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TOP 10 CANINE TOXINS

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INTRODUCTION

Pet Poison Helpline, a 24/7 animal poison control located out of Minneapolis, MN, USA, receives phone calls from both pet owners and veterinarians regarding toxicity cases from accidental or intentional misuse of over-the-counter (OTC) or prescription medications, common garden or outdoor toxins, and common household products. In this lecture, the top 10 canine toxins seen by Pet Poison Helpline will be reviewed.

In veterinary medicine, the primary treatment for toxicant exposure should be decontamination and detoxification of the patient. The goal of decontamination is to inhibit or minimize further toxicant absorption and to promote excretion or elimination of the toxicant from the body. Decontamination can only be performed within a narrow window of time for most substances; therefore, it is important to obtain a thorough history and time since exposure. Decontamination categories may include ocular, dermal, inhalation, gastrointestinal (GI), forced diuresis, and surgical removal to prevent absorption or enhance elimination of the toxicant. For further review on decontamination and specific treatment, attendees are referred to a veterinary toxicology book for more detailed review.

CHOCOLATE

Chocolate, a naturally occurring alkaloid found primarily in the *Theobrema cacao* plant, contains methylated xanthine derivatives (e.g., theobromine, methylxanthine).1 As chocolate is prevalent in pet owners' households, this is a very common toxicosis seen in veterinary medicine. Depending on the type of chocolate ingested, clinical signs may include vomiting, diarrhea, hyperactivity, polyuria, and hyperthermia (secondary to hyperactivity, tremoring, anxiety, etc.). With severe cases, cardiotoxicity (e.g., ventricular premature contractions, tachyarrhythmias, etc.) may be seen, along with neurotoxicity (e.g., tremors, seizures, etc.). With chocolate toxicosis, clinical signs can be seen when the amount of theobromine ingested is > 20 mg/kg (e.g., vomiting, diarrhea). With higher doses (> 40 mg/kg), cardiotoxicity may be seen, while doses > 60 mg/kg can result in neurotoxicity.1 As chocolate often stays in the GI tract for a prolonged period of time, emesis induction up to 4-6 hours post-ingestion may be of benefit, provided the patient remains asymptomatic. Treatment includes multiple doses of activated charcoal, as chocolate undergoes enterohepatic recirculation. Depending on the severity of clinical signs and onset of decontamination (e.g., emesis induction with administration of activated charcoal), treatment may include fluid therapy (either subcutaneously or intravenously), anti-emetic therapy, sedation (if the patient is agitated, tachycardiac, and hypertensive), cardiovascular monitoring (e.g., continuous electrocardiogram monitoring, blood pressure monitoring), and potential beta-blocker therapy (if the heart rate is persistently over 180 beats per minute – canine). As methylxanthines may be reabsorbed through the bladder, frequent walks outside to urinate (or even urinary catheter collection) can be used. As chocolate has a long half-life (approximately 17 hours), clinical signs can be seen for up to 72 hours, and treatment should be continued until clinical signs resolve. Overall, the prognosis is excellent with supportive care. Some patients may develop secondary pancreatitis from chocolate ingestion, particularly if other ingredients were involved (e.g., macadamia nuts).

