Bovine neurologic disease: Demystifying the workup

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Abstract

It is of paramount importance for a bovine practitioner to be proficient in performing a safe and effective neurologic examination that allows the veterinarian to confirm whether neurologic disease is present, and then localize the lesion or lesions to a particular neuroanatomic location. A careful and thorough evaluation involves a good history and signalment, a distance examination evaluating behavior, posture, and gait, and a complete physical examination followed by a thorough neurologic evaluation with a particular focus on mentation, cranial nerve assessment, postural reactions, spinal reflexes and presence or absence of sensation when applicable and possible. Once the clinician has identified the area of the neurologic system most likely to be affected, the list of differential diagnoses can be generated and a diagnostic and/or treatment plan can be instituted.

Key words: bovine, cattle, neurologic, disease

Résumé

Il est d'une importance capitale pour le praticien bovin d'être capable de faire un examen neurologique sécuritaire et performant pour lui permettre de confirmer si une maladie neurologique est présente et d'ainsi localiser la lésion ou les lésions dans un site neuro-anatomique particulier. Une évaluation soigneuse et approfondie demande de bons renseignements sur les antécédents et un examen clinique, un examen à distance pour évaluer le comportement, la posture et la démarche et un examen physique complet suivi d'une évaluation neurologique complète avec un accent sur la lucidité, l'examen des nerfs crâniaux, les réactions posturales, les réflexes spinaux et la présence ou l'absence de sensation si applicable. Lorsque le clinicien a identifié les parties du système nerveux qui semblent affectées, la liste des diagnostics différentiels peut être établie et un diagnostic et/ou un plan de traitement peuvent être instaurés.

Introduction

Conducting an effective neurologic examination on a bovine patient, and particularly an adult bovine patient, can at times seem like a daunting task. This is particularly true the first few times the exam is performed. However, while many components of a neurologic examination in smaller patients cannot physically be achieved in adult cattle, an effective exam can still be accomplished and has the goal of allowing the veterinarian to confirm that neurologic disease is present, and then localize the lesion (or lesions) to a particular area of the nervous system. This in turn drives the generation of an appropriate differential diagnosis list, and then either determines additional diagnostics that could be performed or else delineates potential treatment approaches depending on the available facilities, value and use of the animal, and client budget. If the opportunity arises, it is an excellent idea to perform the neurologic exam (to the extent possible) on a neurologically normal bovine at least a few times.

Neurologic assessment includes obtaining as much information as possible regarding mentation, behavior, posture, gait, postural reactions, musculoskeletal palpation and assessment, cranial nerve and reflex exam, and when possible, spinal nerve and reflex exam. However, always bear in mind that there is some amount of risk involved in performing this exam in larger cattle, based on their temperament (and particularly whether they are aggressive), whether or not they may fall during the exam, and the potential for zoonoses such as rabies.

Neuroanatomic Lesion Localization

Neurologic lesions should be localized to 1 general region of the brain, spinal cord, or peripheral nerves, unless they are suspected to be multifocal which is relatively less common. In cattle, central nervous system (CNS) lesion localization can be simplified if lesions can be considered as located in 1 of 8 general regions in the CNS, 3 in the brain and 5 in the spinal cord. The 3 regions of the brain include the **forebrain (cerebrum and diencephalon,** sometimes described as the thalamocortex[7]), **brainstem (midbrain or mesencephalon, pons, medulla oblongata**[10]), and **cerebellum** (Figure 1). Spinal cord segments can be generally grouped as C1-C5, C6-T2, T3-L3, L4-S1, and S1-Cd (caudal SC segments)[6] (Figure 2). Lesions affecting only peripheral
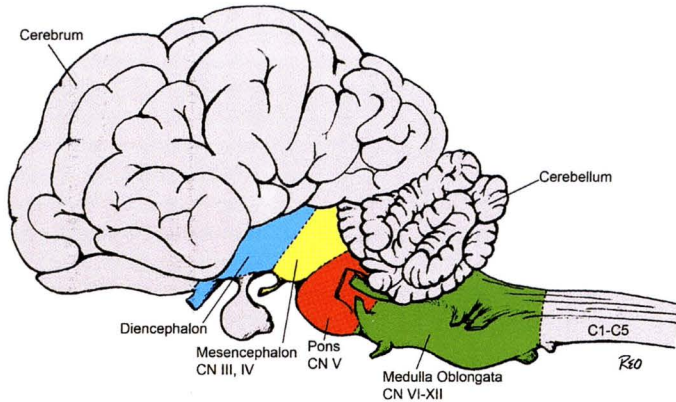
Figure 1. Basic regions of the brain and location of cranial nerve nuclei for neuroanatomic lesion localization.
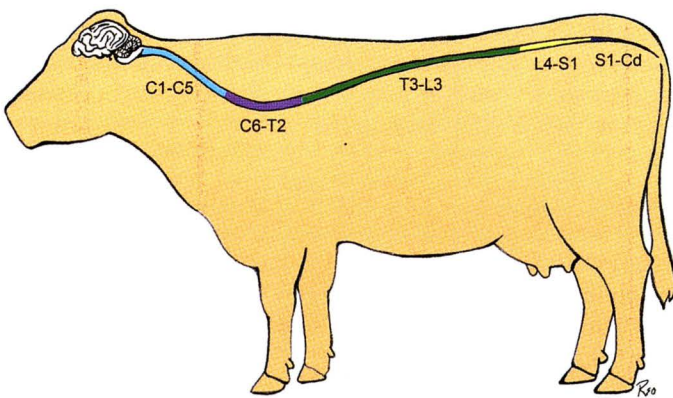
Figure 2. Basic regions of the spinal cord segments for neuroanatomic lesion localization.

