

Clinical Neurology: What do we know, what, do we don't, and everything else in Between!

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Clinical Neurology has evolved as a specialty focus over the last 50+ years. The focus and expertise in clinical neurology has expanded our collective knowledge of neurologic disease pathology, pathophysiology, diagnosis, treatment, and prognosis. What follows is a compilation of perspectives have been generated through clinical observation and scholarly activities. Some of the following statements, observations, and opinions are purely based on anecdotal experiences and therefore should be located at the bottom of the Evidence-based pyramid. However, some may be true. These are all open to discussion and criticism. A great goal for veterinary medicine in general would be to eliminate patient morbidity and mortality which results from ignorance, arrogance, or misdirected ego. Also, we are now existing in an "evidenced-based" medical society. Unfortunately, **over 50%** (and probably more like **90%**) of what we do everyday in veterinary medicine is not evidenced based. There are things we know we know, things we know we don't, and a lot in between that we either don't know we know or know but we really don't.

General

- Clinical signs suggest the location of the lesion, not the etiology – don't definitively diagnosis based on clinical signs alone
- There are exceptions to every rule (all generalizations are false including this one)
- Very few diseases of the nervous system result in pathognomonic clinical signs ("you are only as good as your differential list!") – expand your thought process
- What you "label" it as is very important

- *Ataxia*: Usually associated with diseases of the cerebellum, vestibular system, or spinocerebellar tracts in spinal cord. Possibly associated with disease in other intracranial structures.
- *"Bunny-hopping"*: Seen with various diseases of the spinal cord, peripheral nerves, NMJ, and muscle. May also be seen with musculoskeletal diseases of the pelvic region and limbs. Occasionally seen with diseases that affect vascular perfusion to the pelvic limbs (right to left PDA).
- *Dragging of the feet on dorsal aspect of paw*: Consider abnormalities of conscious proprioception. May be associated with either UMN or LMN diseases. Could be indicative of the lesion in either the intracranial structures, spinal cord, or peripheral nerves.

- *Dysmetria*: Improper measurement of range and force in muscular act, usually associated with diseases of the cerebellum, vestibular system, or in spinal cord (spinocerebellar tracts). Possibly associated with disease in other intracranial structures.
- *Hypermetria*: Voluntary muscular movement results in overreaching of the intended goal, often resulting in high-stepping. Usually associated with diseases of the cerebellum, vestibular system, or in spinal cord (spinocerebellar tracts). Possibly associated with disease in other intracranial structures.
- *Hypometria*: Voluntary movement falls short of the intended goal.
- *Lameness*: Reduced ability or desire to bear weight on a limb due to pain or a mechanical restriction of normal joint movement. In severe instances the limb may be held in a flexed position. Usually indicative of a pain in or around the limb. May be associated with musculoskeletal or soft tissue disease of the limb. May also be associated with pain from a peripheral nerve or spinal cord condition.
- *Myotonia*: Consider diseases of muscle including congenital abnormalities, muscular dystrophies, nutritional myopathies, toxicity (herbicide), and hyperadrenocorticism.
- *Nerve root signature*: A persistent or episodic non-weight-bearing lameness, presumably the result of nerve irritation and pain. Consider diseases that involve peripheral nerves or spinal cord segments in or around the affected limb.
- *Overstepping or overreaching with a limb*: Consider UMN diseases of either the spinal cord or intracranial structures, including vestibular and cerebellar disease. May be seen with supratentorial diseases primarily in the thoracic limb contralateral to the supratentorial abnormality.
- *Paralysis (-plegia)*: Inability to voluntarily move. Usually associated with severe lesions of the spinal cord or peripheral nerves.
- *Paresis*: May be associated with UMN or LMN diseases.
- *Shortened step distance*: Consider diseases associated with muscle weakness, pain (limbs or spine), and other LMN (peripheral nerve, NMJ, or muscle) weakness.
- *Spasticity*: Increased extensor tone of muscles, most often seen in the limbs. Usually indicative of a UMN abnormality (intracranial or spinal cord).
- *Stiffness*: Decreased range of motion and step length when moving. Consider diseases associated with muscle rigidity. If associated with a decreased step distance, consider pain, and LMN (peripheral nerve, NMJ, or muscle) weakness.
- *Wide-based stance*: Standing with the limbs placed more lateral than usual. Usually indicative of a UMN proprioceptive deficit. If involving the thoracic limbs, consider cervical or intracranial disease. If involving the pelvic limbs, consider spinal cord diseases.
- *"Dropped hock"*: Consider diseases of the peripheral nerve (sciatic), gastrocnemius muscle, calcaneon tendon, or calcaneus. Often seen with diabetic neuropathy in cats.

