Title: Effects of Sulfur and Sulfates on Ruminant Health

Jeffery O. Hall, D.V.M., Ph.D., Diplomat A.B.V.T.
Utah Veterinary Diagnostic Laboratory, Utah State University.

1. Objectives
- Provide basic information on sulfur and sulfate toxicosis in ruminants
- Provide clinical points for diagnosis of sulfur and sulfate poisoning cases.
- Provide diagnostic criteria for evaluation of sulfur and sulfate poisoning cases.
- Provide protocols for treatment of sulfur and sulfate toxicoses.

2. General Key Points:
- Both organic and inorganic sulfur compounds are toxic.
- High dietary sulfur intake, as either organic or inorganic, can cause polioencephalomalasia (PEM).
- PEM is associated with conversion of the sulfur to sulfide by the rumen microflora and subsequent absorption.
- Sulfur/sulfate induced PEM does not significantly decrease systemic thiamine or transketolase, but thiamine therapy has been beneficial in treating cases.
- High dietary sulfate can disrupt mineral balance of copper, zinc, and selenium.
- Although the copper-molybdenum-sulfur interaction is well known, adverse affects on copper bioavailability can occur without any increase in the dietary molybdenum.
- Sulfate and selenium directly compete for intestinal absorption, but also directly compete for selenium absorption into plants.

3. Key Clinical Diagnostic Points:
- Clinical signs of PEM include lethargy, anorexia, facial twitching, recumbency, and death.
- Rumen gasses and breath may have the smell of hydrogen sulfide, like rotten eggs.
- Gross lesions may include a darkening of the ruminal material from precipitated sulfide salts, swelling of the cerebral hemispheres, softening of the cerebral hemispheres, yellow discoloration of the cortical gray matter.
- Histological lesions include necrosis of the cortical gray matter and occasional areas of necrosis in the thalamus or midbrain.
- Sulfate/sulfur induced copper deficiency can present as a typical poor growth, poor immune function, and poor reproductive function.
- Sudden death with no gross or histological lesions have occurred.
- Even with short term high sulfur/sulfate exposure (less than 2 weeks), liver copper stores can be depleted to < 5 mg/kg Wet Weight (normal 25 to 100 ppm).
- Sulfate/sulfur induced selenium deficiency can present as the typical poor growth, white muscle disease, poor immune function, and poor reproductive function.

4. Key Etiologic and Pathophysiologic Points:
- In ruminants, both organic and inorganic sulfur is converted to sulfide prior to incorporation into microbial amino acids and proteins. Thus, total ingested sulfate and plant sulfur should be viewed similarly.
- Absorbed sulfide is implicated in the sulfate/sulfur induced PEM.
- The mechanism of sulfide cytotoxic effect is still debated, but most current research is focused on inhibition of cytochrome c oxidase.
• Some literature still implicates a competitive inhibition of thiamine utilization, as thiamine treatment can alleviate clinical signs even in animals with normal circulating thiamine content.
• Common mechanistic effects of sulfate/sulfur on copper bioavailability focus on the precipitation of copper in the rumen rendering it non-bioavailable. But, this does not explain the rapid depletion of hepatic stores. It is possible that binding also occurs systemically resulting in the copper sulfide salts being eliminated.

5: Key Therapeutic Points:
• The primary treatment is to remove the source of excess sulfate/sulfur.
• Supplementation of copper, zinc, and selenium must be evaluated and adjusted to account for the interference by sulfate/sulfur.
• Thiamine treatment has been beneficial in treatment of PEM.

7. Key Prognostic Points:
• For PEM, a positive response from thiamine treatment is indicative of a favorable prognosis, but repeated treatments may be necessary.
• For copper and selenium deficiencies, secondary to high sulfate/sulfur, a good prognosis is common with appropriate mineral supplementation.

8. Overview of the Issue
Sulfur is an essential dietary nutrient in ruminants that is recommended to be in the diet at no more than 0.4%. The sulfur is utilized by microbes for production of sulfur containing amino acids. But, excessive sulfur intake in the form of organic (sulfur containing proteins or amino acids) or inorganic sulfur (sulfates) can result in adverse health effects. Sulfur from either organic or inorganic sources is converted into sulfide by the ruminal microbes prior to being used for incorporation into sulfur containing amino acids and proteins. The adverse health effects of excessive sulfur can be broken down into two primary types, PEM and mineral balance. The conversion to sulfide is responsible for the adverse neurologic health effects and some of the effects on mineral balance.