GRAPES, RAISINS, AND CURRANTS

Grapes and raisins (*Vitis* spp.) have been recently associated with development of acute renal failure (ARF) with ingestion. All types have been implemented with toxicosis, including organic grapes, commercial grapes, homegrown grapes, and seedless or seeded grapes. While the mechanism of toxicosis is unknown, there are several suspected hypotheses, including individual inability to metabolize certain components of the fruit (e.g., tannins, high monosaccharide content),2 the presence of mycotoxins or pesticide residues on the fruit,2 or salicylate-like chemicals within the grape or raisin. Common kitchen items also contain grapes, raisins, or currants in their active ingredient, including raisin bread, trail mix, chocolate-covered raisins, cereal with raisins, etc. Currently, grapeseed extract has not been associated with nephrotoxicity.2 Treatment for grape and raisin ingestion includes aggressive decontamination as the first-line of therapy. Grapes and raisins seem to stay in the stomach for a prolonged period of time, and are not rapidly broken down or absorbed from the GI tract; hence, delayed emesis induction even several hours post-ingestion can still be initiated to maximize decontamination methods. One dose of activated charcoal can also be administered to prevent absorption of the unknown nephrotoxin. As there is no current veterinary peer-reviewed, scientific published toxic dose of grapes and raisins, all ingestions should be treated as potentially idiosyncratic and be appropriately decontaminated and treated. Initially, vomiting may be observed within the first 24 hours of ingestion.2 Within the next 12-24 hours, clinical signs of lethargy, dehydration, vomiting, diarrhea, anorexia, abdominal pain, uremic breath, and diarrhea may be seen.2 Azotemia may develop within 24 hours, with hypercalcemia and hyperphosphatemia occurring first.2 Oliguria and anuria may develop

48-72 hours post-ingestion,2 at which point the prognosis is poorer. Treatment includes decontamination, aggressive IV fluid therapy, anti-emetics, blood pressure and urine output monitoring, and serial blood work monitoring (q. 12-24 hours). In severe cases, hemodialysis or peritoneal dialysis may be necessary. Asymptomatic patients that have been adequately decontaminated and survive to discharge should have a renal panel and electrolytes monitored 48-72 hours post-ingestion. Overall, the prognosis is fair to good, depending on time to decontamination, response to therapy, and prevalence of oliguria or anuria. Overall, 50% of dogs that ingest grapes and raisins never develop clinical signs or azotemia.2

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

NSAIDs are competitive inhibitors of prostaglandin synthesis (cyclooxygenase or "COX" inhibitors) and result in decreased prostaglandin, which is important for normal homeostatic function (including maintaining renal blood flow, maintaining mucous production in the stomach, etc.). Common OTC human NSAIDs include active ingredients such as ibuprofen and naproxen sodium. Common prescription veterinary NSAIDs can also result in toxicosis, particularly when available in the chewable, palatable formulation. Examples of veterinary NSAIDs include carprofen, deracoxib, etogesic, previcoxib, etc. With NSAID toxicosis, the GI tract, kidneys, CNS, and platelets can be affected. Cats and certain breeds of dogs (e.g., German shepherds) seem to be more sensitive to NSAIDs, and should be treated aggressively. With cats, severe ARF is often more clinically seen with NSAID toxicosis at lower doses (as compared to dogs). With dogs, signs secondary to GI ulceration (e.g., vomiting, diarrhea, melena, hematemesis, etc.) are more commonly seen initially, followed by secondary ARF.

With NSAID toxicosis, it is important to keep in mind that each NSAID has a different toxic dose, margin of safety, half-life, and route of excretion, and an animal poison helpline should be contacted to identify what specific NSAID and toxic dose was ingested. For example, in dogs, ibuprofen results in GI signs at doses as low as 16-50 mg/kg, while severe GI signs may be seen at 50-100 mg/kg.3 Renal compromise may be seen at doses of 100-250 mg/kg (resulting in potential ARF), and fatalities have been reported at doses > 300 mg/kg.3 This differs tremendously from naproxen sodium (dogs), where severe clinical signs can be seen at doses as low as 5 mg/kg.3 With naproxen, experimental canine doses of 22 mg/kg orally once a day for 3 days have resulted in perforation of the GI tract with secondary septic peritonitis occurring.

Clinical signs of NSAID toxicosis include anorexia, vomiting, hematemesis, diarrhea, melena, abdominal pain, lethargy, malaise, uremic halitosis, dehydration, etc. Treatment includes decontamination, the use of activated charcoal (often multiple doses due to enterohepatic recirculation, if appropriate), GI protectants (e.g., H2 blockers, sucralfate), aggressive IV fluid therapy (to help maintain renal blood flow) for 24-72 hours, anti-emetic therapy, and symptomatic and supportive care. With high doses, anti-convulsants may also be necessary if CNS signs develop.

