Mineral Toxicoses Most Commonly Encountered in Cattle

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With over thirty years of veterinary diagnostic experience, numerous cases of mineral toxicosis have been encountered. Some mineral poisoning cases occur relatively infrequently, but others are more commonly encountered in cattle. During the previous 5 years, the most commonly encountered mineral toxicoses cases in cattle include sulfur and selenium, but cases involving copper and lead are also relatively common. This presentation will focus on these four most frequently encountered mineral toxicosis etiologies.

SULFUR[1]

In my career, sulfur poisoning has been the most commonly identified type of mineral toxicosis. During the previous five years, 6-14 cases per year were handled. Even though sulfur is a needed dietary mineral, excesses can be toxic. 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, etc.) can results 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 (polioencephalomalasia) and alterations in trace mineral balance. The conversion to sulfide is responsible for the adverse neurologic health effects and most of the effects on mineral balance.

Systemic absorption of toxic amounts of sulfide is predominantly via respiratory absorption. This occurs via eructation, then inhalation of hydrogen sulfide gas. The ruminal microbial conversion of excess sulfur to hydrogen sulfide gas is a gradual adaptive process, which results in a delay from the start of excess sulfur in the diet to the onset of adverse clinical effects. This delay can be a couple of weeks.

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 polioencephalomalasia (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”.

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Since both the organic and inorganic forms of sulfur can be metabolized to sulfide, one must account for both water and forage sources of sulfur. For instance, 0.35% dietary sulfur should not be a problem, but 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 metallic 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 can be 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 as little as a few 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 from selenium deficiency can occur. 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 can be beneficial.

Slow adaptation to increasing dietary 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 can still develop.

Diagnosis of sulfur toxicosis involves analysis of the diet, analysis of water sources, and histologic evaluation of brain tissue from animals that die. Histologic analysis of brain tissue can identify polio lesions, but there are other causes of this specific lesions, including lead poisoning, true clinical thiamine deficiency, and water deprivation/salt poisoning. Tissue sulfur

is not a good indicator of poisoning, as the body has relatively high natural tissue sulfur concentrations. Total dietary sulfur needs to be evaluated to include both water and feed.

SELENIUM[2,3]

Selenium is an essential trace element in cattle that is key in the function of several selenoproteins. These selenoproteins function in free radical clearance, reductases, deiodinases, and other key enzymes. The selenium containing enzymes are essential for normal immune function, reproductive function, biotransformation reactions, neurotransmitter turnover, and anticarcinogenic actions. But, as with many essential minerals, excesses can result in adverse effects. During the previous 5 years, 3-8 cases of selenium poisoning were investigated per year.

Selenium excess can be a result of excess intake of natural diets high in selenium that occur in certain geographic regions of North America, be a result of errors in diet inclusion of selenium supplements, or by excessive dosage of injectable products. In North America the easter slopes of the northern Rocky Mountains and the western areas of the north central great plains have areas of high selenium soils that can result in excessive forage selenium accumulation. Within the areas of high selenium soils, alkaline soils tend to hold selenium in a chemical form that is readily absorbed by plants, selenates. Cases where plant selenium content is over hundreds to thousands of parts per million have been investigated. Some “indicator” or “obligate accumulator” plants that have developed a requirement for high selenium can occur in these areas and can have several thousand PPM of selenium.

Selenium toxicoses cases can be acute, sub-acute, or chronic in nature, dependent on the exposure dose. Acute and sub-acute poisoning are associated with higher exposure rates. With very high exposures, clinical signs can start in less than 24 hours. Clinical presentation is generally associated with respiratory distress, a garlic smell to the breath, lethargy, anorexia, diarrhea, tachycardia, weakness, teeth grinding, and deaths. Tissue lesions include pulmonary edema, systemic congestions, and heart/skeletal muscle necrosis. Chronic selenium poisoning is generally associated with excessive selenium intake over longer periods of time. Clinical signs of chronic selenosis are of weight loss, emaciation, hair loss (bobtail disease), hoof growth abnormalities, lameness, reproductive failure, and deaths.

