Toxicologic Emergencies in Cattle

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Although many plants, metals, industrial products, minerals, and medicines are potentially toxic to cattle, a limited number cause sudden death or respiratory, gastrointestinal, cardiac, or metabolic crises that require emergency treatment or critical care of the affected animal or herd of animals. There are many excellent clinical toxicology reviews and resources for the veterinary clinician that provide detailed information regarding sources of toxins for cattle, toxicokinetics, mechanisms of action, clinical signs, diagnoses, and therapy [1–3]. This article is not a complete review of clinical toxicology of cattle but focuses on the toxins most likely to cause emergencies in cattle. After providing a list of the plants, metals, minerals, industrial products, and feeds that are likely to be responsible for the toxicities that require immediate care for the affected cattle, the authors sort the toxins into categories based on their clinical presentations and follow with diagnostic and treatment recommendations for situations in which the toxin is known and for emergency situations in which the source of toxicity is unknown. The authors’ goal is to provide a useful clinical review of the toxicologic emergencies that bovine practitioners may encounter.

Toxicities requiring emergency treatment of cattle

For most of the potential toxins for cattle discussed in this section, toxicity may vary in severity and clinical presentation depending on the age and sensitivity of the animal; dose, duration, route, and source of exposure; and the nutrition and general health of the subject. There are many classes of potential toxicants for cattle, but the authors have limited this discussion to those that are known to cause clinical emergencies in North American...
cattle and for which exposure or consumption has a high likelihood of producing a consistently serious clinical syndrome. Toxicities resulting in primary photosensitization, abortion, or other nonemergency conditions are not discussed.

**Poisonous plants**

Poisonous plants are frequently cited as the cause of acute toxicity of cattle [4–12]. Cattle that ingest any of the plants listed in Box 1 are at risk of developing a clinical syndrome that requires emergency treatment. These plants are categorized further in the next section. Included in the list are plants that cause photosensitization through liver damage but not those that cause primary photosensitization (photodynamic pigment produced directly by the plant accumulates in the skin) because primary photosensitization is not viewed by the authors as creating an emergency condition of cattle.

**Feed-related toxicities**

Many of the toxicities that require emergency treatment of affected cattle are acquired in feeds. Although some are dose related, others are due to feed contamination, abnormal growing, harvesting or storage conditions, interactions with other ingredients, or other animal, environmental, or management risk factors. The toxicities, briefly summarized in the following text, create critical health risks in exposed cattle.

*Ammoniated feed, urea, nonprotein nitrogen toxicity*

The source of toxicity, characterized by irritability, rapid blinking, ear twitching, salivation, frenzied behavior, and frequent urination and defecation can be ammoniated forages (ammonia added to reduce spoilage and increase nutritional value), feed-grade urea, ammonium salts, and dietary supplements. Although the signs of nonprotein nitrogen or urea toxicosis are due to the accumulating ammonia’s inhibition of the citric acid cycle and subsequent acidosis, the toxicity of ammoniated forages may be due to imidazoles or other metabolites of the ammoniation process.

*Gossypol*

Cottonseed meal or whole cottonseed is the primary source of gossypol, a yellow pigment concentrated in the glands of the cottonseed. Although mature cattle are relatively resistant because the binding of gossypol to rumen protein reduces its toxicity, calves are susceptible to its potent cardiotoxic effects. Labored breathing, abomasitis, and hemoglobinuria have been described in adult cattle.
Box 1. Plants that can cause clinical emergencies in cattle

