# Case Study: Pregnancy Toxemia in a Sheep Flock

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### Abstract

A large sheep flock was experiencing a high prevalence of metabolic diseases early in the lambing season. Pregnancy toxemia and secondary hypocalcemia were diagnosed based on history, physical examination and serum biochemistry results. A new approach to metabolic profiling, using pooled sera samples to reduce costs, was used to assess nutritional status of the flock. Ewes close to the time of lambing were found to be in severe negative energy balance, resulting in excessive fat mobilization and clinical signs associated with pregnancy toxemia and hepatic lipidosis. Inadequate amount of fermentable carbohydrates, which could provide glucose to support late pregnancy requirements, was determined by nutrient analysis. Lower cost by-product feeds had been substituted into the new pellet formulation. Although feed costs are a substantial component of production costs, feed changes based solely on cost may not be appropriate relative to nutritional needs and animal health.

### Résumé

Dans un grand troupeau de moutons, on a observé une forte prévalence de maladies métaboliques au début de la saison des agnelages. Une toxémie de gestation et une hypocalcémie secondaire ont été diagnostiquées, d'après l'anamnèse, l'examen physique et l'analyse biochimique du sérum. Une nouvelle approche d'évaluation métabolique, basée sur des échantillons composés de sérum, pour réduire les coûts, a servi à déterminer le statut nutritionnel du troupeau. Les analyses ont démontré que les brebis prêtes à agneler souffraient d'un grave déséquilibre énergétique ayant provoqué la mobilisation excessive des graisses, générant des signes cliniques typiques de toxémie de gestation et de lipidose hépatique. L'analyse nutritionnelle a révélé un apport insuffisant de glucides fermentescibles, qui autrement auraient pu fournir assez de glucose pour soutenir adéquatement la fin de gestation. Il s'est avéré que des aliments meilleur marché à base de sous-produits avaient été utilisés dans une nouvelle formulation granulée. Bien que les frais d'alimentation constituent une part importante des coûts de production, la substitution d'aliments sur une base uniquement économique peut ne pas convenir aux besoins nutritionnels et à la santé de l'animal.

### Introduction

Under the current economic climate for small ruminant enterprises, veterinarians often are not consulted for individual animal care. The veterinarian can play an important role to the small ruminant producer as a flock-based diagnostician, especially relative to nutrition. As with other agricultural enterprises, feed costs are the largest component of total production costs. Nutritional diseases that potentially affect a large portion of the flock can induce catastrophic losses and warrant investment in preventive practices. Veterinarians willing to provide services to small ruminant clients should be well versed in the role of nutrition in production and disease. This presentation will detail the diagnostic process undertaken to determine etiology and prevention of pregnancy toxemia in a commercial ewe flock.[14]

### History

Multiple health problems were detected in a flock of 320 Polypay and Polypay-cross ewes during late gestation in mid-January in western Oregon. Many of the ewes were being treated with Ca-P-Mg solutions and propylene glycol. This was a well-managed flock, and as a result there were infrequent animal health problems, with the flock maintaining over a 200% lamb crop year after year. One concern about this flock was the general excess body condition of the ewes (4+/5).[12] The situation in January was somewhat alarming, since they had just started lambing and had already lost eight ewes, compared to a total of eight (2%) ewes lost last year over the entire lambing season.

The flock grazed a mixed grass-clover pasture, had access to mineral blocks year-round, and remained on pasture up to four to six weeks prior to lambing. At that time, ewes were grouped according to expected lambing time and brought into an open-end barn containing six straw-bedded group pens, which held 20 to 25 ewes comfortably. First-pregnancy ewes were grouped in the same facility, but penned separately from the mature ewes. Grass hay was available to ewes *ad libitum* when first brought to the lambing facility. A custom pellet (15% crude protein, 72% TDN) was offered at 1 lb (0.45 kg) per head per day initially and increased over a one- to two-week period to an expected intake of 6 to 8 lb (2.7 to 3.6 kg) per head, per day. 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 three weeks into lactation.

The flock feeding program has not fundamentally changed over the past 10 years, but the pellet was reformulated this year to decrease feed costs (Table 1). Intake of the new pellet was less than previous years, reaching a plateau at approximately 3.3 to 4.4 lb (1.5 to 2.0 kg) per head per day. Additionally, grass hay intake by the ewes was approximately 15-20% less than in previous years.