nerves, whether cranial or spinal, must also be considered. Neuromuscular junctions, muscles, and the autonomic nervous system may also be the site affected.[8]

Signalment and History

Signalment should be obtained, including age, sex, breed, use, and stage of production. It is also very important to establish onset, duration, progression, and symmetry of the clinical signs the owner or herd manager has witnessed. However, range cattle may not be seen every day (or even every few days) which can complicate effective history taking. Any information on posture, movement, mentation, and behavior (particularly interactions with other animals or people) is very helpful. Assessment of potential endocrine dysfunction, including whether there has been a change in weight or body condition, hair coat, and whether hydration and urination have been normal is also critical. When possible, evaluation of the environment and feed and water sources can also be performed; this is particularly helpful in cases where a nutritional or toxic etiology is suspected. Enquiring about nutrition and water source(s), housing,

location, vaccination and deworming history, treatment for ectoparasites, previous medical history, and response to any treatments administered is key. Establishing whether other cattle (or even other species) are also affected, and whether other diseases have been noted in the herd previously, is also very informative in narrowing down a differential diagnoses list. Determining what the client's expectations are is also very helpful in formulating a plan for potential diagnostics and treatment.

Distance Examination

Visual assessment of the animal from a distance is often very instructive in cases of cattle with neurologic disease. Observing the patient's interaction with the environment can help the practitioner begin to develop a general idea of the neuroanatomic lesion localization. If aggression, head pressing, aimless wandering, bumping into inanimate objects, or abnormal vocalization s noted, a forebrain (cerebral) lesion should be suspected. If the animal cannot be observed in its normal environment because it has been hauled to a clinic, inquiring about the behavior of the animal at home and during loading into the trailer for transport is of paramount importance. Many blind animals are difficult to load into a trailer, and this is often noticed by the hauler or client. Observe the animal ambulating; watch for evidence of coordination (incoordination implies ataxia) as well as presence or absence of weakness.[5] Also observe the animal at rest and their stance, including their posture. Posture of the head (tilt or turn), trunk, and limbs (abnormal positioning, weakness, knuckling, base-wide or base narrow stance) should be noted.[5] Also note whether or not muscle wasting is present in any of the limbs, and whether head carriage and neck positioning appear normal. Observe recumbent animals, and how they rise if they are able to. Cattle should rise in the hind-end first. Remember that musculoskeletal diseases and disorders can result in muscle wasting from disuse atrophy, and must be differentiated from those that are of primary neurologic origin. Musculoskeletal problems are more commonly encountered.[8]

Close Up Examination

If the animal appears ataxic or has an abnormal gait but is amenable to at least some close up interactions, a more thorough evaluation of ambulation can be performed. It is generally a good idea to do this prior to restraint in a head-catch or chute. The reason this is important is that a weak or ataxic animal may go down in a chute and not be able to get back up. It is often advantageous to work up neurologic cattle in a location that a recumbent animal can be easily moved away from, such as a chute with a side release, or in an alleyway or stall with a side gate that can be opened. Weakness can be assessed by walking behind the animal and pulling the tail from each side to evaluate resistance to the

pull and whether there is weakness, and also if the weakness is symmetrical or asymmetrical. An adult bovine that has normal strength should be able to maintain course when the tail is pulled from 1 side when it is standing or walking. This cannot be performed safely in every patient due to temperament.[12] Keep in mind that weak or ataxic cattle may fall and injure themselves and/or the examiner(s). If the animal is halter-broken, circling them in both directions, walking up and down a gradient, and walking over a curb several times is useful in determining if gait abnormalities exist.[5] Walking on a slippery surface, such as a concrete floor, should be avoided to minimize the risk of the animal slipping and falling. Postural reactions including wheelbarrowing, hopping, hemistanding and hemiwalking, placing, and conscious proprioception are performed with the patient standing still and can be performed in young calves. In adult cattle, conscious proprioception is the only postural reaction that can be assessed,[5] and generally only in very calm animals; this is performed by knuckling each foot onto its dorsum and then releasing it. The foot should be immediately replaced into a normal position. Abnormal responses to postural reactions include paresis, proprioceptive deficits, spasticity, and dysmetria; these can be symmetrical or asymmetrical.

