ANATOMIC DIAGNOSIS

Brain: Prosencephalon, Pons-Medulla, Cerebellum
Cranial nerves
Spinal Cord: C1-C5: UMN/GP all four limbs
    C6-T2: LMN thoracic limbs, UMN/GP pelvic limbs
    T3-L3: UMN/GP pelvic limbs
    L4-S1: LMN pelvic limbs
    S1-Cd: LMN tail, anus, perineum, excretions
Nerves: Radial, Femoral, Sciatic

LOWER MOTOR NEURON (LMN) SIGNS:
In lower motor neuron (LMN) disease, there is a deficiency in the ability to support weight which results in a short stride but no ataxia. The patient walks with a “lame” gait. The patient knows where its paws are located. Postural reactions are normal as long as the limb can be moved.

DIFFUSE LOWER MOTOR NEURON DISEASE (LMN)
- Polyradiculoneuritis
- Tick Paralysis
- Botulism

POLYRADICULONEURITIS: MOLECULAR MIMICRY
Molecular mimicry is a presumed basis for the immune-mediated inflammation in polyradiculoneuritis. The patient is exposed to an antigen that is similar to a component of either the myelin or axon within its nerves. This would include such components as galactocerebrosides or glycolipids. Antibodies made against the exogenous antigen attack and destroy the patient’s antigen (axon and/or myelin). In humans, this polyneuritis is called
the Landry-Guillain-Barre disease. It has occurred in patients exposed to
*Campylobacter jejuni, Mycoplasma pneumoniae*, Cytomegalovirus,
Epstein Barr virus and Zika virus. In dogs, especially coonhounds, the
raccoon saliva is the presumptive source of the common antigen. The
disease can be reproduced only in recovered dogs with the intradermal
injection of raccoon saliva. This suggests that for this disease to
develop, in addition to exposure to the appropriate antigen there needs
to be some alteration of the patient’s immune system as well. Be aware
that this polyradiculoneuritis can occur in dogs without exposure to a
raccoon where the nature of the common antigen is unknown.

**UPPER MOTOR NEURON (UMN) AND GENERAL PROPRIOCEPTIVE (GP) SYSTEM SIGNS**
Lesions of spinal cord white matter affect both the upper motor
neuron (UMN) and general proprioceptive (GP) systems together.
The clinical signs reflect the involvement of both systems. These
include a delay in the onset of limb movement and a prolonged
stride with the joints in extension. This gives an overreaching
appearance to the gait which is easier to appreciate in the thoracic
limbs. Limb placement may be abnormal to either side. Postural
reactions will be delayed to absent.

**CANINE C1-C5 ANATOMIC DIAGNOSIS- PROGRESSIVE COURSE DIFFERENTIAL DIAGNOSIS**
- Compressive myelopathy:
  - Vertebral Stenosis:
    - Malformation/Malarticulation: congenital, acquired.
      - OCD may be involved in the development of the vertebral
        stenosis and malformation of the articular processes.
      - Malarticulation leads to degenerative joint disease that
        involves
        - both the intervertebral disks as well as the articular processes.
  - C2-C3 meningeal fibrosis often accompanied by
    - syringohydromyelia. Large breed dogs, cause unknow
  - Diskospondylitis
  - Intervertebral disc extrusion
  - Neoplasia-extraparenchymal

**Myelitis**
- Parenchymal neoplasm
ROTTWEILER: INHERITED DEGENERATIVE NERVOUS SYSTEM DISORDERS:

1. Neuroaxonal dystrophy: Onset 1 to 2 years, cerebellar signs.
2. Leukoencephalomyelopathy- a primary demyelination: Onset 1.5 to 3.5 years, C1 to C5 signs.
3. Motor neuron disease: Onset 1 month, all lower motor neuron (LMN) signs, no dyspnea.
4. Myopathy-Duchenne type muscular dystrophy, male dogs, a dystrophinopathy: Onset 2 months, muscle disorder, no dyspnea but sialosis and difficult prehension.
5. Polyneuropathy-axonopathy: Onset 2 months, LMN tetraparesis, inspiratory dyspnea, cataracts.
6. Distal neuropathy-axonopathy: Onset adults 1-4 years, LMN signs, no dyspnea.
7. Encephalomyelopathy-polyneuropathy:
   [Neuronal vacuolation, spinocerebellar degeneration: Kortz 1997]
   Onset 1 to 2 months, initially either inspiratory dyspnea or tetraparesis and ataxia (UMN/GP) or both at once; dysphagia, megaesophagus, cerebellar-vestibular signs, cataracts, microphthalmia also reported.

NEPHROBLASTOMA

Nephroblastoma is an embryonic renal neoplasm that in children most commonly occurs in the kidney but in dogs most commonly occurs in the subarachnoid space between the T10 and L2 spinal cord segments. The age range is from a few months to about 3.5 years. In children this is referred to as the Wilm tumor. It is associated with a gene mutation on chromosome 11. Immunocytochemical studies using antibodies prepared against the protein product of this mutated gene, reveal that the canine tumor exhibits a positive stain. Reports in the 70s and 80s mistakenly identified this canine neoplasm as an ependymoma. Recovery follows surgical removal but the tumor readily grows back indicating the need for postsurgical radiation therapy.

