Nitrate Toxicity: Diagnosis and Treatment

Robert Smith, DVM and Glenn Selk

Clinical Signs

Nitrate poisoning in ruminants is an acute or subacute condition. Clinical signs generally are seen within 6 hours following ingestion of high nitrate forage, though as much as a week may pass. Signs are usually related to anoxia resulting from methemoglobinemia. The nitrite ion in blood converts hemoglobin to methemoglobin, and is a vasodilator. The signs of nitrite poisoning appear suddenly due to the tissue hypoxia and low blood pressure resulting from the vasodilation. Rapid, weak heart beat; subnormal body temperature; muscular weakness; ataxia; and brown mucous membranes develop rapidly. Exercise may accentuate the clinical signs and often results in marked dyspnea or collapse or both. Affected animals may die suddenly without evincing any premonitory signs, in convulsions within an hour, or after a clinical course of 3-4 hours. Depression and a cyanotic or brown cast to mucous membranes along with a rapid, weak pulse are often present. Animals occasionally show behavioral changes, muscular tremors, ataxia, and weakness. If not treated, animals may die within several hours to a day after onset of clinical signs. Abortions can result a few days after an episode of acute nitrate intoxication, even in animals that were not obviously affected.

Chronic nitrate intoxication has been reported. Most often this is associated with decreased weight gains and lactation, reproductive failure, and deranged vitamin A and thyroid metabolism. To date these reports are field observations. Nitrate readily passes through the placenta and causes methemoglobinemia in the fetus. Controlled studies to document chronic effects from nitrate have not been reported.

Diagnosis

The blood is chocolate brown because of its methemoglobin content. This characteristic color of the blood is suggestive of the appropriate diagnosis. The submucosa of the rumen, reticulum, and omasum, and the mucosa of the abomasum usually are congested. Petechiae on the serosal surfaces are commonly observed. The dark brown discoloration evident in moribund or recently dead animals is pathognomonic. Animals affected with nitrate intoxication have elevated methemoglobin levels. The percent methemoglobin can be used to evaluate the condition of animals. Methemoglobin is not stable in refrigerated, heparinized blood for more than a few hours. Laboratory determination of methemoglobin must be done within this time or the methemoglobin must be preserved. One part blood may be mixed with 20 parts phosphate buffer (pH 6.6) to preserve the methemoglobin. A 1:20 dilution with distilled water has also been effective in preserving methemoglobin. This sample may then be refrigerated or frozen and delivered to the laboratory. The postmortem lesions are limited to the chocolate brown cast of the blood, mucous membranes, viscera, and muscles, especially if the postmortem investigation is conducted soon after death. Other findings such as pulmonary edema and
emphysema, or agonal hemorrhages associated with respiratory distress, may occasionally be present. Aborted fetuses may be examined for increased nitrate concentrations by diphenylamine testing of the aqueous humor of the eyeball.

Chemical confirmation of elevated nitrate or nitrite levels is required for a firm diagnosis, even if clinical signs, history, and successful treatment all are strongly suggestive of nitrate intoxication. Forage, hay, or feed samples should be analyzed for nitrate content. A field test using diphenylamine should be available to all practitioners. One-half gm of diphenylamine* is added to 20 ml of water, then brought to a volume of 100 ml with sulfuric acid. This stock solution should be stored in a brown glass bottle. The working solution is made by mixing equal parts of the stock solution and 80 per cent sulfuric acid. The working solution should also be stored in a brown glass bottle. Plant material may be tested by placing a drop of working solution on the inside of the split stem at a node or joint. Several plants from different locations should always be tested. A deep blue color will develop within about 10 seconds if 2 per cent or greater nitrate is present. The diphenylamine test can be used readily in the field for testing drinking water, plant material, stomach contents, and urine. While it is not specific, a positive reaction can help to confirm a tentative diagnosis.

Distinguishing between nitrate and cyanide toxicosis

Differentiation between nitrate and cyanide toxicosis is crucial as antidotes for cyanide poisoning exacerbate nitrate toxicity. Livestock poisoning from cyanide is almost always due to the ingestion of plants containing cyanogenic glycosides that liberate cyanide gas upon hydrolysis in the rumen content or the acid media of the stomach. All species of farm animals may be affected with cyanide toxicosis, although cattle, sheep, and horses are most often involved.

Numerous plants contain cyanogenic glycosides at one or all stages of their growth process. Of those, the ones most commonly involved with livestock poisoning are Johnsongrass, Sudan grass, common sorghum, arrowgrass and choke cherry. A venous blood sample provides a quick, accurate test. Cyanide prevents the transfer of oxygen from the blood to its place of molecular utilization in the mitochondria of tissue cells. The circulating blood becomes hyperoxygenated and bright red in color. The venous blood from an animal with cyanide toxicity is bright red while that of an animal with nitrate toxicity is dark or even brownish in color.

Treatment for nitrate toxicity

Methylene blue is the principal therapeutic agent. Methylene blue causes reduction of ferric iron in hemoglobin to the ferrous state so that hemoglobin can again accept and transport oxygen. The suggested dose is 4.4 (Ruhr and Osweiler, 1986) or 9 mg/kg (Merk, 1986) body weight administered slowly via intravenous injection of a 1 to 4 percent solution. The treatment may be repeated if clinical signs recur. Treatment may be repeated in 20-30 min. if the initial response is not satisfactory. Mineral oil (1 L/400 kg)

*Available from Sigma Chemical Company, St. Louis, MO 63166.
orally or saline cathartics (sodium sulfate 0.5 kg/400 kg) orally have been suggested for
lessening the time the high nitrate material remains in the gastrointestinal tract and is
available for conversion to nitrite. (See Table 1 for a summary of drug dosages.) Nitrate
intoxication usually results from feed or water sources, and many animals in a herd will be
exposed. As initially affected animals are treated, others may be developing signs.

Removal of the suspected source of nitrate should also be undertaken. Chemical
confirmation of the nitrate source allows recommendations to be made for preventing
recurrences.

If treatment is prompt and continues for sufficient time and the high nitrate source
can be removed, the prognosis is good, though abortions may still occur within a few
days.

Table 1. Common Drug Dosages

<table>
<thead>
<tr>
<th>Name of Drug</th>
<th>Available From</th>
<th>Species</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylene blue</td>
<td>Mallinckrodt Chemical Co., St. Louis, MO</td>
<td>Bovine</td>
<td>4.4 mg/kg IV (2 to 4 percent solution, Ruhr and Osweiler, 1986)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>9 mg/kg IV (1 percent solution Merck, 1986)</td>
</tr>
<tr>
<td>Mineral Oil</td>
<td>Standard Oil Company Chicago, IL</td>
<td>Bovine</td>
<td>1 L/400 kg orally</td>
</tr>
<tr>
<td>Sodium sulfate orally</td>
<td>Mallinckrodt Chemical Co., St. Louis, MO</td>
<td>Bovine</td>
<td>0.5 kg/400 kg</td>
</tr>
</tbody>
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Sources:
