Neurologic Diseases of Ruminants

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Examination

The goals of physical and neurological examination in animals, in which neurological disease is suspected, should focus on differentiation of primary and secondary neurological disease as well as on localization of suspected lesions within the peripheral or central nervous systems (CNS or PNS). A detailed description of examination procedures has been published previously (Constable, 2004).

In farm animal species, neurological signs most commonly result from an underlying metabolic disease, such as pregnancy toxemia or hypocalcemia. In neonatal patients, sepsis, metabolic acidosis, or hypoglycemia are common causes of neurologic signs. The goal of the physical examination in conjunction with blood work should therefore be exclusion of these common diseases from the differential diagnosis list. Once primary neurologic disease has been determined to be the most likely cause of clinical signs, localization of lesions to one of four functionally different anatomical regions of the nervous system is imperative. These four neuroanatomical regions are: (1) cerebrum, (2) cerebellum, (3) brainstem and cranial nerves, and (4) spinal cord and peripheral nerves. Keeping in mind the three main functions of the nervous system in farm animals (mental state, sensory perceptivity, posture and gait), the localization of lesions by physical and detailed neurological examination is possible (see Table 1).

Clinical signs associated with cerebral disease are mainly those of altered mentation and may include somnolence, depression, stupor, coma, or nervousness and excitation. Central blindness is also common and may result in slow forward locomotion and, at least in a new environment, walking into objects. Many metabolic diseases, especially alterations of the glucose, electrolyte, and acid-base homeostasis may lead to impairment of cerebral function. Evaluation of serum chemistry is helpful in ruling out underlying causes of cerebral disease. Primary causes of cerebral disease in ruminants include polioencephalomalacia, bacterial meningitis, infection with lentiviruses (CAE and Maedi/Visna), herpesvirus encephalitis, rabies, pseudorabies, and plant toxicoses.

Cerebellar disease causes abnormalities of posture and gait with clinical signs of upper motor neuron disease. Typical clinical signs include ataxia, dysmetria, and truncal sway. The presence of weakness should be assessed, which can be performed by pushing on the rump of the animal at a walk or in the standing patient. While normal strength is present in animals with cerebellar disease, signs of weakness may result from vestibular, spinal, or peripheral nerve ataxia, and from muscle disease. Causes of cerebellar disease include transplacental infections with pestiviruses (e.g. cerebellar hypoplasia), congenital lysosomal storage diseases, or grass staggers.

Lesions associated with brainstem and cranial nerves may result in a variety of clinical signs, depending on the region of the brain stem affected and dysfunctional cranial nerves. Mentation is commonly abnormal in patients with listeriosis, and depression and stupor may be

observed. Posture and gait may also be affected when the function of cranial nerve (CN) VIII (vestibulocochlear) is impaired. Cranial nerves are assessed as functional units. Lesions of CN II (peripheral blindness) and CN III, IV, V and VII may be assessed with pupillary light reflex (presence in blind animals suggests central blindness), menace response, palpebral reflex, and corneal reflex evaluations. In addition, lesions affecting CN VII result in drooping of ears, lips, and eyelids, and facial deviation. Lesions of CN VIII result in head tilt, nystagmus, and circling to the affected site. Nystagmus may also occur during cerebellar disease but would be present on the opposite site of the lesion. Dysphagia and decreased tongue tone are seen in patients with impaired CN IX, X, and XII. In ruminants, listeriosis is the most common cause of brainstem and cranial nerve deficits, but otitis media/ interna, pituitary abscess syndrome, and aberrant parasite migration (mostly spinal cord defects) should also be considered.

Spinal cord and peripheral nerve lesions can result in unilateral or bilateral deficits. When gait and postural abnormalities are present, differentiation into upper or lower motor neuron disease is helpful, if possible. Lower motor neuron disease always results in decreased muscle tone (paresis or paralysis), while decreased or increased muscle tone may be seen in upper motor neuron diseases.

Neuroanatomic location	Gait	Mentation	Posture	Spinal reflexes
Cerebrum	Normal	Abnormal	Normal	Normal
Cerebellum	Abnormal	Normal	Abnormal	Abnormal or normal
Brainstem and Cranial Nerves	Abnormal or normal	Abnormal or normal	Abnormal or normal	Abnormal or normal
Spinal cord and peripheral nerves	Abnormal	Normal	Abnormal	Abnormal or normal

Table 1 Neuroanatomic regions and abnormalities associated with neurologic disease (From: (Constable, 2004)

Cerebral diseases

Polioencephalomalacia

Similar clinical signs and (histo-) pathological alterations associated with polioencephalomalacia can be caused by four etiologies: (1) thiamine deficiency, (2) salt toxicity/ water deprivation, (3) sulfur toxicity, and (4) lead toxicity. Thiamine deficiency may be the result of rumen acidosis and disruption of ruminal microflora, which produce thiamine in sufficient amounts in ruminants. Furthermore, bacterial or plant derived (bracken fern, horsetail) thiaminases are able to degrade ruminal thiamine, causing deficiency. In small ruminants, therapeutic use of coccidiostats such as amprolium has caused thiamin-deficiency associated

polioencephalomalacia, as these drugs function as thiamine agonists. Water deprivation, as the result of frozen water troughs during the winter or an insufficient water supply during the summer, commonly results in clinical signs when animals regain access to water after periods of deprivation. Contamination of water or feed sources (e.g. distiller's grain) or the accumulation of sulfur within plants (*Brassica* spp.) may result in neurological disease. Lead toxicity is less common in small ruminants than in cattle, but has been reported.

