Observations on "Nervous" Coccidiosis in Calves

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Summary

Similarities of "nervous" coccidiosis in calves and yearlings to hypomagnesemic (grass) tetany in cows, including clinical signs and response to treatment, are presented. Serum magnesium and calcium levels ranged from below normal to normal. Prevention of coccidiosis, not treatment of the nervous form, is the most economical way to minimize losses.

Introduction

A neurological syndrome associated with coccidiosis in calves and yearling cattle has been known for over sixty years. As early as 1921 nervous system involvement during outbreaks of bovine coccidiosis was described by Bruce: "...fatal cases were preceded by fits. Death occurs in from 8 to 24 hours after first showing fits, the animal dying in convulsions. ... The fits mentioned (which are no doubt due to cerebral anemia) occur at varying intervals. They appear to be induced when the animal is disturbed..., the animal appears frightened, staggers, may brace itself by resting its head on the ground with all four feet widely spread, falls over and froths a little at the mouth; in a little more or less than a minute it gets up and acts as if nothing had happened". This description is as valid today as it was sixty-two years ago. Marsh (1923) also described staggering, convulsions and death in cattle with coccidiosis.

The mechanism of "nervous" coccidiosis has given rise to much speculation, but it remains an enigma. Fitzgerald (1980) has suggested an antigen-antibody reaction involving coccidia and the host may be responsible. Loss of electrolytes has been mentioned by Kemp (1981). Rosenberger (1978) has proposed autointoxication and secondary bacterial sepsis, while Jensen and Mackey (1965) suggest toxemia and anemia are responsible for the convulsions.

Clinical Signs

Early in the course of the syndrome the animal may appear normal until it is disturbed. Then it may show mild muscle tremors, ataxia and fall to the ground. After a short time the animal may get up and appear normal again. In the advanced stages the animal is in lateral recumbency, will show muscle tremors and limb jerking with intermittent convulsions, opisthotonus, converging strabismus, nystagmus, exaggerated snapping of the eyelids, frothing at the mouth and occasional bellowing. Death often occurs in one to four days after lateral recumbency. Convulsions can often be induced by mild stimulation of the recumbent animal. Rectal temperature is usually normal, but may be elevated after the animal exhibits convulsions. Heart and respiratory rates are normal to elevated. Evidence of diarrhea, sometimes bloody, is usually present. The foregoing signs, with the exception of bloody diarrhea, are also seen in cows with grass tetany.

Necropsy Findings

Gross lesions were confined to the ileum, cecum and colon in most cases. Varying degrees of mucosal necrosis, hemorrhage and fibrinonecrotic debris were seen. Microscopically, in addition to the above, intracellular coccidia were observed, mainly in portions of the colon. Gross and microscopic changes in the brains of animals dying from "nervous" coccidiosis were either absent or nonspecific—i.e. edema, congestion and shrunken neurons. One heifer had a purulent bronchopneumonia.

Clinicopathologic Findings

Fecal examination of calves with "nervous" coccidiosis all showed coccidial oocysts in varying numbers. Some animals also had nematode ova present. CBCs from affected calves were within normal limits Serum magnesium levels varied from below normal to above normal, while serum calcium levels were all below normal. Serum free fatty acid levels were below normal in one calf with "nervous" coccidiosis and in a second calf with coccidiosis without nervous signs *(see Table 1).*

Mice injected with CSF from a calf dead from "nervous" coccidiosis were unaffected.

Liver and kidney samples from several affected calves were negative for lead.

Treatment and Results

The cases described were seen from December, 1978, through January, 1983. The area in central Montana consists of cow/calf operations and relatively few calves are wintered. Producers with a coccidiosis problem often do not seek veterinary assistance. For these reasons few cases of "nervous" coccidiosis are seen.