- **Asclepias**—common name is milkweed; neurotoxic in cattle.
- **Calcinogenic glycosides**—plants in this group, like *Cestrum diurnum*, also known as wild jasmine, cause mineralization of many tissues including heart and blood vessels. Although typically toxicity is slow and progressive, some cattle may develop hypercalcemia and cardiac arrhythmias acutely.
- **Cardiac glycosides**—commonly referred to as oleander. All parts of the plant are toxic to cattle, inducing sudden death in many and abdominal pain, rumen atony, and excessive salivation in others.
- **Cicutoxin**—common name is water hemlock; neurotoxic in cattle.
- **Clusiaceae**—*Hypericum* genus, commonly known as Saint-John’s-Wort, Klamath weed, and goatweed. Although most North American species are not toxic or cause primary photosensitization, those that possess pigment glands can cause secondary photosensitization [13].
- **Coumarin glycosides**—commonly found in moldy sweet clovers. Dicoumarol ingestion by cattle interferes with vitamin K function, inducing coagulopathies frequently manifested by hematoma formation in exposed cattle.
- **Cyanobacteria or blue-green algae**—neurotoxic in cattle, inducing acute death and liver failure.
- **Cyanogenic glycosides**—in cattle, the exposure to cyanide is due to accumulation of cyanogenic glycosides in rapidly growing, frost-killed, or drought-stressed grasses (Johnson grass, sorghum, Sudan grass) and corn. With chewing, glycosides are converted to cyanide, which prevents oxyhemoglobin from releasing oxygen to tissues. Affected cattle have respiratory distress that can rapidly progress to convulsions and death. A characteristic lesion is the bright cherry red appearance of blood due to the high oxygen saturation of hemoglobin.
- **Diterpene alkaloids**—common name is larkspur, causing sudden death of range cattle through neuromuscular blockade. Bloat may be observed before death.
- **Furans**—commonly known as perilla mint. The perilla ketone released from the mint plant and from 4-ipomeanol in moldy sweet potatoes causes acute bovine pulmonary edema and emphysema, also known as acute respiratory distress syndrome, in cattle that have access to plants or spoiled potatoes.
• Glucosinolate—commonly known as mustard plants, rape, kale, and others. These plants have toxins concentrated in the seeds that, when ingested by cattle, cause colic, hemorrhagic diarrhea, and blood in the urine.
• Gutierrezia—*Gutierrezia microcephala* and *G sarothrae* (the two perennial species in the United States) can produce acute digestive disease, with crusted muzzle, diarrhea, and anorexia in exposed cattle [14].
• Indolizidine alkaloids—*Astragalus* and *Oxytropis* plants are commonly called locoweeds, vetches, or milk vetches and can produce neurologic disease, infertility, reproductive failure, congenital deformities, right heart failure, weight loss, and poor performance.
• Nitropropanol glycosides—commonly found in *Astragalus* spp. The nitrotoxins cause respiratory and neurologic disease, and affected cattle die within a few hours.
• Oak—most toxicities occur from the ingestion of immature leaves in the spring and acorns in the fall. The classic kidney and gastrointestinal signs of oak poisoning that include anorexia, depression, rumen atony, pigmenturia (brown urine), and diarrhea cannot be reproduced by administration of tannic acid [13].
• Pigweed—*Amaranthus retroflexa* or pigweed. When immature stems are consumed by cattle in large quantities, depression, trembling, and weakness occur, mimicking signs of hypocalcemia.
• Propyl disulfide—the most common sources for cattle are *Allium* sp or onion plants. Although the toxicity depends on the source and type of exposure and the time of year, Heinz body hemolytic anemia is the typical syndrome of exposed cattle [15].
• Ptaquiloside—commonly referred to as bracken fern. Ingestion can cause several different syndromes in cattle depending on age, location, amount ingested, toxin concentration in the plant, and general health of the animal. Aplastic anemia and enzootic hematuria caused by bladder tumors are the most common syndromes of exposed cattle.
• Pyrrolizidine alkaloids—there are numerous plants in this family capable of producing toxicity in cattle. *Senecio jacobaea* (tansy ragwort) and *Crotolaria* sp (rattle pod), two of the prototypic plants in the group, cause liver disease when the plants or their seeds are ingested.
Ionophores

Polyether acid ionophore antibiotics have enjoyed expanded use in the diets of cattle because of their anticoccidal, growth promotion, and feed- and milk production–efficiency claims. Despite the fact that these are approved compounds and cattle are a target species, toxicity can occur with increased dietary levels due to mixing errors, inappropriate delivery methods, overfeeding, or administration to the wrong group of animals [17–22]. The mechanism of monensin and lasalocid toxicity in cattle is related to ion transport and the cellular sodium, potassium, calcium, and hydrogen imbalance that results in excitable tissues. With monensin toxicity, there may be gastrointestinal,