CANINE DEGENERATIVE MYELOPATHY (DM)
MULTISYSTEM CENTRAL AND PERIPHERAL AXONOPATHY.
(J. Coates, D. O'Brien-U.MO)
Affected dogs have a missense mutation in the SOD 1 gene. SOD is superoxide dismutase, a cellular antioxidant that converts the toxic oxygen radicle to H2O2 and oxygen.
Onset of DM is 5 years or older and is slowly progressive over years. Four stages have been recognized by the University of Missouri investigators.
1. Pelvic limb upper motor neuron (UMN) paresis and general proprioceptive (GP) ataxia.
2. Non-ambulatory pelvic limbs to paraplegia with reflex loss in pelvic limbs, mild muscle atrophy and some incontinence.
3. LMN paraplegia, thoracic limb paresis and ataxia.
4. LMN tetraplegia with severe atrophy, mild dysphagia and paretic tongue.
In all of my experience, I never saw a dog with this disorder that was diagnosed at autopsy that had exhibited thoracic limb signs or lower motor neuron signs in the pelvic limbs. In this list, my patients only exhibited stage one clinical signs. This may be due to a shorter period of clinical signs in my patients prior to euthanasia and autopsy.

DNA test for SOD-1 mutation is available through the Orthopedic Foundation of America (OFA).
Results: 1. Clear: 2 normal copies of the gene
               2. Carrier: 1 mutated copy of the gene
               3. At risk: 2 mutated copies of the gene; NOT ALL are affected.
Breeds affected: German Shepherd Dog, Pembroke Welsh Corgi, Chesapeake Bay Retriever, Rhodesian Ridgeback.

DM is being studied as a possible animal model for Amyotrophic Lateral Sclerosis (ALS-Lou Gehrig disease) in humans. The amyotrophy refers to the lower motor neuron degeneration and resultant denervation muscle atrophy. The sclerosis is the spinal cord white matter degeneration of the lateral corticospinal tract secondary to motor cortex neuronal degeneration. A small percentage of humans with ALS have a mutation in their SOD-1 gene. In other patients, the cause is unknown. In these dogs with DM, primary motor neuron cell body degeneration has not been found although degeneration is present in many nerves in these old dogs. The “sclerosis” that is present is widespread in many
spinal cord tracts including both upper motor neuron and sensory pathways. The horse is a model for ALS based on the lower motor neuron degeneration which is caused by deficiency of the antioxidant Vitamin E.

**EQUINE MOTOR NEURON DISEASE**
The chief complaint is often loss of weight despite a good appetite because the weight loss is due to the extensive denervation muscle atrophy. In addition, poor performance, excessive recumbency, excessive sweating, shifting weight when standing, preference to walk rather than stand and muscle fasciculations are observed. Clinical signs slowly progress. These patients are often housed in a stall or dry paddock with no green feed or grain which leads to a deficiency in Vitamin E.

This is a primary degeneration of neurons that innervate Type 1 postural muscles with their high oxidative metabolism. Oxidative stress is from deficiency of antioxidants: vitamin E and superoxide dismutase (SOD 1). No SOD 1 gene mutation has been found in the affected horse. EMND can be produced by a diet deficient in vitamin E for 14 months or more. Clinical signs occur when 30% or more of the motor neurons are depleted.

**RADIAL NERVE - FEMORAL NERVE**
Loss of function of these two nerves results in loss of weight support in the thoracic limb (radial nerve) or pelvic limb (femoral nerve). Protraction of these limbs is normal but when the limb is placed on the bearing surface and expected to support weight, it collapses due to inability to extend the elbow or stifle, respectively. This results in a short stride in the affected limb as the patient depends on the opposite limb for its weight support. The patient will appear to walk “lame.” Nociception is compromised on the cranial surface of the antebrachium or dorsal surface of the forepaw for the radial nerve and the medial surface of the crus and hind paw for the femoral nerve where the skin is innervated by its saphenous nerve branch.

**SCIATIC NERVE**
Sciatic nerve dysfunction is characterized by the preservation of weight support and a protraction of the limb which is uninhibited due to the
loss of hip extensor muscle function. Thus, hip flexion is brisk and the patient may exhibit a skipping form of gait. Stifle flexion is reduced and both extension and flexion of the tarsus and digits is compromised. This is evident when the patient bears weight and a passive overflexion of the tarsus (“a dropped hock”) is exhibited (tibial nerve) and occasionally the patient will bear weight on the dorsal surface of the paw due to the loss of tarsal flexion and digital extensor function (fibular –peroneal nerve). Nociception will be compromised on the cranial, lateral and caudal surfaces of the crus and dorsal, lateral and plantar surfaces of the pelvic limb paw. These surface areas are innervated by the tibial and fibular branches of the sciatic nerve.