## Clinical and Laboratory Findings

During the initial farm visit, three affected ewes were evaluated and diagnostic samples collected (ie, blood, urine, liver tissue, vitreous humor) as appropriate. A recently lambed, mature ewe had died following a uterine prolapse. This ewe was in good body condition (4 of 5 condition score),[12] but had been lethargic with signs of depression prior to lambing. She had improved clinically when treated with propylene glycol (2 oz [60 ml] PO, q 12 h). A field necropsy of this ewe revealed moderate ketonuria 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 normal limits.

Two other ewes in late gestation were also evaluated. One ewe was lethargic, anorectic, and had moderate ketonuria. The other ewe was depressed, recumbent, dehydrated approximately 5%, and had severe ketonuria. Both ewes had good (> 3+) 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 n/µl, < 1%), leukopenia (3.3 x $10^3$ cells/µl; reference range, 4-12 x $10^3$ n/µl), lymphopenia (1.35 x $10^3$ cells/µl; reference range, 2-9 x $10^3$ cells/µl), and hyperfibrinogemia (700 mg/dl; reference range, 100-500 mg/dl), with many toxic neutrophils and dohle bodies evident. Based on history, physical findings and CBC results, septic metritis secondary to fetal death was diagnosed. Serum biochemical analyses from the two affected ewes (Table 2) revealed hypocalcemia, hypoglycemia and hypokalemia, consistent with a diagnosis of pregnancy toxemia with concurrent anorexia and hypocalcemia.[7,10,11] Hypokalemia and hypocalcemia might be attributed to anorexia and metabolic acidosis, respectively, which are often associated with pregnancy tox-

**Table 1**. Ingredient composition of custom pellets and calculated digestible carbohydrate fractions.

| Ingredient | Previous Pellet | | Current Pellet | |
|---|---|---|---|---|
| | Lb | % | Lb | % |
| Ground corn | 650 | 32.5 | | |
| Wheat millrun | 130 | 6.5 | 903.92 | 45.2 |
| Suncured alfalfa | 1200 | 60.0 | 500 | 25.0 |
| Tallow | 10 | 0.5 | 10 | 0.50 |
| Barley screenings | | | 500 | 25.0 |
| Limestone | | | 14 | 0.70 |
| Molasses | | | 50 | 2.5 |
| Salt | | | 10 | 0.5 |
| Vitamin premix | | | 0.5 | 0.025 |
| Mineral premix | | | 1 | 0.05 |
| Selenium 200 | | | 0.58 | 0.029 |
| Oxytetracycline crumbles | 10 | 0.5 | 10 | 0.5 |
| Totals: | 2000 | 100 % | 2000 | 100.0% |
| Carbohydrate fractions[1] | % DM | % NFC | % DM | % NFC |
| Sugar | 4.9 | 11.0 | 5.4 | 18.8 |
| Starch | 28.5 | 64.0 | 12.5 | 43.8 |
| Soluble fiber | 11.1 | 25.0 | 10.7 | 37.4 |
| Nonfiber carbohydrates[2] | 44.5 | 100% | 28.6 | 100% |

[1]Carbohydrate fractions estimated using tabular values for ingredients in Cornell-Penn-Miner software.
[2]Determined by difference, but accounts for neutral detergent insoluble protein fraction in NDF.

**Table 2.** Serum biochemistry values from two clinically affected ewes and pooled samples representing a mean value from seven clinically normal ewes in the same flock.