Once the patient is restrained, a complete physical examination should be performed. This includes the most complete neurologic assessment that can be accomplished given the patient's temperament, behavior, and whether or not they can stand without falling.

From rostral to caudal, the brainstem includes the midbrain (mesencephalon), the pons (ventral metencephalon), and medulla oblongata (myelencephalon).[10] The nuclei of most of the cranial nerves (CNs III-XII) lie in the brainstem and give rise to each nerve (Table 1). Table 1 shows whether CNs have sensory and/or motor function and the location of each of the CN nuclei. The mnemonics in Table 1 are 1 way to remember both the names and the basic functions of the nerves, whether motor, sensory, or both motor and sensory.

Cranial nerves III, VII, IX, and X carry autonomic parasympathetic innervation as well.

Some of the CNs are clinically very relevant in terms of testing and lesion localization, while others are less useful. Cranial nerves I and XI are generally not clinically relevant in ruminants when considered by themselves.[5] The olfactory nerve is sensory (smell) only, can be tested by offering feedstuffs, and is very rarely affected in the absence of other signs of forebrain disease. Signs of dysfunction of the accessory nerve include loss of function and atrophy of the sternocephalicus muscle; the authors have never appreciated this in cattle. The trochlear nerve (IV) is evaluated along with the other cranial nerves that innervate the somatic extraocular muscles (oculomotor and abducens), but is again very rarely solely affected. When the lesion in a CN is peripheral, the neurologic deficit is generally unilateral with no neurologic signs detected that might indicate upper motor neuron involvement (paresis, etc.). When the lesion is within the central nervous system (affecting the CN nucleus), often there will be bilateral deficits (although not always, especially with listeriosis) and/or multiple CN affected. This is due to either other nearby ipsilateral CNs being involved in the disease process, or the contralateral CN being affected. Additionally, if central CN lesions are present often there will be clinical signs such as ataxia or an abnormal gait due to upper motor neuron involvement.

Optic nerve dysfunction can result in partial or total loss of vision. This can be unilateral or bilateral. A multitude of disease processes can affect vision; most commonly these are within the globe or orbit itself, but can also be within the forebrain. If at all possible, it is an excellent idea to have the animal negotiate an obstacle 'course' in order to help assess visual acuity; however, unloading from a trailer and negotiation of an unfamiliar environment may also be very informative. Once the animal is restrained, a complete ophthalmologic exam will help differentiate ocular disease or peripheral nerve disease from a lesion in the CNS. Addi-

Table 1. Cranial Nerve Exam.

Cranial Nerve Number	Cranial Nerve Name	Name Mnemonic	Cranial Nerve Function	Function Mnemonic	Origin (Location of CN nucleus)
I	Olfactory	On	Sensory	Some	Forebrain
II	Optic	Occasion	Sensory	Say	Forebrain
III	Oculomotor	Our	Motor + parasymp	Marry	Midbrain
IV	Trochlear	Trusty	Motor	Money	Midbrain
V	Trigeminal	Truck	Both	But	Pons + Medulla
VI	Abducens	Acts	Motor	My	Medulla
VII	Facial	Funny	Both + parasymp	Brother	Medulla
VIII	Vestibulocochlear	Very	Sensory	Says	Medulla
IX	Glossopharyngeal	Good	Both + parasymp	Big	Medulla
X	Vagus	Vehicle	Both + parasymp	Brains	Medulla
XI	Accessory	Any	Motor	Matter	Medulla
XII	Hypoglossal	How	Motor	More	Medulla

tionally, following restraint of the head, **menace response** and **pupillary light reflexes** should be evaluated. Menace response tests the ipsilateral retina, CN II, the cerebral cortex (for practical purposes, the OPPOSITE CORTEX or contralateral to the eye being menaced[8]), cerebellum, and the facial nerve (CN VII) which provides the normally observed blinking response on the same side. The practitioner should take care not to create air currents that cause the cornea itself to be stimulated, which is a sensory reflex mediated by CN V (trigeminal), and should not touch the eyelashes; try to keep your hand far enough away from the eye that this does not occur. The menace response is a learned response, rather than a reflex, and may not be present in very young animals that are less than a week of age.[7] The **pupillary light reflex (PLR)** should also be performed at this time; ensure the light is as bright as possible (small powerful flashlights work better than penlights in most outdoor environments). The optic nerve carries input to the CN II nucleus in the diencephalon and then signals the parasympathetic nucleus of CN III (oculomotor) in the brainstem to constrict the iris. The 'swinging light test' simplifies performing both a direct and indirect PLR for a person doing the exam solo. A bright light source is directed into 1 eye, and once the pupil has constricted fully the light is shone into the other eye where constriction should continue if the response is normal.[8] Compared to small animals, the PLR tends to be slower in normal cattle. If both menace response and PLR are absent, the lesion is usually in the globe, optic nerve, or optic chiasm (peripheral); if both are absent bilaterally, vitamin A deficiency should be a primary differential diagnosis. **If the menace response is absent but the PLR is still present, the lesion is central (cortical).** This is why loss of menace response bilaterally, with intact PLRs bilaterally, is known as cortical blindness.