Sulfide appears to affect neurologic tissues by either blocking cytochrome c oxidase or interfering with thiamine utilization. The most recent literature suggests that there is no thiamine or transketolase effect in sulfate poisoning, but some literature has shown a beneficial clinical effects when animals are treated with thiamine. This has occurred even when serum concentrations of thiamine are normal.

The outcome of the neurologic effects of excess sulfur is development of polioencephalomalacia (PEM). This necrosis of the gray matter of the brain results in clinical signs of lethargy, anorexia, facial muscle twitching, head pressing, recumbency, seizures, and death. In field cases the most common clinical presentation is “found dead”.

Since both the organic and inorganic forms of sulfur are metabolized similarly to sulfide, one must account for both water and forage sources of sulfur. For instance, 0.35% dietary sulfur should not be a problem, by the addition of 500 mg/L sulfate in the water would push the total intake over the maximum recommended. Since ruminants consume 2-3X the weight of water per day as compared to daily dry matter intake, water can be a critical component of mineral intake.

Gross and histologic lesions are primarily in the brain, but ruminal changes can be observed. Gross pathologic lesions include a darkening of the rumen contents from precipitated sulfide salts, swelling of the cerebral hemispheres, softening of the cerebral hemispheres, yellow discoloration of the cortical gray matter. Histological lesions include necrosis of the cortical gray matter and occasional areas of necrosis in the thalamus or midbrain.

The first component of treatment is removal of the source of high sulfate/sulfur. There is evidence that therapeutic doses of thiamine has beneficial effects on the outcome for PEM cases, even though these animals can have normal plasma thiamine content. This would indicate that the sulfide is competitively
interfering with the tissue thiamine utilization or thiamine may be causing the release of the oxidase bound sulfide in some way. Use of corticosteroids to decrease the cerebral edema has also been suggested. Other than the aforementioned therapies, good supportive care and dietary management is the only other treatment.

Excessive sulfate can also interfere with systemic mineral balance of copper, selenium, and zinc. One means by which this occurs is the precipitation of copper sulfide and zinc sulfide salts, rendering them non-bioavailable from the diet. High sulfur in the form of sulfate in the water and high dietary sulfur caused severe liver depletion of liver copper stores in less than 2 weeks, which indicates that the effects with copper are systemic as well as from the standpoint of bioavailability. In addition, sulfate can directly compete with selenium for digestive absorption sites, competitively inhibiting the bioavailability of selenium.

Clinical signs of copper and selenium deficiency are common with excessive sulfur/sulfate intake. These herds present with poor growth rates, poor immune function (high incidence of infectious disease), and poor reproductive function. In addition, white muscle disease is common.

Treatment of sulfur/sulfate induced mineral deficiency is by removal of the source and adequate supplementation. In cases where removal of the source is not an option, use of chelated mineral supplements as 50% of the total for copper and selenium has been beneficial.

Slow adaptation to increasing sulfur/sulfate occurs. This is likely due to microbial adaptation that results in less sulfide being released and absorbed systemically. In addition, with adaptation, less adverse effects occur with respect to mineral balance, but deficiencies still develop.

9. Additional Detail
Case example 1:
Sixty head of bred beef heifers were transported from Arkansas to Utah and placed on range with some “home raised” replacement heifers. Within 2 weeks, 12 purchased heifers had died. Six animals were necropsied. Two heifers had PEM and all 6 had liver copper content of < 3 ppm (normal – 25 to 100 ppm). Liver biopsies of 5 similar heifers still in Arkansas found liver copper of 36 to 54 ppm. In total, 22 purchased heifers died within 30 days. No native heifers died during the same time period.

The pasture being utilized had 743 ppm sulfate in the water and 0.65% sulfur in the forage tested. No other pasture was available, so the owner opted to treat the animals and leave them in the pasture. With supplementation of chelated copper and thiamine in a “lick tub”, the deaths stopped.

Liver biopsy samples from the native heifers also found a lesser degree of copper deficiency (9 to 15 ppm).

10. Summary
- Excessive sulfur/sulfate results in polioencephalomalacia (PEM) and mineral imbalances in ruminants. Organic and inorganic forms of dietary and water sulfur are uniformly converted to sulfide; so both water and diet sulfur/sulfate must be accounted for in evaluation of poisonings. Sulfide results in PEM, although the exact mechanism by which this occurs is still debated. The primary mineral imbalances caused by excessive sulfur and sulfate are copper and selenium deficiencies. These mineral deficiencies can results in poor animal growth, poor immune function, and poor reproductive efficiency, as well as white muscle disease with selenium deficiency.

11. References/Suggested Reading