SELECTIVE SEROTONIN RE-UPTAKE INHIBITORS (SSRIS)

Selective serotonin re-uptake inhibitors (SSRIs) are a class of medications that are commonly used in human medicine for depression. Common examples include drugs like fluoxetine (Prozac® in human beings; Reconcile™ in veterinary medicine), citalopram (Celexa®), escitalopram (Lexapro®), paroxetine (Paxil®), and sertraline (Zoloft®). Other similar drugs include selective norepinephrine re-uptake inhibitors (SNRIs), which include common drugs like duloxetine (Cymbalta®), nefazodone (Serzone®), and venlafaxine (Effexor®). SNRI and SSRI drugs result in similar clinical signs of toxicosis, and therefore are treated the same. In veterinary medicine, SSRIs are used for a wide array of behavioral problems, including feline urine spraying, canine separation anxiety, lick granulomas, etc. These SSRI drugs work by blocking the reuptake of serotonin in the pre-synapse, thereby increasing the levels of serotonin in the pre-synaptic membrane. In small animal patients, common clinical signs from SSRIs include sedation or central nervous system (CNS) stimulation, anorexia, and lethargy, even at therapeutic doses. Increases in levels of serotonin, even in small doses, may lead to serotonin syndrome. Clinical signs of serotonin syndrome include: CNS stimulation, vomiting, tremoring, seizures, hyperthermia (secondary to tremoring and seizuring), diarrhea, abdominal pain, and mydriasis. Treatment includes decontamination (ideally done at a veterinarian, due to the rapid onset of clinical signs), activated charcoal, hospitalization for sedation (e.g., with acepromazine [0.05-0.1 mg/kg, IV/IM or chlorpromazine), muscle relaxants (e.g., methocarbamol at 22-100 mg/kg, IV/PO q. 4-8 as needed), anticonvulsants (e.g., phenobarbital 4-16 mg/kg, IV as needed), thermoregulation, IV fluid therapy, blood pressure and electrocardiogram (ECG) monitoring, and supportive and symptomatic care.

XYLITOL

Xylitol is a natural sweetener found in small quantities in certain fruit. Xylitol has gained recent popularity because it is sugar-free, and is often found in diabetic snacks, foods, baked foods, mouthwashes, toothpastes, chewing gum, mints, candies, and chewable multivitamins.4 Sugarless products, particularly those with xylitol listed within the first five active ingredients, can result in severe toxicosis within 15-30 minutes of ingestion. Ingestion of xylitol results in an insulin spike in non-primate species, resulting in severe hypoglycemia. Many pieces of candy and gum (e.g., Orbit™, Trident™, Ice Breakers™) contain various amounts of xylitol ranging, on average, from 2 mg/piece to 1.0 grams/piece. Unfortunately, not all sources are disclosed by the company (e.g., how many grams of xylitol may be in each piece of gum) due to a proprietary nature. With xylitol toxicosis, it is imperative to calculate whether a toxic dose has been ingested. Doses > 0.1 g/kg are considered toxic and result in profound, sudden hypoglycemia from insulin stimulation.4 Higher doses (> 0.5 g/kg) of xylitol have been associated with acute hepatic necrosis. Clinical signs of xylitol toxicosis include lethargy, weakness, vomiting, collapse, anorexia, etc. When hepatotoxic doses are ingested, clinical signs and clinicopathologic findings may include melena, icterus, increased liver enzymes, diarrhea, hypoglycemia, hypocholesterolemia, decreased BUN, hypoalbuminemia, etc. When presented a patient that has ingested a toxic amount of xylitol, a blood glucose should be checked immediately upon presentation; if hypoglycemic, a bolus of 1 ml/kg of 50% dextrose, diluted with an additional amount of 0.9% NaCl (in a 1:3 ratio) should be given IV over 1-2 minutes. Emesis induction should not be performed until the patient is euglycemic. Keep in mind that activated charcoal does *not* reliably bind to xylitol, and is not routinely recommended for xylitol toxicosis. Hypoglycemic patients should be hospitalized for IV fluid therapy [supplemented with dextrose (2.5 to 5% dextrose, CRI, IV)] for approximately 24 hours, and frequent blood glucose check should be performed every 1-4 hours. For patients ingesting a hepatotoxic amount of xylitol, the use of hepatoprotectants (e.g., SAMe), anti-emetics, and supportive care (including frequent liver enzyme monitoring) are warranted.