Symmetry of the position of the globe within the orbit should be evaluated. Strabismus can result from a lesion in CN III, IV, or VI, or from a CN VIII lesion. Additionally, the oculomotor nerve should be tested using the 'doll's eye reflex', which is also known as the **oculocephalic reflex**. For this reflex, sensory input is via CN VIII (vestibulocochlear), and motor via CN III, IV, and VI (oculomotor, trochlear, and abducens). For these nerves that innervate the somatic extraocular muscles, remember that motor function is 'LR$_6$, Do$_4$, Rest$_3$'; or, CN VI innervates the lateral rectus and retractor bulbi muscles, CN IV innervates the dorsal oblique muscle, and CN III innervates the rest (levator palpebrae superioris, dorsal, medial, and ventral rectus muscles, and ventral oblique muscle (additionally, it has the aforementioned parasympathetic innervation of the iris). To perform the oculocephalic reflex, the head should be moved up and down as well as side to side. The movement should stimulate cell bodies in the vestibular ganglion, and ultimately impulses are sent to the brainstem and the nuclei of CN III, IV, and VI. The eyes should move slowly in a direction opposite that of the head, and then 'flick' rapidly in the direction the head is moving; this is considered normal vestibular nystagmus.[8] As soon

as movement of the head stops, the nystagmus should also stop. It is considered abnormal if the nystagmus continues. Remember that ptosis of the upper eyelid can result from a lesion in CN III, the sympathetic innervation of the eye (see below), or a lesion in CN VII (also usually includes ptosis of the lower lid with VII involvement).

Loss of sympathetic innervation of the head, including the eye and associated periocular structures, is known as Horner's syndrome. This is very rare in cattle; the authors have only seen it once. It results in ipsilateral miosis, mild ptosis of the upper lid, mild enophthalmos, decreased sweating of the planum nasolabiale on the affected side, and increased warmth of the ipsilateral pinna.[8]

The **palpebral and corneal reflexes** test CN V and VII. Both medial and lateral canthi are touched. If this does not elicit a response, the cornea can also be touched but this is not usually necessary. This stimulates the ophthalmic (and if the lateral canthus is touched, also the maxillary) branch of CN V which ultimately stimulate the motor nucleus of CN VII that innervates the orbicularis oculi muscles of the eyelids. The patient should blink on the ipsilateral side. If this does not happen, there is a lesion in CN V or VII. The trigeminal nerve (CN V) provides sensation to the entire head for pain, pressure, etc., except to the pharynx and larynx (discussed below). The trigeminal nerve also carries motor fibers to the muscles of mastication via the mandibular branch. Thus, if jaw tone is weakened, there may be a lesion in either the left or right mandibular branch. If this is the case, there will be muscle atrophy on that side of the face as well; palpation of the masseter muscles is recommended to help detect asymmetry. If the jaw is dropped, this indicates potential bilateral mandibular branch involvement which is most likely a central lesion. This should make the practitioner consider rabies as a differential diagnosis, as well as space-occupying masses (these are less common).

The facial nerve innervates the muscles of facial expression and is primarily a motor nerve from a clinical perspective. It also has parasympathetic innervation to the lacrimal glands as well as several salivary glands. There are 3 branches, the auriculopalpebral, the dorsal buccal branch, and the ventral buccal branch. CN VII exits the skull via the internal acoustic meatus next to CNVIII. Thus, there may be involvement of both of these nerves in diseases like otitis media and/or interna that occur very close to this region. CN VII can be tested via the corneal and palpebral reflexes, or via the menace response. However, looking at the symmetry of the face usually gives some indication of dysfunction of this nerve as well. Paresis or paralysis of the upper and/or lower eyelid or ear, inability to close the eye, and loss of lacrimation in the eye (which can ultimately result in corneal ulceration) may all be indicators of CN VII dysfunction. Paresis or paralysis of the lip is difficult to ascertain in cattle, as they have a large amount of connective tissue present in this region. The planum nasolabiale does not deviate toward the normal side in cattle as it does in other species for the same reason.

The vestibulocochlear nerve (CN VIII) controls balance and hearing and can be evaluated using the aforementioned oculocephalic reflex. Other signs of dysfunction include complete or partial deafness. Total deafness can be detected by creating a loud and sudden noise behind the animal, such as popping a paper bag behind them. However, if they are only partially or unilaterally deaf, this is extremely difficult if not impossible to detect clinically. If the vestibular system is affected either centrally or peripherally, circling, nystagmus, head tilt, leaning or falling over (all of these would be present toward the side of the lesion in all peripheral disease and most central disease), and ataxia may be seen. To differentiate a peripheral lesion from a central lesion see Table 2.