Be aware that rupture of any component of the common calcanean tendon can result in a “dropped hock” posture identical to that caused by a sciatic/tibial nerve dysfunction. However, this lesion has no effect on hip flexion. This common calcanean tendon includes the gastrocnemius tendon, the tendon of the superficial digital flexor and an extension of the tendons of the biceps femoris laterally and the semitendinosus and gracilis medially. The specific tendon rupture can be defined with MR imaging.

INHERITED POLYNEUROPATHY IN LEONBERGERS – D. SHELTON
The Leonberger dog is a product of breeding Newfoundland, Great Pyrennes and Saint Bernard dogs. The polyneuropathy onset of clinical signs is 1 to 3 years with inspiratory dyspnea, overflexed tarsus (“dropped hocks”) and walking with overflexion of the hips. Be aware that the inspiratory dyspnea may precede the evidence of a gait disorder which may influence your therapy. The gait disorder progresses over months to years to tetraparesis. This is inherited as an autosomal recessive gene but the specific genetic mutation is still being studied. This disorder is more common in males.

AORTIC VASCULAR COMPROMISE IN CATS
Caudal aortic thromboembolism only affects the blood supply to muscles and nerves of the pelvic limbs distal to the mid-thigh level. The blood supply to the lumbosacrocaudal spinal cord, tail, perineum and excretory orifices is unaffected due to the blood supply from the segmental lumbar arteries that branch from the abdominal aorta and
this blood flow can bypass the aortic compromise. The spinal cord is unaffected. Muscle tone is normal in the muscles that control hip joint position and movement as well as the tail and excretory orifices. These cats can move rapidly along the ground by flexing their hips. This unique gait is characteristic of this disorder.

When cats have their abdomen compressed by the tire of a vehicle, the prolonged spasm of the lumbar arteries or possibly their thrombosis causes a poliomyelomalacia of the lumbar, sacral and caudal spinal cord segments. These cats have no muscle function or tone in their abdomen, pelvic limbs, tail, perineum or excretory orifices due to the necrosis of the spinal cord ventral grey columns. These same regions are also usually analgesic due to the necrosis of the dorsal grey columns. This same spinal cord lesion and clinical signs will result when the aorta is ligated in the region of the renal arteries.

**DIFFUSE MYELOMALACIA**

This spinal cord lesion most commonly is associated with a very small percentage of dogs that have an acute severe intervertebral disk extrusion between T10 and L3 that causes a severe focal transverse spinal cord necrosis and hemorrhage. This results in rapid paraplegia and pelvic limb analgesia. At the onset, the paraplegia reflects the loss of upper motor neuron function with hypertonia and hyperreflexia. In a small percentage of these dogs, 1 to 3 days later (occasionally longer), there is a rapid complete loss of muscle tone, spinal reflexes and nociception in the pelvic limbs followed by the tail and perineum and then the abdomen and thorax. In a few days these dogs are totally recumbent and have lost tone and reflexes in the thoracic limbs. This diffuse loss of lower motor neuron activity is associated with a loss of nociception evidenced by analgesia of the entire body caudal to the thoracic limbs and neck. If the myelomalacia extends into the cervical spinal cord, the dog will die from respiratory paralysis. These dogs often exhibit discomfort when handled in the area of the thoracic limbs and neck. These dogs are readily recognized by their clinical signs and are NOT candidates for any ancillary procedures. Surgical decompression at the time of the initial injury will not prevent the development of this diffuse myelomalacia.
The cause of this unique lesion is unknown but may involve an individual variation in the major arterial blood supply to the thoracolumbar spinal cord from the intercostal or lumbar arteries. This progressive myelomalacia may result when a major spinal cord arterial supply is compromised by the intervertebral disc extrusion. I have not observed this disorder in a cat.

MUSCLE DISORDERS
LABRADOR RETRIEVER INHERITED POLYMYPATHY
There are at least three inherited myopathies in Labrador Retrievers:

1. **Centronuclear polymyopathy:** This has been referred to as centronuclear myopathy, Type II fiber deficiency, or autosomal recessive muscular dystrophy. This is NOT a muscular dystrophy which indicates muscle cell degeneration (necrosis) and regeneration. In this inherited polymyopathy, a gene mutation has been identified that is associated with abnormal muscle cell tubules. Onset of tetraparesis is at 2 to 3 months old and the clinical signs slowly progress to 9 to 10 months of age; most dogs remain ambulatory but paretic and have a normal life span. There is no dyspnea or dysphagia. Muscle serum enzymes are normal to slightly elevated. This is inherited as an autosomal recessive gene.