ACETAMINOPHEN/PARACETAMOL

Acetaminophen (N-acetyl-p-aminophenol), a cyclooxygenase (COX)-3 inhibitor, is a popular over-the-counter (OTC) analgesic and antipyretic medication used frequently in humans. It is not considered a true NSAID as it lacks anti-inflammatory properties. Normally, part of this drug is metabolized into non-toxic conjugates via the metabolic pathways (glucuronidation and sulfation);5 some is metabolized into the toxic metabolite, N-acetyl-para-benzoquinoneimine [NAPQI] via the cytochrome P-450 enzyme pathway.5 Typically, NAPQI is detoxified by conjugation with glutathione in the liver.5 Toxicosis occurs when glucuronidation and sulfation pathways are depleted; this results in toxic metabolites building up and secondary oxidative injury occurring.5 While this drug is very safe for human use, it has a narrow margin of safety in dogs and cats; the severity of toxicosis and development of clinical signs is species-dependent. Cats have an altered glucuronidation pathway and a decreased ability to metabolize acetaminophen, making them much more susceptible to toxicosis. In cats, red blood cell injury is more likely to occur in the form of methemoglobinemia (metHb), and toxicity can develop at doses as low as

10 mg/kg.5 In cats, lethargy, swelling of the face or paws, respiratory distress, brown mucous membranes, cyanosis, vomiting, and anorexia may be seen secondary to metHb. In dogs, hepatic injury is more likely to occur; acetaminophen toxicosis can occur at doses > 100 mg/kg, while metHb can develop at doses of > 200 mg/kg.5 Dogs may develop clinical signs of keratoconjunctivitis sicca (dry eye), malaise, anorexia, hepatic encephalopathy, vomiting, melena, and icterus secondary to hepatotoxicity. Treatment includes decontamination, administration of one dose of activated charcoal with a cathartic, IV fluid therapy, antioxidant therapy (Vitamin C), provision of a glutathione source (S-adenosyl-methionine or SAMe), and N-acetylcysteine to limit formation of the toxic metabolite NAPQI by providing additional glutathione substrate. Baseline blood work and follow-up biochemical panels should be performed to monitor for hepatotoxicity. Generally, prognosis is fair with therapy. Those with severe hepatic failure have a poorer prognosis.

RODENTICIDES

One of the most common mistakes seen in the field of veterinary toxicology is assuming that every green or blue block of rat or mouse poison is a long-acting anticoagulant (LAAC) rodenticide. The active ingredient of a rodenticide *cannot* be identified based on physical appearance (e.g., color, shape, size, etc.). When in doubt, the active ingredient (and concentration) must be properly identified to ensure appropriate treatment and management of rodenticide toxicoses. Several different classes of rodenticides exist, including those that contain bromethalin, zinc phosphide, cholecalciferol (Vitamin D3), and LAACs.