If there is a loss of strength (hemi or tetraparesis) or there are CP deficits in conjunction with other vestibular signs, the lesion is CENTRAL (Table 2). When a unilateral central lesion is present in the brainstem, all CP deficits will be ipsilateral. If any other cranial nerve other than VII (which is anatomically very closely associated with VIII) is affected, or abnormal mentation including lethargy or depression is present, the lesion is also most likely central (remember, CN VI-XII all originate at the medulla oblongata or myelencephalon).

Cranial nerves IX and X are usually considered together, and innervate the pharynx and larynx. Clinical signs of pharyngeal dysfunction include dysphagia, gagging, drooling, and food present within the nares.[7] Laryngeal dysfunction (CN X) may result in voice change, loud respirations or dyspnea.[7] Additionally, with CN X involvement there may be GI and cardiovascular disturbances, or megaesophagus; CN X provides parasympathetic innervation to cardiac and smooth muscle of the viscera of the pharynx, larynx, esophagus, and GI tract. In general, these nerves combined provide the sensory and motor function that stimulates swallowing. To avoid placing a hand in the back of the pharynx of cattle to stimulate the **swallowing reflex**, place feed in front of the animal and observe whether or not it can prehend food with its tongue (evaluating CN XII) and whether or not it can masticate (CN V) and then swallow (testing CN IX and X). To stimulate a **gag reflex**, the practitioner can attempt to use a Frick speculum instead; passing an orogastric tube may also help evaluate the swallowing reflex in an anorectic bovine. It is important to keep in mind that 1 differential diagnosis for cattle that cannot swallow is rabies.

The hypoglossal nerve supplies motor innervation to the tongue muscles. It can also be evaluated by the ease with which it is pulled from the mouth. This should be relatively difficult in a normal adult bovine. The tongue may also deviate to the contralateral side, protrude, or else develop atrophy if there is a lesion in CN XII either peripherally or centrally.

Spinal Reflex Exam

Spinal reflexes test a reflex arc consisting of a sensory component, influence of descending motor pathways, and a motor component.[10] Spinal reflexes tested in cattle include the patellar reflex, withdrawal reflex, perineal reflex, and panniculus (cutaneous trunci) reflex. Ideally the patient would be in lateral recumbency to most effectively perform these tests, and thus usually these can only be performed in young calves or adult patients that are recumbent and unable to rise. Evaluating spinal reflexes can help differentiate between upper and lower motor neuron abnormalities and should be evaluated if paresis or paralysis is noted during gait and posture evaluation. As a brief review, the upper motor neurons (UMN) present within the CNS synapse with the lower motor neurons (LMN) in the spinal cord ventral gray matter and in addition to excitatory stimuli, provide inhibition to refine and control spinal reflexes. If UMN are damaged, and the descending inhibition of the LMN is lost, exaggerated responses to testing of spinal reflexes is usually seen. Damage to the LMN results in decreased to absent responses to spinal reflexes and often there is loss of muscle tone.[10] Some spinal reflexes can only be performed in young calves, or in recumbent adult patients (patellar reflex).

The **withdrawal or flexor reflex** for each limb is reliably present in normal animals and can be performed

Table 2. Differentiating Peripheral from Central Vestibular Disease.

Clinical Sign	Peripheral Dz (CN VIII)	Central Dz (CN VIII Nuclei in Brainstem)
Paresis	-	+
Postural response deficits (ie., lack of conscious proprioception)	-	+
Mentation change	-	+
Additional CN dysfunction	VII	Any of CN V-XII
Spontaneous nystagmus, either horizontal or rotary	+	+
Spontaneous vertical nystagmus	-	+
Normal physiologic nystagmus	Decreased/-	Decreased/-
Strabismus	+	+
Strabismus present that resolves or occurs when head position changes	-	+
Spontaneous nystagmus that changes direction when head position changes	-	+
Bilateral strabismus present with globes oriented in different directions	-	+

whether the animal is standing or recumbent. However, the tendon reflexes, other than the patellar reflex, are not very consistent. Additionally, the tendon reflexes all must be done with the patient in lateral recumbency. Start by pinching the toes or pressing a ballpoint pen just above the coronary band[5] to elicit a withdrawal reflex. If this is not sufficient to elicit a withdrawal, use a pair of hemostats on the skin above the coronary band or touch with a needle instead (take care to avoid the coffin, pastern, and fetlock joints if a needle is used). If the patient is in lateral recumbency, the examiner can also pinch between the toes.[5] Flexion of all joints of the limb should occur and to confirm intact pathways to the brain, the animal should also show a pain reaction such as looking toward the site of stimulus[5]. The withdrawal reflex in the front limbs is mediated by sensory innervation from a peripheral nerve (radial), with motor innervation from the lower motor neurons of the brachial plexus (C6-T2 spinal cord segments), and peripheral nerves that innervate the flexor muscles (median, ulnar, and axillary nerves). In the hind limbs, the withdrawal reflex is mediated by the sciatic and femoral nerve and the LMN of the lumbosacral plexus (L4-S1 SC segments). If the afferent nerve and/or the lower motor neurons are affected, there will be diminished or no response. If the upper motor neurons in the spinal cord are damaged, the reflex is still present, but may be exaggerated, even to the point of clonus. Additionally, if UMN are impaired in adult cattle, a 'crossed extensor reflex' identified by extension of the opposite limb, may also occur.