- Quinolizidine alkaloids—commonly known as lupines. This group of plants rarely causes acute toxicity in cattle.
- Ryegrass toxicity—although rarely reported in the United States, the corynetoxins in the seed heads of annual ryegrass and fescue can produce neurologic disease, recumbency, and death in exposed cattle [16].
- Senna—formerly known as Cassia sp. This group of plants is myotoxic to cattle as evidenced by weakness, recumbency, and myoglobinuria.
- Taxine alkaloids—Taxus sp (yew). These plants are the readily recognized ornamental evergreen shrubs, trees, and ground hemlock. They are potent cardiotoxins, causing sudden death in cattle even when a small amount of clippings has been consumed.
- Trematone—common name is white snakeroot. The toxicity, which is dependent on the amount consumed, is usually manifested as an abnormal gait, muscle tremors, myoglobinuria, and cardiac signs in cattle.
- Tropane alkaloids—Datura sp, commonly known as jimsonweed. It is unpalatable, but the toxin, which is concentrated in the seeds, is a competitive antagonist of acetylcholine at muscarinic cholinergic receptors, producing mydriasis, muscle tremors, bloat, and respiratory paralysis.
- Tryptamine alkaloids—commonly known as canary grass. Phalaris canariensis toxicity induces muscle tremors, uncoordinated gait, staggers, and occasionally sudden death in exposed cattle.
- Tryptophan—L-tryptophan from lush green forages is converted to 3-methylindole in the rumen, is absorbed and concentrated in the lung of cattle, and produces acute bovine pulmonary edema and emphysema, also known as acute respiratory distress syndrome.
musculoskeletal, or cardiac signs exhibited by the affected group [17,18]. Lasalocid toxicity reported in calves has primarily neurologic manifestations, including ataxia, recumbency, seizurelike activity, dyspnea, and death [20,21]. Monensin toxicity may resemble vitamin E and selenium deficiency, senna, or trematone (Eupatorium sp) toxicity described earlier. Lasalocid toxicity of calves must be distinguished from septicemia, sodium toxicity, bovine viral diarrhea, polioencephalomalacia, or congenital defects. Reported toxic doses of monensin and lasalocid have recently been reviewed [23].

**Mycotoxins**

Of most concern in cattle feeds are aflatoxin, fumonisins, zearalenone, deoxynivalenol, ergot alkaloids, T-2 and other trichothecene mycotoxins, ochratoxin, and citrinin. Feed refusal, decreased feed intake, reproductive failure, and immunosuppression—signs attributed to many of these mycotoxins—do not require emergency treatment. The classic dry gangrene of extremities due to ergot alkaloids does not develop acutely. Aflatoxicosis of cattle is usually chronic, with clinical signs reflective of liver disease. Tremorgenic forages produce a syndrome often referred to as “staggers” because of the fine tremors of the head and neck when animals are excited. More severe signs of ataxia, seizures, opisthotonus, and convulsions can occur when fungi growing on perennial ryegrass, Dallis grass, Bahia grass, or Bermuda grass are ingested by cattle.

**Nitrate/nitrites**

The rumen microbes of cattle that (1) ingest nitrate-laden plants (frequently drought-stressed, frost-injured, hail-damaged, herbicide-treated, or grown on nitrate-rich soil); (2) drink high-nitrate water; or (3) accidentally consume nitrate-based fertilizer rapidly metabolize nitrate to nitrite, resulting in the development of methemoglobinemia. Depending on the rate and amount consumed, cows can become critically oxygen deprived when methemoglobin levels exceed 30% in blood [24].

**Salt**

Salt poisoning can occur from ingesting too much sodium or from water deprivation. Although salt is limited in most rations fed to cattle, protein and mineral supplements and selected milk replacers may have high salt levels [25,26]. Oral or intravenous (IV) fluids used to treat calves and cows may be the source of excess sodium. The clinical signs of salt toxicity, although somewhat dependent on the rate of development of hypernatremia, may begin with gastrointestinal signs but rapidly progress to neurologic signs indistinguishable from polioencephalomalacia.

**Selenium**

Selenium toxicity of cattle is most often attributed to overconsumption or overdosing parenteral administration of selenium supplements. Forage or plant-based selenium toxicity is less likely because of palatability issues.
The toxicity, believed to be linked to oxidative stress, produces lesions strikingly similar to vitamin E and selenium deficiency [27]. Signs of acute toxicity are weakness, abdominal pain, and respiratory and circulatory failure that progresses to recumbency, coma, and death.

**Sulfur**

Excessive dietary intake of sulfur, usually in the form of protein, amino acid supplements, inorganic sulfur (ammonium sulfate, magnesium sulfate), high-sulfate water, or molasses-rich diets, can cause polioencephalomalacia in cattle after ruminal reduction to sulfide. The characteristic clinical signs that include blindness, stargazing, recumbency, convulsions, and death are thought to be due to sulfide impairment of neuronal energy metabolism or cerebral blood flow impairment.