The mechanism of action for selenium poisoning in cattle is thought to be multifactorial. With acute poisoning, depletion of intermediate metabolic substrates and development of free radical damage are likely mechanisms. With chronic poisoning, those mechanisms may also play a role, but incorporation of seleno-amino acids, like selenomethionine or selenocysteine, in place of their respective sulfur containing amino acids may alter a broader array of proteins. The incorporation of selenium in place of sulfur in sulfur containing amino acids could result in loss of key disulfide bridges and structural integrity of key enzymes/proteins.

The amount of selenium that will result in either acute or chronic selenosis can be variable. Different chemical form of the selenium have different relative toxic potentials. In general, selenate is slightly more toxic than selenite. Similarly, different organic selenium compounds differ in toxic potential. It has been recommended that total dietary selenium of less than 5 ppm is safe. Some have suggested that this value is inappropriately too low, but this author has

been involved with dosing studies where 10 ppm total dietary selenium caused over 50% reproductive failure in sheep.

Some adaptation to higher dietary selenium can occur. This is predominantly a result of rumen microbial adaptations, which can convert some of the dietary selenium to elemental. Elemental selenium is insoluble which prevents it from being available to be absorbed systemically.

Post-mortem diagnosis of selenium poisoning can be accomplished by liver selenium analysis. Cases of acute and sub-acute selenium poisoning in cattle will generally have liver concentrations greater than 7 ppm on a wet weight basis. Chronic selenosis can start to occur at liver selenium concentrations of greater than 1.5 ppm, but most cases have concentrations greater than 2 ppm on a wet weight basis. Care must be taken in evaluation of liver selenium content, as recent use of an injectable product containing selenium can cause liver selenium concentrations to be higher than normal. It is common for liver selenium content to increase to concentrations of up to a non-toxic 3-4 ppm after an injection of a selenium containing product. This increase will gradually decrease over a period of up to 10-14 days. Without an appropriate history, an injected animal could be erroneously identified as one with chronic selenosis.

The only treatment for selenium poisoning is removal of the dietary over-exposure, supportive care and time. Animals will gradually eliminate the excessive accumulated tissue selenium.

Lead[4]

Lead poisoning cases in cattle have historically been relatively common, but case numbers have diminished over the years due to decreased lead use in many products. However, this author has investigated 2-7 cases per year of lead poisoning in cattle over the past 5 years. The cases involved ingestion of lead from batteries, ingestion of old lead-based paint materials, ingestion of lead caulking materials, ingestion of lead shot, and cases where the source was not identified. Almost half of the diagnosed lead poisoning cases were identified when very high liver lead concentrations were identified during routine liver mineral analyses. In one case, lead shot was identified in the rumen and omasum of dead yearlings. It was later found that silage being fed to the yearlings had lead shot in it. The source of the lead shot was a shooting range next to the corn field. Apparently, the shot got lodged in the corn stalks and was present when the corn field was chopped for silage.

Lead poisoning cases in cattle most commonly present as neurologic disease with ataxia, blindness, weakness, muscle tremors, and seizures or just as animals that are found dead. Lead can also be a reproductive and developmental toxin. Gross lesions of lead poisoning are minimal, but pieces of lead plates from batteries or lead shot can sometimes be identified in the rumen or omasum.

Metallic lead that gets caught in the rumen or omasum can slowly dissolve, allowing for some delay from the time of absorption to the onset of clinical disease. Lead material that reaches the abomasum will more rapidly dissolve in the much lower pH environment, allowing for a more rapid systemic absorption. Thus, when multiple animals are exposed from the same source, animals may have onset of clinical signs over a wide time frame.