To perform the **patellar reflex**, restrain the animal in lateral recumbency, but without restraining the upper hind limb. Support the distal femur with 1 hand, or have an assistant help with this. A pleximeter (in calves) or a metal tool such as hoof testers or a short piece of rebar (in adult cattle) can then be used to strike the middle patellar tendon. Normally this results in extension of the stifle joint. Ideally this should be performed on both hind limbs with the tested limb being uppermost. If the reflex is decreased to absent, the femoral nerve and/or spinal cord segments L4-L6 are damaged, or else myonecrosis is present[5]. If the reflex is exaggerated, there is an UMN injury cranial to the L4 cord segment.

The sensory innervation of the **perineal reflex** is mediated through the perineal branch of the pudendal nerve originating from spinal cord segments S1-S3. The motor function is mediated by the caudal rectal branch of the pudendal nerve originating from S1-Co.[8] To perform this reflex, stroke the perineal region, or pinch the anal sphincter and the patient should clamp its tail down and contract the sphincter. If the LMN are affected, this reflex is decreased to absent. If the UMN are affected, the response may be normal to exaggerated (the authors have not seen this before, however). Tail tone is often evaluated during the general physical exam. A normal adult bovine tail should be relatively difficult to lift up at the base as they tend to clamp down the tail. Decreased tail tone can be an indication of decreased motor innerva-

tion or muscle weakness from metabolic conditions such as hypocalcemia.

The **cutaneous trunci or panniculus reflex** can be performed by running the end of a hemostat from back to front along the lateral trunk of the animal. The spinal cord segments involved are T3-L3 for the sensory component of the reflex arc, and C8-T2[2] and the lateral thoracic nerve as the efferent motor component that innervates the cutaneous trunci muscle. If the afferent portion of the reflex is absent, work from caudal to cranial to try to localize the affected spinal cord segment. This may be difficult to elicit in some cases, and is not always reliable.

Examination of spinal reflexes can reliably localize lesions to spinal cord segments C6-T2, L4-S1, and caudal to S1. Other SC cord segments are not as definitively evaluated by the reflex exam.

Forebrain Disease

The forebrain includes the cerebral hemispheres and the diencephalon. Alteration in cerebral function can result in abnormal mentation, behavior changes, seizures, circling (toward the side of the lesion if unilateral), cortical blindness (visual or menace deficits with PLRs maintained), and mild proprioceptive deficits. Often, lesions in this region also involve the thalamus (a portion of the diencephalon). In cattle, behavioral changes may include aggression, frequent yawning, abnormal vocalization, compulsive pacing, and 'head pressing', which may be attributed to compulsive walking that is halted by an immovable barrier.[5] All of these signs are usually indicative of diffuse forebrain disease. If the cortical lesion is unilateral, both proprioceptive deficits as well as visual deficits will be detected on the OPPOSITE or contralateral side. Unilateral disease can also result in a head turn (not tilt) or circling toward the affected side. Opisthotonus may be present in cattle with cerebral disease that are either sternally or laterally recumbent.[12] It is important to differentiate generalized seizures from other causes of lateral recumbency with paddling, such as tetanus.

Importantly, the diencephalon (which includes the thalamus) is immediately adjacent to the cerebral hemispheres. The optic nerve originates from this region, and space-occupying masses in this region may ultimately affect other CNs, including III, IV, and VI.[10] As with cortical lesions, any postural deficits noted would be on the contralateral side.[10] The diencephalon also includes the hypothalamus, which regulates the autonomic nervous system, visceral motor activity, water consumption (via the pituitary gland), appetite, and temperature control.[6] Hypothalamic lesions can therefore result in a variety of clinical signs.

Diffuse cerebral disease in cattle has a relatively long list of differential diagnoses: polioencephalomalacia (from thiamine deficiency or sulfur toxicity), lead toxicity, salt toxicity (hypernatremia or water deprivation), encephalitis or meningoencephalitis from *Listeria monocytogenes* or else

gram-negative coliforms in neonatal calves, thromboembolic meningoencephalitis from *Histophilus somni*, hepatic encephalopathy, nervous ketosis, viral diseases including rabies, BHV1, BHV5, and less commonly pseudorabies, nervous coccidiosis (in relatively young animals), and bovine spongiform encephalopathy should be considered. Urea toxicity and locoweed ingestion are also possibilities. Because many electrolyte and acid-base abnormalities can result in signs of symmetric forebrain disease in cattle, evaluating these is critical[5] and can easily be done in the field with point-of-care blood analyzers. Unilateral or asymmetrical forebrain disease can be caused by space-occupying masses including cerebral abscesses, granulomas, or very rarely, neoplasia. In very young animals, congenital or heritable defects or disorders including hydrocephalus and hydranencephaly may be present.