BROMETHALIN

Bromethalin, a neurotoxic rodenticide, is marketed under several common brand names of Assault®, Tomcat Mole Killer®, Talpirid®, Real Kill®, Clout®, Fastrac®, Vengeance®, etc. Bromethalin is *not* an anticoagulant rodenticide and should *not* be treated with Vitamin K1 as an antidote. Bromethalin works by uncoupling oxidative phosphorylation in the brain and liver mitochondria.6 This results in decreased ATP production, which affects sodium and potassium pumps; as a result, lipid peroxidation occurs, resulting in sodium accumulation within the cell.6 Edema of the central nervous system (CNS) may result.6

In dogs, the LD50 of bromethalin is 2.38-3.65 mg/kg, with a minimum lethal dose being 2.5 mg/kg.6 Cats are more sensitive to the effects of bromethalin, and the LD50 is significantly lower (0.54 mg/kg).6 Clinical signs are dose-dependent, and the onset of clinical signs depends on the amount ingested. Typically, with acute ingestion, signs may be seen within 2-24 hours.6 Clinical signs of CNS stimulation or depression, abnormal behavior, ataxia, hyperesthesia, seizures, and coma may be seen.6 Other common signs include paresis, hind limb paralysis, anisocoria, nystagmus, changes in the pupillary light reflex, and tremors may also be seen. Treatment includes early decontamination, prevention of cerebral edema, and symptomatic supportive care. With recent ingestion in an asymptomatic patient, the use of decontamination (e.g., emesis induction, activated charcoal) is warranted. As bromethalin undergoes enterohepatic recirculation, the use of multiple doses of activated charcoal (without a cathartic) can be administered q 6 hours for 24 hours. Patients should be monitored for signs of neurotoxicity. The use of IV fluid therapy, oxygen support, head elevation, mannitol (to decrease cerebral edema), anticonvulsant therapy, and thermoregulation is warranted if clinical signs develop. The prognosis varies depending on the amount ingested and the severity of clinical signs. If persistent seizures or paralytic syndrome is seen, the prognosis is poorer.

PHOSPHIDES

Phosphide rodenticides have been used since the 1930's and are still readily available on the market.7 Aluminum phosphide is a pelleted product used as a fumigant in grain storage silos, while the more common zinc phosphide is labeled for use in control of rats, mice, ground squirrels, prairie dogs, voles, nutria, muskrats, feral rabbits, and gophers. 7 Zinc phosphide, a crystalline, grey powder, is available in 2-10% concentrations as grain or sugar-based baits in a powder, pellet, tablet, or paste formulation.7 Trade names of some of the commercially available zinc phosphide products include: Gopha-Rid, Gopher Bait II, Rodenticide AG, This is the Way, Prozap, Hopkins, and Sweeney's Poison Peanuts Mole.7 Formulations of phosphides have a unique, distinctive odor similar to rotten fish, garlic, or acetylene.7 You should care about this type of rodenticide because it is potentially poisonous to you, your pet owner, and your staff too! The toxic dose of zinc phosphide in dogs is approximately 20-40 mg/kg, but up to 300 mg/kg on empty stomachs.8 With zinc phosphide, the administration of food (e.g., bread, milk, etc.) is contraindicated, as it may potentially release gastric acid, promoting hydrolysis and further production of phosphine gas.8

Phosphide rodenticides result in the production of phosphine gas. When zinc phosphide combines with gastric acid or moisture (or the presence of food!), liberated phosphine gas is rapidly absorbed across gastric mucosa and distributed systemically, where it exerts its toxic effect. Phosphine gas is considered a corrosive and a direct irritant to the gastrointestinal tract (GIT). Clinical signs can be seen within 15 minutes to 4 hours; death has been reported within 3-48 hours.8 Clinical signs include severe gastrointestinal (GI) signs (e.g., vomiting, bloat, abdominal pain, hematemesis, melena, etc.), CNS signs (e.g., tremoring, seizuring, death), and rarely, cardiopulmonary signs (e.g., pulmonary edema, tachypnea, pleural effusion, etc.) or organ dysfunction.8

Zinc phosphide also carries a public health risk. Emesis – whether intentionally induced or occurring due to clinical signs - can result in poisoning to the pet owner or the veterinary professional secondary to exposure of phosphine gas. Clinical signs of nausea and difficulty breathing have been reported in humans exposed. To minimize these risks, emesis induction should always be performed in a well-ventilated area (e.g., opening the car window if the patient vomits or inducing emesis outside or in a well-ventilated area). Pet owners should be appropriately educated on the toxic gas exposure to themselves also. Pet owners should be informed *not* to feed their pet to prevent further production of phosphine gas. In addition, the administration of an antacid (e.g., aluminum hydroxide) prior to emesis induction may help decrease the presence of phosphine gas. With recent ingestion in an asymptomatic patient, the use of emesis induction (following antacid administration) and one dose of activated charcoal with a cathartic is warranted to minimize toxic effects of zinc phosphide. Symptomatic supportive care, including anti-emetic therapy, IV fluid therapy, gastric protectants, and analgesics are warranted.