2. **X-linked myotubular myopathy:** This occurs in male Labrador Retrievers with an onset of signs at 7 to 14 weeks of age. Clinical signs include a progressive short choppy stride and muscle atrophy. A flexed vertebral posture with a low head carriage is present. Patellar reflexes are absent. Recumbency may occur after 3 or 4 weeks of progressive paresis. In severely affected puppies there may be difficulty in mastication along with abnormal laryngeal and esophageal function. Serum creatine kinase levels are normal or slightly elevated. EMG exhibits non-specific positive sharp waves and fibrillations. The mutated gene normally codes for a myotubular protein.

3. **Dystrophinopathy:** Duchenne type muscular dystrophy. This is a sex-linked recessive, spontaneous mutation. Therefore male dogs of many breeds are affected. The onset of tetraparesis occurs at 1 to 2 months of age along with dysphagia with excessive drooling and limited range of mouth opening. Both muscle atrophy and hypertrophy are observed in different muscle groups. In addition, a myotonia occurs and
contributes to the stiffness observed in the gait. A marked elevation of serum muscle enzymes is present.

LABRADOR RETRIEVER EXERCISE INDUCED COLLAPSE
DR. SUSAN MERIC TAYLOR, UNIVERSITY OF SASKATCHEWAN.
The onset of this disorder occurs at 7 months to 2 years in muscular, excitable, aggressive field trial Labrador Retrievers engaged in strenuous activity with a high level of excitement. After a brief period of vigorous exercise of 5 to 15 minutes, the affected dog starts to collapse in the pelvic limbs but does not become short-strided. The dog struggles to continue moving but loses its ability to stand and collapses usually in sternal recumbency. As they struggle to stand, they often show a loss of balance and fall to one side. When collapsed, the pelvic limbs are hypotonic and patellar reflexes are absent. For 3 to 5 minutes after the end of the exercise they often get worse. In severe cases, all four limbs are affected. After 15 to 20 minutes of rest, complete recovery occurs.

The anatomic diagnosis is not clear. It is unlikely to be solely neuromuscular as these dogs are not short-strided and some evidence of balance loss is present. It seems likely that the collapse reflects some loss of caudal brainstem UMN facilitation of the central pattern generators and includes some deficiency of vestibular nuclear function. Significant hyperthermia (107-108F) and panting are present in these collapsed dogs which is similar to normal Labrador Retrievers that do not collapse. All ancillary metabolic studies are normal. No lesions of the nervous or musculoskeletal systems are observed at autopsy.

Genetic studies have determined that this syndrome is inherited as an autosomal recessive disorder. A mutation in the dynamin 1 (DMN1) gene has been identified in affected dogs. DMN1 is a protein involved in repackaging neurotransmitters into synaptic vesicles for release in the brain and spinal cord and is required when there is an increase demand for neurotransmitters as occurs during intense exercise. DNA testing for this gene can be obtained at the College of Veterinary Medicine at the University of Minnesota.

Be aware that if dogs with this disorder are excessively exercised, they may collapse and die.
INFRASPINATUS CONTRACTURE
This occurs primarily in hunting dogs that are in the the field and thought to step in a depression or hole that causes them to overextend one thoracic limb. The distal end of the spine of the scapula is adjacent to where the tendon arises from the infraspinatus muscle. Overextension of this joint forces the distal end of the scapula into the infraspinatus muscle-tendon junction causing injury to that muscle. The affected dog walks lame for a few days, followed by a period of normal gait. After a few weeks to months, this dog will develop an unusual posture and action in that thoracic limb but without any evidence of discomfort. When the dog bears weight on standing, the humerus at the shoulder is partially rotated laterally which positions the elbow more medially under the thorax. When the dog protracts the limb to walk and the affected limb is not weight bearing, the humerus suddenly further rotates laterally causing the elbow to assume a more medial position. The paw will appear to be positioned more laterally during the stride. All of this is the result of the healing of the torn infraspinatus muscle which resulted in fibrosis and a shortening of the muscle. This shortened muscle causes a passive but persistent excessive lateral rotation of the humerus at the shoulder joint and the characteristic gait that represents this disorder. If you stand over this affected dog when it is bearing weight on both thoracic limbs, grasp both brachia and rotate them medially and laterally, you will feel resistance to medial rotation of the humerus at the shoulder of the affected limb. Surgical removal of the fibrotic portion of this affected infraspinatus muscle should correct the abnormality.

FIBROTIC MYOPATHY OF THE CAUDO-MEDIAL THIGH MUSCLES
This is the name of a disorder that is poorly understood. It is most common in large breed working dogs, especially the German Shepherd Dog. The pelvic limb gait disorder is usually a subtle change unassociated with any recognized traumatic experience or any discomfort in the use of the affected pelvic limb. When these affected dogs walk, at the end of the protraction (swing) phase of the affected pelvic limb, the paw is abruptly slightly elevated as the stride is prematurely stopped and it is turned slightly medially. This medial rotation of the leg and paw can be seen at the stifle. This is considered to be due to a fibrosis of a caudomedial thigh muscle that inserts on the
proximomedial surface of the tibia. The fibrosis is thought to be due to an injury of the affected muscle followed by healing with fibrosis that resulted in a shortened muscle. Most commonly the gracilis and semitendinosus muscles have been implicated. This might occur following intramuscular injections of large volumes of drugs into these muscles but most of these dogs do not have this history and the onset of clinical signs is usually insidious. Surgical removal of a portion of the affected muscle has had variable success as the clinical signs have often recurred a few weeks to months postoperatively.