- *Decerebellate rigidity*: Characterized by opisthotonus with thoracic limb extension and flexion of the pelvic limbs up under the body due to contraction of the sublumbar muscles. Mental status is normal. Associated with diseases of the cerebellum.
- *Decerebrate rigidity*: Characterized by opisthotonus (extreme dorsal extension of the head and neck toward the back) and extension of all limbs; usually the animal is stuporous or comatose. Associated with midbrain lesions.
- *Extension (rigid, fixed) of a limb*: Consider myopathic or LMN disease. Seen in pelvic limbs with toxoplasmosis and neospora infection in young animals. Also consider UMN spasticity.
- *Falling*: Consider diseases of that result in weakness or ataxia. Often associated with vestibular or cerebellar dysfunction if animals fall to the side rather than straight ventrally. Can sometimes be associated with dysfunction of the intracranial structures, spinal cord, or peripheral nerves. Falling directly ventrally and becoming sternally recumbent may indicate syncope, cataplexy, other forms of muscle weakness.
- *Flexing of a limb*: Most often be associated with a painful reaction in or around the limb. Consider lameness, musculoskeletal or orthopedic abnormalities, nerve root signature (from spinal or peripheral nerve pain). If in the pelvic limbs of a Doberman pinscher, also consider Dancing Doberman syndrome.
- *Head tilt*: Assess for vestibular (central or peripheral) or cerebellar disease. Rarely associated with primary ear pain. Tilting is usually, but not always, toward the side of the lesion.
- *Head turn*: Usually associated with supratentorial diseases, usually structural. Head usually turns in the direction of the side of the lesion.
- *Kyphosis*: An abnormal flexion primarily of the thoracolumbar spine, results in a "hunched-back" appearance. Associated with cervical, abdominal, back pain; diseases of the spine or vertebrae; paraspinal muscle abscess. If occurs during walking may be associated with weakness.
- *Lordosis*: Abnormal extension of the vertebral column particularly in the thoracolumbar region; this results in a concave appearance of the vertebral column when the animal is viewed from the side. May be associated with muscle weakness, spinal disease, possibly abdominal pain.
- *Opisthotonus*: May be associated with decerebrate or decerebellate posture. Diseases of the central nervous system and brain stem.
- *Schiff-Sherrington posture*: Characterized by thoracic limb extension with normal tone and reflexes in the pelvic limbs; this results from a severe lesion between the third thoracic (T3) to lumbar spinal cord segments that interrupts the ascending inhibitory impulses to the extensor muscles of the thoracic limbs.
- *Scoliosis*: An abnormal lateral deviation of the vertebral column usually associated with spinal cord or vertebral diseases. Often associated with syringomyelia and other cystic spinal cord defects in animals.