**Cholinesterase inhibitors**

Organophosphate and carbamates can be found in insecticides, herbicides, and fungicides used in agriculture. Organophosphate deworming products are another potential source of toxicity for cattle. Toxic effects occur by binding with cholinesterase and by inhibition of acetylcholine catabolism. Accumulation of acetylcholine results in overstimulation of the cholinergic nerve synapses at the neuromuscular junction, resulting in death from respiratory and cardiovascular failure. With acute poisoning, clinical signs progress from apprehension and nervousness to abdominal discomfort, bloat, salivation, defecation, miosis, and urination to muscle tremors, ataxia, seizures, bradycardia, respiratory failure, and death.

**Hydrogen sulfide**

The source of hydrogen sulfide that poses the greatest risk to cattle is liquid manure storage tanks or pits under slatted floors or other holding areas. Toxicity occurs when the manure slurry is agitated, an action that can produce hydrogen sulfide concentrations up to 1000 ppm, levels that obtund the ability to detect the characteristic odor that serves as a warning [28]. Inhalation of the gas induces ocular and respiratory inflammation, pulmonary edema, and death from asphyxiation.

**Metals**

**Arsenic**

The sources for arsenic poisoning in cattle can be environmental (mining and smelting sites), old pesticides, ashes from arsenic-treated wood products, rodenticides, herbicides, and insecticides [29–31]. Clinical signs, although dependent on rate, type, duration, and dose of exposure, target the gastrointestinal system with symptoms of abdominal pain, atony, and diarrhea. Weakness, ataxia, recumbency, and shock are common.
Copper

Although cattle are much more resistant than sheep, copper toxicity is associated with excessive supplementation or overtreatment of copper deficiency [32–34]. Clinical signs of depression, anorexia, and weakness are followed by watery, dark, or blood-tinged diarrhea. In acute toxicity, cattle may be neurologic, with head pressing, ataxia, and circling, whereas in chronic toxicity, evidence of hemolysis (anemia and hemoglobinuria) may be present.

Lead

Most lead sources for cattle are inorganic compounds such as paint, solder, automotive batteries, gasoline or oil, caulking compound, roofing felt, and putty. Signs of toxicity depend on the dose, the type and duration of exposure, and the age of the animal. In acute exposure, cattle show neurologic signs of depression, hyperesthesia, muscle tremors, ataxia, blindness, seizures, head pressing, and dementia. Gastrointestinal signs of straining, teeth grinding, bloat, and diarrhea may be present. Chronic toxicity is associated with similar signs that develop over a more protracted period.

Molybdenum

Cattle are more sensitive to molybdenum toxicity than other ruminants. The interactions of molybdenum, copper, and sulfur are responsible for the toxicity. Increasing levels of sulfur in the diet increases the toxicity of molybdenum by decreasing the absorption of copper. Balancing the molybdenum-to-copper ratio is the best way to prevent molybdenum toxicity [35]. Chronic diarrhea is the most common sign of toxicity.

Therapeutic agents

Neomycin

Nephrotoxicity was exhibited by calves given doses of neomycin greater than 2.25 mg/kg [36].

Propylene glycol

Commonly used as a vehicle for drugs, propylene glycol is also one of the most commonly used oral drenches for ketosis. Accidental overdose is the cause of toxicity, manifested by ataxia, depression, and recumbency in cattle [37].

Tetracyclines

In cattle, cardiovascular and renal toxicoses are reported with tetracycline overdose [38–41].
**Nitrofurazone**

Formerly approved for treatment of respiratory and gastrointestinal disease of cattle, this illegal antimicrobial can cause neurologic signs after prolonged feeding or administration of high doses [42].

**Toxicity characterized by clinical presentation**

The clinical signs that prompt an emergency response by cattle producers and their veterinarians are

- Sudden death
- Neurologic signs (abnormal behavior, ataxia, blindness, head pressing, opisthotonus, convulsions)
- Muscular weakness, tremors, or collapse
- Dyspnea or respiratory failure
- Cardiac failure signs
- Severe digestive system disturbance (pain, bloat, salivation, severe diarrhea, atony)
- Hemorrhage or hemolysis
- Hepatogenous photosensitization or signs of liver failure
- Pigmenturia
- Kidney failure signs

Because the clinical signs are not specific and toxin exposure may not be identified as a cause when the veterinarian is called to respond, the considerations relative to cause, prevention, diagnosis, and treatment are summarized in the following lists and discussion.