CHOLECALCIFEROL

Cholecalciferol, the chemical name for vitamin D3, is one of the most deadly – and costly – rodenticides to pets. Ingestion of toxic levels of cholecalciferol can result in severe hypercalcemia and hyperphosphatemia, with secondary ARF developing as a result of dystrophic mineralization to the soft tissue and kidneys. Common sources of Vitamin D3 include over-the-counter (OTC) or prescription vitamins (typically found in a calcium/Vitamin D3 combination), psoriasis creams (in the form of calcipotriene), and rodenticides. With cholecalciferol-containing rodenticides, only a tiny amount of rodenticide needs to be ingested before clinical toxicosis occurs due to a very narrow margin of safety within these products. In dogs, cholecalciferol has an LD50 of 85 mg/kg (based on the rodenticide concentration of 0.075%).9 Doses of Vitamin D3 > 0.1-0.5 mg/kg can result in clinical signs and hypercalcemia, respectively.9

Typically, clinical signs often do not develop for 1-3 days until the patient has already developed clinical signs of ARF.9 That said, renal failure can occur within 12-36 hours following toxic ingestion. Clinical signs and clinicopathologic findings include increased thirst and urination, weakness, lethargy, anorexia, vomiting, generalized malaise, uremic halitosis, dehydration, hypercalcemia, hyperphosphatemia, azotemia, melena, hemorrhagic diarrhea, and death.9

Aggressive treatment must be initiated with cholecalciferol toxicosis, due to the narrow margin of safety. Decontamination should include emesis induction, if ingestion was recent and the patient is asymptomatic. As cholecalciferol undergoes enterohepatic recirculation, the

administration of multiple doses of activated charcoal (without a cathartic) is warranted q 6 hours X 24 hours. Additional treatment includes the aggressive use of IV fluid therapy to promote calciuresis (e.g., 0.9% NaCl), calcium monitoring, gastrointestinal support (e.g., anti-emetics, H2 blockers, sucralfate, phosphate binders, etc.), and the use of medications to increase calciuresis (e.g., prednisone, furosemide) and prevent hypercalcemia (e.g., pamidronate, calcitonin). Treatment is often expensive, and requires hospitalization for an extended period of time. Most patients are continued on oral furosemide and prednisone for weeks, following discharge from the hospital. Frequent monitoring of renal function and electrolytes is imperative. Calcium, phosphorous, BUN, creatinine, and ionized calcium should be evaluated every 12-24 hours while hospitalized, and then every 2-3 days thereafter for the next 2-4 weeks. This will allow one to assess the ability to titrate the prednisone and furosemide therapy, and to ensure that the patient does not develop secondary ARF [or potentially chronic renal failure (CRF)]. Even with aggressive treatment, CRF may be a secondary sequela.

LONG-ACTING ANTICOAGULANTS (LAAC)

First and second generation LAAC anticoagulants result in inhibition of Vitamin K epoxide reductase, resulting in inactivation of clotting factors II, VII, IX, and X. First generation rodenticides (e.g., warfarin, pindone)10 have been largely replaced by more potent second generation anticoagulants (e.g., brodifacoum, bromadiolone, diphacinone, chlorophacinone, etc.).10 Second generation LAACs are more recently developed and are generally considered to be more toxic with a longer duration of action (requiring a longer duration of treatment compared to first generation anticoagulants).10 Each individual LAAC varies in the margin of safety and LD50. Some have very narrow margins of safety (e.g., brodifacoum), while some have very wide margins of safety (e.g., bromadiolone). When in doubt, the toxic dose should be calculated, or Pet Poison Helpline contacted to determine if a toxic dose has been ingested. Finally, keep in mind that species differences exist; cats are much more resistant to the effects of LAAC as compared to dogs.

