

JOURNAL OF ANIMAL SCIENCE

The Premier Journal and Leading Source of New Knowledge and Perspective in Animal Science

Polioencephalomalacia

D. H. Gould

J Anim Sci 1998. 76:309-314.

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://jas.fass.org>



American Society of Animal Science

www.asas.org

Polioencephalomalacia¹

Daniel H. Gould

Department of Pathology, College of Veterinary Medicine and Biomedical Sciences,
Colorado State University, Fort Collins 80523

ABSTRACT: Polioencephalomalacia (PEM) is a neuropathologic condition of ruminants that can be induced by a variety of neural metabolic disruptions. These include altered thiamine status, water deprivation-sodium ion toxicosis, lead poisoning, and high sulfur intake. Investigations of sulfur-related PEM have demonstrated that the onset of the clinical signs

coincides with excessive ruminal sulfide production. A number of ruminal factors could modulate the production and absorption of ruminal sulfide. The development of a convenient method to estimate ruminal gas cap H₂S has made it possible to identify cattle with high levels of ruminal H₂S and evaluate their risk of developing PEM.

Key Words: Ruminants, Hydrogen Sulfide, Toxicology, Polioencephalomalacia, Cerebrocortical Necrosis

©1998 American Society of Animal Science. All rights reserved.

J. Anim. Sci. 1998. 76:309-314

Introduction

Polioencephalomalacia (**PEM**) is a neurologic disorder of ruminants (Jensen, et al., 1956; Radostits et al., 1994; Summers et al., 1995) characterized by necrosis of the cerebral cortex. Clinical signs include blindness, ataxia (incoordination), and sometimes recumbency with seizures. Early in the disease, the damaged tissue autofluoresces under ultraviolet (360 nm) illumination. With time, the affected tissue softens and undergoes cavitation (Jubb and Huxtable, 1993). Polioencephalomalacia literally means softening (malacia) of the gray matter (polio) of the brain (encephalo). Cerebrocortical necrosis is a synonym for PEM. Confusion sometimes arises because the term PEM can be used in two ways: 1) a brain lesion lacking etiological specificity or 2) a neurological disease syndrome caused by disturbed thiamine status. When used to denote a lesion, PEM refers to a group of tissue changes that are the nonspecific final common expression of a number of different pathophysiological states. Despite this, there has been a tendency to assume that outbreaks of PEM are caused by altered thiamine status. This often is because the affected cattle responded favorably to thiamine administration even though specific tests to assess thiamine status were not performed.

To diagnose, treat, and prevent PEM in ruminants, one must recognize the nature of the tissue alterations underlying the neurologic impairment, and identify the cause. Frequently the term PEM is used loosely, and it is unclear whether the lesion or the syndrome is under consideration. To facilitate investigation of the cause and epidemiology of PEM, I recommend that use of the term PEM be limited to denote the lesion name. When this lesion is identified, a number of etiological considerations are raised. These can be systematically investigated by gathering appropriate types of supporting laboratory or epidemiological information.

Causes of Polioencephalomalacia

Although the main focus of this article is sulfur-associated PEM, it should be emphasized that PEM can have other causes. These include altered thiamine status, acute lead poisoning, and water deprivation-sodium ion toxicosis. A brief review of the nature of some of these forms provides the necessary diagnostic perspective.

Thiamine

Worldwide, there is a large body of literature regarding the relationship between altered thiamine metabolism and PEM. Several investigators have measured markedly decreased concentrations of thiamine in body tissues, decreased activity of a thiamine diphosphate dependent enzyme (transketolase) in blood, (Edwin and Jackman, 1973; Roberts and Boyd, 1974; Spicer and Horton, 1981; Jackman, 1985;

¹Presented at a symposium titled "Bud Britton Memorial Symposium on Metabolic Disorders of Feedlot Cattle," July 1996, following the ASAS 88th Annu. Mtg., Rapid City, SD.

Received September 30, 1996.

Accepted July 15, 1997.

Rammell and Hill, 1986; Fakhruddin et al., 1987a), and increased levels of thiamine-destroying thiaminases in the gastrointestinal tract of animals with PEM (Edwin et al., 1968; Morgan, 1974). Thiamine analogues with impaired biological activity may be produced in the rumen by thiaminase I (Edwin and Jackman, 1982). In this case, direct measurement of blood and tissue thiamine concentration may not be appropriate to demonstrate altered thiamine status; microbiological methods may provide a better indication of availability of biologically active thiamine (Olkowski and Gooneratne, 1992). One can induce PEM by feeding thiamine antagonists for prolonged periods (Spicer and Horton, 1981; Fakhruddin, 1987b). The disease also has been associated with ingestion of thiaminase-containing bracken and nardo ferns (Pritchard and Eggleston, 1978). Furthermore, affected animals often recover if high doses of parenteral thiamine are administered (Davies, 1965).