**Causes of sudden death**

Although individual animals may suddenly die with no obvious prior clinical signs, investigations of most sudden death complaints reveal clinical signs in the affected group of cattle. Infectious, metabolic, nutritional, physical, traumatic, and toxic causes are given primary consideration. Infectious diseases like anaplasmosis, anthrax, clostridial disease, liver flukes, and bacterial septicemia should be considered. Other causes include internal exsanguinations; abomasal ulcer perforation; metabolic conditions like severe hypokalemia, hypocalcemia, or hypomagnesemia; nutritional myodegeneration (vitamin E or selenium deficiency); acute bloat; grain overload; and lightening, stray voltage, gunshot, or other trauma.

**Toxic causes of sudden death in cattle**

The list of toxic causes (Box 2) is confined to those that cause death within a very short time of exposure or have a limited number of defining clinical signs other than death.
Toxic causes of neurologic disease in cattle

The list of toxic causes that follows (Box 3) must be differentiated from infectious causes like thromboembolic meningoencephalitis, listeriosis, rabies, pseudorabies, bovine spongiform encephalopathy, and malignant catarrhal fever. Vitamin A deficiency, brain abscess, congenital and familial neurologic conditions, hypomagnesemia, nervous ketosis, and trauma are other differential diagnoses that should be considered.

Toxic causes of muscle weakness, tremors, and collapse

In addition to the following toxic causes, these nonspecific signs can be exhibited by cattle that have hypokalemia, hypocalcemia, and hypomagnesemia and that have congenital brain defects such as cerebellar abiotrophy, hypoplasia, or lysosomal storage disease.

- Calcinogenic glycosides (Cestrum diurnum, Solanum sp, Trisetum sp)
- Indolizidine alkaloids (Astragalus and Oxytropis sp)
- Ionophores (monensin and lasalocid)
- Senna sp
- Thermopsis montana (quinolizidine alkaloid)

Toxic causes of dyspnea or respiratory failure

To be distinguished from the toxic causes of respiratory difficulty in cattle (Box 4) are infectious (bacterial, mycoplasmal, viral, and parasitic) causes of pneumonia, aspiration pneumonia, anaphylaxis, necrotic laryngitis, pharyngeal trauma, and nutritional myodegeneration from vitamin E or selenium deficiency.
Toxicities targeting the cardiovascular system

Heart failure from any cause, including endocarditis, other valvular insufficiencies, lymphosarcoma, pericarditis, myocarditis, cor pulmonale, or congenital disease should be differentials for cardiac toxins (Box 5). Cardiac myodegeneration from vitamin E or selenium deficiency should also be considered.

Toxicities presenting with severe digestive system disturbance

Along with the toxic causes of gastrointestinal pain, bloat, salivation, severe diarrhea, and atony that are listed in Box 6, other differential diagnoses include infectious causes like salmonellosis, bovine viral diarrhea, hemorrhagic bowel syndrome, acute grain overload, clostridial enterotoxemia, functional or mechanical intestinal obstruction, and abomasal volvulus.
Toxicities causing hemorrhage or hemolysis

Toxins and other agents can act systemically, damaging vessels and interfering with coagulation. Immune-mediated coagulopathy, bovine virus diarrhea, virus-induced thrombocytopenia, disseminated intravascular coagulopathy, and other infectious agents are capable of inducing coagulopathies that serve as differential diagnoses for toxicity-induced hemorrhage or hemolysis. Blood loss due to internal or external parasitism, perforation of an abomasal ulcer, pulmonary abscess rupture, and hemolysis in anaplasmosis and leptospirosis infections should be considered.

- Acute copper toxicity
- Bracken fern
- Brassica sp
- Onion toxicity
- Moldy sweet clover
- Propylene glycol

Box 5. Toxicities of the cardiovascular system

- Calcinogenic glycosides (Cestrum diurnum, Solanum sp, Trisetum sp)
- Gossypol
- Locoweed
- Monensin
- Oleander
- Selenium
- Tetracycline
- White snakeroot
Toxicities causing hepatogenous photosensitization

Although primary photosensitization is not considered a critical emergency condition of cattle, secondary or hepatogenous photosensitization is discussed in this article because it may be associated with severe concurrent hepatobiliary disease that puts cattle at risk for hemorrhage, hepatoencephalopathy, weight loss, diarrhea, and death.

