails to elicit a behavioral response such as

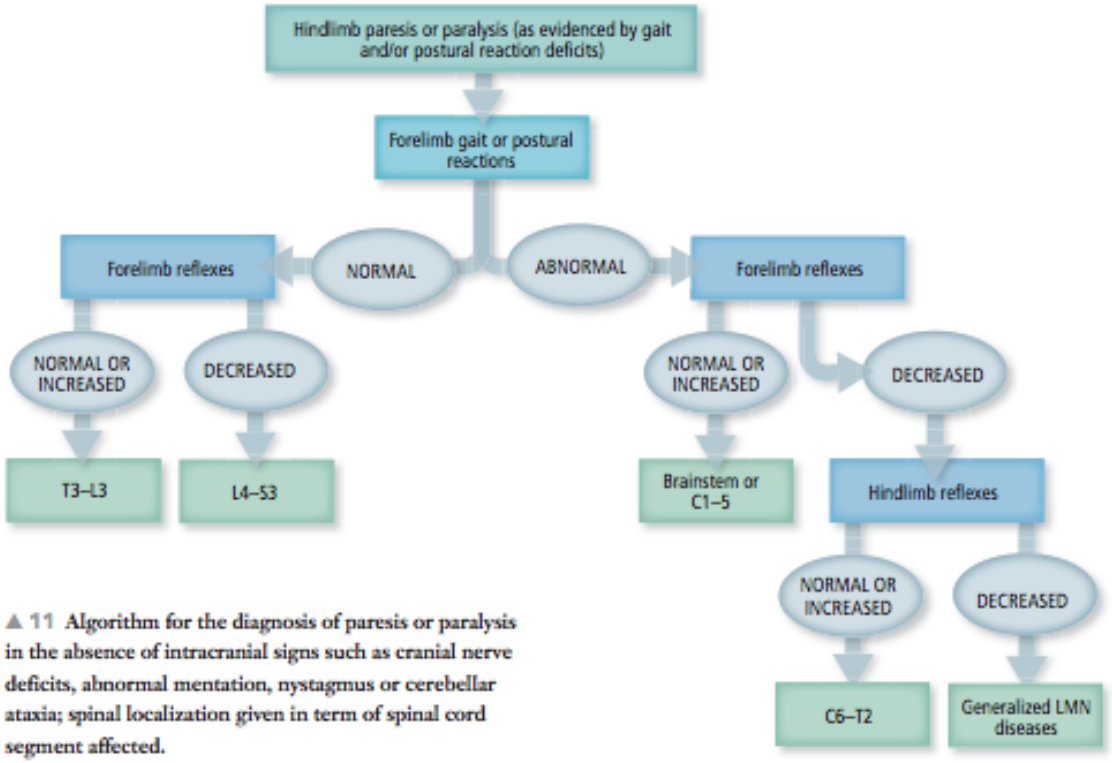
turning of the head, vocalizing or an escape behavior. Withdrawal of the limb is only the flexor reflex and should not be taken as evidence of pain sensation.

STEP 6: Cutaneous trunci reflex and spinal palpation/manipulation

The cutaneous trunci reflex enables accurate localisation within the T3 to L3 UMN spinal cord segments, and additionally assesses the C8 to T1 region of the brachial plexus (efferent arm of the reflex) via the lateral thoracic nerve from spinal cord segments C8 or T1. The cutaneous trunci reflex can be decreased or absent caudal to a lesion anywhere in this pathway. In the occasional normal animal the cutaneous trunci reflex is either unreliable or totally absent. This test is conducted by stimulating the skin with a pinprick or by pinching with a pair of haemostats, starting at the iliac crest, about one inch lateral to the midline. This should result in a bilateral contraction (or twitch) of the cutaneous trunci muscles. In the absence of such muscle contraction, the point of skin stimulation should be moved cranially until a normal reflex is observed (i.e. cut-off point).

Paraspinal palpation is performed near the end of the examination to ensure the continued cooperation of the patient. The clinician should palpate down the spine feeling for focal pain, muscle spasm and heat. If the dog does not react to light palpation then moderate pressure is applied. The neck is flexed from side-to-side, dorsally and ventrally. The lumbosacral junction is flexed and extended while trying not to flex other joints. A behavioural reaction to what should be an innocuous stimulation can be interpreted as pain.





▲ 11 Algorithm for the diagnosis of paresis or paralysis in the absence of intracranial signs such as cranial nerve deficits, abnormal mentation, nystagmus or cerebellar ataxia; spinal localization given in term of spinal cord segment affected.

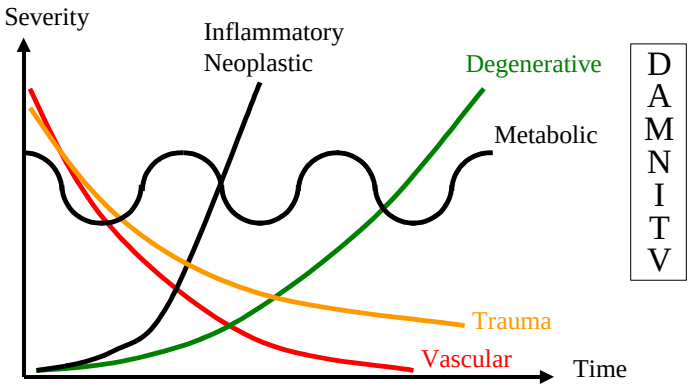
HOW TO ESTABLISH A DIFFERENTIAL DIAGNOSTIC LIST?