However, findings such as these are not consistent. Low thiamine concentrations have been associated with medical conditions that do not involve PEM (Gupta et al., 1976). Induction of severe thiamine deficiency in lambs did not cause PEM (Mueller and Asplund, 1981). Several investigators have been unable to demonstrate that thiamine levels are decreased in tissues and rumen fluid of PEM-affected animals (Loew et al., 1975; Mella et al., 1976; Sager et al., 1990; Gould et al., 1991). The activity of blood transketolase and gastrointestinal thiaminases can be altered nonspecifically in conditions other than PEM (Loew et al., 1975; Linklater and Dyson, 1977). Thiamine treatment has been shown to be beneficial in cases of lead encephalopathy and, therefore, may have nonspecific therapeutic benefits in cerebral diseases (Bratton et al., 1981; Coppock et al., 1991; Dey et al., 1995).

High dietary sulfate can alter blood thiamine concentrations and reduce duodenal thiamine flow (Goetsch and Owens, 1987; Gooneratne et al., 1989b). Sulfite, an intermediate in the reduction of sulfate, cleaves thiamine. However, a thiamine-destroying effect could not be demonstrated in sheep fed a thiamine-free, high-sulfate, semisynthetic diet, even though ruminal sulfide concentrations increased (Oliveira et al., 1996).

Acute Lead Poisoning

The lesions of acute lead encephalopathy have been described (Little and Sorenson, 1969; Christian and Tryphonas, 1971), and cortical neuronal necrosis is a common feature. Diagnosis of lead poisoning is based on demonstration of elevated blood or tissue lead concentrations. Frequently the source of the lead can be discovered and eliminated.

Water Deprivation-Sodium Ion Toxicosis

Padovan (1980) described PEM in cattle subjected to water restriction, although this may be a less

common response in bovines than in other animals. This disorder is due to either deprivation of water or subsistence on water with a high sodium content. Diagnosis is based on demonstration of elevated concentrations of sodium in plasma and(or) cerebrospinal fluid. Frequently a lapse in management resulting in water deprivation or a high sodium source can be demonstrated.

Sulfur-Associated Polioencephalomalacia

This type of PEM has been reported with increasing frequency in the literature. Sulfate-associated PEM seems to represent a distinct epidemiological form of PEM. In some instances the sulfate source is water (Harris, 1987; Gooneratne et al., 1989b; Beke and Hironaka, 1991; Hamlen et al., 1993; James et al., 1994), and in others the sulfate or other sulfur form is a dietary component (Raisbeck, 1982; Gibson et al., 1988; Jeffrey et al., 1994; Bulgin et al., 1996; Low et al., 1996; Hill and Ebbett, 1997). In some reports, a high sulfate source was likely but not directly identified (Dickie et al., 1979; Haven et al., 1983; Hibbs and Thilsted, 1983). A putative sulfur-associated form of PEM may be represented by the PEM that occurs with molasses-urea feedlot diets (Mella et al., 1976). Molasses can be high in sulfur. This molasses-associated form of PEM lacks alterations in thiamine status.

Polioencephalomalacia and "Blind Staggers"

An area of potentially confusing terminology concerns sulfate-associated PEM of range cattle and the clinical syndrome denoted by the term "blind staggers". The clinical signs of PEM often feature blindness and staggering, thus inviting confusion with so-called selenium-induced blind staggers. Selenium-induced blind staggers recently has been critically reviewed, and the existence of such a syndrome is open to question (O'Toole et al., 1996). Some cases of selenium-induced blind staggers actually may be sulfate-associated PEM (James et al., 1994; O'Toole, et al., 1996).

Experimentally Induced Polioencephalomalacia

Polioencephalomalacia induced experimentally with diets high in sulfate also has been reported. Investigators in Canada reported that sheep fed high-sulfate diets developed PEM 3 to 6 wk after the beginning of the experimental feeding period (Gooneratne et al., 1989a; Rousseaux et al., 1991). A modest decrease in blood thiamine was demonstrated. However, thiamine-supplemented groups also manifested PEM, even though clinical signs were not observed (Olkowski et al., 1992).