- *Brassica napus, Triticale* (rape, wheat, rye hybrid pasture)
- Moldy alfalfa hay, wheat straw, or other mycotoxin-contaminated feeds
- Pyrrolizidine alkaloids
- *Setaria* sp, *Dactylis glomerata* (foxtail, orchard grass hay)
- *Trifolium pratense* (red clover)

**Diagnostic sample submission for suspected toxicities**

The emergency management of a suspected toxicity requires a detailed history that includes timing, number of animals affected, presenting clinical
Box 7. Toxicities causing pigmenturia or kidney failure

- Arsenic toxicity
- Ptaquiloside (bracken fern) toxicity
- Calcinogenic glycosides (Cestrum diurnum, Solanum sp, Trisetum sp)
- Chronic copper poisoning (hemoglobinuria)
- Mercury toxicity
- Monensin (myoglobinuria) toxicity
- Neomycin (hematuria) toxicity
- Oak poisoning (hemoglobinuria)
- Oxalate toxicity
- Pigweed toxicity
- White snakeroot (myoglobinuria) toxicity
- Senna sp (myoglobinuria) toxicity
- Tetracycline (hematuria, hemoglobinuria) toxicity

signs, time course of events, potential feed or environmental sources, and management changes. Careful examination of affected and unaffected animals, evaluation of potential risk factors, and collection of diagnostic samples complete the investigation. Complete blood count, biochemical profile, and electrolyte concentrations serve as discriminating information to distinguish infection, inflammation, type of toxicity, metabolic derangements, and the target organ system. A coagulation-testing panel is frequently useful. From live animals, blood samples should be taken and stored appropriately. Whole blood with ethylenediaminetetraacetic acid (EDTA) as the anticoagulant is preferred to heparinized blood. A refrigerated 10-mL sample of whole blood is useful for ammonia, anticoagulant, carbamate, cyanide, lead, mercury, nitrate, organophosphate, selenium, and urea toxicity diagnosis. Clotted blood samples, serum and plasma, should be separated immediately and chilled or frozen until ammonia, copper, drug, ionophore, magnesium, mercury, nitrate, potassium, sodium, selenium, urea, vitamins A and E, or zinc analysis can be performed. Hemolyzed samples are not useful. Rubber stoppers may be inappropriate for some samples; other samples may need specialized tubes and still others may require foil-covered tubes to prevent breakdown with heat and light exposure. Large-volume urine samples (20–100 mL) chilled until submission in leak-proof containers can facilitate the diagnosis of arsenic, carbamate, chlorinated hydrocarbon, ionophore, magnesium, mercury, and urea toxicity. A 30-mL sample of refrigerated milk may be used to look for antibiotics, organochlorines, or polychlorinated biphenyls. Ingesta (rumen contents) and feces (minimum of 100 g) chilled until submission in leak-proof containers may complement other diagnostic samples to confirm ammonia, arsenic, carbamate,
chlorinated hydrocarbon, herbicide, nitrate, organophosphate, plant, or urea toxicity. Two aliquots of feed, forage, and water samples should be placed in airtight containers. One sample should be frozen and one refrigerated because sample preference differs with different toxins. Cerebrospinal fluid that is kept chilled until analysis provides definitive evidence for magnesium and sodium toxicity.

From the postmortem examination, 1-kg samples of rumen contents should be frozen and chilled, along with 100-g fecal samples. Depending on the tests desired, frozen or refrigerated samples may be preferred. A liver sample (100–200 g) should be obtained and chilled until submission for arsenic, carbamate, chlorinated hydrocarbon, copper, cyanide, drug, herbicide, lead, mercury, molybdenum, mycotoxin, organophosphate, selenium, vitamin, and zinc analysis. Formalin-fixed liver is used for copper, gossypol, and vitamin analysis. Fresh liver can be submitted for mercury and mycotoxin screens. A chilled kidney sample (100–200 g) is used for arsenic, copper, herbicide, lead, mercury, molybdenum, selenium, and zinc analysis. Formalin-fixed kidney is used for copper diagnosis, and fresh samples can be submitted for mercury and mycotoxin screens. Half of the brain sample is used for submission of fresh (mercury diagnosis), chilled (carbamate, chlorinated hydrocarbon, mercury, and salt toxicity), and frozen (petroleum or fuel oil) samples, whereas the second half is used for formalin-fixed histopathologic examination (salt toxicity). Ocular fluid from one eye or a 2-mL sample chilled until submission is useful for analysis of nitrates, nitrite, chloride, potassium and sodium concentrations, ammonia, drugs, urea, and magnesium. Fat samples (100 g) can be used to confirm chlorinated hydrocarbon and polychlorinated biphenyl exposure. Formalin-fixed skeletal and cardiac muscle samples are used for gossypol, ionophore, and vitamin A and E analysis.