On two occasions, surgeons have submitted the muscle that they removed for study and in each dog, on one side of the muscle specimen, a prominent longitudinal band of collagen was present in the epimysium with no lesion in the muscle itself. Why and how this band of connective tissue develops remains an enigma. From a practical viewpoint, if you make this diagnosis, consider leaving the dog alone as this band does not cause obvious discomfort or interfere with their physical activity at all.

**PERIPHERAL VS. CENTRAL VESTIBULAR SYSTEM CLINICAL SIGNS**

A lesion limited to the vestibular nerve causes a head tilt, loss of balance and an abnormal nystagmus. There is no upper motor neuron paresis and no general proprioceptive ataxia. The affected dog knows exactly where its limbs are located and can generate very fast normal limb movements to help compensate for its loss of balance. Postural reactions are **normal**.

Lesions in the caudal brainstem (pons and medulla) that affect the vestibular nuclei also cause a head tilt, loss of balance and abnormal nystagmus. **However,** these lesions also usually affect the adjacent tracts and reticular formation nuclei which results in a variable degree of upper motor neuron paresis and general proprioceptive ataxia. Postural reactions are **abnormal**. Cranial nerve involvement other than VII and VIII also implicates a brainstem anatomic diagnosis

A unique form of central vestibular disease is referred to as **paradoxical vestibular syndrome** in which the head tilt and balance loss are directed toward the side opposite to the central lesion which usually involves one caudal cerebellar peduncle. An explanation for this
paradox is based on the rule that the direction of the head tilt and balance loss is towards the side of least vestibular system activity. With peripheral vestibular system disorders such as otitis interna, the loss of facilitatory activity of vestibular nerve axons results in decreased activity of the ipsilateral vestibular nuclei. The head tilt and balance loss are directed towards this decreased vestibular nerve activity. In the cerebellum, the Purkinje neurons of the flocculus and nodulus are unique in that instead of projecting to a cerebellar nucleus, these inhibitory neurons project directly via the caudal cerebellar peduncle to the ipsilateral vestibular nuclei. When this pathway is interrupted, the overactive, disinhibited vestibular nuclei cause a head tilt and balance loss directed to the opposite side.

CEREBELLAR CORTICAL ABIOTROPHY
Cerebellar cortical abiotrophy is most common in dogs and in most breeds consists of a progressive premature degeneration of Purkinje neurons as the primary lesion. In most breeds the clinical signs are first observed at a few weeks of age and progress at a variable rate. Advanced lesions can be recognized on T2W median plane images where the sulci between dorsal vermal folia are enlarged secondary to the atrophy of the cerebellar cortex. In the Kerry Blue Terrier and Chinese Crested breeds, following the clinical signs of Purkinje neuronal abiotrophy, other systems in the brain degenerate which is the basis for this being called a multiple system degeneration in these two breeds. A late onset of many years before clinical signs of Purkinje neuronal degeneration is recognized has been reported in the Gordon Setter, Old English Sheepdog, Scottish Terrier, American Staffordshire Terrier, and Brittany Spaniel. At the onset, the clinical signs are subtle and they progress slowly. In many of these breeds a genetic mutation has been identified and genetic testing for the identification of carrier animals is available. When the clinical signs of cerebellar ataxia are subtle in the early stages of the abiotrophy, we have found that having the patient climb or descend stairs will markedly exacerbate the ataxia.

SCOTTIE CRAMPS VS. CEREBELLAR CORTICAL ABIOTROPHY
Scottie cramps is an example of a movement disorder which is defined as an episodic, uncontrolled, involuntary contraction of various muscle groups in a conscious patient with a normal sensorium during rest or
activity. In the Scottish Terrier this has been related to an abnormal metabolism of serotonin resulting in a decrease in its activity. In subtle cases, methysergide, which blocks serotonin receptors, will increase the incidence and severity of the clinical signs. This disorder is inherited as an autosomal recessive gene. This is an episodic disorder associated with activity.

In cerebellar cortical abiotrophy, the clinical signs may be subtle but are ALWAYS present whereas the clinical signs in Scottie cramps are EPISODIC and associated with activity. In addition, the cerebellar ataxia will be exacerbated when the dog goes up or down stairs.

**UNILATERAL PROSENCEPHALIC ANATOMIC DIAGNOSIS** is associated with three clinical signs.

1. Normal gait (unless an acute episode): Contralateral postural reaction deficits
2. Contralateral visual deficit with normal pupil size and responses to light.
3. Contralateral hypalgesia of entire surface of patient: Test nasal mucosa

**CASE EXAMPLE**

9-year-old female Toy Fox Terrier

3 seizures in 2 months, less responsive for 1 month, recent circling to the left.