| Analyte | Ewe #1 | Ewe #2 | Pregnant Ewe Group[1] | | | Reference Range |
|---|---|---|---|---|---|---|
| | | | 1 | 2 | 3 | |
| BUN | 8 | 48 | 13 | 13 | 19 | 10 - 35 mg/dl |
| Creatinine | 0.7 | 3.7 | 1.0 | 0.9 | 1.0 | 0.9 - 2 mg/dl |
| Glucose | 24 | 17 | 62 | 62 | 72 | 50 - 85 mg/dl |
| Total Protein | 6.6 | 6.1 | 6.8 | 6.1 | 6.8 | 5.5 - 7.5 g/dl |
| Albumin | ND | ND | 3.5 | 3.1 | 3.4 | 2.5 - 3.9 g/dl |
| Bilirubin, total | 0.4 | 0.3 | 0.2 | 0.2 | 0.2 | 0 - 0.5 mg/dl |
| Alkaline Phosphatase | 74 | 24 | 123 | 63 | 193 | 10 - 70 IU/L |
| GGT | 39 | 45 | 39 | 52 | 56 | 30 - 94 IU/L |
| Aspartate transaminase | 84 | 1,243 | 108 | 99 | 109 | 60 - 280 IU/L |
| Sodium | 149 | 146 | 150 | 151 | 151 | 145-155 mEq/L |
| Potassium | 4.0 | 3.9 | 4.7 | 4.6 | 5.2 | 4.5 - 6.0 mEq/L |
| Chloride | 105 | 104 | 111 | 114 | 110 | 95 - 112 mEq/L |
| Calcium | 7.2 | 7.0 | 9.8 | 8.8 | 9.9 | 8.5 - 12 mg/dl |
| Phosphorus | 6.7 | 6.6 | 5.4 | 5.8 | 7.2 | 5 - 7.5 mg/dl |
| Triglycerides | 27 | 13 | 17 | 18 | 28 | < 100 mg/dl |
| Cholesterol, total | 59 | 38 | 74 | 53 | 72 | > 75 mg/dl |
| Nonesterified Fatty Acids | 1.43 | 0.29 | 0.43 | 0.20 | 0.19 | < 0.4 mEq/L |

[1]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.

emia.[10,11] Both ewes had low cholesterol concentrations, and one ewe had high nonesterified fatty acid (NEFA) concentrations, consistent with anorexia and potential liver dysfunction associated with fatty infiltration.[4,5] During the next two days, two more 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). The 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 calcium, phosphorus and dextrose solution (30-50 ml, one treatment), administered intravenously prior to lambing, and had good clinical response.

## Nutritional Evaluation

To evaluate the metabolic status of the flock, serum was collected from three groups of seven clinically normal ewes from this flock for biochemical analyses. The three groups were defined as mature ewes due to lamb within two-to-three weeks (Close-up), mature ewes due to lamb between four and six weeks (Far off), and young ewes lambing for the first time (Young). Serum from the seven individuals in each group was pooled equally into a single sample per group.[13] Biochemical analysis of pooled samples (Table 2) revealed high alkaline phosphatase activity (Close-up and Young groups), high NEFA (Close-up), and low cholesterol concentration (all groups). These data suggest that mature ewes approaching lambing are experiencing 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. Concurrent low cholesterol concentrations suggest the liver's ability to export fat as VLDL is compromised, thus inducing hepatic fat accumulation. These metabolic changes in conjunction with the high prevalence of high body condition score (>3+) for pregnant ewes suggested a high risk potential for continued problems with pregnancy toxemia in the flock.

The nutrient analysis of the newly formulated custom pellet was compared to the previous pellet (Table 3). Higher cost feed ingredients, such as ground corn and alfalfa meal, were replaced with wheat mill run and barley screenings (Table 1). Energy, protein and fat content were essentially the same and consistent with desired guidelines and specifications. 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). Additional mineral and vitamin ingredients improved nutrient quality of the new pellet because

**Table 3.** Nutrient content (dry matter basis) of feed ingredients fed to a flock of sheep with health problems associated with pregnancy toxemia.

| | Nutrient Content | | | |
|---|---|---|---|---|
| Nutrient | Current pellet | Previous pellet | Grass hay[1] | 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 |
| Non-fiber Carbohydrates, %[2] | 22.7 | 38.4 | 16.8 | 0 |
| 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, IU/lb | 3,182 | 4,864 | N/A | N/A |
| Vitamin D, IU/lb | 699 | 322 | N/A | N/A |
| Vitamin E, IU/lb | 9.7 | 6.9 | N/A | N/A |

[1]Mean composition for five grass hays fed to the flock.
[2]Determined by subtraction (NFC = 100 – CP – NDF – Ash – EE).
N/A = Not applicable



there was no vitamin or trace mineral supplement in the previous pellet. Molasses was added as a palatability agent.