The ages of the calves observed ranged from seven months

TABLE 1. Serum and Cerebrospinal fluid Chemistry 4/

Calf No.	Age (mo.)	Sex	Breed	Serum 5/ Mg mg/dl	Ca mg/dl	Na mEq/L	K mEq/L	Glucose mg/dl	Free Fatty Acids mEq/L	Status at time of Initial treatment	Response to treatment
Normal Values 6/				2.0-3.5	8.0-11.0 (9-12) 7/	132-152	3.9-5.8	33-55	0.45-0.90		
Herd A											
1	9-11	Steer	Angus-Hereford	1.5*	7.5	—	5.8*	—	—	Standing, ataxic	Recovered
2	9-11	Steer	Angus	2.4	6.8	140	3.5	—	—	"	Died
3	9-11	Steer	Angus	2.4*	8.1	143	9.0*	—	—	"	Died
			Hereford	0.3*	7.9	139	8.7*	After treatment			
4	9-11	Steer	Angus-Hereford	5.6*	6.1	142	5.1*			Recumbent	Died
5	9-11	Heifer	Angus	2.1	7.5	146	3.3			Standing, ataxic	Died
				2.6	8.6	142	4.2	24 hr after treatment			
				2.4	7.6	149	3.1	24 hr after 2nd treatment			
6	9-11	Heifer	Angus Charolais	1.7	7.7	144	2.6			Recumbent	Died
7	9-11	Steer	Angus-Hereford	2.3	9.0	147	7.4	Normal control:		No coccidiosis	
Herd B											
1	7	Heifer	Hereford	1.4	7.6	—	—	68		Standing, ataxic	Recovered
			Simmental	1.4	9.1	—	—	Convalescent			
2	8	Heifer	Hereford-Simmental	2.4	8.1	—	—	76		Recumbent	Died
Herd C											
1	10	Heifer	Angus	1.6	8.4	—	—	334		Recumbent	Died
				2.5	8.3	—	—	87 After treatment			
				CSF (4.8)	(8.5)			(103)			
Herd D											
1	8-10	Heifer	Hereford	2.0	10.0	—	—	—	0.48		Normal control: No coccidiosis
2	8-10	Steer	Hereford	3.4	9.5	—	—	—	0.20		"Nervous" coccidiosis:
3	8-10	Steer	Hereford	3.2	8.3	—	—	—	0.20		Died before any treatment
				CSF (2.0)	(4.9)						

4/ All serum and CSF chemistries were conducted by the Veterinary Research Laboratory, Montana State University, Bozeman, Montana 59715, except the free fatty acid determinations which were done by Smith Kline Chemical Laboratories, Inc., St. Louis, Missouri.

5/ All samples were taken before any treatment was given except in the cases where multiple samples were taken throughout the course of the disease. CSF samples were taken shortly after death.

6/ Normal values taken from Blood, D.C., Henderson, J.A. and Radostits, O.M., *Veterinary Medicine,* 5th ed., Lea and Febiger, 1979.

7/ Other sources give slightly different normal ranges for some of the electrolytes: Dukes, H.H., *Physiology of Domestic Animals,* 7th ed., Cornell University Press, 1955 and Maynard, L.A. *Animal Nutrition,* 3rd ed., McGraw-Hill Book Company, 1951.

* Samples were hemolyzed. Figures given may be elevated above true values, especially magnesium and potassium which are primarily intracellular.

to one year. No sex predilection was observed. Hereford, Angus and crosses involving these two breeds predominate in this area, and therefore were most often observed.

Calves with coccidiosis exhibiting CNS signs were treated initially with 250 ml of a commercial calcium, magnesium and dextrose solution[1] intravenously and an additional 250 ml subcutaneously. In addition, sustained release sulfamethazine boluses[2] were given at the rate of one bolus per 150 lbs, orally. Animals in convulsions were treated with a 7% chloral hydrate solution or a 6% chloral hydrate/magnesium sulfate solution intravenously to effect. Additional supportive therapy consisted of balanced electrolyte solutions (IV and oral), thiamine, dextrose, and amino acids, given as needed. Calves that responded to initial calcium/magnesium therapy were given one ounce of magnesium oxide per head per day, orally in gelatin capsules for three or four days.

[1] *Cal-Dextro No. 2, Fort Dodge Laboratories, Inc., Fort Dodge, Iowa 50501.*

[2] *Sulfamethazine Spanbolt II, Norden Laboratories, Lincoln, Nebraska 68501.*

Herd A: December, 1978. Comprises 475 calves, both steers and heifers, weaned about six weeks. Fifty-eight calves showed clinical signs of coccidiosis, i.e. bloody diarrhea, tenesmus, weight loss, anorexia and coccidia in the feces. Seven of the affected calves exhibited CNS signs, six of which died. During this outbreak the temperature approached 0° F, and a ten-to-twenty mile an hour wind developed most afternoons. The calves had little shelter.

Herd B: November, 1980. Group of 150 calves, mostly heifers; about one-third of the calves showing diarrhea, weight loss and coccidia in the feces. Three calves died in convulsions.

Herd C: January, 1981. Fifty heifers branded, vaccinated against blackleg and malignant edema, and put on feed. Heifer found recumbent on ice in the feedlot. Ambient temperature near 0° F. Animal showing diarrhea and coccidia oocysts in feces.

