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# Case Report - Use of Calcium Sulfate to Alleviate Signs of Copper Toxicosis in Ewe Lambs

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## Abstract

Thirty-one Debouillet ewe lambs were exposed to elevated dietary copper (Cu) after being fed pelleted alfalfa from two separate feed mills which contained 33 and 45 ppm Cu. After consuming about 5.5 lb/day of this diet for approximately 50 days, signs of Cu poisoning became apparent (hemoglobinemia, hemoglobinuria). Cu toxicity was confirmed by a liver Cu concentration of 439 ± 36 (mean ± SE) ppm in five dead animals. During the course of Cu exposure, eight of 31 ewe lambs died. Serum was collected from 10 ewe lambs showing extreme signs of Cu poisoning. Total, direct, and indirect bilirubin, and creatine kinase (CK) were elevated in ewes consuming Cu. Ten extremely affected ewe lambs that had stopped consuming any feed received gelatin capsules (gavage) containing about 2 oz of a livestock salt/gypsum (76% calcium sulfate) mixture (2:1, weight basis) daily for 10 days. After 10 days of calcium sulfate treatment, serum bilirubin and CK were at or near normal concentrations and neither hemoglobinemia nor hemglobinuria were observed. Calcium sulfate administered in gelatin capsules appears to aid in the treatment of acute Cu toxicosis in sheep.

## Résumé

Trente et une agnelles Debouillet ont été exposées à des doses alimentaires élevées de cuivre présent dans des comprimés de luzerne provenant de deux meuneries différentes avec des concentrations de cuivre de 33 et 45 ppm. Des signes apparents d'empoisonnement au cuivre (hémoglobinémie, hémoglubinurie) étaient présents suite à la consommation d'un tel régime au taux de 5.5 livres par jour (2.2 kg) pendant 50 jours. L'empoisonnement au cuivre a été confirmé par une concentration du cuivre dans le foie de 439 ± 36 (moyenne ± 1 écart type) ppm chez cinq individus décédés. Durant la période d'exposition au cuivre, un total de huit individus sur 31 sont morts. Du sérum a été prélevé chez 10 agnelles montrant des signes extrêmes d'empoisonnement au cuivre. La concentration totale, directe et indirecte de bilirubine et de la créatine-kinase (CK) était plus élevée chez les brebis qui consommaient du cuivre. Dix agnelles très affectées qui avaient cessé de se nourrir ont reçu à tous les jours pendant dix jours des capsules de gélatine (gavage) contenant approximativement 2 onces d'un mélange (2 :1, basé sur la masse) sel/gypse (76% sulfate de calcium). Après 10 jours de traitement au sulfate de calcium, la bilirubine du sérum et la CK atteignaient un niveau presque normal et ni l'hémoglobinémie ni l'hémoglobinurie n'étaient présentes. Le sulfate de calcium dans des capsules de gélatine semble efficace pour le traitement de l'empoisonnement aiguë au cuivre chez le mouton.

## Introduction

Copper (Cu) poisoning can be a serious problem for sheep producers because of the low tolerance sheep have for Cu. The pathogenesis of Cu toxicosis has two distinct stages: a primary phase of Cu accumulation in the tissues and a stage of acute illness resulting from hemolytic crisis.[5] The phase of accumulation is caused by intake of forages or processed feed high in Cu and may take several weeks or months. The condition is most often observed in feedlot situations, but is also prevalent when show lambs are fed the same diet as calves being fitted for exhibition. McCosker[9] found that during the accumulation or pre-hemolytic phase, liver Cu levels (dry weight basis) increased from a normal range of 6 to 279 ppm to a range of 1,000 to 3,000 ppm. Copper toxicosis may remain unnoticed until the ani-

mal is stressed by factors such as transportation, lactation, strenuous exercise, or a declining plane of nutrition.[10] Stress leads to a sudden increase in blood Cu concentration and intravascular hemolysis, along with severe gastroenteritis, icterus, dehydration, depression of appetite, hemoglobinemia and hemoglobinuria.[1,10] Necropsy findings show liver concentrations > 150 ppm (wet basis) in chronic poisoned sheep.[10]

Treatment of copper toxicity is often unrewarding because of the sudden, severe hemolysis and resulting detrimental effects. The Merck Veterinary Manual[10] states that analgesic drugs, penicillamine and calcium verserate may be useful if administered in the early stages of the disease. Harker[6] indicated that addition of ammonium molybdate to the concentrated diet might be a useful method for reducing the risk of nutritional Cu poisoning in sheep. Administration of intravenous tetrathiomolybdate to Cu-loaded sheep showed that even though Cu accumulated in the kidneys, less damage was observed.[4] Intravenous and subcutaneous administration of ammonium tetrathiomolybdate have been suggested as effective means of treating the acute phase of Cu toxicosis in sheep.[7,8]

## History and Clinical Findings

Thirty-one Debouillet ewe lambs born during the spring of 1999 were allowed free access to a pelleted alfalfa diet, salt, water and shade until they were 8 months of age (mid-November). Over the previous 8 years, the pelleted alfalfa was supplied primarily by a single feed mill and contained 96% alfalfa, 3% molasses, 0.5% sodium phosphate, and small amounts of vitamin A and feed grade oxytetracycline. Average chemical analysis of the diet was 18% crude protein, 40% acid detergent fiber, 16% acid detergent lignin, 12% ash, 0.6% P and 1.6% Ca. In addition, ewe lambs received cracked corn fed at an amount to approximate 30% of their alfalfa intake.

In September 1999, the ewe lambs were approximately 6 months old, weighed 120 lb and were eating the pelleted alfalfa at about 4% of their body weight. At this time, a new load of feed was received from the same feed mill that had supplied pellets for several years. After the lambs had consumed the new pellets for about 50 days, one became sick. Visual examination of her serum and urine revealed signs of Cu toxicosis (hemoglobinemia, hemoglobinuria), and within 3 days the lamb died.