Observations of chocolate-colored (nitrate) or cherry red (cyanide) blood, gross lesions, appearance of tissues, and rumen pH measurement should be recorded and submitted to the diagnostic laboratory and may speed up the diagnostic process. A hair sample obtained from the flank, although rarely a confirming diagnostic test, can be submitted after washing the area with nonselenium-containing shampoo, rinsing with deionized water, and shaving to obtain a 1- to 2-g sample that is submitted in a collection vial for diagnosis of chronic selenosis. Ruminal hydrogen sulfide concentration can be used to diagnose sulfur toxicosis.

Principles of therapy

When the toxicity is unknown or has no specific antidote, supportive care is administered to stabilize affected animals. For oral toxicants, ruminal evacuation (surgically or nonsurgically by lavage) may be useful. Alternatively, binding agents, adsorbents, or mineral oil can be given to decrease
absorption. Cathartics or laxatives may hasten the excretion of unabsorbed toxicant, and antacids may neutralize the toxic effect of others. Cattle that have life-threatening respiratory or cardiac distress, hyperexcitability, or toxicity syndromes that pose human risk should be observed from a distance and treated only when the agent can be administered in the feed or water or by other noncontact methods.

Sedatives or anesthesia may be required in cattle that have severe neurologic signs. Thiamine administration may be palliative, sparing, or restorative in cattle that have neurotoxic conditions. Correction of hypokalemia, hypocalcemia, or hypomagnesemia or of metabolic derangements like dehydration, acidemia, rumen acidosis, or alkalosis are other important aspects of supportive care for cattle that have a toxicity. Administration of vitamin E and selenium may help arrest myotoxic changes in affected animals or cattle at risk of deficiency syndromes. Pain management constitutes another aspect of supportive care.

**Antidotes**

Antidotes are not readily available and are not approved for use in cattle. As a result, the drugs are used in an extralabel manner and, by necessity, may be compounded from bulk drug sources. Although compounding an animal drug from bulk substances is illegal, emergency treatment of a toxicity that threatens the life of untreated animals may necessitate the compounding of an antidote that would otherwise be unavailable. Under those circumstances, a valid veterinarian-client-patient relationship must be established, along with guidelines that eliminate the chance of milk or meat residues in treated cattle. Food Animal Residue Avoidance Databank (FARAD) is the best source of information regarding appropriate withdrawal times for the antidote and the toxicant.

**Activated charcoal**

Activated charcoal is a nonspecific adsorbent administered to cattle that have ingested potential toxicants, feeds, feed additives, or drugs capable of inducing toxicity. Activated charcoal, frequently used in combination with mineral oil, other saline cathartics, or gastric protectants, may reduce absorption and increase the rate of elimination of some ingested toxins. Because activated charcoal is not soluble or absorbed, there is no concern for milk or meat residues.

**Atropine sulfate**

Atropine sulfate is indicated for the treatment of organophosphate toxicity (cholinesterase inhibitor) in cattle. Administration of a subcutaneous dose of 0.1 mg/kg body weight is repeated at 4- to 6-hour intervals until pupil dilation is achieved. The recommended milk and meat withdrawal times
of 6 and 28 days, respectively, may be exceeded by the time required for de-
pletion of the organophosphate residues in surviving cattle [43].

**Copper glycinate, sulfate, and edetate disodium**

Copper glycinate, sulfate, and edetate disodium are used to treat cattle
that have molybdenum toxicity. There are limited data to establish the route
of administration, dosage, efficacy, and safety for cattle, and no approved
formulations are marketed. To establish appropriate milk and meat with-
drawal information, FARAD should be contacted with specific herd
information.

**Corticosteroids**

Corticosteroid administration may be recommended for treatment of
acute allergic reactions, toxicities that result in acute respiratory collapse,
pulmonary edema, or inflammation of the gastrointestinal, respiratory, or
nervous system of cattle. Because of accessibility, efficacy, and cost, dexam-
ethasone is usually the drug of choice. It is administered (IV) at a dose
of 0.05 to 0.1 mg/kg body weight.

**Dimercaprol**

Dimercaprol, also known as British antilewisite, is a chelating agent used
to complex the heavy metals arsenic, lead (in conjunction with EDTA), and
mercury. No animal product exists, so the drug must be compounded from
bulk human drug formulations [43]. To the authors’ knowledge, pharma-
koenic and pharmacodynamic studies have not been done in cattle, leaving
treatment dose, frequency, and residue depletion information somewhat
speculative and based on studies in rabbits, dogs, and humans [43]. It has
been recommended that a dose of 2.5 to 5 mg/kg of a 10% solution in oil
be given intramuscularly every 4 hours for 2 days, then twice daily until re-
cover [44].