Herd D: January 1983. Approximately 100 calves purchased through a sales ring and added to 400 home grown calves. Coccidiosis outbreak confined to the purchased calves. About one-half were affected. One steer developed the "nervous" form and died in convulsions.

Differential Diagnosis

Diseases to be considered when the "nervous" form of coccidiosis is encountered include lead poisoning, polioencephalomalacia, thromboembolic meningo-encephalitis, listeriosis, rabies, sporadic bovine encephalomyelitis and salt poisoning. Consideration of history, clinical examination, necropsy, laboratory tests, histopathology and response to treatment should differentiate these diseases.

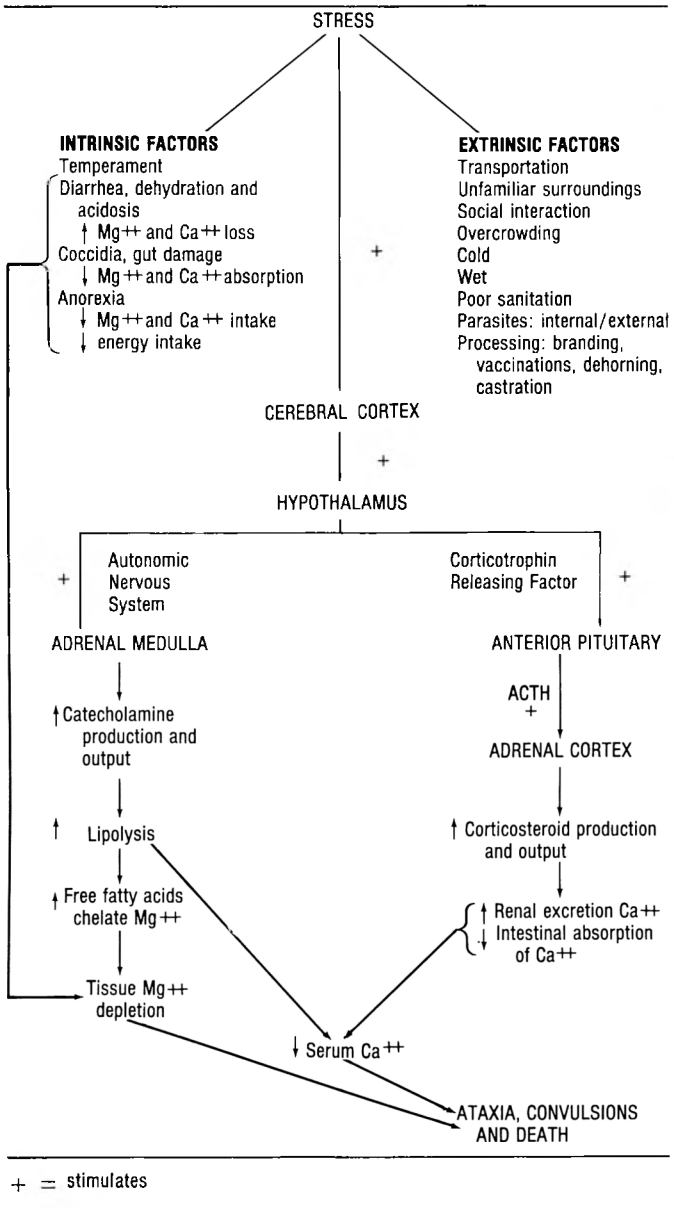
Discussion

The signs exhibited by calves with "nervous" coccidiosis parallel those seen in cows with hypomagnesemic (grass) tetany. Both conditions are usually associated with stress, and the response to treatment with parenteral magnesium, calcium and glucose is similar: those animals treated early in the course of the disease (those that are still standing) respond more favorably; those animals that are recumbent for any period of time usually succumb.