- *Tetanus/tetany*: Extensor rigidity of the limbs, neck, trunk, and/or tail. If persistent, consider tetanus, other forms of muscle rigidity (myotonia). If episodic, consider muscle cramping, muscle depolarization, reflex myoclonus.
- *Torticollis*: A contracted state of the cervical muscles producing twisting of the neck and head. Usually associated with brain stem or cranial cervical abnormalities.
- *Ventral flexion of the neck*: Consider diseases associated with muscle weakness. In cats, consider diseases such as hypokalemic myopathy, myasthenia gravis, organophosphate toxicity, hyperthyroidism.
- *Anisocoria*: Consider diseases of the eyes, pupils, visual system, intracranial neurologic system, parasympathetic and sympathetic innervation to the pupils. Can occasionally be associated with cerebellar disease. The miotic pupil may be too small, or the mydriatic pupil may be too large.
- *Anosomia*: Usually associated with nasal diseases, viral infections. Rarely occurs with intracranial diseases (olfactory bulb area).
- *Dysomia*: Usually associated with nasal diseases, viral infections. Rarely occurs with intracranial diseases (olfactory bulb area).
- *Blindness (visual deficit)*: Consider diseases of the eye, ocular pathways, and intracranial structures necessary for visual integration.
- *Corneal ulcer*: Consider primary corneal disease, often the result of poor corneal sensation (cranial nerve V), corneal dryness (cranial nerves V and VII), or inability to protect the eye through blinking (cranial nerve VII).
- *"Dropped jaw"*: Inability to close the jaw-usually due to bilateral trigeminal nerve disease, possibly due to TMJ locking or jaw fracture.
- *Facial asymmetry*: Unequal facial expression; usually due to disease of the facial nerve.
- *Hemifacial spasm*: Persistent contraction of the muscles of facial expression on one side; most often associated with disease of the facial nerve, internal ear disease.
- *Megaesophagus*: Dilated esophagus due to numerous causes; often seen with cranial nerve, muscle, and neuromuscular junction disease; esophagitis; myasthenia gravis; esophageal parasites; esophageal reflux; vascular ring anomalies; lead toxicity; hypothyroidism; hypoadrenocorticism.
- *Miosis*: Consider diseases of the eye (painful eye, uveitis), abnormalities of sympathetic innervation to eye (Horner's syndrome or pupil), parasympathomimetic drug therapies or toxicity (pilocarpine, organophosphate intoxication), supratentorial diseases.
- *Muscle atrophy (temporalis and masseter)*: *Bilateral*-consider disease of muscles such as masticatory myositis, age-related degeneration, disuse if associated with abnormalities of jaw movement or pain; *Unilateral*-consider disease of cranial nerve V.
- *Mydriasis*: *With blindness*-consider diseases of the eye, retina, and optic nerve. Possibly intracranial disorders such as brain herniation if the animal has concurrent severe alteration of consciousness; *With normal vision*-consider diseases of the pupil (iris atrophy, parasympatholytic drug therapies), abnormalities of parasympathetic innervation to eye (cranial nerve III abnormalities), supratentorial diseases, dysautonomia.

- *Neurotropic keratitis*: Loss of corneal integrity due to loss of innervation from the trigeminal nerve; suggests disease of the ophthalmic branch of CN V.
- *Nystagmus (spontaneous or positional)*: Consider vestibular or cerebellar disorders, inner ear disease.
- *Poor blinking, inability to close the eyelids*: Usually associated with poor palpebral reflex function and cranial nerve V or VII disease.
- *Ptosis*: Consider abnormalities of cranial nerve III or the sympathetic innervation to the eyelid. Gravitational ptosis may occur with facial nerve disease.
- *Regurgitation*: Usually indicates megaesophagus.
- *Salivation, excessive*: Consider local problems with the mouth (inflammation, tumor, toxicity, burn); hepatic encephalopathy (especially in cats); swallowing problems; cranial nerve V, VII, IX, and X disease; megaesophagus; nausea; facial muscle weakness.
- *Strabismus: Positional*-consider abnormalities of the vestibular system, possibly other intracranial structures; *Spontaneous or resting*-consider abnormalities of cranial nerves III, IV, or VI, or the extraocular muscles.
- *Swallowing abnormality*: Usually the result of cranial nerve IX and X dysfunction; can also be associated with some intracranial abnormalities and muscle lesions; Cricopharyngeal dysphagia.
- *Tongue paresis/paralysis*: Inability to use the tongue normally; often associated with disease of the hypoglossal nerve, occasionally seen with supratentorial abnormality.
- *Vomiting: Rarely a reflex of seizure activity; may be associated with vestibular disease.*