Despite varying etiologies, clinical signs associated with polioencephalomalacia are the result of disruption of cerebral energy metabolism, with accumulation of sodium and shifts in free water, resulting in the development of cerebral edema and pressure necrosis. Clinical signs include incoordination, depression, aimless wandering, dorsomedial strabismus (especially with thiamine deficiency), opisthotonos, central blindness, and convulsions. Thiamine administration (10mg/ kg IV q3-6h) is the mainstay of therapy regardless of etiology. Administration of diuretics (mannitol 1-2 g/kg slowly IV) and steroidal anti-inflammatory drugs may be useful in some cases. Lead toxicity can be treated by chelation with CaEDTA, and careful rehydration is the mainstay of therapy for salt toxicity.

Small ruminant lentiviruses

Small ruminant lentiviruses of the family retroviridae are closely related and include caprine arthritis encephalitis virus (CAEV), Maedi-Visna virus (MVV), and ovine progressive pneumonia virus (OPPV). Transmission is mainly by colostrum and milk, but also by direct contact with infected animals. Lentiviruses are able to incorporate their genome into that of the host, causing a life-long carrier state. Infection rates are relatively high in many herds and progressive diseases, including arthritis, mastitis, and interstitial pneumonia can be observed. The neurological disease associated with CAEV is seen in goat kids between 2 - 4 month of age and often begins with unilateral or bilateral posterior paresis, which progresses to tetraplegia. Head tilt, circling, and cerebral disease later follows these signs. In contrast, neurologic disease of sheep has an adult onset and is mainly caused by MVV, which is rare outside of Europe. The clinical disease is not unlike scrapie and is characterized by a progressive development with wasting, hind limb ataxia, and paralysis. Diagnosis is based on serological tests such as AGID or ELISA.

Viral encephalitis

Viral diseases affecting ruminants include herpesvirus encephalitis (e.g. bovine herpesvirus I and V), rabies, and pseudorabies. Although these diseases are rather uncommon, they should be considered in ruminants with cerebral disease.

Both BHV 1 and 5 are alphaherpesviruses that can cause neurologic disease in cattle, and BHV 5 has a strong tropism for nervous tissues. Neurologic disease occurs more commonly in calves, but can be observed in adult animals. After infection by the respiratory route, the virus spreads to the CNS centripetally, within sensory axons originating in the nasopharynx. Animals

surviving initial infection can become latently infected and upon reactivation can shed the virus to susceptible cohorts. While BHV1 causes marked respiratory disease in conjunction with neurologic signs, respiratory signs are mild in most BHV5 infections. Neurologic signs are typical of cerebral disease and infections are commonly fatal.

Non-suppurative encephalitis caused by rabies virus can affect all farm animals, and in the US approximately 50 cattle and 30 small ruminants are affected annually. The disease is associated with spillover infections from wildlife populations, including the skunk (South-central to North-central US and California), raccoon (Southeastern US and East Coast), fox (southern US and Alaska), and mongoose (Puerto Rico). Transmission of rabies virus occurs by bite of an affected animal that contains the virus in its saliva. The virus replicates in muscle cells, then spreads to the CNS by centripetal axoplasmic flow and replicates in the CNS gray matter. Via parasympathetic nerves, the virus invades several tissues including salivary glands. Although the disease usually affects individual animals, herd outbreaks are not uncommon in sheep. Early clinical signs may include depression, ataxia and anorexia. Proprioceptive deficits, hyperesthesia, muscle twitching, and ascending paralysis may develop as the disease progresses. Pharyngeal paralysis results in inability to swallow, stertorous breath, and accumulation of frothy saliva around the oral cavity. Behavioral abnormalities, such as aggression towards handlers and inanimate objects and sexual hyperactivity may be intermittent. The disease is rapidly progressive and affected animals become recumbent within 3-5 days, followed by coma and death by 10 days of clinical illness.

Pseudorabies is caused by suid herpesvirus 1 (SHV1), an alphaherpesvirus of swine. The virus has been eradicated from commercial swine in the U.S., but feral pigs may continue to serve as a reservoir. Severe neurological disease may occur in piglets, but low case fatality rates are seen in older pigs, which are the reservoir for SHV1. Other farm animal species, including cattle, sheep, and goats may also develop clinical disease, but are considered dead-end hosts. Few reports of pseudorabies in ruminants exist. Infection may occur by bite of an infected pig, exposure of open wounds or mucous membranes, iatrogenically, and by airborne route. Clinical signs develop within 2-7 days of exposure. In infected ruminants, paresthesia and intense local pruritus at the site of inoculation are common. Pyrexia and self mutilation result in abrasions, swelling and alopecia. Other clinical signs include fever, ataxia, circling, excitement, and aggression, although affected animals are often depressed. Death is preceded by recumbency, convulsions, vocalization, and other signs of severe cerebral disease.