The differential diagnosis list is entirely dependent on the anatomic diagnosis. Determination of a differential diagnosis list is essential in choosing and interpreting any diagnostic test however sophisticated they may be. The aim of performing such diagnostic tests should only be to confirm or exclude the differentials in the list and not replace the clinical evaluation. The differential diagnosis list can be developed taking into account:

- Signalment
- Historical data: questioning of the owner should be aimed at defining the mode of onset (acute, subacute, chronic or episodic) and evolution of the condition. Furthermore, historical data can give clues as to how widespread or focal the disease process is in the nervous system, whether there was evidence of asymmetry, and how severe the signs have been.
- Neurological findings: the aim of the neurological evaluation being to define the lesion localisation (forebrain, brainstem, cerebellum, spinal cord segment, peripheral nerve, neuromuscular junction and muscle) and distribution of the disease (focal, multifocal, diffuse) within the nervous system.

Disease processes that can affect the nervous system are classically classified according to the mnenomic VITAMIN D (Vascular - Inflammatory/Infectious - Traumatic/Toxic - Anomalous – Metabolic – Idiopathic Neoplastic – Nutritional - Degenerative). Each of these disease processes has a typical signalment, onset and progression as well as distribution within the nervous system.

ONSET AND PROGRESSION



SPINAL CORD DISEASES THAT CAN CAUSE TETRAPARESIS ([C1 – C5] OR [C6 – T2] LOCALISATION)

Disease mechanisms (Vitamin D)	**Specific diseases that affect dogs and cats- unique diseases to dog (D) and cats (C) as specified.**
Vascular	Fibrocartilaginous embolism Vascular malformations Spinal cord hematoma or haemorrhage
Inflammatory/infectious	Meningo(encephalo)myelitis (viral, bacterial, protozoal, fungal or immune-mediated) Discospondylitis/osteomyelitis/physitis Spinal epidural empyema Aseptic suppurative meningo arteritis (D) (note that meningitis is not a cause of tetraparesis unless concurrent parenchymal involvement but pain often localised to the cervical spine)
Trauma	Spinal fracture/luxation Traumatic disk herniation Spinal cord contusion Epidural hemorrhage
Toxic	Tetanus

Anomalous	Atlanto-axial luxation Atlanto-occipital overlap (D) Intra-arachnoid cysts Dermoid sinus Syringohydromyelia Vertebral and spinal cord anomalies Osteochnodromatosis
Metabolic	None
Idiopathic	None
Neoplastic	Primary or metastatic spinal or spinal cord tumor
Nutritional	Hypervitaminosis A (C)
Degenerative	Intervertebral disk disease (Hansen types I and II) Cervical spondylomyelopathy (Wobbler syndrome) (D) Discal cyst (D) Synovial cyst Inherited neurodegenerative diseases

SPINAL CORD DISEASES THAT CAN CAUSE PARAPARESIS ([T3 – L3] LOCALISATION)

Disease mechanisms (Vitamin D)	**Specific diseases that affect dogs and cats- unique diseases to dog (D) and cats (C) as specified.**
Vascular	Fibrocartilaginous embolism Vascular malformations Spinal cord hematoma or haemorrhage
Inflammatory/infectious	Meningomyelitis (viral, bacterial, protozoal, fungal or immune-mediated) Discospondylitis/osteomyelitis/physitis Spinal epidural empyema
Trauma	Spinal fracture/luxation Traumatic disk herniation Spinal cord contusion

Toxic	None
Anomalous	Syringohydromyelia Verterbral and spinal cord anomalies Intra-arachnoid cyst Dermoid sinus Osteochondromatosis
Metabolic	None
Idiopathic	None
Neoplastic	Primary or metastatic spinal or spinal cord tumor
Nutritional	Nutritional hyperparathyroidism Hypervitaminosis A (C)
Degenerative	Intervertebral disk disease (Hansen types I and II) Degenerative myelopathy Synovial cyst

SPINAL CORD DISEASES THAT CAN CAUSE PARAPARESIS ([L4 – S3] LOCALISATION)

Disease mechanisms (Vitamin D)	**Specific diseases that affect dogs and cats- unique diseases to dog (D) and cats (C) as specified.**
Vascular	Fibrocartilaginous embolism Aortic and/or iliac thromboembolism Vascular malformations Spinal cord hematoma or hemorrhage Ascending and descending haemorrhagic myelomalacia
Inflammatory/infectious	Meningomyelitis (viral, bacterial, protozoal, fungal or immune-mediated) Discospondylitis/osteomyelitis/physitis Spinal epidural empyema

Trauma	Spinal fracture/luxation Traumatic disk herniation Spinal cord contusion Sacro-coccygeal luxation
Toxic	None
Anomalous	Syringohydromyelia Vertebral and spinal cord anomalies Spinal stenosis Sacrocaudal dysgenesis
Metabolic	None
Idiopathic	None
Neoplastic	Primary or metastatic spinal or spinal cord tumor
Nutritional	Endocrine neuropathies Hypervitaminosis A (C)
Degenerative	Intervertebral disk disease (Hansen type I and II) Degenerative lumbo-sacral disease Spondylosis deformans

COMMON SPINAL DISEASE IN DOGS AND CATS

- DISC HERNIATION

Intervertebral disc disease (IVD) can occur in any area of the spinal cord caudal to C1-2. The presence of the intercapital ligament contributes to the low incidence of intervertebral disc extrusions in the thoracic spine between T2 and T11. Middle-aged dogs are most often affected. Clinical signs of IVD disease in all ages of cats are rare. Older cats often have protrusions of intervertebral discs, but rarely do these results in clinical signs.

Two basic types of IVD disease are seen. A type I (Hansen's) intervertebral disc abnormality is seen in chondrodystrophic breeds of dogs which have chondroid metaplasia of their discs beginning early in life. The discs usually extrude rather than protrude. The type II IVD seen most commonly in older,

larger non-chondrodystrophoid dogs with fibroid metaplasia of the disc. These discs usually protrude rather than extrude.

Clinical signs of IVD disease include spinal pain and varying degrees of limb dysfunction. Root signature, where an affected limb may be held flexed off the ground may occur as a reflection of pain. Spinal pain may be the only clinical sign in some dogs.

