Toxicology: What Did They Get Into?

Jo-Annie Letendre, DMV, DACVECC
Clinical lecturer in Emergency and Critical Care
Faculté de médecine vétérinaire, Université de Montréal

Toxicology 101

Intoxication is a common presentation to the emergency room in small animal veterinary medicine. According to the ASPCA, top toxins affecting animals in 2022 were over-the-counter medications, human foods, human prescription medications, plants, household toxins, veterinary products, rodenticides, insecticides, and recreational drugs. In this presentation, we will first talk about the importance of taking a complete and detailed history when managing a case of pet poisoning. Indeed, when an animal is presented following exposure to a known toxin, it will be important to obtain information about the exposure, such as the concentration of the substance, the quantity ingested, the time at which the exposure took place, if signs were observed, if treatment was attempted. If it is an exposure to a medication, it will also be important to determine if it is an extended-release formulation. In some cases of poisoning, exposure to the toxic substance has been observed. In other cases, intoxication should be suspected even if exposure has not been witnessed. Indeed, intoxication should be suspected in cases where a previously healthy animal suddenly falls ill, especially if the animal is young, if the animal has been exposed to a new or changed environment, if the patient has been left outdoors or in a garage, if the patient has access to compost, or if clinical signs develop after contact with guest belongings or food offerings.

An important part of managing poisoned patients is decontamination. This decontamination will take different forms depending on the route of exposure to the toxic substance (bath in the case of a topical product, eye cleaning in the case of contact with the eyes, etc.). Most cases of poisoning occur following the ingestion of a substance. Inducing vomiting is therefore a commonly used method to decontaminate an intoxicated patient. In dogs, apomorphine (0.03 mg/kg IV) is used as an emetic agent. In cats, we instead use dexmedetomidine (7-10 mcg/kg IM) or hydromorphone (0.1 mg/kg SQ). A new molecule, ropinirole, has recently been made available to induce vomiting in dogs. However, this molecule is not yet available in Canada. Before inducing vomiting, you must ask yourself if it is necessary (is the dose ingested sufficient to cause significant clinical signs?), if the timing to induce vomiting is good (generally vomiting should be induced within 2 hours of ingestion), and if it is safe to induce vomiting. Complications of emesis induction include regurgitation, aspiration pneumonia and oesophageal inflammation if the substance is caustic or irritant. Hydrogen peroxide, although often recommended to induce vomiting, should only be used as a last resort. Indeed, studies have shown that the use of hydrogen peroxide to induce vomiting, even at usual doses, results in significant irritant damage to the gastric mucosa. The administration of hydrogen peroxide is contraindicated in cats, which seem even more sensitive to irritant effects than dogs. In addition, cases of acute respiratory failure have also been reported following the administration of hydrogen peroxide.

Decontamination can also be carried out by the administration of activated charcoal, which will allow the adsorption of toxic substances present in the digestive system. Toxins have varying affinity for activated charcoal and in certain cases, multidose administration should be considered.

Intravenous lipid emulsion (ILE) can also be administered in cases of intoxication. The precise mechanism of action of ILE is unknown, though there have been several proposed theories such as the lipid sink theory (accumulation of the lipophilic substance into the lipid) and the lipid shuttle theory (transport of the toxins within the lipid sink to the liver for degradation, which is followed by renal excretion of the lipophilic toxicants after their removal from the plasma pool). Furthermore, for some toxins that have cardiac effects, lipid emulsion can also have cardioprotective effects. The most used dose of ILE in veterinary patient is 1.5 mg/kg IV bolus over 15 minutes followed by 0.25 mL/kg/min constant rate infusion (CRI) over 1 hour. The key parameter to determine the indication for ILE application is log P, which is the logarithm of the partition coefficient calculated for the respective substance from a two-phase system (octanol and water) and reflects its lipophilicity. Substances with a lop P > 1.0 accumulate in lipophilic solvents because of the concentration gradient that is created between the lipophilic and hydrophilic phases (lipid sink) and can thus be removed from the tissue. However, just because a substance has a high log P does not mean that ILE will be effective. Furthermore, administration of ILE can be associated with side effects such as hyperlipidemia, pancreatitis, corneal lipidosis, hemolysis, fluid overload, hypersensitivity, and acute respiratory distress syndrome. In people, adverse effects of ILE, although not reported in dogs, are acute kidney injury, embolism, fat overload syndrome, and sepsis secondary to contamination of the bag or delivery system. It is also possible that ILE may interfere with the activity of lipid soluble medications that the patient is receiving. It is therefore important, before using ILE, to weigh the pros and cons.

Tetrahydrocannabinol

THC intoxication resulting from cannabis exposure, is a significant concern in veterinary medicine. Clinical signs of THC toxicosis in companion animals include urinary incontinence, disorientation, ataxia, lethargy, hyperesthesia, and bradycardia. Edibles are commonly implicated in toxicosis, with ingestion being the primary route of exposure. Supportive clinical signs are often used to diagnose cannabis toxicosis, and outpatient monitoring is a common treatment approach. In more severe cases, intravenous fluid therapy with or without administration of ILE can be used as supportive treatments. The severity of clinical signs can vary, with synthetic cannabinoids potentially leading to more severe effects. While death secondary to THC exposure in dogs and cats has been reported, the lethality of cannabis in pets remains uncertain, with conflicting reports on lethal doses and causes of death. Further research is needed to determine the potential lethality of non-synthetic cannabis in dogs and other pets.