Studies of Experimental Polioencephalomalacia in Colorado

We have studied various aspects of the experimental disease in steers and sheep. Our interest in PEM was stimulated by the occurrence of PEM in association with copper deficiency and high-sulfate waters in our region. During the course of experiments on diet-induced copper deficiency in cattle, we observed that a copper-deficient experimental diet with added sulfate consistently induced PEM in cattle. The PEM-inducing capability of the high-sulfate diet was not due to copper deficiency (Sager et al., 1990). Before and during the expression of the diet-induced PEM, no significant decreases in rumen or plasma thiamine (Sager et al., 1990) were noted, nor were there alterations of thiamine or its mono- and diphosphate esters in whole blood, brain, cerebrospinal fluid, or liver indicative of thiamine deficiency (Gould et al., 1991). Blood thiamine pyrophosphate effect on transketolase was unaltered (Sager et al., 1990). Thus, evidence of thiamine deficiency was not demonstrable in this form of PEM.

During these experiments, we recognized that the eructed odor of hydrogen sulfide (H_2S) was associated with the onset of PEM in steers fed the PEM-inducing diet. We demonstrated a positive association between elevated sulfide concentrations in rumen fluid (Gould et al., 1991) and gas cap (Gould et al., 1997) and the onset of PEM in steers fed the PEM-inducing diet. Additional studies concerned the effects of direct sulfide administration on sheep. These studies demonstrated that sublethal doses of sodium sulfide given by gavage produce PEM (McAllister et al., 1992). Thus, PEM seemed to be the direct result of sulfide exposure and not the result of some other rumen-derived neurotoxin associated with the altered ruminal conditions.

Our recent studies have focused on developing a simple method for estimating rumen gas cap H_2S concentrations to facilitate field investigations of dietary risk factors and allow disease diagnosis. The method involves passing a known volume of rumen gas obtained percutaneously through a calibrated, commercially available H_2S detector tube (Gould et al., 1997). In steers with high sulfate diet-induced PEM, rumen gas cap H_2S concentrations were increased to a much larger degree than rumen fluid sulfide concentration increases (Gould et al., 1997).

The elevated concentrations of ruminal fluid sulfide and ruminal H_2S gas associated with the onset of experimentally induced PEM provide a plausible pathophysiologic basis for the PEM (i.e., sulfur-associated PEM is a form of subacute H_2S toxicity). Furthermore, it raises a more general question concerning the causes for and consequences of pathologic ruminal H_2S production.

Pathologic Ruminal H_2S Production

Episodes of excessive production and absorption of ruminal sulfide are a toxicologic hazard to ruminants. Notably, H_2S and its ionic forms are highly toxic substances with important biological effects. Traditionally H_2S has been thought to interfere with cell respiration in a manner similar to hydrogen cyanide (Beaucamp et al., 1984). However, other mechanisms of action also could be involved. These include the formation, during sulfur metabolism, of a sulfate anion free radical that is thought to have the tissue-damaging capacity of the hydroxyl radical (Mottley and Mason, 1988). In addition, endogenous H_2S may function as a neuromodulator in the brain (Abe and Kimura, 1996).

In general, H_2S is a normal product of rumen microbial metabolism (Lewis, 1954; Bray and Till, 1975; Kandyliis, 1983). Part of ruminal sulfur metabolism involves the sulfate-reducing bacteria. The sulfate pathway involves ATP to form adenosine-3-phosphosulfate, which either reacts with ATP to produce 5'-phospho-adenosine-3'-phosphosulfate (**PAPS**) or releases H_2S by dissimilatory reducing bacteria. Assimilatory reducing bacteria utilize PAPS as a source of reduced sulfur for the synthesis of sulfur-containing amino acids (Bray and Till, 1975). Sulfate and sulfide form a recycling system. Sulfur is reduced to sulfide mostly in the rumen. The sulfide is absorbed or used for microbial protein synthesis. The absorbed sulfide is oxidized to sulfate in blood and liver and is distributed to extracellular fluid. Sulfate is recycled to the rumen via saliva or directly to the large intestine (Bray and Till, 1975).

Alterations in ruminal microbes associated with the high sulfate diet-induced form of PEM were investigated. There were no demonstrable increases in numbers of sulfate-reducing bacteria in steers associated with the development of high sulfate diet-induced PEM. However, the capacity of ruminal microbes to generate H_2S from sulfate was enhanced by adaptation to a high-sulfate diet (Cummings et al., 1995b) and the presence of known sulfate-reducing bacteria *Desulfovibrio* spp. was confirmed (Cummings et al., 1995a).