Abnormalities such as collapse of the intervertebral disc space, deformities of the intervertebral foramina, radiopaque material in or around the spinal cord, and decrease in the size of the dorsal articular joint space may be noted with survey radiographs of the spine. While suggestive of disc disease, these changes do not always correlate with clinical significant spinal or nerve compression. Accurate assessment of spinal compression is aided by myelography or advanced imaging studies (CT or MRI). An extradural spinal compression centered over or around the disc space is characteristic. Cerebrospinal fluid collected caudal to the lesion may contain elevated protein concentration and/or pleocytosis.

General guidelines have been established for selecting therapy of dogs with intervertebral disc disease. These decisions usually depend upon severity of clinical signs. Mildly affected animals (animals with pain alone or mild paresis) may be managed with cage confinement for at least two weeks. If after two weeks signs are improved, definitive diagnosis and surgery should be considered. If the animal worsens during this time, diagnosis and surgery should be considered earlier. If improvement is noted, continuation of cage confinement is indicated for up to one to two weeks after the animal is clinically normal. More severely affected animals are considered surgical candidates and require timely diagnosis and surgical treatment. Animals that retain nociception have an 80 – 90% chance of being able to walk at some time after surgery. When nociception is absent, the prognosis for walking falls to 50%. If nociception is absent for longer than 48 hours, the prognosis for return to walking falls below 5%.

- ISCHAEMIC MYELOPATHY

Fibrocartilaginous embolism (FCE) of the spinal cord is a syndrome of acute spinal cord infarction caused by embolisation of fibrocartilage material. FCE has been described in many species including man, dog, cats, horses and sheep. Histopathology evaluation is necessary to establish its definitive diagnosis as other conditions (even if rare) can also cause spinal cord infarction (neoplastic emboli, parasitic embolism associated with microfilariasis, or septic emboli associated with bacterial endocarditis or other infection, hyperlipidemia and possible microinfarction or hyperviscosity).

FCE should be suspected in dogs with acute, paroxysmal, and then non-progressive signs of a focal myelopathy. Many hypotheses have been proposed to explain the origin and possible migration routes of the fibrocartilaginous material. Unfortunately, most of these hypotheses are extrapolated from a small number of cases and none of them can satisfactorily explain all cases seen in affected species.

The most common breeds predisposed to FCE are giant breeds, especially Great Danes but it can also occur in small breeds mainly the Miniature Schnauzer and the Shetland Sheepdog. It does not tend to occur in chondrodystrophoid dogs. The mean age varies between 3 and 7 years.

Fibrocartilaginous embolism results in an ischaemia of the spinal cord parenchyma. As a vascular disorder, its onset is peracute and its evolution non-progressive. More than half of cases are presented following an episode of trauma or exercise. Exercise or trauma need not be severe but may be factors in increasing pressure within the intervertebral disc, inducing embolisation. Due to the development of secondary spinal cord injury, the clinical signs can occasionally get worse over the first 24 hours. Thereafter, FCE is usually a non-progressive phenomenon unless ascending and descending myelomalacia develops.

Being a non-compressive spinal cord disease, affected patients are classically non-painful on palpation/manipulation of the spine. A very small percentage of dogs may initially shows mild spinal hyperaesthesia associated with the actual extrusion of fibrocartilaginous material and stimulation of nociceptive receptors in bone, periosteum, ligaments, and meninges.

Clinical signs vary with the severity of the ischemic episode and the localisation of the embolus. The neurological examination is consistent with focal or multifocal spinal cord neurolocalisation that can be either symmetrical or asymmetrical (due to the asymmetric branching of the intrinsic spinal cord vasculature). Emboli can occur anywhere in the spinal cord so LMN or UMN signs can be observed, however a large proportion of FCE localise to the cervico-thoracic or lumbo-sacral intumescence.

Histopathology evaluation is necessary to establish a definitive diagnosis of FCE. Its antemortem diagnosis is essentially a rule-out one. Its suspicion is based on the clinical history (peracute to acute onset of non-progressive spinal cord dysfunction in a non-chondrodystrophoid breed), results of neurological examination (focal or multifocal a/symmetrical non-painful spinal cord neurolocalisation) and imaging findings.

Differential diagnosis of acute spinal cord dysfunction includes: 1) FCE, 2) acute disc herniation, 3) spinal fracture/luxation, 4) inflammatory CNS diseases. Focal myelitis and spinal neoplasia may sometimes produce comparable asymmetric neurologic deficits. However, their onset is expected to be more gradual and their course progressive.

Survey radiographs are indicated to investigate the possibility of spinal fracture/luxation. Myelogram should be considered to eliminate an extra-medullary spinal cord compression (disc herniation, fracture/luxation) that may require surgical treatment. This contrast study is usually normal or on occasion can reveal an intramedullary pattern associated with spinal cord edema at the site of the myelopathy. CSF analysis could be normal in case of FCE or may reveal xantochromia, elevated total protein (related to rupture of the blood brain barrier), and/or pleocytosis with majority of non-degenerate polymorphonuclear in the acute phase.

If available, MRI scan of the suspected spinal cord segment involved might reveal intraparenchymal hyperintense lesion on T2-weighted scan with or without contrast-enhancement.

Definitive diagnosis of FCE is only obtained at postmortem examination.