**Calcium ethylenediaminetetraacetic acid**

Calcium EDTA is approved for use in humans but is administered par-
tenterally to cattle to chelate divalent ions like lead, zinc, cadmium, copper,
iron, and manganese in the case of toxicity. Edetate calcium disodium is the
chelator of choice for lead toxicity after decontamination of the gastrointes-
tinal tract is complete. It is administered (IV) slowly at 73 mg/kg body
weight, divided into two or three doses per day for 3 to 5 days or given
as an IV 110 mg/kg dose twice daily for 2 days [45]. Additional treatment
may be necessary, and treated cattle should be well hydrated. A short
milk and meat withdrawal time of 2 days has been established because of
the drug’s limited distribution within the body [43].
**Epinephrine**

Epinephrine is a nonspecific antidote recommended for treatment of acute allergic reactions, drug sensitivities, or toxicities that result in cardiopulmonary collapse. Its rapid inactivation has resulted in a 0-day milk and meat withdrawal at the usual dose of 0.01 mg/kg (approximately 5 mL for adult cattle and 0.5 mL for a calf) of a 1:10,000 (0.1 mg/mL) dilution.

**Methylene blue (1%)**

Methylene blue (1%) is used to treat methemoglobinemia from nitrate, nitrite, and chlorate toxicity of cattle. The dose range is 4 to 15 mg/kg IV, which may be repeated in 6 to 8 hours [44]. The potential for carcinogenicity has resulted in an extended meat withdrawal time of 180 days and a milk withdrawal time of 4 days [43]. Currently, no veterinary or human formulations are available for veterinarians to use, making the compounding from a bulk drug source a necessity.

**Molybdenum salts**

Molybdenum salts are used to treat copper toxicity, which is relatively rare in cattle. Ammonium molybdate (oral dose of 200 mg/d for 3 weeks) and ammonium tetrathiomolybdate (IV or subcutaneous dose of 1.7–3.4 mg/kg on alternate days for three treatments) are used, with recommended milk and meat withdrawal times of 5 and 10 to 30 days, respectively [43,44]. Doses for cattle have been extrapolated from sheep.

**Penicillamine**

Penicillamine (d-penicillamine, 3-mercaptovaline) may be useful in combination therapy for copper and lead toxicity. It has an advantage of being effective orally but, like calcium EDTA, it can enhance the intestinal absorption of lead, so treatment should be initiated after all lead is removed from the gastrointestinal tract. Pharmacokinetic data for cattle have not been reported, but a daily oral dose of 110 mg/kg for 1 to 2 weeks has been recommended for lead toxicity [44]. Three- and 21-day withdrawal times have been recommended for milk and meat, respectively [43].

**Pralidoxime chloride (2-PAM)**

Pralidoxime chloride (2-PAM) can be used as an adjunct to atropine to reactivate acetylcholinesterase in the event of organophosphate toxicity in cattle. It is contraindicated in cases of carbamate toxicity. No animal formulation is marketed in the United States, but the use of a human formulated product at an intramuscular or subcutaneous dose of 20 to 30 mg/kg has been recommended [44,46,47]. Used in conjunction with atropine, the 6-day milk and 28-day meat withdrawal times for atropine are appropriate.
Sodium nitrite and sodium thiosulfate

Sodium nitrite and sodium thiosulfate are used IV for treatment of cyanide toxicity. Sodium nitrite is given once at 16–22 mg/kg of a 1% solution, whereas the sodium thiosulfate dose of 30 to 40 mg/kg of a 20% solution can be repeated [44]. The latter drug has also been used to treat arsenic toxicity. Sodium sulfate, a saline cathartic agent, can be used orally to hasten excretion of many oral toxicants. Because of their rapid elimination, recommended milk and meat withdrawal times are 48 hours for lactating cattle.

Vitamin K₁

Vitamin K₁ is used for sweet clover toxicity in cattle. Used at a dose of 0.5 to 2.5 mg/kg, there is no requirement for milk and meat withdrawal [43].

Summary

Although many plants, metals, industrial products, minerals, and medicines are potentially toxic to cattle, a limited number cause respiratory, gastrointestinal, cardiac, or metabolic crises that require emergency treatment or critical care of the affected animal or herd of animals. This article presents the plants, metals, minerals, industrial products, and feeds that are likely to be responsible for the toxicities that require emergency care for the affected cattle, reviews the clinical presentations, and provides diagnostic and treatment recommendations.

References