Factors Affecting Pathologic Ruminal H_2S Production

The occurrence of pathologic concentrations of ruminal H_2S could involve a variety of potential pathogenetic factors. The two main factors probably are total sulfur intake and state of the sulfur-reducing ruminal microbes.

Total Sulfur Intake

The recommended level of dietary sulfur is less than .3%, and the maximum tolerated is .4% (NRC,

1996). Overall, many sulfur sources may be important for pathologic ruminal sulfide production and PEM. As indicated above, PEM has been associated with high-sulfate water, molasses, elemental sulfur, and gypsum or ammonium sulfate added to concentrate diets. Cruciferous forages and certain grain processing by-products can be high in sulfur (NRC, 1996; Hill and Ebbett, 1997).

Assessment of the total sulfur intake in terms of percentage S in dry matter may be a convenient approach to evaluate the potential for pathologic ruminal H₂S production. One needs to account for sulfur from all sources and then calculate intake as part of the total dry matter consumed. Sulfur in the water is especially important; it can represent a significant amount of sulfur consumed. Sulfur in water usually is reported as parts per million of sulfate. To calculate the contribution of water to overall sulfur intake, one must estimate daily water intake, convert sulfate to sulfur, and then equate the grams of sulfur consumed in the water to the estimated total daily dry matter consumption. When the sulfur contributed by the water is added to the sulfur contributed by the diet, estimated total intake is in an appropriate form to compare with the NRC guidelines (1996).

Such estimation can sometimes reveal surprisingly high total sulfur intake. For example, if a steer is consuming 10 kg of feed containing .2% sulfur and 50 L of water at 600 ppm sulfate (equals 200 ppm sulfur), total intake of sulfur would be 30 g, or the equivalent of .3% dietary sulfur. In the high plains and intermountain regions of North America, water sulfate concentrations of 2,000 ppm or more are associated with the occurrence of PEM. With the same estimation assumptions as above, use of water with 2,000 ppm sulfate at moderate ambient temperatures results in a total intake of sulfur equivalent to .53% dietary sulfur, well above the maximum of 0.4% tolerated (NRC, 1996). Large increases in water intake occur at higher ambient temperatures, increasing total sulfur intake even more and increasing the likelihood of PEM.

Microbial Factors

Because H₂S generation is due to microbial sulfur reduction mechanisms, increased ruminal microbial sulfur reducing capacity could be a crucial factor even in the face of a modest level of total sulfur intake. Rumen fluid from steers fed a high-sulfate concentrate diet has an increased capacity for H₂S generation compared to rumen fluid in cattle fed an identical diet without added sulfate (Cummings et al., 1995b). Other findings with potential relevance to pathologic ruminal sulfide production are that cysteine is readily used for ruminal microbial H₂S generation. Thus, ruminally degraded protein is a relevant sulfur source. When H₂S accumulates in the head space of cultures

of sulfate reducing bacteria *in vitro*, H₂S generation is suppressed, whereas if the H₂S is removed periodically, total H₂S production is enhanced (Cummings et al., 1995a).

Other Factors

Ruminal H₂S production also could be affected by the type of carbohydrate, pH of ruminal fluid, and dietary metals. The carbohydrate source and content affect microbial metabolism and pH of the rumen fluid. The pK_a of the first proton of H₂S is approximately 7.04 (Beaucamp et al., 1984). The relative concentrations of H₂S in the rumen gas cap and the hydrosulfide anion in the rumen fluid change with pH. Ruminants inhale a sizable fraction of eructed gases (Dougherty and Cook, 1962). Acidic conditions favor an increased rumen gas cap concentration of H₂S, so inhalation of eructed H₂S could be a route of systemic sulfide absorption. Although the principal route of sulfide absorption is not known, cattle exposed to atmospheric manure gas (H₂S) developed PEM (Dahme et al., 1983), indicating that the respiratory system could serve as a primary entry route.

Because a large fraction of eructed gas may be inhaled, the respiratory tract is exposed to H₂S during episodes of pathologic ruminal sulfide production. H₂S damages pulmonary tissue in rats (Lopez et al., 1988) and has been incriminated in acute interstitial pneumonia of cattle (Kerr and Linnabary, 1989). The pneumotoxic potential of H₂S under field conditions remains to be established.