- **Abnormalities of Cognition and Awareness**

- *Abnormal mentation, stupor, or coma*: Consider supratentorial and infratentorial diseases. Also consider systemic disease processes that may secondarily affect intracranial functions.
- *Aimless wandering or walking*: Consider supratentorial and infratentorial diseases. Also consider systemic disease processes that may secondarily affect intracranial functions. Sometimes occurs in animals with pain such as from the abdominal cavity.
- *Circling, compulsive and unidirectional*: May result from either supratentorial or vestibular disease. Animals usually, but not always, circle in the direction of either a supratentorial or vestibular abnormality.
- *Compulsive (stereotypic) behavior*: Consider primary behavioral abnormalities, seizure activity, localized pain in the region of the animal's attention, or intracranial diseases.
- *Head pressing*: Usually indicates abnormalities of cognition, awareness, or consciousness. Consider supratentorial and infratentorial diseases. Also consider systemic disease processes that may secondarily affect intracranial functions.

- *Hemianattention*: Usually associated with supratentorial disease.
- *Narcolepsy/cataplexy*: Usually occurs without a definable pathologic abnormality. Rarely associated with anatomical disease of the brain stem. Some toxicities, such as organophosphate toxicity in cats, can result in similar appearing episodes.
- *Pacing*: Consider supratentorial and infratentorial diseases. Also consider systemic disease processes that may secondarily affect intracranial functions. Sometimes occurs in animals with pain such as in the abdominal cavity.
- *Seizures*: Consider diseases of the supratentorial structures. Also consider systemic metabolic diseases that secondarily alter intracranial function.
- *Syncope*: Short, episodic loss of consciousness that results from transient cerebral hypoxia or anoxia. Consider diseases of the cardiopulmonary and vascular systems, or autonomic nervous system.
- *Vocalizing*: May be indicative of a disorder of cognition, consider intracranial diseases and metabolic encephalopathies. Also consider as a reaction to pain, especially if associated with abnormal posturing, limb carriage, or movement.

Imaging- When, why, how?

One of the significant influences on the practice of veterinary neurology in the last 15 years has been the use of magnetic resonance (MR) imaging for evaluating intracranial, spinal, and even peripheral nerve disorders. Certainly the physics associated with the MR image production is complex, and the sequence choices requires some functional knowledge of the process of MR imaging, but what does the practicing clinician really need to know about MR as a diagnostic modality?

- MR should be used as a diagnostic modality if you are looking to define or exclude **structural (anatomical)** abnormalities of the nervous system
- Therefore, ask yourself during your clinical evaluation, "***Is this disease structural?***"
- From a cost/benefit standpoint, MR is financial more expensive, relatively patient safe, and the **gold standard** for anatomical imaging of the nervous system
- There are standard MR sequences that should be performed in animals
- Use a facility with **experience** in MR imaging of **animals**
 - **Positioning** of the patient (important)
 - Sequences (some better than others)
 - Experience with neurologic disease (got to know what you are looking for!)
 - Artifacts (what are they and when do they occur?)
 - **Who's** doing the **interpreting?**
- You still need to perform a physical (neurological) **examination** to know where to image (neuroanatomical localization) and to place the MR results in clinical **context!** (If you don't know where to look you will never find)
- MR imaging does not afford a histologic diagnosis
- MR imaging cannot be used to prognosticate

Intracranial Diseases

- A **variety of diseases** may affect the same region of the nervous system!
- Very infrequently, a disease process may have a characteristic group of clinical signs that help in the identification of that particular disease
- As clinical signs reflect the region of the nervous system that is involved with the disease process, but not the individual disease, multiple disease processes may result in similar clinical signs, and need to be considered as potential causes of the clinical signs.
- Disease processes described historically may be referred to by different names in the current era.

