

Nitrate poisoning in animals

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Abstract: Nitrate toxicity in animals is a significant concern in agriculture and livestock industries, where animals are exposed to high levels of nitrates through contaminated feed, water, or the environment. Nitrates are naturally occurring compounds found in soil, water, and plants, and they are essential for plant growth and nutrition. However, excessive accumulation of nitrates can lead to harmful effects on animal health.

Nitrate poisoning is a condition that typically arises when animals consume excessive amounts of nitrate-rich fodder, which the plant has not converted to protein. Cattle, in particular, are more susceptible to this condition compared to sheep and horses. Nitrates and nitrites, composed of nitrogen and oxygen, naturally occur in the atmosphere as part of the Nitrogen cycle, serving as the fundamental building blocks of these compounds. Notably, nitrites pose a greater hazard than nitrates, being 6–10 times more toxic.

The Nitrogen cycle involves free-living or symbiotic bacteria converting nitrogen into nitrates and nitrites through atmospheric, industrial, and biological processes, a phenomenon known as nitrogen fixation. Nitrification, on the other hand, involves soil-dwelling nitrifying bacteria transforming ammonia into nitrates and nitrate ions.

Plants engage in the process of assimilation by absorbing nitrates or ammonium from the soil through their root hairs. Within the plants, nitrates are converted into nitrites and then ammonium ions, making them available for incorporation into amino acids. Facultatively anaerobic bacteria facilitate the reduction of nitrates back to nitrogen gas, a process termed denitrification.

Sources of nitrate poisoning can arise from various plants such as barley, maize, lucerne, oats, linseed, soybean, sorghum, and wheat. Herbicides,

specifically 2,4-dichlorophenoxyacetic acid, can also contribute to nitrate contamination. Additionally, sewage and industrial waste contaminating drinking water can pose a risk. After periods of drought, plants may have increased nitrate uptake. Although high concentrations of nitrate are not toxic to plants, animals grazing on such plants may suffer from poisoning.

Factors that can lead to higher levels of nitrate in plants include moisture stress, reduced light, cold temperatures, and nutritional deficiencies like phosphorus, sulfur, and molybdenum. Young or immature plants are more likely to accumulate nitrate.

Toxicity varies among animal species. Pigs are more susceptible to nitrate poisoning than cattle and sheep. Fasting can enhance toxicity, and factors like rate of ingestion, gastrointestinal nitrate reduction, nutrition, metabolic status, and pregnancy can influence toxicity levels. Neonatal animals and fetuses are at a greater risk.

Non-ruminant animals are not susceptible to nitrite poisoning from high nitrate ingestion because they lack a digestive system that can convert nitrate to nitrite. However, they are highly vulnerable to nitrite poisoning if they ingest preformed nitrites (e.g., from eating moldy hay) as they cannot convert nitrite to ammonia.

The toxicity of nitrate varies among different animal species. For adult humans, the lethal dose (LD50) of nitrate is estimated to be between 80 to 300 mg/kg of body weight. In cattle, the LD50 ranges from 330 to 620 mg per kilogram of body weight, while in sheep, it is approximately 308 milligrams per kilogram of body weight.

Overall, nitrate poisoning is influenced by various factors, including animal species, health status, and environmental conditions. It is crucial to be aware of these factors to prevent and manage nitrate poisoning effectively.

Toxicokinetics: The elimination of nitrate differs in ruminants and non-ruminants. In most cases, nitrate is converted to nitrite. Rumen microbes facilitate the conversion of nitrate to ammonia, which is then used to produce amino acids. However, during excessive intake of nitrate, the conversion to nitrite occurs at a faster rate than the conversion to ammonia. This leads to an accumulation of nitrite in the gastrointestinal tract, where it is rapidly absorbed into the bloodstream, resulting in toxicity.

Once in the bloodstream, nitrite interacts with haemoglobin, the oxygen-carrying protein in red blood cells (RBCs). Nitrite converts haemoglobin to methaemoglobin, a form of haemoglobin that is unable to efficiently deliver oxygen to the lungs and body tissues. The enzyme NADH Methaemoglobin reductase reduces methaemoglobin back to haemoglobin under normal physiological conditions. However, during nitrate poisoning, the formation of methaemoglobin exceeds the turnover rate of these reducing enzymes, leading to an abnormally high concentration of methaemoglobin that cannot effectively carry oxygen.

Nitrate is excreted by the kidneys, and some of it is recycled back into the gastrointestinal tract. Nitrate can also cross the placental barrier, leading to the conversion of fetal haemoglobin to methaemoglobin.