Poisonous plants in cerebral disease

Many toxic plants are associated with neurological signs of cerebral disease. These signs include weakness, trembling, convulsion, coma; and with some plant species, hypersalivation and vomiting. Poison hemlock, spotted water hemlock, milkweed, red buckeye, white snakeroot, mountain laurel, and rhododendron species, including azaleas are common cause of intoxication in the US.

Cerebellar disease

Pestiviral infections

Pestiviruses affecting ruminants are Border disease virus (BDV) and Bovine viral diarrhea virus (BVDV). Infection with BVDV has caused great concern for the alpaca industry , but infections are possible in many other cloven-hoofed animals, such as small ruminants, swine, and deer. In immunocompentent animals, pestiviral infections result in pyrexia, pneumonia, reproductive disease and impairment of the immune system. Although encephalitis has been reported in young sheep infected with BDV, neurologic disease as a result of pestiviral infection is most commonly seen in offspring that were infected in-utero at the time of organogenesis (100 – 150 days in calves). Coarse, abnormally pigmented hair coat and cerebellar hypoplasia are the result of a transplacental infection with BDV or BVDV in sheep and are well described by the term ‘hairy shaker lambs’. Affected calves show dysmetria, intention tremors, and truncal sway. Affected animals are bright and alert, but ataxia and intention tremors worsen at attempts to nurse. In alpacas, deer, goats, pigs, and sheep, in utero infection with BVDV may result in persistently infected offspring, which commonly suffer from ill-thrift, poor weight gain, chronic diarrhea, and recurrent bacterial infections.

Grass staggers

Perennial Rye-grass, Dallis grass, Bermuda grass, and Canary grass have been associated with grass staggers in small and large ruminants. Fungal toxins are causative in perennial Rye-grass and Dallis grass staggers. Canary grass contains a tryptamine alkaloid which has also been associated with cardiovascular disease in sheep. The toxic principle of Bermuda grass staggers has only recently been identified, and is a mycotoxin produced by *Claviceps cynodontis* on ergotized Bermuda grass, similar to that of *C. paspali* of Dallis grass. In affected animals (usually multiple animals within a herd), a stiff gait, trembling, and hypermetria can be observed. Clinical signs worsen with excitement and removal of affected animals from the offending pasture should be performed in a calm and quiet fashion.

Brainstem and cranial nerve disease

Listeriosis

Infection with *Listeria monocytogenes* is among the most frequent causes of neurologic disease in small ruminants. *L. monocytogenesis* is commonly found in the environment of farm animals and is shed in the feces of healthy animals. In cattle, feeding of spoiled silage is the most common risk factor for clinical listeriosis; however, rotting forages (grass clippings) and the bottoms of large round hay bales may be more important sources of infection in small ruminants. Small ruminants, especially goats, are more susceptible to infection and clinical signs are

variable. Presence of severe depression and unilateral cranial nerve deficits are frequently observed. Depression and dysphagia lead to decreased feed intake, and the presence of exposure keratitis make supportive care an important part of therapy. The choice of appropriate antimicrobial therapy is matter of discussion, but it appears that some cases respond better to repeated procaine penicillin administration, while oxytetracycline may be better in other cases. Florfenicol (Nuflor) has also been successfully used in clinical listeriosis. Further supportive therapy has to be chosen according to the case and may include steroidal or non-steroidal anti-inflammatory drugs, intravenous balanced electrolyte containing fluids, and eye medications.

Spinal cord and peripheral nerves

Aberrant parasite migration – meningeal worm infestation

Infestation with *Paralephostrongylus tenuis* may occur in all ruminants but small ruminants and especially llamas and alpacas are most commonly affected. Definitive host of the nematode is the white-tailed deer and snails and slugs are obligate intermediate hosts. After ingestion of infectious larvae within snails, the parasite migrates through the abomasal wall and enters blood vessels of the spinal cord. In aberrant hosts, parasite development is not completed and an inflammatory response at the spinal cord results in neurological signs. Clinical signs of upper motor neuron disease include hind limb ataxia, proprioceptive deficits especially in the hind limbs, recumbency, and paralysis. Although signs of impaired brain stem function, including circling, have been reported, spinal cord disease is predominant. Definitive diagnosis can only be established by necropsy; however clinical signs, increased eosinophil counts within cerebrospinal fluid and response to treatment are diagnostic aids. Treatment is based on administration of anthelmintic (avermectins and/or benzimidazoles) and anti-inflammatory drugs, but despite improvement, full recovery cannot be expected in all cases. Since prevention of contact of small ruminants with intermediate and definitive hosts is difficult, some owners administer a monthly regimen of ivermectin to alpacas, which is effective in disrupting parasite development during its migration from abomasum to the spinal cord, but causes resistance to anthelmintics in intestinal parasites.

Further reading:

Constable, P.D., 2004. Clinical examination of the ruminant nervous system. Vet Clin North Am Food Anim Pract 20, 185-214.

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