Comparison of rumen fluid sulfide concentration and H₂S gas cap concentration indicates that the H₂S in the gas compartment increased to a larger degree than the sulfide in ruminal fluid (Gould et al., 1997). As indicated above, pH is one important determinant. For example, at pH 5.2 the percentage of H₂S vs hydrosulfide anion is 97.2 and 2.8, whereas at pH 6.8 it is 46.8 and 50.4, respectively (Bray and Till, 1975). In addition, H₂S in the gas cap tends to be sequestered in a less dynamic metabolic compartment than metabolites in the ruminal fluid. Sulfide concentrations in the ruminal fluid probably reflect all sulfur cycle processes occurring in the fluid phase. Thus, the total sulfur in the pool can fluctuate independent of the hydrosulfide anion. Conversely, the accumulation of H₂S in rumen gas is determined partly by pH-governed ion partitioning. Once in the gas phase, H₂S is separated from sulfur cycle processes and remains more stable. The difference in the volume of the fluid compartment and the gas compartment also could play a role in accentuating H₂S gas accumulation. Overall, the processes that are likely to determine rumen gas cap H₂S concentrations include sulfide generation in the rumen fluid, rumen fluid pH, eructation frequency, and absorption by the ruminal mucosa.

Dietary metals also could play an important role in pathologic ruminal H₂S production. Copper, zinc, iron,

and molybdenum could modify sulfur toxicosis. Molybdenum, copper, and sulfur combine to form insoluble copper-thiomolybdate (Suttle, 1980). Copper, zinc, and iron all form insoluble salts with sulfide (Chemical Rubber Company, 1996). Although these elements could not be expected to exert an effect on the total amount of sulfide potentially produced, they could have an effect on some fraction of the sulfide. Sulfide formation decreases absorption of most minerals, so extra amounts of copper, zinc, and iron may be needed for cattle with high sulfate intake. Molybdate, at sufficient dietary concentrations, depresses ruminal sulfide concentrations (Bryden and Bray, 1972). Such an effect represents another potential modifying influence on sulfide formation.

Recent Field Studies

We investigated PEM associated with high-sulfate water (approximately 2,400 ppm sulfate) under feedlot conditions. Using the method of Gould et al. (1997), the ruminal H₂S gas cap concentrations in six cattle with signs of advanced PEM were not markedly elevated. This is not unexpected, because PEM-affected cattle, being depressed and lethargic, have reduced feed and water intake. However, when ruminal H₂S gas cap concentrations were measured concurrently in six clinically normal pen mates of the affected cattle, four of the clinically normal steers had H₂S concentrations over 2,000 ppm (range, 2,800 to 8,000 ppm H₂S). Based on the study of PEM that was experimentally induced with a high-sulfate concentrate diet, ruminal H₂S levels over 2,000 ppm can precede the development of PEM (Gould et al., 1997). Ruminal H₂S concentrations in steers fed the same concentrate diet without added sulfate remained under 500 ppm (Gould et al., 1997). Total blood thiamine concentrations in PEM-affected cattle and clinically unaffected pen mates remained within normal reference ranges when measured with the bioassay method of Olkowski and Gooneratne (1992), a method that may indicate availability of biologically active thiamine even when potential analogues are formed.

Implications

Episodic excessive ruminal sulfide production is a hazard of ruminant life. Although polioencephalomalacia (PEM) is a conspicuous manifestation of sulfide toxicity, sulfide has other more subtle effects. As a nonspecific cell poison, hydrogen sulfide probably affects other organs. Pneumotoxicity could be a subtle but important adverse effect of pathologic ruminal sulfide production. Further research is needed to examine the various factors involved with production of pathologic ruminal sulfide concentrations and the

absorption of sulfide so that dietary and ruminal microbial intervention can be used to prevent PEM.