Lily

Lily toxicity in cats is a well-documented concern, leading to various clinical signs such as vomiting, ptyalism, anorexia, diarrhea, and signs of acute kidney injury (AKI). The toxic component in lilies from the Lilium and Hemerocallis genera remains unidentified. Treatment for lily toxicity typically involves decontamination methods like inducing

vomiting and administering activated charcoal, along with intravenous fluid diuresis to support renal function. Monitoring of renal parameters is crucial, with baseline creatinine levels and regular rechecks recommended. Studies have shown that early diagnosis and treatment of lily toxicity in cats can lead to a good prognosis, but AKI may still develop in some cases. The efficacy of decontamination, IV fluid diuresis, or a combination of both within 48 hours post-ingestion has shown positive outcomes with a low incidence of AKI. While most cats respond well to treatment, there have been instances of chronic renal failure in some cases, highlighting the importance of long-term monitoring and care post-exposure to lilies.

Xylitol

Xylitol, a sugar substitute commonly found in various products, is toxic to dogs but not to cats. In dogs, xylitol ingestion can lead to acute toxicity, primarily due to its ability to stimulate pancreatic insulin secretion, resulting in rapid-onset hypoglycemia. Xylitol is quickly absorbed from the gastrointestinal tract, with increased insulin concentrations observed within 20 minutes and hypoglycemia as early as 40 minutes post-ingestion in dogs. Other mechanisms contributing to hypoglycemia include inhibition of carbohydrate metabolism, slowed intestinal glucose absorption, depletion of liver glycogen, and hepatocellular damage. Hypokalemia and hypophosphatemia are common in xylitol toxicosis, with hypophosphatemia likely due to insulin-mediated intracellular shifts in phosphorus. Severe cases of xylitol toxicity can lead to liver failure, marked by increases in liver enzyme activities and hepatocellular necrosis. Liver failure can contribute to coagulopathy, thrombocytopenia, and hemorrhage, indicating a poor prognosis. Treatment for xylitol toxicity involves supportive care, monitoring for hypoglycemia, liver function tests, and potentially the administration of N-acetylcysteine to protect the liver. The prognosis for dogs exposed to xylitol varies based on the severity of the toxicity, with early intervention and aggressive supportive care playing a crucial role in the outcome. Monitoring for signs of hypoglycemia, liver failure, and coagulopathy is essential in managing xylitol toxicity in dogs.

Grapes and raisins

Grapes and raisins are known nephrotoxins for dogs, causing toxicity that can lead to severe health issues. Until recently, the toxic compound responsible for clinical signs of AKI in dogs following the ingestion of grapes or raisins was unknown. It is now thought that tartaric acid may be the part of grapes and raisins that cause them to be toxic to companion animals. The amount of tartaric acid can vary in grapes by their type, how they were grown, and how ripe they are, which could explain why some pets get very sick while others seem unaffected after eating similar amounts of grapes or raisins. Ingestion of grapes or raisins can result in vomiting within 12-24 hours and azotemia within 24-48 hours post-ingestion. The approach to managing grape and raisin ingestion is like that of lily exposure in cats, involving decontamination (maybe up to 12 hours after ingestion) by emesis induction, and intravenous fluid therapy to maintain renal perfusion. In cases of grape and raisin toxicity, monitoring renal parameters for 48-72 hours is crucial to assess kidney function and detect any signs of acute kidney injury (AKI). It appears that cats can

also develop gastrointestinal signs following the ingestion of grapes and raisins. However, no cases of AKI secondary to grape or raisin ingestion have been reported in this species. Many variables related to the toxicity of grapes and raisins in cats and dogs remain unknown.

Amphetamine and ADHD medications

Amphetamine, dextroamphetamine, and methylphenidate are first-line therapies in treating attention-deficit/hyper-activity disorder (ADHD) in humans and are a potential source of toxicity for companion animals. Amphetamine intoxication can lead to severe health issues in animals, with cardiovascular and neurological symptoms being common. The toxic effects of amphetamines include hypertension, tachycardia, hyperactivity, agitation, tremors, and potential seizures. The mechanism of action involves the release of catecholamines, leading to stimulation of alpha and beta-adrenergic receptors. Amphetamines can also cause hyperthermia and, in severe cases, rhabdomyolysis, nephrotoxicity, or disseminated intravascular coagulopathy (DIC).Treatment for amphetamine intoxication involves controlling stimulatory signs with sedatives, treating hyperthermia with active cooling methods, and managing tachyarrhythmias, hypertension, and seizures if present. Intravenous lipid emulsion (IVLE) therapy has been used in cases of amphetamine toxicosis to reduce amphetamine levels and potentially improve clinical signs.

References available upon request.