Pregnancy toxemia in a flock of sheep

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SWINE/CAMELIDS/ RUMINANTS

- Pregnancy toxemia in sheep is a metabolic disease initiated by negative energy balance and results in excessive lipid metabolism, ketosis, and subsequent hepatic lipidosis.
- The diet provided to sheep during late gestation should contain sufficient glucose precursors to maintain adequate glucose availability to maternal and fetal tissues.
- To minimize the physiologic decline in dry-matter intake during late gestation (which results in accentuation of negative energy balance), high-quality feed ingredients should be fed to ewes during this period.

Multiple health problems were detected in a flock of 320 Polypay and Polypay-cross ewes during late gestation in mid-January in western Oregon. At least 8 ewes died from periparturient metabolic disorders during the first 3 weeks of lambing. This flock historically had > 200% lamb crop, with < 2% total ewe death loss through the entire lambing season. During the initial farm visit, 3 affected ewes were evaluated, and appropriate diagnostic samples were collected (ie, blood, urine, hepatic tissue, and vitreous humor). A recently lambed mature ewe had died following a uterine prolapse. This ewe was in good body condition (4 of 5 condition score)[1] but had been lethargic and had signs of depression prior to lambing. She had improved clinically when treated with propylene glycol (2 oz, PO, q 12 h). A field necropsy of this ewe revealed moderate ketonuria[a] and gross evidence of hepatic lipidosis. Biochemical analysis of vitreous humor revealed hypocalcemia (3.5 mg/dl; reference range, 5.1 to 5.7 mg/dl) and hypophosphatemia (2.1 mg/dl; reference range, 4.7 to 7.0 mg/dl); magnesium concentration was within reference limits.

Two other ewes in late gestation were also evaluated. One ewe was lethargic, anorectic, and had moderate ketonuria. The other ewe was recumbent, dehydrated approximately 5%, and had signs of depression and severe ketonuria. Both ewes had good (3 to 4) body condition scores. A blood sample was collected from the second ewe, and a CBC revealed increased band neutrophils (462 cells/µl, 14%; reference range, 0 cells/µl, < 1%), leukopenia (3.3×10^3 cells/µl; reference range, 4 to 12×10^3 cells/µl), lymphopenia (1.35×10^3 cells/µl; reference range, 2 to 9×10^3 cells/µl), and hyperfibrinogemia (700 mg/dl; reference range, 100 to 500 mg/dl), with many toxic neutrophils and Dohle bodies evident. On the basis of history, physical examination findings, and CBC results, septic metritis secondary to fetal death was diagnosed. Serum biochemical analyses from the 2 affected ewes revealed hypocalcemia, hypoglycemia, and hypokalemia consistent with a diagnosis of pregnancy toxemia with concurrent anorexia (**Table 1**).[2-4] Hypokalemia and hypocalcemia may be attributed to anorexia and metabolic acidosis, respectively, which are often associated with pregnancy toxemia.[3,4] Both ewes had low cholesterol concentrations, and 1 ewe had high **nonesterified fatty acid** (**NEFA**) concentrations consistent with anorexia and potential hepatic dysfunction associated with fatty infiltration.[5,6] During the next 2 days, 2 other prepartum ewes with similar clinical signs were evaluated and had moderate ketonuria, hypocalcemia (2.7 and 6.6 mg/dl, respectively; reference range, 8.5 to 12 mg/dl), and hypermagnesemia (3.6 and 4.7 mg/dl, respectively; reference range, 2.2 to 2.8 mg/dl). One ewe with severe hypocalcemia (2.7 mg/dl) was also hypophosphatemic (2.3 mg/dl; reference range, 5 to 7.5 mg/dl). These ewes were treated with a calcium, phosphorus, and dextrose solution (30 to 50 ml, 1 treatment), administered IV prior to lambing and had good clinical responses to treatment.

To evaluate the metabolic status of the flock, blood was collected and serum obtained for biochemical analyses from 3 groups of clinically normal ewes. The 3 groups were defined as mature ewes scheduled to lamb within 2 to 3 weeks (group 1; n = 7), mature ewes scheduled to lamb within 4 to 6 weeks (group 2; 7), and young ewes lambing for the first time (group 3; 7). Serum from the 7 ewes in each group were pooled equally into a single sample per group. Biochemical analysis of pooled samples revealed high alkaline phosphatase activity (groups 1 and 3), high NEFA concentrations (group 1), and low cholesterol concentration (group 2; Table 1). These results suggested that mature ewes approaching lambing have a negative energy balance, with mobilization of NEFA from adipose tissue. Nonesterified fatty acids are taken up by the liver where they can either be exported as fat in **very low density lipoprotein (VLDL)** or partially metabolized as ketone bodies.[7] Concurrent low cholesterol concentrations suggest that the liver's ability to export fat as VLDL is compromised, thereby inducing accumulation of fat in the liver.[5,6] These metabolic changes, in conjunction with the increased prevalence of high body condition score (> 3+) for pregnant ewes, suggested a high-risk potential for continued problems with pregnancy toxemia in this flock of sheep.