Toxicodynamics: The toxicity of nitrate involves its interaction with haemoglobin, smooth muscles, and red blood cells.

1. **Interaction with Haemoglobin:** One mole of nitrite ion interacts with two moles of haemoglobin, converting them to produce methaemoglobin. Under normal conditions, a small percentage of methaemoglobin (1-2%) is always present in the blood, which is converted back to normal ferrous haemoglobin by two reducing enzymes in the blood, namely NAD-dependent diaphorase I and NADP-dependent diaphorase II.
2. **Effect on Smooth Muscles:** Nitrate ions directly affect vascular smooth muscles, contributing to the vasodilation and hypotension observed in nitrate poisoning.
3. **Effect on Red Blood Cells (RBCs):** Nitrate can easily enter erythrocytes in exchange for chloride ions. This process further contributes to the accumulation of methaemoglobin in the blood, leading to reduced oxygen-carrying capacity and potential tissue hypoxia.

Overall, the toxicokinetics and toxicodynamics of nitrate poisoning involve complex interactions that disrupt normal oxygen transport and lead to various clinical manifestations in affected animals.

Effect on Smooth Muscles: Nitrite exerts its effect on smooth muscles by increasing K⁺ efflux through the Ca²⁺-sensitive K⁺ channel, leading to hyperpolarization. This causes vascular relaxation and vasodilation, resulting in hypotension and reduced cardiac output. The subsequent inadequate perfusion of tissues leads to a shortage of oxygen, contributing to tissue hypoxia.

1. **Effect on Red Blood Cells (RBCs):** Nitrate ions cause an exchange of chloride ions within RBCs, forming methaemoglobin. Methaemoglobin inhibits the normal oxygen-carrying capacity of RBCs, leading to tissue hypoxia, which manifests as clinical signs such as convulsions, coma, and eventually, death. Methaemoglobinemia can arise from either insufficient enzyme activity or excessive methemoglobin synthesis.
2. **Effects on the Gastrointestinal Tract (GIT):** Excessive consumption of nitrates can have a direct caustic effect on the lining of the gut. This can lead to irritation and damage to the gastrointestinal mucosa.

Clinical Signs of Acute Nitrate Poisoning:

Symptoms typically appear 6 to 24 hours after ingestion of the toxic material. The first symptom is a grayish to brownish discoloration of nonpigmented skin and mucous membranes in areas like the mouth, nose, eyes, and vulva. This discoloration results from the chocolate-brown color of the blood, a characteristic feature of nitrate poisoning that persists for several hours after death.

Other clinical signs include a staggering gait, muscle tremors, abdominal colic, rapid pulse, labored breathing, frequent urination, diarrhea, marked dilation of pupils, signs of vitamin A deficiency, and cyanotic membranes.

As the poisoning progresses, affected animals may experience collapse, coma, and ultimately death.

It is important to promptly recognize these clinical signs and seek veterinary attention to mitigate the effects of nitrate poisoning and provide appropriate treatment.

Chronic Signs of Nitrate Poisoning: In chronic cases of nitrate poisoning, animals may exhibit various long-term health issues and reproductive complications:

1. **Weight Loss:** Chronic nitrate exposure can lead to weight loss in affected animals.
2. **Abortion:** A condition known as "Low land abortion syndrome" may occur, most

commonly observed 3 to 5 days after an acute toxicosis. This syndrome can hinder foetal implantation during the first trimester and result in the death of the foetus during the final trimester. Foetuses that do survive may be prone to convulsions and seizures, often dying within 10 to 24 hours after delivery.

3. **Poor Growth and Reduced Milk Production:** Animals exposed to chronic nitrate poisoning may experience impaired growth and reduced milk production.
4. **Goitre:** Chronic nitrate toxicity can cause goitre, particularly in sheep, due to interference with iodine metabolism.
5. **"Blue Baby Syndrome" in Humans:** In humans with a congenital methaemoglobin reductase enzyme impairment, nitrate exposure can lead to a condition known as "blue baby syndrome." This syndrome results in a decreased ability to carry oxygen in the blood, leading to cyanosis and potentially severe health issues.
6. **Brain Damage and Asphyxia:** In extreme untreated cases of nitrate poisoning, brain damage and death from asphyxia due to oxygen deprivation are possible.

Developmental and Reproductive Effects:

Nitrates can also have developmental and reproductive effects. Increased nitrate exposure is associated with a higher prevalence of neural tube abnormalities in both children and adults.