Diagnosis of lead poisoning is based on high liver or whole blood lead content. Normal background liver lead content is less than 1 ppm, while normal whole blood lead content is less than 0.1 ppm. Liver lead concentrations greater than 5 ppm or whole blood lead greater than 0.35 ppm can be diagnostic of lead poisoning. Lead concentrations between normal and that which is diagnostic of lead poisoning indicate excessive exposure to lead. In some states, diagnosis of lead poisoning in a food producing animal is reportable disease. In several cases where lead poisoning was diagnosed, other animals in the herd had higher than normal whole blood lead, even though they were not showing clinical disease. These animals were deemed not to be suitable for sale/slaughter (quarantined) until blood lead concentrations returned to normal background values. Cases where systemic lead remained high for months have occurred, likely due to slow systemic absorption of lead that was retained in the digestive tract.

Treatment for lead poisoning is possible, but in most cases cost prohibitive. For particulate lead (plates, shot, etc.), rumenotomy to remove any remaining lead from the rumen and omasal folds can prevent further lead absorption. Use of chelating agents, such as EDTA, BAL, or Succimer, to aid in the removal of tissue lead can also help eliminate lead.

Copper[5]

Copper is an essential trace element for cattle. Copper toxicosis in cattle is not very common, as they are much more resistant to excess accumulation than sheep. In fact, copper deficiency is much more commonly encountered in cattle than toxicosis. However, higher than normal, but less than toxic, liver copper is routinely identified in some mature dairy cattle. Even though copper toxicosis is relatively uncommon in cattle, an increasing number of cases have presented over the past 5 years.

Prior to 2017, this author averaged less than one case per year of copper poisoning in cattle. However, during the past 5 years 3-5 cases per year have been investigated. Almost all of the cases have been in younger dairy calves, with most being calves sent to feedlots from calf raising operations. However, colleagues have discussed cases in heifer development operations.

Cases of copper poisoning in calves primarily are associated with hepatic accumulation followed some time later by liver failure and deaths. Copper poisoning in cattle generally presents as an acute development of liver failure, jaundice, weakness, anorexia, and deaths. The inciting cause of the sudden hepatic release of copper stores is generally unknown. Several cases investigated by this author involved 250 to 300+ pound calves that had been moved to a feed yard from a calf raising operation. Many of the calves were beef-dairy cross calves that were being pushed harder for growth. Almost all the cases occurred within the first 30 days after arrival.

In discussions with colleagues, several factors many be at play in the increasing occurrence of copper poisoning in these dairy calves. Many dairy cows are over-supplemented with copper, as indicated by frequent findings of higher than normal liver copper concentrations. Movement of copper to the fetus may give these calves higher liver copper at birth. In the past 10 years, many calf raising operations have increased the amount of milk replacer being fed to each calf per day, some by as much as double what was used historically. But, the trace mineral pack in the milk replacer has stayed the same, resulting in the calves getting double the amount of trace mineral supplementation as would have historically occurred. Many calf starter rations

contain high concentrations of trace minerals and young animals tend to have higher absorption capability for trace minerals than adult animals. And, many feedlots that are accustomed to feeding beef calves use higher trace mineral content in their starter rations to counteract potential deficiencies often encountered in typical beef calves. One or several of these factors may be at play in the increased occurrence of copper poisoning cases.

Diagnosis of copper poisoning cases involves analysis of the copper content in both liver and kidney. High liver values alone only prove that the liver has accumulated excess. High kidney copper values verify that excessive copper was dumped into systemic circulation. High liver copper with appropriate histologic pathology can also be suggestive of copper poisoning.

Treatment is limited to supportive care, as use of chelation therapy is cost prohibitive in most cases. Removal of excessive copper from the diet plus animal growth will gradually dilute the excessive liver copper stores in younger animals. In more mature animals, use of increased sulfur and molybdenum in the diet can aid in the reduction of liver copper, but how much and how long are difficult to answer.

Normal liver copper values in cattle tend to vary depending on the source of the information. This author uses the following for copper: Liver normal = 25 to 100 ppm on a wet weight basis (normal for early neonates is 65 to 150 ppm), Toxic concentrations tend to be greater than 250 ppm, but if significant systemic dump occurs then values may be lower; Normal kidney copper = 4-6 ppm on a wet weight basis, Toxic concentrations are greater than 10 ppm but most are much higher.

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