The mechanism proposed for the nervous form of coccidiosis involves stresses which result in the depletion of tissue magnesium and a lowering of serum calcium *(see Figure 1).* Rayssiguier (cited in Seelig, 1980) showed fasting or cold stress of shorn sheep caused lypolysis and hypomagnesemia similar to the infusion of epinephrine. Catecholamines increase lipolysis and the free fatty acids chelate magnesium ions. Rayssiguier (1980) demonstrated that cows tetany had elevated free fatty acid levels and hypomagnesemia. In other studies cited, the administration of a beta blocking agent (propanolol) or an antilipolytic agent (sodium nicotinate) inhibits the increase in free fatty acids and the reduction in plasma magnesium. Sabbot and Costin (1974 a and b) demonstrated an increased uptake of calcium and magnesium by brain tissue of cold-stressed rats. It is not known if this occurs in calves with "nervous" coccidiosis. Catecholamine-induced lipolysis has also lowered the serum calcium level of sheep, and adrenal corticosteroids decrease intestinal absorption and increase renal excretion of calcium (cited in Anderson, 1980). The ten calves with "nervous" coccidiosis all had below-normal levels of serum calcium before any treatments were given, whereas the two normal controls (no coccidiosis) and the one steer with non-"nervous" coccidiosis had normal serum calcium levels *(Table 1).*

Some affected calves had normal or elevated serum magnesium levels. The serum magnesium level is not a true

Figure 1. Proposed Mechanism For "Nervous" Coccidiosis



indication of the magnesium status of the body. Sixty per cent of the magensium in the animal body is in the skeleton, about twenty-nine percent is in the muscle, and only one per cent is in the extracellular fluid (Aikawa, 1981). Initial tissue magnesium depletion may produce a transient elevation in serum magnesium before the level falls below normal. Pauli and Allsop (1974) demonstrated low levels of magnesium in the CSF of cows with grass tetany, and Kershaw and Wilson (1969, cited in Aikawa, 1981) found magnesium levels of heart muscle of cattle and sheep that died from hypomagnesia were significantly lower than those of normal animals. Tissue and CSF magnesium levels would appear to give a truer evaluation of the magnesium status of the body than serum or plasma concentration. Ventriculolumbar perfusion of sheep with a synthetic CSF with a low magnesium content (<0.6 mg/dl) produced tetany which was abolished by the perfusion of a solution with a normal magnesium concentration (cited in Aikawa, 1981).

The free fatty acid level in the one steer tested was below normal; just the opposite of what one would expect. The time at which the sample was drawn in relation to the onset of the disease may be important. Samples drawn in the initial stages may show the elevated free fatty acids, while those taken later (as this sample was) may show decreased values. Kruse *et al* (1933) found decreased fatty acid values in magnesium-deficient rats.

The suggestion that electrolyte losses resulting from diarrhea and subsequent dehydration are responsible for the neurological signs does not appear to be valid, for the calves exhibiting the most severe dehydration are usually not the ones with CNS signs. Also the calves with the greatest blood loss and anemia are usually not the ones affected with the nervous form of coccidiosis. If "nervous" coccidiosis were due to an immune-mediated response one would expect a beneficial effect from the administration of corticosteroids such as dexamethasone. In reality, the use of these drugs has just the opposite effect: the animal seems to die a little sooner. This is not surprising when one considers that these drugs can lower the serum calcium.

No conclusions can be drawn from the preceding observations and discussions. There is enough evidence to suggest that the proposed mechanism, or some variation, is workable. No comprehensive studies of the "nervous" form of coccidiosis have been done to date. Some parameters that might elucidate this condition are the calcium and magnesium levels in serum (or plasma), CSF, skeletal and heart muscle, brain, bone, urine and feces of normal calves, those with non-neurological coccidiosis and calves with "nervous" coccidiosis. Serum free fatty acid levels throughout the course of the disease, blood glucose and cortisol levels should also be evaluated. The absolute values of electrolytes (Na, K, Mg, Ca) may not be as important as the ratios to each other in which they are present.

The effect of beta blocking and antilipolytic agents on magnesium concentration and free fatty acids in calves with coccidiosis should be studied to determine their effect on the production (or prevention) of neurological signs.

It is proposed that so-called "nervous" coccidiosis in calves and yearling cattle is not due to the coccidia *per se,* but to a combination of stressors, including the damage by the coccidia to the intestinal tract, which results in tissue magnesium and serum calcium depletion and the production of the neurological syndrome observed. It is also suggested that the temperament of the individual animal is an important factor; the more nervous individuals more likely to respond adversely to a given stress.

Treatment of affected animals with IV and SC calcium, magnesium and dextrose solution, balanced electrolyte solutions, oral magnesium oxide and sulfamethazine has been relatively successful when given early, while the animal is still able to stand and appears normal until disturbed. Treatment in the later stages (even when the animal is still standing) or when the calf is recumbent has been disappointing.

The most logical approach to the problem of "nervous" coccidiosis is the prevention of all coccidiosis through good herd management, sanitation, the reduction of stress and the use of coccidiostats.

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Several of the references listed are not cited in the body of this report but are included because they provide a broader background for the subject.