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Polioencephalomalacia

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Polioencephalomalacia (PEM) is a morphological diagnosis of a lesion in the brain characterized by necrosis of gray matter of the cerebral cortex. However, the term is most often used to indicate a specific central nervous system disease in ruminants assumed to be caused by the disruption of normal thiamine metabolism. The pathological lesion polioencephalomalacia is not caused only by thiamine problems. Therefore, it is important in communications between pathologists, practitioners, and producers that everyone realizes how the others are using the term. In some countries such as Great Britain and Australia, the term cerebrocortical necrosis is used instead of PEM.

Epidemiology

In cattle the disease is usually associated with 6- to 18-month-old cattle and in sheep weaned to 18 months old. PEM is rare in adult cattle. It is more commonly seen in feedlot animals on high concentrate, low roughage diets. Pastured animals can get PEM. The disease is sporadic but can affect 25% of the animals, of these 25% to 50% may die.

Clinical Signs

In the book Diseases of Cattle: A Manual of Diagnosis (Blood et al., 1990), the percentage of time an animal presents with a certain sign is as follows:

Acute PEM

5	temperature > 39.5
5	heart rate > 100 per minute
30	weight gain reduced or weight loss
95	feed intake < 50 of normal
70	milk yield below normal
5	gait abnormal
70	opisthotonos
70	recumbency
95	hyposensitive to external stimuli
95	behavior indicated blindness
5	aggressive actions
5	frenzy
50	aimless or compulsive walking
50	head pressing
50	jaw champing
70	nystagmus
5	strabismus
30	pupil constriction
70	papilledema
95	menace response absent
95	pupillary light response absent
30	drooling saliva
70	saliva frothy
50	convulsions
5	tremor

Subacute PEM

70	weight gain reduced or weight loss
95	feed intake < 50 of normal
70	standing preferred
70	eat slowly
70	hyposensitive to external stimuli
70	behavior indicates blindness
95	aimless or compulsive walking
95	head pressing
80	menace response absent

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Pathology

Morphological brain lesions in acute cases of PEM may be difficult to see grossly. Edema is evidenced by paleness and softness of cerebral cortex. There may be some caudal displacement of brain resulting in coning of cerebellum as it is forced into foramen magnum. Lesions are more severe over dorsal and caudal cerebral cortex. Lesions are approximately symmetrical.

Subacute and chronic lesions are more severe. In 2 to 3 days cerebral cortex gray matter becomes softer and yellow brown as necrosis can be seen grossly. Lesions over cerebral cortical ridges (gyri) are most prominent. As lesion progresses, there is separation of cerebral white and gray matter. If the animal survives 2 weeks or more, necrosis progresses with collapse of gray matter, resulting in decortication of cerebral hemispheres.

Pathogenesis

The total picture is not clear as to causes and mechanisms of PEM production. Current information indicates multiple factors are involved and all need not be present in all cases. The most commonly accepted cause (and most documented) is one of thiamine deficiency or inadequacy. This is supported by the therapeutic value of thiamine (parental) when given to animals early in the course of PEM. Studies show low thiamine levels or low thiamine dependant functions in herds where PEM is present. Low tissue brain thiamine is present in animals with PEM. Also, thiamine antagonists can be used to produce PEM. It is easily theorized how thiamine deficiency would cause PEM, since thiamine is an important factor in carbohydrate metabolism. The blocking of glucose (carbohydrate) metabolism in the brain would cause cell injury with swelling proceeding to death and therefore necrosis in the brain.

Since adequate thiamine is produced in the rumen normally, deficiency could be caused by:

-Decreased ruminal thiamine production
-Decreased thiamine absorption
-Decreased activation of thiamine to thiamine (pyrophrophate) diphosphate
-Increased amounts of thiamine inhibitors (e.g., analogues)
-Decreased amounts of other substances essential for thiamine function (e.g., apoenzyme)
-Increased thiamine demand
-Increased thiamine excretion
-Increased thiamine destruction by thiaminases

PEM has been produced in preruminant lambs with a thiamine free diet. Decreased brain thiamine phosphated ester concentrations were found in brains of lambs on thiamine free milk. Once the rumen is fully functional, it produces enough thiamine so no exogenous sources are needed.

Considerable attention has been given to ruminal thiaminases as the cause of thiamine deficiency. Thiaminases are found in high concentrations in rumen contents and feces of many animals with PEM. Thiaminase are classified as I or II. Thiaminase II cleaves thiamine at the methylene bridge between the thizole and pyrimidine rings. Thiaminase I in the rumen will not only destroy thiamine by cleavage but also, with the thiamine fragments plus a cosubstrate, produce a thiamine analog. The analog could be absorbed and inhibit thiamine dependent reactions.

Even though ruminal production of endogenous thiaminase is likely, there are exogenous sources, also. High levels of thiaminase I are present in rhizomes of bracken fern (Ptendium equilinium) and horsetail (Equisetum arvense). Kochia scorpia (Mexican fireweed) had thiamine destroying properties in two of six sources examined. This thiamine destroying property in Kochia may or may not be due to thiaminase. Field cases have associated grazing Kochia with polioencephalomalacia in cattle. However, in both cases cattle were consuming water high in sulfates. The role of

sulfur in polioencephalomalacia will be covered later. Evidence of moldy feed inducing PEM is subjective and inconclusive.