Literature Cited

- Abe, K., and H. Kimura. 1996. The possible role of hydrogen sulfide as an endogenous neuromodulator. *J. Neurosci.* 16:1066.
- Beauchamp, R. O., J. S. Bus, J. A. Popp, C. J. Boreiko, and D. A. Andjelkovich. 1984. A critical review of the literature on hydrogen sulfide toxicity. *CRC Crit. Rev. Toxicol.* 13:25.
- Beke, G. J., and R. Hironaka. 1991. Toxicity to beef cattle of sulfur in saline well water: A case study. *Sci Total Environ* 101:281.
- Bratton, G. R., J. Zmudaki, N. Kincaid, and J. Joyce. 1981. Thiamine as treatment of lead poisoning in ruminants. *Mod. Vet. Pract.* 62:441.
- Bray, A. C., and A. R. Till. 1975. Metabolism of sulphur in the gastro-intestinal tract. In I. W. McDonald and A.C.I. Warner, (Ed.) *Digestion and Metabolism in the Ruminant. Proceedings of the IV International Symposium on Ruminant Physiology.* pp 243–260. The University of New England Publishing Unit, Armidale, Australia.
- Bryden, J. M., and A. C. Bray. 1972. The effect of dietary molybdenum on the reduction of inorganic sulphate in the rumen. *Proc. Aust. Soc. Anim. Prod.* 9:335–340.
- Bulgin, M. S., S. D. Lincoln, and G. Mather. 1996. Elemental sulfur toxicosis in a flock of sheep. *J. Am. Vet. Med. Assoc.* 208:1063.
- Chemical Rubber Co. 1996. *Physical constants of inorganic compounds. Handbook of Chemistry and Physics.* (77th Ed.). pp 34–98. CRC Press, Boca Raton FL.
- Christian, R. G., and L. Tryphonas. 1971. Lead poisoning in cattle. Brain lesions and hematologic changes. *Am. J. Vet. Res.* 32:203.
- Coppock, R. W., W. C. Wagner, J. D. Reynolds, R. S. Vogel, H. B. Gelberg, L. Z. Florence, and W. A. Wolff. 1991. Evaluation of edetate and thiamine for treatment of experimentally induced lead poisoning in cattle. *Am. J. Vet. Res.* 52:1860.
- Cummings, B. A., D. H. Gould, D. R. Caldwell, and D. W. Hamar. 1995a. Identity and interactions of rumen microbes associated with dietary sulfate-induced polioencephalomalacia in cattle. *Am. J. Vet. Res.* 56:1384.
- Cummings, B. A., D. R. Caldwell, D. H. Gould, D. R. Caldwell, and D. W. Hamar. 1995b. Rumen microbial alterations associated with sulfide generation in steers with dietary sulfate-induced polioencephalomalacia. *Am. J. Vet. Res.* 56:1390.
- Dahme, E., T. Blitzer, and G. Dirksen. 1983. Zur neuropathologie der jauchegasvergiftung (H₂S-vergiftung) beim rind (neuropathology of manure gas [hydrogen sulfide] poisoning in cattle). *Dtsch. Tieraerztl. Wochenschr.* 90:316.
- Davies, E. T. 1965. Cerebrocortical necrosis in calves. *Vet. Rec.* 77:290.
- Dey, S., D. Swarup, Kalicharan, and B. Singh. 1995. Treatment of lead toxicity in calves. *Vet. Hum. Toxicol.* 37:230.
- Dickie, C. W., R. J. Nelson, D. G. Frazee, L. D. Krugman, and E. Bronner. 1979. Polioencephalomalacia in range cattle. *J. Am. Vet. Med. Assoc.* 175:460.
- Dougherty, R. W., and H. M. Cook. 1962. Routes of eructated gas expulsion in cattle—a quantitative study. *Am. J. Vet. Res.* 23:997.
- Edwin, E. E., and R. Jackman. 1973. Ruminal thiaminase and tissue thiamine in cerebrocortical necrosis. *Vet. Rec.* 92:640.
- Edwin, E. E., and R. Jackman. 1982. Ruminant thiamine requirement in perspective. *Vet. Res. Commun.* 5:237–250.
- Edwin, E. E., G. Lewis, and R. Allcroft. 1968. Cerebrocortical necrosis: a hypothesis for the possible role of thiaminase in its pathogenesis. *Vet. Rec.* 83:176.
- Fakhruddin, P. D. Mathur, S. N. Sharma, and J. S. Yadav. 1987b. Experimental studies on polioencephalomalacia (cerebrocortical necrosis) in goats induced by amprolium. *Indian J. Anim. Sci.* 57:377.