**Anatomic Dx:** Left prosencephalon

**Differential Dx:**

Neoplasm

Inflammation: Small breed, young adults develop meningoencephalitis of unknown cause which may represent a disorder of the immune system in these patients.

**GME-Granulomatous meningoencephalitis:** A vessel-related lesion (angiocentric), diffuse in white matter of cerebrum, cerebellum, brainstem or spinal cord. Lesions consist of large perivascular cuffs of lymphocytes, plasma cells and histiocytes or an accumulation of these affected vessels in a granuloma-like lesion. No infectious agent has been identified. Possibly this involves a lymphoproliferative disorder. This is presently considered to be a dysregulation of the immune system.

**NME-Necrotizing meningoencephalitis:** Primarily an inflammation in
the cerebral meninges and inflammation and necrosis of the adjacent cerebral cortex with extension into the white matter of the corona radiata. May also affect the hippocampus and thalamus (ie. Pug Dog encephalitis)

Considered to be a disorder of the immune system.

NLE-Necrotizing leukoencephalitis: Primarily in the deep prosencephalic white matter with cavitation of the internal capsule and thalamocortical projections. Lesions may also occur in the hippocampus, mesencephalon and cerebellum. This disease is common in Yorkshire Terriers. Considered to be a disorder of the immune system.

NORMAL CUTEREBRA SPECIES LIFE CYCLE
Spring: Bot fly hatches from pupa in the soil and lays eggs on browse. Body heat of host (rabbit) hatches the egg. This first stage larva attaches to host’s hair coat, migrates to a body opening (usually the mouth) and enters the submucosa and migrates to the host species-selective subcutaneous site. Here it molts to a 3rd stage larva, forms a pupa and opens to the skin surface. The pupa drops to the ground where it spends the winter months.

CUTEREBRA SPECIES LIFE CYCLE IN THE CAT:
This may be the same as in the normal host species. However, if the 1st stage larva enters the nasal cavity, it migrates caudally and may migrate through the cribiform plate of the ethmoid bone to enter the cranial cavity and the brain where it is unable to complete the life cycle. Clinical signs of sneezing may reflect this migration through the nasal cavity. Neurological signs reflect the areas of the brain involved in the migration as well as areas deprived of their blood supply from arterial thrombosis. The middle cerebral artery is a common site for this thrombosis and the basis for the designation feline ischemic encephalopathy.

In cats, the intracranial migration of a Cuterebra larva is the most common cause of thrombosis of the middle cerebral artery. T2 weighted MR images will show the ethmoidal bone destruction and the parasitic tract within the brain parenchyma. In addition, the surface of the invaded cerebral hemisphere may show a hyperintensity which reflects
a degeneration of the surface of the cerebral cortex. This degeneration may be due to the toxic effect of secretions from the invading larva that gain access to the cerebrospinal fluid.

Be aware that hyperthyroid cats are at risk for developing hypertension and subsequent vascular compromise in the brain resulting in ischemia or infarction. On rare occasions, hypothyroidism in dogs has been associated with cerebrovascular atherosclerosis and acute compromise of their blood supply.

**UNCONTROLLED INVOLUNTARY SKELETAL MUSCLE CONTRACTIONS IN A CONSCIOUS PATIENT:**

**MUSCLE OR NEURONAL ORIGIN**

**MUSCLE ORIGIN:**

**MYOTONIA** – This is a sustained contraction of muscle fibers, a delay in relaxation, a repetitive depolarization of muscle cell membranes. It is a muscle cell disorder.

**INHERITED NON-DYSTROPHIC MYOTONIA**

Inherited non-dystrophic myotonia is often referred to as congenital myotonia although the clinical signs are not usually observed before a few weeks of age. It has been observed in Pygmy goats, Montadale sheep, Murrah water buffalo, and Chow Chow and Miniature Schnauzer dogs. Where it has been studied, a mutation has been found in the chloride channel 1 DNA. The sarcolemmal chloride channel 1 has a role in membrane repolarization after muscle cell contraction. The myotonia reflects the delay in muscle cell relaxation. This is inherited as an autosomal recessive gene. DNA testing of Miniature Schnauzer dogs is available through the University of Pennsylvania: www.vet.upenn.edu/penngen

**INHERITED DYSTROPHIC MYOTONIA – MUSCULAR DYSTROPHY**

Dystrophinopathy (Duchenne muscular dystrophy). Myotonia occurs in many of the affected muscle groups.

**ACQUIRED MYOTONIA**
Chronic hyperadrenocorticoidism is a cause of myotonia and is most often due to inappropriate prolonged corticosteroid therapy.