Because nutrition plays an important role in the pathogenesis of pregnancy toxemia and hypocalcemia, the feeding program for gestating ewes was examined. The flock grazed a mixed grass-clover pasture, had access to mineral blocks year-round, and remained on pasture up to 4 to 6 weeks prior to lambing. At that

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Table 1—Serum biochemical values from 2 ewes with clinical signs of pregnancy toxemia and pooled samples representing a mean value from 3 groups (n = 7 each) of clinically normal ewes in the same flock

Analyte	Ewe 1	Ewe 2	Pregnant ewe group* 1	2	3	Reference range
BUN (mg/dl)	8	48	13	13	19	10–35
Creatinine (mg/dl)	0.7	3.7	1.0	0.9	1.0	0.9–2
Glucose (mg/dl)	24	17	62	62	72	50–85
Total protein (g/dl)	6.6	6.1	6.8	6.1	6.8	5.5–7.5
Albumin (g/dl)	ND	ND	3.5	3.1	3.4	2.5–3.9
Total bilirubin (mg/dl)	0.4	0.3	0.2	0.2	0.2	0–0.5
Alkaline phosphatase (U/L)	74	24	123	63	193	10–70
GGT (U/L)	39	45	39	52	56	30–94
Aspartate transaminase (U/L)	84	1,243	108	99	109	60–280
Sodium (mEq/L)	149	146	150	151	151	145–155
Potassium (mEq/L)	4.0	3.9	4.7	4.6	5.2	4.5–6.0
Chloride (mEq/L)	105	104	111	114	110	95–112
Calcium (mg/dl)	7.2	7.0	9.8	8.8	9.9	8.5–12
Phosphorus (mg/dl)	6.7	6.6	5.4	5.8	7.2	5–7.5
Triglycerides (mg/dl)	27	13	17	18	28	< 100
Total cholesterol (mg/dl)	59	38	74	53	72	> 70
Nonesterified fatty acids (mEq/L)	1.43	0.29	0.43	0.20	0.19	< 0.4

*Group 1 = Mature ewes within 2 to 3 weeks of lambing. Group 2 = Mature ewes 4 to 6 weeks from lambing. Group 3 = First-time pregnant ewes 4 to 6 weeks from lambing.
ND = Not determined. GGT= γ–Glutamyltransferase.

Table 2—Nutrient content (dry-matter basis) of feed ingredients fed to a flock of sheep with health disorders associated with pregnancy toxemia

Nutrient	Nutrient content: Current pellet	Previous pellet	Grass hay*	Trace mineral salt
Dry matter (%)	89.8	89.7	91.6	98
Crude protein (%)	15.0	14.6	7.1	N/A
Digestible energy (Mcal/kg)	3.07	3.11	2.55	N/A
Acid detergent fiber (%)	22.9	26.7	40.7	N/A
Neutral detergent fiber (%)	49.1	36.1	66.1	N/A
Crude fat (%)	3.7	3.6	N/A	N/A
Ash (%)	9.5	7.3	N/A	100
Calcium (%)	0.80	0.82	0.48	13.0
Phosphorus (%)	0.67	0.34	0.21	5.0
Magnesium (%)	0.39	0.28	0.18	0.5
Sodium (%)	0.31	0.14	0.1	23.9
Potassium (%)	1.34	1.20	1.69	N/A
Copper (mg/kg)	10.6	8.2	5.8	0
Cobalt (mg/kg)	0.33	0.03	N/A	60
Iron (mg/kg)	217	290	116	2300
Manganese (mg/kg)	89	30	266	3500
Selenium (mg/kg)	0.28	0.26	N/A	90
Zinc (mg/kg)	199	12.6	25.6	3500
Vitamin A (U/kg)	7,000	10,700	N/A	N/A
Vitamin D (U/kg)	1,537	708	N/A	N/A
Vitamin E (U/kg)	21.4	15.2	N/A	N/A

*Mean composition for 5 grass hays fed to the flock.
N/A = Not applicable. To convert mg/kg to mg/lb, divide given value by 2.2.