Thiabendazole, tetramisole, piperazine, oxyclozanide, trimeprazine, and acepromazine have been shown to be thiaminase I cosubstrates. Antihelmintics levamisole hydrochloride, and thiabendazole have been associated with PEM outbreaks.

Amprolium, a thiamine analog which inhibits thiamine phosphorylation, induces polioencephalomalacia. This supports the theory of analog induced PEM.

There appears to be multiple ways that increased sulfur intake can result in PEM. One way is thiamine destruction. Sulfhydryl or sulfinic acid can act as a cosubstrate with thiaminase I to destroy thiamine. Sulfite ion will destroy thiamine by cleaving it at methylene bridge independent of thiaminase. Sodium sulfate (Na_2SO_3) will also destroy thiamine without thiaminase.

$MgKSO_4$ has been shown to produce PEM. Animals fed $CaSO_4$-$2H_2O$ (gypsum) as a feed intake limiter developed PEM. Cattle on rations of above 2% sulfate had a much greater incidence of PEM. Plasma thiamine concentrations are depressed by addition of $MgKSO_4$ or $NaSO_4$ to the diet. Cattle with .72% sulfate (as $MgKSO_4$) added to their diet gained 50% less than control groups. Three of 20 cattle in the sulfate added group and none of the controls developed PEM.

One study showed that when cattle drank water with more than 1000 ppm sulfate blood thiamine concentrations were significantly lowered compared to cattle drinking water with less than 200 ppm sulfate. This study gave no information of occurrence of PEM in these populations. Both feed and water contributed significantly to sulfur total intake.

Some researchers believe that sulfur independent of thiamine metabolism can cause PEM. In a study authors concluded that depression of blood and tissue thiamine concentrations were not severe enough to induce PEM. In this study, five of nine steers developed PEM when given diets with added sodium sulfate, resulting in .36% total sulfur. Calves were fed a high concentrate, low fiber diet. These authors concluded PEM can be induced by sulfur toxicosis. Again, in sheep given diets of .63% sulfur, all sheep had brain lesions consistent with PEM. Dietary thiamine at 230 mg/kg DM did have some protective effect as evidenced by no clinical signs and milder brain lesions. This same research group from the University of Saskatchewan showed sheep on .19% dietary sulfur did not develop PEM. As in the previous study, high dietary thiamine (243 mg/kg DM) as HCl protected sheep from clinical nervous signs but not PEM brain lesions. McAllister et al. (1992) induced central nervous system signs within 45 to 120 minutes of oral administration of sulphide solution to lambs. The theory is that thiamine related PEM takes much longer to develop. Therefore, researchers concluded lambs got PEM from the direct effect of sulfur on the brain.

It has been proposed that dietary sulfur may result in higher metabolic demand for thiamine in sheep. Therefore, it has been proposed that sulfur may induce PEM by one of or a combination of three ways: thiamine destruction, direct toxic effect, and/or increasing thiamine requirements.

In Cuba a molasses-urea based diet induced PEM without altering brain or liver thiamine levels. Molasses can have high concentrations of sulfur and this may explain PEM production.

Other causes of PEM that are independent of thiamine include lead and chronic cyanide toxicosis. PEM has been induced in sheep on a cobalt deficient diet. Pathogenesis is not clear.

Treatment

Treatment is effective in acute cases. However, as days pass, damage is most likely irreversible. Thiamine hydrochloride should be given intravenously. Supportive care to treat edema is also indicated.

Measures for prevention of others in the herd from developing PEM include thiamine added to diet at 50 mg/kg of feed for 2 to 3 weeks followed by 20 to 30 g/kg of feed as long as animals are at risk. For healthy groups of animals fed diets that could cause thiamine inadequacy, thiamine should be added to diet at 5 to 10 mg/kg of dry feed.

The Merck Index (1991) states supplemental dietary thiamine is contraindicated. There is some concern that dietary thiamine (thiamine hydrochloride) may increase production of thiamine analogues if thiaminase I is present in rumen. To avoid this scenario, use of thiaminase resistant thiamine-containing compounds are indicated. Two such compounds are thiamine propyl disulfide or thiamine tetrafurfuryl disulfide.

References

Blood, D. C., P. Brightling, and M. T. Larcombe. 1990. Diseases of Cattle: A Manual of Diagnosis. Bailliere Tindall, London.

Blood, D. C., and O. M. Radostitis. 1989. Veterinary Medicine (7th Ed.). Bailliere Tindall, London.

Brent, B. E., and E. E. Bartley. 1984. Thiamin and niacin in the rumen. J. Anim. Sci. 59:813-822.

McAllister, M. M., D. H. Gouold, and D. W. Hamar. 1992. Sulphide-induced polioencephalomalacia in lambs. J. Comp. Path. 106:267-278.

The Merck Index. 1991. An Encyclopedia of Chemicals, Drugs and Biologicals. Merck & Co., Inc. Rahway, NJ.