FCE is exclusively a medical spinal cord disorder. Its treatment is essentially conservative and based on supportive care and physiotherapy. Free radical scavengers are recommended in the acute phase

to limit the secondary ischaemic complications. Methylprednisolone sodium succinate 30 mg/kg i/v might be indicated only if given during the first eight hours after the onset. This first injection can be followed by an infusion of the same drug at 5.4 mg/kg/hour for 24 hours or alternatively serial bolus of 15 mg/kg at 2 hours, 7.5 mg/kg at 6 hours and 12 hours. Unfortunately, there is no clinical data available to support its use and such therapeutic information is extrapolated from clinical trial in human with acute spinal cord injury. Passed this therapeutic window, corticosteroid treatment is not indicated and could potentially be harmful. Physical therapy plays on other hand an important role in the successful management of these patients. Recumbent animals must be placed on thick bedding and turn every four hours. Bladder function should be appropriately monitored with three times daily check/manual expression, intermittent catheterisation or undwelling catheter if necessary.
Physiotherapy, assisted walking using harness or supporting sling as well as hydrotherapy are all extremely important adjunctive treatment.
Recovery from FCE is determined by the degree of spinal cord damage. The prognosis for functional recovery is usually good with some animal keeping residual deficit (especially in case of intumescence involvement and LMN signs). Failure to make any improvement after two weeks is usually suggesting of poor prognosis. Animal with absent nociception (deep pain perception) have a guarded to poor outcome.

- DEGENERATIVE MYELOPATHY

Degenerative myelopathy (also known as CDRM) is a degenerative disease of the spinal cord commonly recognised in dogs, mainly in the larger breeds and particularly the German shepherd. It has also been described in the cat, but it is a much rarer diagnosis in this species. It affects both the axon and the myelin sheath in the spinal cord and nerve roots of middle aged animals (5-11 years).
The clinical signs are those of a non-painful, slowly progressive thoraco-lumbar myelopathy causing an UMN bilateral paraparesis. Some dogs may also show loss of patellar reflex due to involvement of the dorsal nerve root of the femoral nerve (true cases of CDRM). The onset is often insidious and mistaken for arthritis or hip dysplasia. The course of the disease can be between 5 months and 2 years.
The diagnosis is based on the breed, age and history. It is essentially a rule out diagnosis as spinal radiographs, CSF analysis and myelography are unremarkable. DNA testing is now available. The aetiology is unknown and at this point no treatment is reported.

- CAUDA EQUINA SYNDROME

The cauda equina is defined as the spinal cord segments, the adjacent nerve roots, and spinal nerves lumbar 7 (L7), sacral 1-3 (S1-3), and caudal 1-5 (Cd1-5) contained within the vertebrae L5-7, S1-3, and Cd1-5. Diseases that affect these structures may result in cauda equina neuropathy. Terminology regarding cauda equina dysfunction is confusing, as lumbosacral disease has been used synonymously with cauda equina syndrome. Lumbosacral disease is a collective term encompassing

many diseases that can lead to pathologic changes of the cauda equina. Cauda equina syndrome (CES) is a definitive term describing sensory and/or motor neural dysfunction that results in compression, destruction or displacement of the nerve roots or the blood supply in the region of the cauda equina. Common causes of CES in the dog include vertebral malformation, idiopathic stenosis, discospondylitis, neoplasia, intervertebral disc disease, sacral osteochondrosis, vasculopathy, degenerative lumbosacral arthropathy, and trauma. Common clinical signs of CES are lumbosacral pain, hyperesthesia (especially over the L/S region), reluctance to sit or jump, pelvic limb lameness, unilateral or bilateral paraparesis, muscle atrophy in the caudal thigh, cranial tibial and gastrocnemius, tail paresis, and, in severely affected dogs, urinary and fecal incontinence. Animals with CES usually have normal pelvic limb spinal reflexes although the patellar reflex may be slightly exaggerated. This results from flaccidity of the caudal thigh musculature that is innervated by the sciatic nerve and increased action of the quadriceps muscle groups. Diagnostic protocol for CES should include: 1) electromyography and motor nerve conduction velocity, 2) survey radiographs of at least L5 to Cd5 vertebrae, regardless of the results of electrodiagnostic studies, to be sure that conditions that may cause apparent pain without EMG abnormalities (such as discospondylitis or vertebral tumour) are not overlooked, 3) flexion-extension myelography and CSF analysis for structural lesion and for inflammatory/infectious causes, 4) if diagnosis cannot be made: L7/S1 discography, 5) if diagnosis cannot be made: epidurography, 6) if diagnosis cannot be made: CT and/or MRI.

- MENINGITIS AND MENINGO-MYELITIS

Can be infectious (especially associated with Distemper in dog or FIP in cats) but more often non-infectious (suspected immune-mediated).

<u>Granulomatous Meningoencephalomyelitis (GME)</u>

GME is an inflammatory disease of the CNS of unknown origin. It affects mainly middle-aged dogs of mainly mid-size breeds, although it has been reported to affect very young or very old individuals occasionally. It is believed to be either pre-neoplastic or possibly related to an undetected viral infection. It has three forms. Two affecting the central nervous system (intra-cranial structures and the cervical spinal cord mainly although less frequently the rest of the spinal cord as well): A granulomatous form causing space occupying masses and a diffuse infiltrative form. The third form causes an optic neuritis. The clinical signs vary with the neuro-anatomical localisation and the onset can be acute or chronic.

The treatment is based on immuno-suppression with cortico-steroids (prednisolone, 0.5-1 mg/kg BID 4-6 weeks then taper slowly whilst monitoring the clinical signs to avoid a relapse that would be more resistant to treatment) or other chemotherapeutic agents (azathioprine, cytosine arabinoside/cytarabine) if corticosteroids fail to control the problem. Radiation therapy has been used successfully in the isolated granulomatous form. The prognosis is guarded.

Non-Infectious meningitis (Steroid-responsive)

Meningitis in dogs is most frequently idiopathic and possibly immune-mediated as it responds most of the time to treatment with immuno-suppressive doses of corticosteroids, once the possibility of infection has been ruled out. However it can also occur subsequent to sub-arachnoid hemorrhage, or post-myelography. It is observed in young middle and large breed dogs (7-16 months) with no pathogen. The clinical signs are the same as septic meningitis and the CSF analysis is the same as for septic meningitis. The neutrophils however should not show any bacterial inclusions. Culture and sensitivity should be negative.