Seizures

- They happen a lot
- There is more than 1 clinical feature
- They can be hard to diagnose based on clinical signs
- Everyone has a device to electronically capture movement- do it!
- 3 General categories of causes, but numerous specific causes
- Treatment – a bunch – therefore none superior?
- Individualized treatment?
- How aggressively do you treat? Do all seizures stop?
- Valium works to acutely stop seizures if you give enough
- Corticosteroids help straighten out idiopathic epileptics that present in status epilepticus

Brain Tumors

- In a retrospective review of 97 dogs with brain tumors diagnosed at our hospital, 95% of the affected dogs were 5 years or older at the time of diagnosis.
- The median age of dogs diagnosed with brain tumor was 9 years (range 4 to 13 years).
- Seizures are sometimes the only sign of a structural intracranial abnormality with the remaining neurological examination findings being normal. This is especially true with more rostral and olfactory lobe lesions
- Meningiomas are the most common brain tumors in dogs and cats

Meningitis/encephalitis

- There are a lot of names but these may only be “fashion”
- Incidence of infectious agents causing meningitis varies with geographic location
- Cervical pain is common with intracranial disease
- In general, most encephalitis and meningitis syndromes (~ or greater 60 %) in small animals do not have a definable infectious cause.

- A non-infectious disease of the brain which is commonly **over-diagnosed** is **granulomatous meningoencephalitis (GME)**.
- All **breed-specific meningitis** is not the same
- Initial treatment for non-specific encephalitis without a definitive etiology: the “**inflammatory protocol**” (Trimethoprim sulfa, doxocycline, clindamycin, and corticosteroids)?

Head Injury

- Intravenous volume support (**fluids**) and **mannitol** are probably the most helpful
- 60% or greater of animals suffering a head injury will recover useful function
- Corticosteroids are **not** currently recommended for treatment of head injury in humans

Toxicity

- **Metronidazole toxicity** is commonly associated with neural toxicity in dogs and cats.
- **Vestibular signs** in dogs
- **Diazepam** may help speed up recovery

Cerebrovascular diseases

- Cerebrovascular diseases is **much more common** in dogs and cats than historically thought
- Underlying hypercoagulation is commonly a factor
- Hypertension may be a factor
- Disorders of coagulation (coagulopathies, DIC) and platelet function (thrombocytopenia and thrombopathies) may result in intracranial hemorrhage
- Many dogs improve

Spinal cord Disease

When you identify one disease, there may be more

Imaging

- Magnetic resonance imaging is far superior in imaging the spinal cord parenchyma and the associated spinal canal than other imaging modalities

All of the aforementioned statements regarding MR imaging of the head are also true for the spine

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Diseases

Intervertebral disk disease

- Intervertebral disk disease is **not** a simple disease process such as “Type I “ or Type II” (What about “Type III”?)
- There can be **extrusion** of disk material into the canal but also in other directions
- Lateral IVD extrusions result in painful animals
- Conversely, the annulus may be squeezed or bulged into the spinal canal, and this is commonly referred to as a **protrusion**.
- Intervertebral disk disease is also an important component of other spinal cord compressive diseases such as “wobbler’s” syndrome and lumbosacral stenosis
- Cats can get intervertebral disk disease
- Acute extrusions of otherwise healthy nucleus pulposus is **Very Common (see FCE)**!

Wobblers Syndrome

- Two general clinical presentations of this disease exist.
- One of these is classically seen in middle-aged to older Doberman pinschers.
- The disease as seen in the middle-aged to older Doberman is characterized by ventral compressive lesions of the caudal cervical area from ligamentous hypertrophy and intervertebral disk (usually annulus fibrosis) protrusion.
- Younger, large breed dogs such as the Great Danes, Mastiffs, and Saint Bernard’s have a similarly named disease, but most likely with a differing pathophysiology.

- In these younger and larger dogs there is disease of the dorsal articular facets with secondary hypertrophy of the associated joint capsules and ligaments.
- Is this disease associated with vertebral instability??
- The “best” surgical treatment is controversial
- What about the “domino” effect?

Lumbosacral Disease

- One of the most commonly over-diagnosed while at the same time under-diagnosed diseases of dogs (i.e. often misdiagnosed)
- Clinical signs may result from a variety of structural abnormalities in the lumbosacral region
- MR imaging can be difficult to interpret
- The “best” surgical treatment is controversial
- Is this disease associated with vertebral instability??