**NEURONAL ORIGIN:**

**TETANUS, TETANY, MYOCLONUS, MOVEMENT DISORDER**

**TETANUS:** Tetanus is a tonic sustained contraction of extensor antigravity muscles that is NOT INTERMITTENT. Diffuse and focal forms exist. The clinical sign of tetanus most commonly follows infection with *Clostridium tetani* and its production of tetanospasmin which interferes with the release of the inhibitory neurotransmitter glycine from spinal cord interneurons and gamma aminobutyric acid from brainstem interneurons. Tetanus refers to both a clinical sign as well as to a disease.

**TETANY:** Tetany is an INTERMITTENT tonic sustained contraction of extensor antigravity muscles. An autosomal recessive inherited congenital tetany occurs in Polled Hereford calves that was incorrectly published as myoclonus. This mutation results in an abnormal alpha 1 subunit of the neuronal glycine receptor. Glycine is an inhibitory neurotransmitter. This disinhibition of alpha motoneurons results in tetany. There are no lesions in the nervous system. In humans, this is referred to as hyperekplexia or startle disease because of the abrupt onset of tetany when stimulated by physical, visual or auditory stimuli.

A similar disorder occurs in Labrador Retrievers and was published as “familial reflex myoclonus”. However, this is a tetany and not a form of myoclonus.

**MYOCLONUS:** Myoclonus is a sudden contraction of muscle cells immediately followed by relaxation. Sporadic and repetitive forms are recognized.

**SPORADIC MYOCLONUS:** This is either benign or a component of a seizure.

**REPETITIVE MYOCLONUS:**

**CONSTANT:** Constant myoclonus occurs during activity, rest and sleep and is a presumptive disorder of the involved central pattern generators. This myoclonus is commonly related to canine distemper viral encephalomyelitis. Some dogs respond to procainamide or mexiltiline.
ACTION RELATED: Action related repetitive myoclonus occurs in the awake animal that is contracting muscles for posture or movement. It appears as a tremor and requires a diffuse CNS myelin or axonal disorder.

CONGENITAL ACTION-RELATED REPETITIVE MYOCLONUS:

SWINE: HYPOMYELINATION – DYSMYELINATION
Viral: Hog Cholera, Swine Fever, Circa Inherited: Landrace, British Saddleback breeds Toxic: Trichlorfon

RUMINANTS:
CALVES: HYPOMYELINATION-DYSMYELINATION
Bovine virus diarrhea virus

CONGENITAL CEREBRAL EDEMA
Autosomal recessive in Herefords

LAMBS: HYPOMYELINATION
Border disease virus

HORSE: ARABIAN FOALS: Inherited diffuse CNS axonopathy

DOGS: HYPOMYELINATION-DYSMYELINATION
Presumptive inheritance in Samoyeds (lethal) and Dalmatians (recover)

ACQUIRED ACTION-RELATED REPETITIVE MYOCLONUS

MENINGOENCEPHALITIS: This is mild, diffuse and responsive to corticosteroid therapy. Occurs most commonly in small breeds often with a white hair coat. MR images are usually normal. CSF is normal or indicates a mild inflammation. Complete recovery follows treatment with corticosteroids. TOXICITY: This may cause diffuse myoclonus (tremors) followed by seizures, coma and death. Examples include metaldehyde (snail bait), pyrethrins, lead, hexachlorophene, chlorinated hydrocarbons, organophosphates, macademia nuts, and numerous mycotoxins.

POSTURAL REPETITIVE MYOCLONUS
This benign action related myoclonus occurs primarily during weight support of the affected part and not during movement. It involves the head and neck in young dogs and is common in Doberman Pinschers and English Bulldogs. It may occur in episodes. This may occur in the pelvic limbs of old dogs of any breed.

An orthostatic postural repetitive myoclonus occurs in young adult
Great Danes. The tremors are associated with standing or during efforts to lie down or when posturing to eat or excrete. They are absent when the patient is recumbent or moving at a walk, trot or run or when picked up. This disorder is slowly progressive despite therapy with gabapentin (10-20 mg per os bid) which may decrease the intensity of clinical signs.

**MOVEMENT DISORDERS**
A movement disorder is an involuntary spontaneous contraction of skeletal muscles in a conscious patient with a normal sensorium during rest or activity. Some of the terms used for these involuntary movements include:
- **Chorea:** an abrupt, nonsustained contraction of different muscle groups in the same patient.
- **Dystonia:** a sustained involuntary contraction of a single group of muscles.
- **Tetany:** a sustained contraction of extensor muscles that is variably intermittent.
- **Athetosis:** a prolonged contraction of trunk muscles causing a bending or writhing motion.
- **Ballism:** an abrupt contraction of limb muscles causing a flailing movement.

Repeated examples of a movement disorder have been observed in the Scottish Terrier, (Scotty cramps), Bichon Frise, Cavalier King Charles Spaniel (tetany, deer stalking), Soft Coated Wheaton Terrier, Boxer (paroxysmal dystonic choreoathetosis), Norwich Terrier and the Border Terrier (paroxysmal dystonic choreoathetosis, Spike’s disease).

