Toxicoses of the Ruminant Nervous System

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KEYWORDS

• Ruminant • Toxicosis • Polioencephalomalacia • Lead • Neurologic disease • Infectious agents • Poisonous plants

KEY POINTS

- Damage to the nervous system of ruminants can be caused by organic compounds, inorganic compounds, metals, infectious agents, and plants.
- Specific agents that can cause damage include lead, salt, pesticides, insecticides, mountain laurel, nightshades, and milkweeds.
- Not all syndromes can be cured, and it is important that caution is used when using unapproved drugs to treat ruminant brain injuries.

INTRODUCTION

Numerous organic compounds, inorganic compounds, metals, infectious agents, and plants cause damage to the nervous system of ruminants. This article reviews many of these agents. This review is not meant to be exhaustive but rather a brief overview of the agent, its mechanism of action, clinical signs, diagnosis, and treatment of the most common neurotoxicoses encountered in ruminant medicine. Readers must use caution when using unapproved drugs to treat brain injuries to ruminants to avoid tissue residues.

NONINFECTIOUS AGENTS

Polioencephalomalacia

Polioencephalomalacia (PEM) is a diagnostic term describing necrosis of the gray matter of the brain. This lesion has become synonymous with the neurologic disease termed *polio*, which is documented in cattle, sheep, goats, cervids, camelids, and camels. Cerebrocortical necrosis and cortical laminar necrosis are synonymous with PEM. Historically, thiamine deficiency or destruction of thiamine by thiaminases, present in a variety of plants; by-products of rumen acidosis; and amprolium

Disclosure Statement: The author has nothing to disclose.
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Vet Clin Food Anim 33 (2017) 111–138
http://dx.doi.org/10.1016/j.cvfa.2016.09.009
vetfood.theclinics.com

administration were listed as the causes of this disease. Other causes of PEM include excess dietary sulfur, lead poisoning, and salt poisoning.

Excess dietary sulfur has been known to cause PEM for more than 30 years. Although numerous investigators have documented sulfur-induced PEM during this time period, the specific mechanism of action is open for debate. Historically the mechanism of action is thought to be that excess dietary sulfur leads to formation of excess hydrogen sulfide (H_2S), entering the bloodstream and causing direct damage to the brain. Rumen bacteria metabolize elemental, inorganic, and organic sulfur; therefore, the total sulfur content in feed and water must be determined to determine total sulfur intake.[1,2] These bacteria use sulfates for their own metabolic needs and the production of sulfur-containing amino acids releasing H_2S into the rumen.[1,2] It takes 7 days for these bacteria to acclimate to this process.[1–3] The H_2S accumulates in the rumen gas cap where it dissociates to HS^-, $HSO3^-$, S2, and S0. The amount of H_2S in the gas cap compared with the other ions is dependent on the rumen pH. When the rumen pH is 7.4, one-third is in the form of H_2S; this value increases to 97.2% when the rumen pH is 5.2. This explains why the incidence of PEM is much greater in animals fed concentrates. H_2S trapped in the rumen gas cap diffuses across the rumen wall entering into the portal blood stream. When large amounts of H_2S enter the blood, the liver's ability to convert it back to sulfate is overwhelmed, allowing direct access of excessive amounts of H_2S to the brain.

H_2S is produced endogenously and serves to protect the brain cells.[4] At normal physiologic levels it functions as a neuromodulator and protector of brain cells. It protects brain function by scavenging free radicals and reactive oxygen species, reducing oxidative stress and modulating glutathione and intracellular $Ca2^+$ levels.[4] When excess amounts enter the brain, the added H_2S, HS^-, and $HSO3^-$ interfere with the electron transport chain by blocking cytochrome C, leading to cell death.[5–7] Damage occurs to the brain because of its high energy demand, with the greatest demand involving the gray matter due to the increased number of synapses compared with white matter.[8,9] Acute death due to respiratory failure can result from paralysis of the carotid body.[5,10,11]

Inhalation of eructated rumen gas is another proposed route of H_2S access into the blood. This route of entry is questioned by some investigators.[4,12,13] When expired air from weaned beef heifers receiving up to 7010 ppm sulfur in their ration and exhibiting clinical signs of PEM was analyzed for H_2S and other biomarkers indicative of oxidative lung damage, none was detected with repeated sampling. Also, histology did not reveal any lung damage in these animals when euthanized during episodes of clinical illness.[12] Other investigators question whether the amount of H_2S in rumen gas reaches amounts that are high enough to be significant even if appreciable amounts of eructated gas are inhaled.[4] This subject merits additional research to establish how H_2S enters the bloodstream.

Thiamine is a sulfur-containing water-soluble vitamin. It is synthesized in the stomach and intestines of all animals but nonruminants require additional dietary sources. Rumen bacteria are capable of synthesizing adequate amounts of thiamine even with less than optimal nutrition.[14]

Thiamine monophosphate (TMP) and thiamine pyrophosphate (TPP) are phosphate esters of thiamine that are essential for normal metabolism. TPP is an essential coenzyme in 6 different decarboxylation reactions in aerobic respiration.[6,15] This coenzyme is the catalyst to convert pyruvate to acetyl coenzyme A, which reacts with oxaloacetate in the citric acid cycle in aerobic respiration.[15] Thiamine is essential for normal cellular membrane function and the conduction of nerve impulses.[6] Because of the high energy demands of the central nervous system (CNS), adequate thiamine is