Degenerative myelopathy

- This disease is over-diagnosed if the diagnosis is based on clinical signs alone
- German shepherds have most commonly been diagnosed with this disease, however, other breeds may also be affected
- Don't forget about IVD
- A similar disease affects **Corgis** and other breeds

Spondylosis Deformans/Ventral Bridging Spondylosis

- Debate continues as to its clinical significance in animals with vertebral pain.
- While often this bony change does not cause obvious clinical disease, if the proliferative bone extends dorsally and laterally to compress exiting peripheral nerves, pain and limb dysfunction may result
- If spondylosis results secondarily to intervertebral disk disease, alterations in vertebral articulation resulting in pain may also occur.

Atlantoaxial subluxation

- When you see AA instability, look for other associated diseases
- Surgical treatment does not have to have a high morbidity and mortality rate
- What about the “domino” effect?

Syringomyelia and Hydromyelia

- Syringomyelia is one of the most commonly diagnosed diseases of the spinal cord.
- The pathologic mechanisms that result in syringomyelia and hydromyelia are many and varied and no single pathologic mechanism adequately explains all instances of the diseases.
- Often times syringomyelias is associated with posterior fossa abnormalities (referred to as Chiari malformations) or other abnormalities of the foramen magnum/cranial cervical spinal cord region
- A variety of clinical signs of spinal cord abnormality may be found including ataxia, paresis, and pain.
- Some Cavalier King Charles spaniels affected with syringomyelia in association with a malformation of the caudal aspects of the foramen magnum and brain stem (Chiari malformation) have an unusual facial rubbing behavior.
- Intramedullary cystic spinal lesions such as syringomyelia and hydromyelia have been associated with scoliosis and other spinal deformities (such as scoliosis) in dogs

Arachnoid cysts

- Spinal arachnoid cysts have been reported with increasing frequency in dogs. The term arachnoid cyst is misleading as there is extramedullary expansion and cord cavitation rather than cyst formation
- Additionally, there is no epithelial lining to the cyst
- A congenital etiology for lesion is most likely, although trauma has been implicated in both human beings and dogs
- Scarring of the pia or other meninges may result in the creations of pockets of CSF accumulation (“Pug scar”)
- Two more commonly affected breeds of dogs are Rottweilers and Pugs
- May be associated with fecal incontinence

External Trauma to the Spinal Cord

- Corticosteroids for spinal injury? Who knows?
- Braces or surgery?

Fibrocartilagenous Emboli

- A reasonable pathophysiologic explanation for this disease has been elusive.
- There are certain clinical features that have been commonly identified with fibrocartilagenous emboli and have been used to separate this disease from other similar spinal diseases, however these clinical signs are not pathognomonic.
 - Fibrocartilagenous emboli tends to occur in non-chondrodystrophoid breeds of dogs.
 - Clinical signs of spinal cord dysfunction occur acutely and progress rapidly.

- Affected dogs usually have no spinal hyperesthesia when examined, however, they may seem painful initially (within the first 24 hours) after onset.
 - In one study in Schnauzers, however, up to 30% of affected dogs had some degree of spinal pain.
 - Spinal cord involvement is usually asymmetric and the infarction commonly involves a spinal intumescence.
 - Therefore, LMN signs in one or more limbs are frequently seen. The signs are usually not progressive after the first 24 hours.
- When clinically suspected, many dogs thought to have FCE in the modern era have undergone evaluations with MR imaging as part of their diagnostic evaluation.
 - In a surprising number of these dogs, diseases other than FCE were found.
 - The most common of these diseases are acute, non-compressing nucleus pulposus extrusions (sometimes referred to as a Hansen's type III IVD).
 - In these instances, local associated spinal cord edema and probable contusion is found, however, the extruded intervertebral disk material has been dissipated within the spinal canal and therefore does not form a compressive mass.
 - An important clue to this disease, in addition to the focal spinal cord disease, is an alteration in the appearance of the nucleus pulposus within the associated annulus fibrosus of the intervertebral disk space.
 - These dogs often do not require surgery to recover

Peripheral Nerve Disease

- Peripheral nerve disease is often overlooked (more common than you think)
- Paraneoplastic neuropathies are often missed
- **Nerve sheath tumors** (Schwannoma, neurofibroma, neurofibrosarcoma) commonly involve any peripheral nerves and result in **pain** and **lameness!**
- **Muscle and nerve biopsy** the way to go for now