Although the newly formulated pellet intuitively seemed to be a better formulation based on the balance of available nutrients, the fiber and digestible carbohydrate fraction differences between the pellets was of concern. Notable differences in NDF and NFC carbohydrate fractions, which may account for the health problems in this flock, were identified when comparing the nutrient profile of the two pellet formulations (Tables 1 and 3). Replacement of ground corn and some alfalfa meal with barley screenings and wheat mill run resulted in increased neutral detergent fiber (NDF) (49.1 vs. 36.1%) and lower non-fiber carbohydrates (NFC) (22.7 vs. 38.4%) content in the new, compared with the old, pellet formulation. Retrospectively, using newer computer software packages, the NFC component (digestible carbohydrates) was further subdivided into sugar, starch and soluble fiber fractions for each of the pellets based on tabular composition data of all ingredients (Table 1). The estimated starch content of the new pellet (12.5%) is only 44% of the starch content in the old pellet (28.5%). Inclusion of barley screenings did not compensate for the starch loss from removing the 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.[1] 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).[9] 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 the 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.

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.[8] During gestation, NDF intake is decreased as a result of physical expansion of the gravid uterus in the abdomen.[3] In the current situation, total NDF intake was increased as a result of poor forage quality (66.1% NDF) and the increase in pellet NDF 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 most likely lower than estimated, leading to greater negative energy balance consistent with the severe health problems observed.

## Therapeutic Management

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 to improve forage quality and add some cereal grain to the diet at a rate of 0.5 to 1.5 lb (0.23 to 0.68 kg) per head per day. In the short-term, recommendations were made to provide aggressive prophylactic treatment of late-pregnant ewes with oral propylene glycol and oral (calcium propionate drench) or subcutaneous calcium therapy. 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 problems that had been observed in this flock were minimized over a two-week period, and no further ewes died.

## Discussion

The variety of disease problems in this flock is consistent with clinical signs of pregnancy toxemia with secondary hypocalcemia as a result of decreased feed intake. The observed decline in feed intake was the direct result of the changes made to ingredient composition of the custom pellet fed to the late-gestation and lactating ewes. In this situation, forage quality was poor (66.1% NDF) and the pellet NDF increased from 36 to 49%. Sugar and starch content of the NFC fraction can provide a rapid form of glucose, if not fermented, or indirectly via fermentation to propionate and being converted to glucose in the liver. Although the calculated energy content of the two pellets was minimal, one must remember that these are digestible energy values and they do not account for fermentation and metabolic losses in the digestive and metabolic processes.

Glucose is a primary metabolic substrate that supports metabolism of pregnancy and lactation.[2,6,7] To facilitate glucose availability to the fetus, the dam's body increases gluconeogenesis and minimizes maternal tissue glucose usage.[2] Maternal tissues preferentially use lipids for energy metabolism, thus sparing glucose for fetal demands. To facilitate lipid usage, adipose tissue becomes more sensitive to metabolic signals that induce lipolysis and inhibit lipogenesis.[2] Lipid mobilization can become excessive during states of negative energy balance, which can overwhelm the liver's ability to process the lipid influx. Gluconeongenesis from dietary precursors, primarily propionate and lactate, accounts for the majority of glucose production in ewes. Although 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, 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. A recommendation to provide approximately 1.5 lb (0.68 kg) cereal grain per day to ewes in late gestation is suggested to prevent pregnancy toxemia. This recommendation was adequately met when the original pellet formulation was fed. Severity of the pregnancy toxemia outbreak and hypocalcemia problems experienced by this flock appeared to result from confounding effects of limited glucose precursors, excessive dietary fiber limiting intake and reduced dietary energy availability.

## Conclusions

The transition from late pregnancy into lactation invokes severe physiologic adaptations to nutrient partitioning, and homeostatic derangement will result in common metabolic disease conditions. Like dairy cattle, sheep and goats are prone to disturbances of glucose and lipid metabolism around the time of parturition, resulting in similar metabolic conditions of hyperketonemia and fatty infiltration of the liver. Quality of nutrition, as well as feeding and environmental management considerations to minimize stress conditions, are primary mediators in the pathogenesis of the disease. To ensure the ability of the pregnant ewe to consume an adequate amount of feed and have sufficient glucose precursors, it would be recommended that dietary NDF not exceed 40-45% and the diet contain a minimum of 15-20% starch. This case underscores the need to monitor feed quality and give careful consideration to feed substitutions based solely on costs.

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