time, ewes were grouped according to expected lambing time and brought into an open-end barn containing 6 group pens that were bedded with straw and hold 20 to 25 ewes comfortably. First pregnancy ewes were grouped in the same facility but in pens separate from the mature ewes. Grass hay was available ad libitum to ewes when first brought to the lambing facility. A custom pellet was offered at 0.45 kg/head/d (1 lb/head/d) initially and increased over a 1- to 2-week period to an expected intake of 2.7 to 3.6 kg/head/d (6 to 8 lb/head/d). Grass hay and pellet were placed in wooden feeders in group pens, and there was ample bunk space for all ewes. Trace mineral salt was available ad libitum. Following lambing, ewes and lambs were moved into a second set of group pens of similar size on the other side of the barn. Ewes and lambs were moved back onto pasture approximately 3 weeks into lactation.

The feeding program for this flock had not been fundamentally changed for 10 years. However, the custom pellet was reformulated for this year to help decrease feed costs. Higher cost feed ingredients such as ground corn and alfalfa meal were replaced with wheat mill run and barley screenings. Additional mineral and vitamin ingredients improved the nutrient quality of the new pellet, because there was no vitamin or trace mineral supplement in the previous pellet. Molasses was added as a palatability agent. Intake of the new pellet was less than previous years, reaching a plateau at approximately 1.5 to 2 kg/head/d (3.3 to 4.4 lb/head/d), rather than the expected intake of 2.7 to 3.6 kg/head/d (6 to 8 lb/head/d). Additionally, grass hay intake by the ewes was approximately 15 to 20% less than in previous years. Nutrient analysis of the available grass hays revealed they were mature and of low quality (**Table 2**). Comparison of nutrient analyses from the 2 pellet formulations revealed that energy, protein, and fat contents were essentially the same. Increased content of most other minerals and vitamins was attributed to specific ingredients added to the new pellet formulation. Increased phosphorus content of the new pellet formulation was attributed to the high inclusion rate of wheat mill run, which contained approximately 1% phosphorus (dry-matter basis).[8]

Notable differences in carbohydrate fractions, which may account for the health problems in this flock, were identified when comparing the nutrient profile of the 2 pellet formulations. Replacement of ground corn and some alfalfa meal with barley screenings and wheat mill run resulted in increased fermentable fiber. This change was evidenced by

increased **neutral detergent fiber (NDF)** and decreased acid detergent fiber content in the new, compared with the old, pellet formulation (Table 2). Sugar and starch content of a feed or diet is defined as the **nonstructural carbohydrate (NSC)** fraction and is estimated by the following calculation:

NSC = 100 – crude protein % – NDF % – fat % – ash %

All values are on a dry-matter basis.[9] With the elimination of ground corn in the new pellet formulation, calculated NSC content (dry-matter basis) decreased from 38.4 to 22.7%. Inclusion of barley screenings did not compensate for the starch loss from ground corn. Grain screenings, by definition, include only light or broken grains and agricultural seeds, weed seeds, chaff, hulls, and straw, along with elevator or mill dust, sand, and dirt.[10] Grain screenings vary greatly in nutrient content and quality.

Predicted nutrient intake for this flock, on the basis of feed analysis and estimated intake, was compared with published requirements for ewes in late gestation (175 to 225% lambing crop).[8] Protein, calcium, and phosphorus intakes exceeded National Research Council requirements, whereas energy intake was slightly deficient. Although dietary negative energy balance was consistent with a diagnosis of pregnancy toxemia, the magnitude of the deficit did not appear to be consistent with the severity of the clinical signs in this flock. Additionally, there was no evidence to support a diagnosis of primary hypocalcemia as a result of deficient calcium intake. However, serum calcium concentrations in clinically affected ewes were lower than typically seen in instances of pregnancy toxemia and were more consistent with a diagnosis of primary hypocalcemia. This suggested that the decreased feed intake was greater than estimated, nutrient availability was reduced, or both. On the basis of nutrient intake analysis and concerns over forage quality, a recommendation was made to replace some of the grass hay with alfalfa hay and add cereal grain to the diet at a rate of 0.2 to 0.7 kg/head/d (0.5 to 1.5 lb/head/d). Because more custom pellet needed to be ordered, a decision was made to use the original pellet formulation. Once the original pellet formulation was fed again, the metabolic disorders that had been observed in this flock were minimized over a 2-week period, and no other ewes died.