A complete list of differential diagnoses for neurologic disease in cattle, including congenital and heritable defects and disorders and the breeds most commonly affected, has been previously published.[5,8]

Brainstem Disease

The brainstem includes the midbrain (mesencephalon), pons, and medulla oblongata. Cranial nerves III-XII originate from these regions (Figure 1). The ascending reticular activating system (ARAS) is in the rostral brainstem and is responsible for arousing the cerebral cortex and awakening it to consciousness.[6] Alterations in the brainstem can affect cranial nerve function in 1 or more cranial nerves on the ipsilateral side. They also result in ipsilateral hemiparesis or tetraparesis. Animals with brainstem disease can demonstrate normal mentation, or they can show abnormal signs such as depression, obtundation, stupor, or coma if the ARAS is involved. The respiratory centers reside within the medulla, and abnormal respiration (usually a terminal event) can also result if severe injury occurs to this portion of the brainstem.[5]

Listeriosis is the most common cause of brainstem disease and multifocal cranial nerve deficits in ruminants.[9] Other major differentials include otitis media/interna, brainstem abscess, and pituitary abscess.[9] The pituitary gland is situated immediately ventral to the hypothalamus, and ruminants appear to be at increased risk (compared to other species) of developing abscesses in this region.[11] Asymmetric cranial nerve signs are usually present, and can include blindness, pupillary abnormalities, facial paresis/paralysis, circling, head tilt, strabismus, nystagmus, dysphagia, and reduced jaw or tongue tone.[9] These signs are likely secondary to extension of inflammation or else compression of the adjacent structures, including the diencephalon and brainstem.[9] Bradycardia has been described in 50% of cattle diagnosed with pituitary abscess in 1 report.[11] This may be due to hypothalamic involvement, or could be related to anorexia. Additionally, rabies in cattle may present with dysphagia, suggesting brainstem involvement.

Cerebellar Disease

The cerebellum coordinates all voluntary motor function, or skeletal muscle movements[8] including posture, muscle tone, and smoothness and synergy of muscle activity. It does not initiate motor activity; however, the cerebellum modulates it. When dysfunction of the cerebellum occurs, it is most often diffuse. The patient will present with a bilaterally symmetrical ataxia, but WITHOUT PARESIS as strength is preserved. If the lesion is unilateral, the ataxia will be ipsilateral. Additionally, cerebellar disease may result in dysregulation of range and force of movement resulting in hypermetria, truncal sway, a wide-based stance, or tremors (particularly intention tremors). The menace response can be absent with cerebellar disease but without visual deficits, as an avoidance response is often noted.[8] Nystagmus may also be present. In differentiating cerebellar disease from true vestibular disease, note that with cerebellar disease alone there will NOT be circling, a head tilt, or strabismus; however, spontaneous nystagmus in any direction can occur. Mentation is **normal** if only the cerebellum is affected.

In cattle, acquired cerebellar disease could be due to grass staggers, or else a space-occupying mass (abscess, granuloma). Congenital or hereditary cerebellar diseases include cerebellar hypoplasia (often from in utero viral infection, such as BVDV), abiotrophy, malformations, and lysosomal storage diseases (mannosidosis).[5]

Spinal Cord Lesions

Lesions within the SC segments C1-C5 often cause abnormal movement or position of the head and/or neck.[12] These also result in quadrilateral signs including ataxia, spastic paresis or paralysis, normal to increased muscle tone, and hyperreflexic responses to spinal reflexes in all 4 limbs.[6] In C6-T2 lesions, all 4 limbs may also show ataxia and paresis to paralysis; the front limbs have decreased tone and hyporeflexia to areflexia in response to spinal reflexes, and the hind limbs have normal to increased muscle tone and hyperreflexia. T3-L3 lesions do not affect the forelimbs, but cause hindlimb ataxia, proprioceptive deficits, and normoto hypertonia and reflexia with normal tail and anal tone.[6] Lesions in SC segments L4-S1 result in hypotonia and hypo to areflexia of the hind limbs. This can be difficult to differentiate from T3-L3 lesions without performing a spinal reflex exam[12] (but this is not always possible or safe). Decreased anal tone, tail tone, and loss of the perineal reflex can also occur with lesions from S1 caudally, as can urinary incontinence with constant urine dribbling (Table 3).[6,12]

Spinal cord lesions can result from trauma (vertebral fractures, luxations, or subluxations), neoplasia (most commonly epidural lymphosarcoma from enzootic BLV), vertebral body abscesses or osteomyelitis (which can result in pathologic fractures), discospondylitis, parasite migration (including *Hypoderma bovis*), and less commonly organophosphate