Lesions: In cases of nitrate poisoning, various characteristic lesions can be observed:

1. **Blood Discoloration:** Blood appears dark brown or coffee-colored and clots improperly.
2. **Petechial Hemorrhages:** Petechial hemorrhages are observed on the serous surfaces, leading to tissue brown discoloration. Widespread vascular dilation and cyanosis are also common findings.
3. **Placental Necrosis:** Nitrate poisoning can lead to necrosis of the placenta.
4. **Gastrointestinal Congestion:** Congestion of the ruminal or abomasal mucosa may be present.



5. **Neonatal Calves:** Neonatal calves exposed to high maternal nitrate levels may exhibit ascites, edema, and hemorrhage in the lungs and digestive system, and stillborn calves have been recorded.

Diagnosis: Diagnosing nitrate poisoning involves considering the animal's history and clinical signs, particularly the presence of dark chocolate-colored blood. Various testing methods can be used in the field and laboratory.

Field approaches include qualitative spot color techniques and some quantitative techniques using colorimeters and nitrate electrodes. Plasma is the preferred antemortem specimen, while maternal and perinatal serum, plasma, ocular fluid, and similar biologic fluids are indicative of excessive nitrate or nitrite exposure in most domestic animal species. For postmortem samples, ocular fluid is the preferred sample for nitrate poisoning.

Plasma or serum nitrate and nitrite concentrations in acutely poisoned ruminant cattle can reach 300 ppm and 25-50 ppm, respectively. Blood samples for methemoglobin analysis should be collected within 2 hours of death and rapidly frozen or preferably preserved in phosphate buffer to stabilize methemoglobin. Forage, ingesta, and water can also be examined to assess nitrate levels.

Differential Diagnosis: It is important to differentiate nitrate poisoning from other toxicoses and diseases with similar clinical signs. Differential diagnoses include toxicosis due to cyanide, urea, pesticides, toxic gases (e.g., carbon monoxide, hydrogen sulfide), chlorates, aniline dyes, aminophenols, or drugs (e.g., sulfonamides, phenacetin, and acetaminophen). Additionally, various infectious or noninfectious diseases like grain overload, hypocalcemia, hypomagnesemia, pulmonary adenomatosis, or emphysema should be considered. Any other cause of sudden, unexplained death must also be ruled out.

Treatment: The treatment for nitrate poisoning involves removing the source of nitrate exposure and providing supportive care.

It is essential to address the condition promptly to prevent further absorption and to manage the animal's clinical signs effectively. Supportive therapies may include intravenous fluids, oxygen therapy, and medications to stabilize the cardiovascular system.

However, specific treatment protocols may vary depending on the severity of the poisoning and the animal's overall health status.

Veterinary consultation is crucial to determine the most appropriate treatment plan for affected animals.

Treatment: In cases of nitrate poisoning, the administration of 1%–2% methylene blue via slow intravenous injection in distilled water or isotonic (0.9% NaCl) saline solution is recommended. The dosage should be adjusted based on the severity of exposure, typically ranging from 4–15 mg/kg or more.

Prevention: To prevent nitrate poisoning in livestock, several measures can be taken:

1. **Avoid High-Nitrate Forages:** Refrain from feeding forages with potentially toxic levels of nitrate. Analyze feeds and forages for nitrate levels before grazing or feeding them.
2. **Dilute High-Nitrate Forages:** If harvested forages are high in nitrate, they can be safely fed by mixing them with other feeds to reduce the overall dietary intake of nitrate.
3. **Proper Harvesting:** When cutting drought-stressed forages, harvest them a few inches above the ground level, as the lower stalk contains the highest concentration of nitrates.

Management: Implement the following management practices to mitigate the risk of nitrate toxicity:

1. **Test Forages:** Drought-stressed small-grain forages and other forages suspected of having high nitrate levels should be tested before feeding.
2. **Gradual Intake:** Allow livestock to consume small amounts of high-nitrate feed frequently. This helps them adjust to high-nitrate feeds and increases the total amount of nitrate they can consume daily without adverse effects.

3. **Fresh Water Access:** Provide livestock with access to fresh, nitrate-free water at all times.
4. **Controlled Access:** Do not allow hungry cattle to have access to high-nitrate forages or pastures. Feed them hay or forages low in nitrates before turning them onto high-nitrate pastures.

Conclusion: Nitrite toxicity in animals is a complex issue that requires collaboration among researchers, veterinarians, and policymakers to safeguard animal health and ensure the production of safe and nutritious animal-derived products for human consumption. By implementing preventive measures, managing nitrate-rich feeds carefully, and providing appropriate treatment when needed, the impact of nitrate poisoning on livestock can be minimized, ensuring the well-being of both animals and consumer.