The treatment of steroid responsive meningitis is based on protracted immuno-suppression with corticosteroids. The treatment can be initiated with dexamethasone (0.25 mg /kg BID I.V.) then switched to oral prednisolone (0.5-1 mg/kg BID for 4-6 weeks beyond clinical remission then switch to EOD for 2 weeks then 0.5 mg/kg SID EOD for 2 weeks then discontinue).

The prognosis is good if severe encephalomyelitis is avoided but recurrences are reported, particularly if the treatment is tapered off too rapidly.

WORKING UP THE WEAK

The neuromuscular system is composed of motor units that consist of a neuron cell body, its axon, the neuromuscular junction, and muscle fibers. Consequently, an abnormality in any portion of this motor unit can result in clinical signs of neuromuscular disease. The lower motor neuron (LMN) is an integral part of this unit and is an efferent neuron connecting the central nervous system to a target muscle. Its cell body lies within the ventral horn of the spinal cord grey matter or within the cranial nerve nucleus of the brainstem. Its axon leaves the central nervous system by the ventral nerve roots to join successively a spinal nerve and a peripheral nerve before it synapses via a cholinergic (nicotinic) neuromuscular junction with a muscle. The motor unit composed of the LMN, the neuromuscular junction and the muscle fibres innervated is the final common pathway for motor activity.

CLASSIFICATION OF NEUROMUSCULAR DISORDERS

Neuromuscular disorders may be classified based on their underlying cause or according to the disease location within the motor unit as:

- **Motorneuron disorders** or diseases affecting the lower motor neuron cell body within the spinal cord ventral grey matter
- **Neuropathies** or diseases affecting the peripheral nerve or nerve root. Depending the nerve components affected (axon and/or myelin), neuropathies are further subdivided into axonopathies (axon involvement), demyelinating disease (Schwann cells involvement) or mixed axonal-demyelinating disease (axon and Schwann cells)
- **Junctionopathies** or diseases affecting the neuromuscular junction (further divided in pre-synaptic, synaptic or post-synaptic)

- **Myopathies** or diseases affecting the muscles
- **Neuromyopathies** or diseases affecting elements of both the motorneurons and muscles

CLINICAL SIGNS OF NEUROMUSCULAR DISORDERS

Peripheral nerve, neuromuscular junction and muscle diseases most often produce lower motor neuron signs with varying degree of paresis, hypotonia, hyporeflexia and muscle atrophy. A paretic gait is usually manifested as a stilted stride that becomes progressively shorter with accompanying ventroflexion of the neck, reluctance to walk or run, lying down, and collapse. Many cats will present a plantigrade stance or a crouched pelvic limb gait and cervical ventro-flexion. As other signs of neuromuscular disorder, these signs are not pathognomonic of an underlying cause but only reflect neuromuscular weakness associated with lower motor neuron involvement. Some exceptions might be worth mentioning such as some primary muscle diseases characterised by muscle hypertrophy rather than atrophy (as seen in muscular dystrophy), pure sensory neuropathy causing only sensory signs (sensory ataxia, hypermetria, depression or absence of nociception, reduced postural reaction, depression or loss of spinal reflexes without muscle atrophy, self-mutilation,) in the absence of motor signs or neuromuscular junction disease causing in some cats only intermittent signs of exercise-induced weakness (as seen in some cases of myasthenia gravis).

DIAGNOSIS OF NEUROMUSCULAR DISORDERS

Diagnosis of lower motor neuron disorders requires a complete physical and neurological examination in order to confirm the anatomic diagnosis (localisation to the lower motor unit) and rule-out other neurological differentials (disease involving the spinal cord or brain) and non-neurological differentials (cardio-respiratory disease, joint disease, endocrine and systemic disease as cause of weakness).

Minimum database

Each suspected dogs or cats should have a minimum database including complete blood count (CBC), serum biochemistry panel (especially creatine kinase [CK] and electrolytes) and urinalysis. The CBC may reveal abnormalities such as a stress leukogram supportive of hyperadrenocorticism, a mild normocytic, normochromic nonregenerative anemia supportive of hypothyroidism or immune-mediated thrombocytopenia or anemia indicative of possible systemic lupus erythematosus or an immune basis for the neuromuscular disease. The chemistry panel may reveal electrolyte abnormalities, ionic imbalances, hypercholesterolemia suggestive of hypothyroidism and blood glucose aberrations, which may be responsible for myopathic or neuropathic signs. The serum half-life of CK is very short, lasting only 6 hours; a persistent elevation of 4-5 times the normal level in two tests carried out between 24 and 48 hours of each other is an indication of a recent and active muscle lesion. Creatine kinase may be normal in the presence of muscle disease; but muscle disease should not be ruled out based on a normal CK concentration. Serum CK may also be mildly elevated in the

absence of neuromuscular disease related to factors such as exercise, recumbence, trauma such as needle injections, or markedly elevated in anorexic cats. Elevated levels of serum aspartate aminotransferase, alanine aminotransferase, and lactate dehydrogenase can also be compatible with muscle disease, but as for CK, they are not disease specific and can be normal.

Other minimally invasive blood tests such as serology for anti-acetylcholine receptor antibody, 2M antibody, Toxoplasma IgM/IgG, Neospora, FelV, FIV and cholinesterase serum level are also indicated as second intention and are aimed at specific etiologies. In case of suspicion of endocrine disease based on preliminary blood and urine profile, an ACTH stimulation test in combination with an endogenous ACTH assay for hyper- and hypoadrenocorticism, a combination of serum total T4, endogenous thyroid-stimulation hormone (TSH) assay and free T4 levels for hypothyroidism, serum fructosamine levels for diabetes mellitus should be included in the work up. Radiographs of the thorax and abdomen and ultrasonography of the abdomen are indicated to investigate the possibility of neoplasia as a cause for the neuropathy, junctionopathy or myopathy (paraneoplastic syndrome) as well as detecting complications such as megaoesophagus or aspiration pneumonia.

Electrophysiological assessment

Electrophysiological tests such as electromyography (EMG), motor nerve conduction studies (electroneurography) and repetitive nerve stimulation are helpful to try to further localise the level of dysfunction (nerve, neuromuscular junction or muscle), determine the extent of the disease and site of muscle or nerve biopsy. Unfortunately these tests do not provide information on the underlying cause.

EMG is used to identify denervated muscles and to identify and characterise myopathies. With EMG, muscles are explored using a concentric needle electrode, which measures the electrical activity in a small muscle volume at its tip. Nearly all striated muscles can be probed including limb, masticatory, facial, laryngeal, pharyngeal, paraspinal, tail and anal sphincter muscles. A normal relaxed muscle is electrically silent except in the end plate region; this is where endplate noise due to miniature endplate potentials and endplate spikes, thought to be caused by the presence of the electrodes near the endplate, are recorded. During concentric needle electrode movements, mechanical triggering of muscle fibre potentials generates insertion potentials. Five to ten days after the development of a peripheral motor nerve lesion (the time needed for degeneration of the distal axonal segment), denervated muscle fibres exhibit spontaneous depolarization, which is most often recorded in the form of fibrillation potentials and positive sharp waves. Spontaneous activity objectively confirms a peripheral or muscular problem. EMG alone is unable to discriminate between these possible localizations and poorly correlates to the severity of the problem. Follow-up nerve conduction studies and frequently muscle and nerve biopsy are therefore indicated.

Motor nerve conduction studies are used to investigate suspected peripheral neuropathies. Motor NCV is obtained by stimulating a motor nerve at a minimum of two sites and recording the evoked electrical activity, the compound muscle action potential (CMAP), in one of the target muscles each

time. Expected normal ranges for conduction velocity, CMAP amplitude and duration for each nerve have been established. However, it should be noted that the age of the patient and limb temperature can have an effect on the motor NCV of specific nerves. The difference in latency of the CMAP when the nerve is stimulated at two different sites is determined. The resulting latency difference (in ms) is divided by the distance between the two stimulating electrodes (in mm) and represents the maximum conduction velocity of the motor fibres in the nerve segment between the two stimulating electrodes (in m/s). The amplitude, duration and waveform of the CMAP are also recorded. Three different types of changes may be observed:

1- CMAP amplitude is severely diminished and the conduction velocity slightly decreased with motor axon loss

2- The conduction velocity is severely diminished and CMAP components dispersed with disorders of the myelin sheath

3- CMAP to distal stimulation is normal but CMAP to proximal stimulation is altered or suppressed in conduction block as a result of focal demyelination

Repetitive stimulation investigates patients with suspected myasthenia gravis. The quantity of neurotransmitter delivered at the nerve fibre terminals normally decreases during repeated stimulation; however, it always remains above what is needed to efficiently trigger all muscle fibres in a normal animal. The neurotransmitter excess is called the 'safety factor'. Should the number of functional motor plate receptor diminish, such as in myasthenia gravis, the neurotransmitter quantity becomes relatively insufficient. Consequently, the action potentials are not triggered in some muscle fibres, which then do not contribute to the CMAP after several stimuli. The amplitude of CMAP therefore diminishes as the train of stimuli proceeds. A consistent >10% decrease in the CMAP amplitude during a train of 10 stimulations at a rate of 3 Hz is suggestive of myasthenia.

Muscle and nerve biopsy

Muscle and nerve biopsy (including histopathology and histochemical analysis) are therefore necessary if all other preliminary tests are inconclusive. Evaluation of only paraffin embedded muscle, however, is of very limited value. The most information from the muscle biopsy specimen is obtained primarily from evaluation of fresh frozen specimens reserving the fixed muscle specimens for ultrastructural studies when required.

More specialized tests involved evaluation of resting and post-exercise plasma lactate and pyruvate concentrations, urine, plasma and muscle concentrations of total, free and esterified carnitine as well as urinary organic acids and plasma amino acids. Evaluation of plasma lactate, pyruvate and their molar ratios (L/P) can provide important information in the evaluation of possible metabolic myopathies and is critical for the diagnosis of mitochondrial diseases. The analysis of urinary organic

acids and plasma amino acids profiles can be useful in determining the etiology of muscle metabolism disorders. Evaluation of the complete carnitine status is necessary for rational therapeutics of primary or secondary disorders of carnitine metabolism.

COMMON NEUROMUSCULAR DISORDERS

- **Acute polyradiculoneuritis**

Acute canine polyradiculoneuritis (inflammation of the nerve roots and peripheral nerves) is considered the most common peripheral neuropathy in dogs. This condition was initially suggested to be an animal model for the acute polyradiculoneuropathy of people, Guillan-Barre syndrome, although some divergences in the pathological findings are now recognised. A similar condition has been reported in cats but seems to be less common than in dogs. Acute canine polyradiculoneuritis can be subclassified according to the presumptive cause as Coohnound paralysis, idiopathic polyradiculoneuritis and post-vaccinal polyradiculoneuritis. The exact pathogenesis is overall unknown however an immune-mediated process involving both a humoral and cell-mediated process is suspected. In North America, the most common form of acute polyradiculoneuriits is Coonhound paralysis and appears in dogs 7 to 10 days after they have been bitten or scratched by a raccoon. It is thought that a protein constituent of raccoon saliva may induce a delayed hypersensitivity against myelin. Dogs that have recovered from coonhound paralysis are not immune to future attacks. A condition that appears to be identical to Coonhound paralysis with respect to onset, clinical signs and course, and pathological findings occurs worldwide in dogs that have had no possible exposure to raccoons and named idiopathic polyradiculoneuritis. Finally, recent vaccination (especially against rabies) has been incriminated as a possible cause of acute canine polyradiculoneuritis. In all instance, signs are caused by an inflammatory reaction to axons and myelin sheaths affecting mainly the ventral nerve roots and ventral root components of spinal nerves.