Table 3. Spinal Cord Lesion Localization

	C1-C5	C6-T2	T3-L3	L4-S1	S1-Cd5
Thoracic limbs	Ataxia Paresis/paralysis UMN signs	Ataxia Paresis/paralysis LMN signs	Normal	Normal	Normal
Pelvic limbs	Ataxia Paresis/paralysis UMN signs	Ataxia Paresis/paralysis UMN signs	Ataxia Paresis/paralysis UMN signs	Ataxia Paresis/paralysis LMN signs	Normal (LMN to perineum/tail/ bladder)

UMN signs: normal to increased mm. tone/spasticity, normo to hyperreflexia, decreased proprioception/pain, minimal/no disuse mm. atrophy
LMN signs: decreased mm. tone/flaccidity, hypo to areflexia, hypo to analgesia of innervated regions, acute neurogenic mm. atrophy

toxicity. In a report of 112 cattle with clinical lymphosarcoma, 26% had extradural tumors with clinical complaints including hind end ataxia and weakness.[3] Epidural LSA of the lumbar, sacral, and coccygeal regions combined accounted for 64% of these cattle with extradural tumors.[3] Always consider that rabies can present as ataxia, with gradually ascending paresis or paralysis (paralytic form).[4] Epidural abscesses, or caudal epidurals performed with alcohol can also result in signs consistent with caudal and/or ascending spinal cord disease. Congenital or hereditary diseases presenting with spinal signs include vertebral anomalies, spastic paresis (Elso Heel), and spastic syndrome, among others.

General Characterization of Differential Diagnoses in Neurologic Disease

The 'DAMN IT V' scheme in conjunction with a good history can be helpful in generally differentiating potential categories of disease that may be responsible for the patient's clinical signs (Table 4). Metabolic, toxic, and nutritional

Table 4. Characterizing Categories of Differential Diagnoses for Neurologic Diseases[1]

Differential Dx Category	Onset	Progression	Unilateral or Bilateral	Symmetry	Comments
Degenerative	Chronic	Progressive; sometimes rapidly	Bilateral	Symmetric	Usually occur in animals 4-6 months of age or older
Anomalous (congenital, hereditary, familial, etc.)	Present from birth OR acute onset	Anatomic malformation: Nonprogressive Metabolic: Progressive	Bilateral	Symmetric	May occur from birth; in some disease manifestations, clinical signs don't appear until 1-3 years of age
Metabolic	Acute to subacute	Progressive and/or intermittent	Bilateral	Symmetric	
Nutritional	Acute to subacute	Progressive and/or intermittent	Bilateral	Symmetric	
Neoplastic	Acute or chronic	Progressive	Unilateral or bilateral	Symmetric or asymmetric	IF BLV-associated LSA, often cattle 4-8 yrs old (recent data indicates cattle 2-21 yrs may be affected by LSA, with median age of 5 years[11])
Infectious/inflammatory	Acute	Rapidly progressive	Bilateral	Asymmetric if focal/multifocal; symmetric if diffuse	Multifocal: viral, bacterial, parasitic, protozoal, fungal Focal: abscess, granuloma, discospondylitis
Toxic	Acute to subacute	Progressive and/or intermittent	Bilateral	Symmetric	
Traumatic	Acute	Nonprogressive	CNS: bilateral PNS: unilateral	CNS: symmetric PNS: asymmetric	In traumatic brain injury, edema/hemorrhage often progressive
Vascular	Acute	Nonprogressive	Bilateral	Symmetric or asymmetric	Rare; fibrocartilaginous embolic myelopathy and aortoiliac thrombosis reported in cattle[13,14]

diseases usually affect many animals in a herd at once, particularly if the animals are managed similarly and in the same location. In cattle, the major neoplastic disease to consider is lymphosarcoma (LSA) from enzootic bovine leukemia virus (BLV), which targets a specific age group (often adults 4 to 8 years of age; Table 4). When BLV positive cattle with enzootic lymphosarcoma develop neurologic disease, the signs are often referable to the spinal cord as the tumors are usually extradural. In non-BLV associated lymphosarcoma, the brain may rarely be affected.[3] Infectious and/or inflammatory diseases can be focal (abscess or granuloma) or multifocal (viral, bacterial, fungal, protozoal, parasitic) in nature. These are usually acute in onset, progressive, and often are bilateral but asymmetrical; this depends on the site of infection, however, and diffuse or multifocal evidence of disease may be present.

Conclusions

While a complete neurologic exam as performed in small animals is not feasible in adult cattle, a good history combined with careful observation and an effective and systematically performed neurologic evaluation can allow the clinician to neuroanatomically localize the lesion(s). Generation of a differential diagnoses list is then more easily accomplished, and can help dictate potential ancillary diagnostics as well as treatment decisions.

Acknowledgements

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