Within a 3-week period, four more ewe lambs began to show signs of Cu toxicosis and subsequently died. At this time, a feed sample and liver tissue from dead animals were submitted for Cu analysis. Lambs were promptly switched to a 50% pellet and 50% alfalfa hay diet to reduce the Cu exposure, and a new load of pellets was ordered from a second feed mill. When the second load of feed arrived, lambs were switched back to the all-pellet diet (over a 10-day period). As a precaution, a sample of the new feed was analyzed for Cu and found to contain more Cu than the initial feed. At this point, the lambs had received toxic levels of Cu for about 80 days and several were extremely sick. Ewe lambs were subsequently placed on a 100% alfalfa hay diet.

Because livers were already burdened with excess Cu and the dietary source had been removed, supplementation with molybdenum was not considered to be beneficial. Based on previous experience of one of us (M. K. Petersen), a treatment regimen using calcium sulfate (gypsum) was initiated. Livestock salt[a] and gypsum[b] (76% calcium sulfate) were mixed at a ratio of 2 parts salt to 1 part gypsum (weight basis). All ewe lambs were allowed free access to this mixture. In addition, the 10 lambs that showed signs of Cu poisoning (off feed, hemoglobinemia, hemoglobinuria) were given the salt/gypsum mix orally in gelatin capsules[c] (size 12 EL) at a dosage of 2 oz/day for 10 days.

## Laboratory Data

Samples of feed from both loads were analyzed[d] for Cu and found to contain 33 and 45 ppm Cu. Cu toxicity was confirmed by liver Cu concentrations of 439 ± 36 ppm (mean ± SE, > 150 ppm is diagnostic of Cu poisoning[e]). Serums collected twice weekly from all 23 lambs throughout the outbreak were grossly examined for evidence of both toxicosis as well as possible recovery from Cu poisoning. Samples from seven of the 10 lambs showing signs of extreme Cu poisoning were used to characterize Cu effects on serum bilirubin and creatine kinase (CK). Serums from the three remaining lambs that received the calcium sulfate in gelatin capsules over a 10-day period were used to more intensively monitor effects of oral dosing on signs of Cu toxicosis.

## Discussion

During the course of Cu exposure, eight of 31 (26%) ewe lambs died. Once these eight lambs showed signs (hemoglobinemia, hemoglobinuria), none recovered. Of the remaining 23 lambs, 10 showed clinical signs of Cu toxicity. Bolusing of these 10 affected lambs with the calcium sulfate mixture began as soon as they were observed not eating, indicating that they were not voluntarily eating the free-choice mineral mixture.

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[a]United Salt Corp., Houston, TX
[b]Kelly Lime and and Rock Co., Inc., Newark, MO
[c]Torpac Inc., Fairfield, NJ
[d]Pope Testing Labs, Dallas, TX
[e]Texas Vet. Med. Diag. Lab.

Total, direct and indirect serum bilirubin were greatly elevated in ewe lambs exhibiting signs of Cu poisoning. Total bilirubin was 10.7 ± 1.9 mg/dL in serum from seven of the Cu-poisoned animals (normal laboratory[f] reference range = 0 to 1.2 mg/dL). Major elevations in serum bilirubin in sheep are usually observed in cases of hemolytic crisis, and increased direct bilirubin in sheep usually results from hepatic disease and (or) obstruction of bile ducts.[2] The hemolytic disease induced by Cu poisoning often is accompanied by hepatic necrosis and bilirubinuria.[2]

Creatine kinase concentration in seven of the lambs exposed to Cu was 9086 IU/L (normal laboratory[f] reference range = 0 to 225 IU/L). This large elevation in serum CK likely resulted from Cu induced hemolysis. Goonerate and Howell[3] suggested that CK values would decline at the conclusion of a hemolytic crisis.

Visual examination of serum from the 10 ewes that were bolused revealed marked changes in serum color. The serum taken at the onset of Cu toxicity was dark brown to black in color; however after several days of calcium sulfate treatment (gavage), the serum returned to normal "straw" color.

Serum was collected from the three severely affected ewes beginning on the first day of calcium sulfate treatment (day 0) and again on days 3, 7 and 10. On day 0 (extreme signs of Cu toxicosis), total, direct, and indirect bilirubin averaged 6.8 ± 1.7, 3.2 ± 0.9, and 3.6 ± 0.8 mg/dL, respectively (normal laboratory[f] reference ranges = 0 to 1.2, 0 to 0.4, 0 to 0.8 mg/dL, respectively). In addition, serum CK was 8477 ± 1636 IU/L (normal laboratory[f] reference range = 0 to 225 IU/L) on day 0. Likewise, serum constituents remained elevated after 3 and 7 days of calcium sulfate treatment, but all values were much lower on day 7 than they had been on day 3. After 10 days of calcium sulfate treatment, total, direct, and indirect bilirubin were 0.7 ± 0.1, 0.3 ± 0.1, and 0.4 ± 0.1 mg/dL, respectively, and serum CK was 1725 ± 656 IU/L. Likewise, after 10 days, all 10 treated ewes had regained their appetite and hemoglobinemia and hemoglobinuria were no longer present, as evidenced by grossly normal serum and urine.

## Conclusions

These data demonstrate that Cu toxicosis induces marked changes in serum bilirubin and creatine kinase. Treatment of affected ewes with 2 oz/day of a salt/calcium sulfate (gypsum) mixture over a 10-day period may assist in reversing the signs of Cu poisoning.

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[f]Southwest BioLabs, Las Cruces, NM