Clinical signs initially consist of a stiff, stilted, short-strided gait. The weakness then develops on the pelvic limbs and ascends rapidly, resulting in a flaccid symmetric tetraparesis or tetraplegia that usually peaks within 10 days of the onset. Occasionally the weakness appears first in the thoracic limbs and descends. Cranial nerves are rarely affected, although there may be signs of facial weakness and aphonia. Nociception remains intact but some dogs seem to experience considerable discomfort on light palpation on the extremities. Some dogs can develop significant respiratory compromise as a result of paralysis of the intercostals muscles and diaphragm that can progress to complete respiratory paralysis.

Differential diagnosis of acute canine polyradiculoneuritis should include conditions such as botulism, tick paralysis and fulminant myasthenia gravis. Diagnosis is based on the history and clinical findings. A number of diagnostic tests may help to re-enforce the clinical suspicion. CSF may be normal (particularly if collected by cisternal puncture) or may reveal an increased total protein concentration

with a normal nucleated cell count (albuminocytological dissociation). The most reliable electrophysiologic indicators of acute canine polyradiculoneuritis are electromyographic changes, significantly decreased compound muscle action potential amplitudes, increased minimum F-wave latencies, increased F ratios and decreased F-wave amplitudes. An enzyme-linked immunosorbent assay (ELISA) test is available and reported to be highly sensitive and specific to detect specific circulating antibodies to raccoon saliva in dogs with known coonhound paralysis.

Results of randomised trials in man have shown equivalent efficacy of both plasma exchange and intravenous immunoglobulin, but not corticosteroids, in hastening recovery from Guillain-Barre syndrome. Plasma exchange or immunoglobulin therapies have not been tried in dogs with acute canine polyradiculoneuritis. Treatment is mainly based on supportive care. Affected dogs should be closely monitored for respiratory depression. Most dogs tend to recover fully within a few weeks to up to 6 months depending on the severity of the disease.

- **Acquired myasthenia gravis**

Immune-mediated myasthenia gravis (MG) is a relatively common neuromuscular disease affecting dogs and occasionally cats. This acquired form of MG is due to antibody-mediated (predominantly IgG) destruction of nicotinic acetylcholine receptor (AChR) on the postsynaptic membrane of the neuromuscular junction. The deficiency of functional receptors results in reduces sensitivity of the postsynaptic membrane to the neurotransmitter acetylcholine and failure of the neuromuscular transmission. Acquired MG has been reported as a paraneoplastic syndrome in association with a variety of tumour including thymoma, cholangiocellular carcinoma, osteosarcoma, anal sac adenocarcinoma, lung carcinoma and cutaneous lymphoma. Hypothyroidism, hypoadrenocorticism, systemic lupus erythematosus and polymyositis have been recognised in dogs with MG. Acquired MG has been reported in hyperthyroid cats receiving methimazole therapy.

The characteristic clinical presentation of acquired MG is appendicular muscle weakness that worsens with exercise and improves with rest. Concurrent megaoesophagus causing regurgitation and aspiration pneumonia is also common in dogs because of the large amount of skeletal muscle in the oesophagus in this species. Occasionally, facial, laryngeal, or pharyngeal weakness accompanied the appendicular muscle weakness. In cats, a breed predisposition for acquired MG has been recognised in Abyssinians (and related Somalis).

Acquired MG has been reported in dogs ranging in age from 7 weeks to 15 years with all breeds and both genders being potentially affected. Breeds with the highest risk of acquired MG are Akitas, several terrier breeds, German Shorthaired Pointers, and Chihuahuas. A familial predisposition has been suggested in Newfoundlands. Rare cases of juvenile-onset autoimmune MG have also been documented.

Clinical signs of acquired MG may be focal in nature, associated with regurgitation (megaoesophagus), dysphagia (pharyngeal dysfunction) and decreased palpebral reflex (facial muscles), without detectable limb muscle weakness. The reason for selective involvement of particular muscle groups is not known. An acute fulminating form of MG has also been described in dogs and characterised by frequent regurgitation of large volumes of fluid associated with megaoesophagus and rapid loss of muscle strength resulting in recumbence. Respiratory failure, presumably caused by aspiration pneumonia and loss of strength in muscles involved in respiration, is a consistent complication of acute fulminating MG and a common cause of death.

The diagnosis of acquired MG can be a challenge. The definitive diagnosis of acquired MG is based on demonstration of serum antibodies to muscle AchRs by immunoprecipication radio-immunoassay. This test is objective and quantitative, and proves an autoimmune response to AchRs which differs from other causes of muscle weakness. The prevalence of seronegative canine myasthenics is considered to be very low and false positive results have not been documented. Seronegative, acquired MG may occur due to very low titer but high-affinity AChR antibodies with all antibodies complexed to AChRs in muscles or antibodies directed against other end-plate proteins. Other diagnostic tests that are relatively specific for acquired MG include the edrophonium chloride (Tensilon) challenge test, immuno-cytochemical staining of muscle endplates, repetitive nerve stimulation, and single fiber electromyography (SF-EMG). The response to the ultrashort-acting anticholinesterase drug edrophonium chloride (0.1 to 0.2 mg/kg intraveinously) may help to establish a clinical diagnosis of MG while the results of antibody testing are pending especially if a dramatic response is observed. This testing method has been shown to be neither sensitive nor specific as a negative response to Tensilon does not rule-out the diagnosis of MG (especially in cases of acute fulminating MG) and some dogs with other myopathic and neuropathic disorders can also show mild improvement in their neuromuscular weakness. Occasionally this test can cause a cholinergic crisis by overstimulation of Achr producing a depolarising blockade. Dyspnoea, bradycardia, profuse salivation, miosis, cyanosis and limb tremor may result and can be reversed with atropine (0.05 mg/kg intraveinously).