- Fakhrudin, S. N. Sharma, and J. S. Yadav. 1987a. Haematobiochemical and therapeutic studies on polioencephalomalacia in cattle. *Indian J. Vet. Med.* 7:19.
- Gibson, D. M., J. J. Kennelly, and G. W. Mathison. 1988. The performance of dairy and feedlot cattle fed sulfur dioxide-treated high-moisture barley. *Can. J. Anim. Sci.* 68:471.
- Goetsch, A. L., and F. N. Owens. 1987. Effect of supplement sulfate (Dynamate) and thiamine-HCl on passage thiamine to duodenum and site of digestion in steers. *Arch. Anim. Nutr.* 37:1075.
- Gooneratne, S. R., A. A. Olkowski, and D. A. Christensen. 1989a. Sulfur-induced polioencephalomalacia in sheep: Some biochemical changes. *Can. J. Vet. Res.* 53:462.
- Gooneratne, S. R., A. A. Olkowski, and R. G. Klemmer. 1989b. High sulfur-related thiamine deficiency in cattle: A field study. *Can. Vet. J.* 30:139.
- Gould, D. H., B. A. Cummings, and D. W. Hamar. 1997. In vivo indicators of pathologic ruminal sulfide production in steers with diet-induced polioencephalomalacia. *J. Vet. Diagn. Invest.* 9:72.
- Gould, D. H., M. M. McAllister, J. C. Savage, and D. W. Hamar. 1991. High sulfide concentrations in rumen fluid associated with nutritionally induced polioencephalomalacia in calves. *Am. J. Vet. Res.* 52:1164.
- Gupta, G. C., B. P. Joshi, and P. Rai. 1976. The levels of thiamine in the rumen fluid and blood serum in the spontaneous bovine rumen dysfunctions. *Acta Vet. Brno* 45:205.
- Hamlen, H., E. Clark, and E. Janzen. 1993. Polioencephalomalacia in cattle consuming water with elevated sodium sulfate levels: A herd investigation. *Can. Vet. J.* 34:153.
- Harris, W. N. 1987. Polioencephalomalacia in feedlot cattle drinking water high in sodium sulfate. *Can. Vet. J.* 28:717.
- Haven, T. R., D. R. Caldwell, and R. Jensen. 1983. Role of predominant rumen bacteria in the cause of polioencephalomalacia (cerebro cortical necrosis) in cattle. *Am. J. Vet. Res.* 44:1451.
- Hibbs, C. M., and J. P. Thilsted. 1983. Toxicosis in cattle from contaminated well water. *Vet. Hum. Toxicol.* 25:253.
- Hill, F. I., and P. C. Ebbett. 1997. Polioencephalomalacia in cattle in New Zealand fed chou moellier (*Brassica oleracea*). *N. Z. Vet. J.* 45:37.
- Jackman, R. 1985. The diagnosis of CCN and thiamine deficiency in ruminants. *Vet. Annu.* 25:71.
- James, L. F., W. F. Hartley, K. E. Panter, B. L. Steglemeier, D. Gould, and H. F. Mayland. 1994. Selenium poisoning in cattle. In: S. M. Colegate and P. R. Dorling, (Ed.) *Plant Associated Toxins: Agricultural, Phytochemical and Ecological Aspects.* p 416. CAB International, Oxon, U.K.
- Jeffrey, M., J. P. Duff, R. J. Higgins, V. R. Simpson, R. Jackman, T. O. Jones, S. C. Mechie, and C. T. Livesey. 1994. Polioencephalomalacia associated with ingestion of ammonium sulfate by sheep and cattle. *Vet. Rec.* 134:343.
- Jensen, R., L. A. Griner, and O. R. Adams. 1956. Polioencephalomalacia of cattle and sheep. *J. Am. Vet. Med. Assoc.* 129:311.
- Jubb, K.V.F. and C. R. Huxtable. 1993. The nervous system. In: K.V.F. Jubb, P. C. Kennedy, and N. Palmer (Ed.) *Pathology of Domestic Animals* (4th Vol.). p 267. Academic Press, New York.
- Kandylis, K. 1983. Toxicology of sulfur in ruminants: Review. *J. Dairy Sci.* 67:2179.
- Kerr, L. A., and R. D. Linnabary. 1989. A review of interstitial pneumonia in cattle. *Vet. Hum. Toxicol.* 31:247.
- Lewis, D. 1954. The reduction of sulphate in the rumen of the sheep. *Biochem. J.* 56:391.
- Linklater, K. A., and D. A. Dyson. 1977. Faecal thiaminase in clinically normal sheep associated with outbreaks of polioencephalomalacia. *Res. Vet. Sci.* 22:308.
- Little, P. B. and D. K. Sorenson. 1969. Bovine polioencephalomalacia, infectious embolic meningoencephalitis and acute lead poisoning in feedlot cattle. *J. Am. Vet. Med. Assoc.* 155:1892.