**SEIZURES:**
Any patient that experiences a seizure has a disorder within its prosencephalon that alters the environment of neurons to a level below that patient’s seizure threshold. The prosencephalon is the anatomic diagnosis for any seizure disorder. The period of the seizure is the *ictus*. The period of depressed cerebral function after the seizure is the *postictal* period which can last from a few minutes to an hour or more in small animals, and more than a day in horses. The *interictal* period is the period between seizures when the patient should have a neurologic examination.

**EPILEPSY:** Epilepsy means that the patient has more than one seizure, regardless of cause. An animal that has two or more seizures has epilepsy.

**SEIZURE CLASSIFICATION:**
Seizures may be classified by type and etiology. Defining the type of seizures does not per se support a specific etiology or choice of anticonvulsant therapy in veterinary patients in our experience. There are two types of seizures: generalized and focal.

**Generalized seizures** are the most common in domestic animals. A generalized seizure results when there is a sudden disinhibition of neurons in both cerebral hemispheres. This disinhibition may be initiated in one hemisphere and rapidly spread to the other hemisphere via the corpus callosum or it may spread to the thalamus which in turn spreads the disinhibition to both hemispheres through its neurons that function in the diffuse cortical projection system. In some patients, the disinhibition may be initiated in the thalamus and spread to both hemispheres from there. Most commonly, the result is a loss of the conscious state by the patient, a tonic contraction of most of the antigravity skeletal muscles, recumbency followed by periods of rigidity (tonic muscle contractions) and uncontrolled thrashing of the head, neck, trunk and limbs (clonic muscle activity). Running-like movements of the limbs occur along with jaw clinching or chewing movements, sialosis, dilated pupils, hair erection, and sometimes urinary and fecal excretions. This is the form of seizure observed in the 9-year-old Quarter Horse in the web site Video 18-1 and is the most common form observed in domestic animals. Apnea may occur during a tonic phase of the seizure. A generalized seizure usually lasts from 30 seconds to 3 minutes, followed by a variable period of postictal clinical signs and then complete recovery.

This form of generalized seizure is sometimes referred to as a *grand mal seizure*. *Petit mal seizures* that are described in humans consist of brief lapses in the conscious state with a specific electroencephalographic pattern. This type of seizure has not been recognized in domestic animals and this term should be discouraged in veterinary medicine.

A generalized seizure also includes those patients that exhibit episodes of profound somnolence, an episodic change in behavior, bilateral blindness, chewing movements with salivation, bilateral facial twitching, mydriasis, tearing, and urine and fecal excretions. The patient may remain standing during these episodes. It is presumed that these patients are experiencing disinhibition of cerebral neurons in both hemispheres but to a lesser degree than the recumbent thrashing patient and limited to specific populations of neurons. It is important to carefully describe in the medical record the appearance of the seizure to better document recurrent episodes.

A **focal seizure** occurs when the disinhibition is confined to one cerebral hemisphere and the uninhibited muscular activity occurs only on the
opposite side of the patient’s body. Focal seizures that involve uncontrolled muscle activity on one side of the body or a specific part of one side of the body strongly indicate a seizure focus in the contralateral cerebral hemisphere but these are rare in animals. An example of this can be seen in the web site Video 18-12 that shows a 20-year-old palamino Saddle Horse with episodes of muscle twitching on the right side of the body presumably caused by the injury to its left cerebral hemisphere associated with an adjacent calvarial fracture. Another example is a 10.5-year-old Boxer Dog with brief episodes of profound unilateral tearing with a normal ocular exam and an altered mentation. The MRI in this patient revealed a large intraparenchymal mass, contralateral to the side of the tearing. It is assumed that the episodes of tearing represent focal seizures. The frequency of these episodes was dramatically reduced with anticonvulsant therapy. In many instances a seizure may begin as a focal event but then generalize with the uncontrolled muscular activity occurring on both sides of the patient. Focal motor seizures may be difficult to differentiate from a movement disorder. Recognition of a focal seizure and the associated contralateral seizure focus does not automatically allow for the conclusion of a mass lesion. The addition of further characterizing names is of no value in determining the anatomic diagnosis or the cause of the seizures.

**SEIZURE ETIOLOGY:**

The etiology of seizures includes idiopathic, genetic and structural disorders.

**IDIOPATHIC:** This is epilepsy where the cause of the seizures is unknown based on a normal clinical examination and normal CSF evaluation and MR imaging.

**GENETIC:** This is epilepsy where an inherited or a genomic basis has been determined as the cause of the seizures. All ancillary studies including CSF analysis and MR imaging are normal.

**STRUCTURAL:** These epileptics include acquired and genetic disorders of the prosencephalon such as malformation, inflammation, neoplasia, injury, degeneration, metabolic disorder and toxicity. This includes both intracranial as well as extracranial disorders that affect the prosencephalon.