Therapy for acquired MG should be tailored to the individual needs of the patient. The three main aspects of therapy are anticholinesterase therapy, immunomodulatory therapy and supportive care. The natural course of autoimmune canine MG was recently determined in a large number of dogs treated with anticholinesterase therapy, without immunosuppression. Spontaneous clinical and immunologic remission occurred in more than 85% of dogs with an average of 6.4 months. Neoplasia was identified in the 15% of dogs that did not spontaneously remit. Anticholinesterase therapy comprises the cornerstone of treatment of acquired MG in dogs. Anticholinesterase agents prolong the action of ACh at the neuromuscular junction by reversibly inhibiting acetylcholinesterase. Pyridostigmine is the most commonly used anticholinesterase drug, and is administered by mouth or a stomach tube at a dosage of 0.5 to 3.0 mg/kg q8-12h in dogs and 0.25 mg/kg q8-12h. Common side effects include nausea, cramps, diarrhoea, salivation and lacrimation. Overdosing leads to weakness

as a result of depolarization and desensitization of the postsynaptic membrane. To avoid a cholinergic crisis, it is recommended to start at the low end of the dose and increase as needed. If oral treatment is not possible due to severe regurgitation, neostigmine can be given (0.04 mg/kg intramuscularly q6h). For critical animals, a constant rate intraveinous infusion of pyridostigmine (0.01-0.3 mg/kg/h) may be given until oral feedings are resumed or a feeding tube is placed. Adjunctive immuno-suppressive treatment is indicated if limb muscle strength has not returned to normal following symptomatic treatment with anticholinesterase therapy and if there is no evidence of aspiration pneumonia. Other indications include dogs with persistently elevated AChR antibody titres, seropositive dogs with a negative edrophonium test, dogs with less than optimal response to anticholinesterase agents and/or unacceptable side-effects. If prednisolone is to be given to a myasthenic dog or cat, anti-inflammatory doses (e.g. 0.5 mg/kg q12-24h) should be given initially, gradually building to immuno-suppressive levels (2 to 4 mg/kg q12-24h) over 7 to 10 days to avoid initial exacerbation of muscle weakness. Once muscle strength has returned, dosage of prednisolone can be reduced very slowly whilst monitoring carefully for relapse. If there is no response to immunosuppressive dosage of prednisolone, other immunosuppressive drugs such as azathioprine (1 to 2 mg/kg orally every 24 hours), cyclosporine (4 mg/kg q12h) or mycophenolate mofetil (20 mg/kg orally q12h) can be used. The potential benefits of thymectomy for canine MG patients are unknown; however a complete removal of thymomas has been associated with normalization of the AChR antibody titre and resolution of clinical signs. Decision regarding duration and treatment regimen should be based on clinical ground (resolution of clinical signs of weakness) and periodic testing of AChR antibody titres (at least in dogs or cats that are not on immuno-suppressive treatment).

Overall, the prognosis for acquired MG is guarded. Approximately 84% of patients have megaoesophagus. Aspiration pneumonia is the main cause of death in canine patient and the 1-year mortality rate has been reported to be as high as 60%. Because fewer cats develop megaoesophagus and aspiration pneumonia, the 1-year mortality rate for cats is only 15%. Response to treatment of congenital MG is usually poor and the complete resolution of clinical signs is uncommon although reported by 6 months of age without medical therapy in two Dachshunds.

- **Idiopathic polymyositis**

Polymyositis (PM) is an idiopathic diffuse inflammation of skeletal muscle that is presumed to have an immune-mediated basis. Signs of polymyositis are variable and may was and wane initially. They include mild to severe weakness, which may be precipitated or exacerbated by exercise, lameness, stiff stilted gait and muscle atrophy. The disease may or may not be painful and pyrexia may be part of the clinical picture in acute severe case or as a consequence of aspiration pneumonia. The neurological examination is usually normal aside for reduction in the myotatic reflexes depending the severity of the disease. Occasionally PM can manifest as a more focal disease affecting one limb, pharyngeal, laryngeal or oesophageal muscles group causing unilateral lameness, dysphagia, dysphonia, stridor or regurgitation. Any age and breed of dog and cat may be affected. In a recent

study, Boxers and Newfoundlands were overrepresented. Unlike other breeds, Newfoundland had circulating autoantibodies against an unidentified sarcolemmal antigen supporting a humoral immune component. The diagnosis of idiopathic PM is based on clinical signs, elevation of serum CK (although can be low in end-stage disease), negative infectious disease titres (*Toxoplasma gondii*, *Neospora caninum* and tick-related disease when appropriate in dogs - *Toxoplasma gondii,* FeLV and FIV in cats) and histologic confirmation of lymphocytic infiltrates in skeletal muscle biopsy. EMG can be used to determine the distribution of the disease and to help selecting the most severely affected muscle prior to tissue biopsy. The absence of EMG changes does not rule-out PM. Systemic connective tissue diseases such as systemic lupus erythematosus and neoplastic diseases should be investigated as possible underlying cause of PM. Thoracic radiographs should be performed to investigate the presence of megaoesophagus, aspiration pneumonia or primary or metastatic neoplasia. Abdominal ultrasound is also indicated to search for underlying neoplasia. Recently, a series of Boxer initially diagnosed with PM that several months later were diagnosed with lymphoma was published. It was suggested that inflammatory myopathy might be a preneoplastic syndrome in that breed. Treatment is based primarily on the use of immuno-suppressive dosage of prednisolone (initially at 1 to 2 mg/kg every 12 hours orally). The prognosis is generally favourable unless there is presence of megaoesophagus, aspiration pneumonia, pharyngeal dysfunction or if initiation of treatment has been delayed with resultant marked muscle atrophy and fibrosis. Prednisolone should be continued for at least 12 weeks at decreasing dosages. Life-long treatment is occasionally necessary. Other immuno-suppressive drug such as azathioprine can be used in addition to prednisolone if there is a poor response to this first drug or if the animal relapses when the dosage is reduced.