- Loew, F. M., J. M. Bettany, and C. E. Halifax. 1975. Apparent Thiamine status of cattle and its relationship to polioencephalomalacia. *Can. J. Comp. Med.* 39:291.
- Lopez, A., M. Prior, L. E. Lillie, C. Gulayets, and O. S. Atwal. 1988. Histologic and ultrastructural alterations in lungs of rats exposed to sublethal concentrations of hydrogen sulfide. *Vet. Pathol.* 25:376.
- Low, J. C., P. R. Scott, F. Howie, M. Lewis, J. FitzSimons, and J. A. Spence. 1996. Sulphur-induced polioencephalomalacia in lambs. *Vet. Rec.* 138:327.
- McAllister, M. M., D. H. Gould, and D. W. Hamar. 1992. Sulphide-induced polioencephalomalacia in lambs. *J. Comp. Path.* 106:267.
- Mella, C. M., O. Perez-Oliva, and F. M. Loew. 1976. Induction of bovine polioencephalomalacia with feeding system based on molasses and urea. *Can. J. Comp. Med.* 40:104.
- Morgan, K. T. 1974. Thiaminase type 1-producing bacilli and ovine polioencephalomalacia. *Vet. Rec.* 95:361.
- Mottley, C., and R. P. Mason. 1988. Sulfate anion free radical formation by peroxidation of (bi)sulfite and its reaction with hydroxyl radical scavengers. *Arch. Biochem. Biophys.* 267:681.
- Mueller, R. E., and J. M. Asplund. 1981. Evidence in the ovine that polioencephalomalacia is not a result of an uncomplicated thiamin deficiency. *Nutr. Rep. Int.* 24:95.
- NRC. 1996. *Nutrient Requirements of Beef Cattle* (7th Ed). p 60. National Academy Press, Washington, DC.
- Oliveira L. A. de, C. Jean-Blain, V. D. Corso, V. Benard, A. Durix, and S. Komisarczuk-Bony. 1996. Effect of a high sulfur diet on rumen microbial activity and rumen thiamine status in sheep receiving a semisynthetic, thiamine-free diet. *Reprod. Nutr. Dev.* 36:31.
- Olkowski, A. A., and S. R. Gooneratne. 1992. Microbiological methods of thiamine measurement in biological material. *Int. J. Vitam. Nutr. Res.* 62:34.
- Olkowski, A. A., S. R. Gooneratne, C. G. Rousseaux, and D. A. Christensen. 1992. Role of thiamine status in sulphur induced polioencephalomalacia in sheep. *Res. Vet. Sci.* 52:78.
- O'Toole, D., M. Raisbeck, J. C. Case, and T. D. Whitson. 1996. Selenium-induced blind staggers and related myths. A commentary on the extent of historical livestock losses attributed to selenosis on Western US rangelands. *Vet. Pathol.* 33:104.
- Padovan, D. 1980. Polioencephalomalacia associated with water intoxication in cattle. *Cornell Vet.* 70:153.
- Pritchard, D., and G. W. Eggleston. 1978. Nardoo fern and polioencephalomalacia. *Aust. Vet. J.* 54:204.
- Radostits, O. M., D. C. Blood, and C. C. Gay. 1994. *Veterinary Medicine.* (8th Ed.). Bailliere Tindall, London.
- Raisbeck, M. F. 1982. Is polioencephalomalacia associated with high-sulfate diets? *J. Am. Vet. Med. Assoc.* 180:1303.
- Rammell, C. G., and J. H. Hill. 1986. A review of thiamine deficiency and its diagnosis, especially in ruminants. *N. Z. Vet. J.* 34:202.
- Roberts, G. W., and J. W. Boyd. 1974. Cerebrocortical necrosis in ruminants. *J. Comp. Path.* 84:365.
- Rousseaux, C. G., A. A. Olkowski, and A. Chauvet. 1991. Ovine polioencephalomalacia associated with dietary sulphur intake. *J. Vet. Med. Ser. A* 38:229.
- Sager, R. L., D. W. Hamar, and D. H. Gould. 1990. Clinical and biochemical alterations in calves with nutritionally-induced polioencephalomalacia. *Am. J. Vet. Res.* 51:1969.
- Spicer, E. M., and B. J. Horton. 1981. Biochemistry of natural and amprolium-induced polioencephalomalacia in sheep. *Aust. Vet. J.* 57:230.
- Summers, B. A., J. F. Cummings, and A. de Lahunta. 1995. *Veterinary Neuropathology.* Mosby-Year Book Inc., St. Louis MO.
- Suttle, N. F. 1980. The role of thiomolybdates in the nutritional interactions of copper, molybdenum and sulfur: Fact or fantasy? *Ann. N. Y. Acad. Sci.* 335:195.

Citations

This article has been cited by 7 HighWire-hosted articles:
<http://jas.fass.org#otherarticles>