Pregnancy toxemia in sheep results from inadequate dietary energy intake and subsequent metabolic changes associated with excessive lipid mobilization.[2-4] Metabolic derangements of hyperketonemia and ketonuria, hypoglycemia, metabolic acidosis, hypocalcemia, and altered liver function attributable to hepatic lipidosis are all associated with pregnancy toxemia. Ewes in late gestation with multiple fetuses and pregnant ewes with excessive body condition are at the greatest risk of developing pregnancy toxemia. Cold weather conditions, poor feed quality, and environmental stressors may induce a state of negative energy balance and increase the risk of pregnancy toxemia.

Biochemical analyses are commonly used as an aid in the diagnosis of individual animal health disorders. Application of this diagnostic procedure on a flock basis has been limited primarily because of the perceived cost. However, obtaining biochemical analyses from other sheep at risk within a flock is useful information with which to initiate appropriate preventive management changes prior to evidence of illness within the flock. Use of pooled samples from individuals is a method that may be used to minimize total costs and to better assess the health status of the flock by including larger numbers of sheep. Metabolite values from pooled samples are equivalent to arithmetic means of individuals and can be used as an economic method of evaluating a population by reducing the total number of samples for analysis.[11,b] However, pooled sample results need to be interpreted differently from individual samples. A pooled sample represents a mean of a group; thus, there are individuals above and below the determined value. Therefore, pooled sample results should be compared with the midpoint of a given reference range, rather than anywhere within the range.

Glucose is a primary metabolic substrate that supports metabolism of pregnancy and lactation.[2,7,12] To facilitate glucose availability to the fetus, the dam's body increases gluconeogenesis and minimizes maternal-tissue glucose usage.[12] Maternal tissues preferentially use lipids for energy metabolism, thereby sparing glucose for fetal demands. To facilitate lipid usage, adipose tissue becomes more sensitive to metabolic signals that induce lipolysis and inhibit lipogenesis.[12] Lipid mobilization can become excessive during states of negative energy balance, which can overwhelm the liver's ability to process the lipid influx. Gluconeogenesis from dietary precursors, primarily propionate and lactate, accounts for the majority of glucose production in ewes. Increased fermentable fiber in a ruminant's diet can have positive effects on animal performance through minimizing effects of ruminal acidosis from excess starch fermentation. However, some ruminal starch fermentation is necessary to provide propionate. In the flock of this report, an appropriate propionate precursor was removed when ground corn was eliminated from the pellet formulation. It is recommended that approximately 1 kg of cereal grain/d (2.2 lb cereal grain/d) be provided to ewes in late gestation to prevent pregnancy toxemia. This recommendation was adequately met when the original pellet formulation was fed to this flock.

It has been reported that intake of NDF influences dry-matter intake capacity in ruminants, with optimal NDF intake between 1.1 and 1.3% of body weight.[13] During gestation, NDF intake is decreased as a result of physical expansion of the gravid uterus in the abdomen.[14] In the sheep of this report, total NDF intake was increased as a result of poor forage quality (66.1% NDF), and pellet NDF increased from 36.1 to 49.1%. On the basis of estimated feed intake used to evaluate nutrient intake, predicted NDF intake exceeded 1.4% of body weight. Thus, actual dry-matter intake was lower than estimated, leading to a negative energy balance consistent with the severe health problems observed.

Feed costs are a substantial component of overall production costs in sheep raising operations. Producers are often seeking ways to decrease feed costs. As in the

flock of this report, the practice of substituting low-cost by-product feeds in ruminant diets has become more common. By-product feeds generally contain high amounts of fermentable NDF and lesser amounts of NSC. Structural carbohydrates comprising the NDF fraction are fermented by microbes to acetate or butyrate and are used by the sheep for energy but cannot contribute to net glucose production. Although energy density of the 2 pellet formulations was essentially equal, these are digestible energy values and do not account for fermentation and metabolic losses in the digestive and metabolic processes (Table 2). In actuality, the energy available to ewes to support maintenance and pregnancy needs was much less for the new pellet formation as a result of greater fermentation losses. Severity of the pregnancy toxemia outbreak and hypocalcemia observed in this flock appeared to result from confounding effects of limited glucose precursors, excessive dietary fiber-limiting intake, and decreased availability of dietary energy. This report underscores the need to monitor feed quality and give careful consideration to feed substitutions based solely on costs.

[a]Ketostix, Bayer Corp Diagnostic Division, Elkhart, Ind.

[b]Tornquist SJ, Van Saun RJ. Comparison of biochemical parameters in individual and pooled bovine sera (abstr). *Vet Pathol* 1999;36:487.

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