	Canine LD50	**Feline LD50**
Difethialone:	4 mg/kg	> 16 mg/kg
Brodifacoum:	0.25-4 mg/kg	25 mg/kg
Bromadiolone:	11-20 mg/kg	> 25 mg/kg
Diphacinone:	3-7.5 mg/kg	> 15 mg/kg

When a toxic ingestion of LAAC has occurred, prolongation in coagulation factors [prothrombin (PT) or activated partial thromboplastin time (aPTT)] is not seen for 36-48 hours, due to the half-life of factor VII. Clinical signs typically do not develop for 3-5 days. Clinical signs are due to clotting factor depletion, resulting in generalized hemorrhage. The most common clinical signs include lethargy, exercise intolerance, inappetence, pallor, dyspnea, coughing, hemoptysis, etc. Hemoabdomen, hemothorax, pericardial effusion may also occur. Rarer clinical signs include gingival bleeding, epistaxis, ecchymoses, petecchia, hematuria, bleeding into the subcutaneous space or joint space, and melena.10

Errors are often made by veterinary professionals when it comes to the medical management of LAAC rodenticides. While it is often appropriate to decontaminate a patient with emesis induction and activated charcoal administration, with non-toxic ingestions (based on the LD10), this is often unnecessary (unless the patient is neonatal, geriatric, has an underlying hepatopathy, or has previously ingested a LAAC before). Next, the administration of a “one-time,” parenteral injection of vitamin K1 at the time of decontamination is unnecessary and potentially detrimental. First, vitamin K1 is faster absorbed *orally* than parenterally (particularly with a fatty meal). Another reason why the “one-time shot” should be avoided is because it will skew point-of-care, accurate blood results of the PT test. As factor VII has the shortest half-life, PT will be the first blood test to be prolonged with LAAC ingestion; however, this prolongation of the PT will not normally occur until approximately 36-48 hours post-LAAC ingestion. Testing prior to this time is unnecessary (unless the patient has been chronically ingesting a LAAC over several days), as the PT will be normal prior to 36-48 hours. By administering a “one-time shot” of Vitamin K1 therapy, the patient’s PT will be falsely normal at 48 hours, and instead, the patient will be coagulopathic days later (3-5 days, instead of 2 days). Normally, clinical signs of acute, LAAC toxicosis typically occur at 3-5 days post-ingestion. With a “one-time shot,” the patient can potentially develop clinical signs of coagulopathy at 5-7 days instead of 3-5 days!

When treating LAAC rodenticides, two considerations for treatments should be utilized.

1. With an acute, one-time ingestion of a LAAC, one can decontaminate and check a PT 48 hours post-initial ingestion. If the PT is prolonged at 48 hours, 3-4 weeks of Vitamin K1 therapy should be initiated (3-5 mg/kg PO, divided SID-BID X 4 weeks). A recheck PT should be performed 48 hours after the last dose; if prolonged, an additional 2 weeks of therapy is indicated, with another PT performed 48 hours after the last dose OR
2. With an acute one-time ingestion of a LAAC, one can just prophylatically treat with Vitamin K1 therapy, particularly if the patient is young, debilitated, geriatric, or has underlying liver pathology. Treatment includes Vitamin K1 therapy (3-5 mg/kg PO, divided SID-BID X 4 weeks), with a recheck PT being performed 48 hours after the last dose; if prolonged, an additional 2 weeks of therapy is indicated, with another PT performed 48 hours after the last dose.

Clinical application:

1. You don’t typically need to bother testing the patient’s PT while they are on chronic Vitamin K1 administration – it will be normal while on therapy (unless the owner is not appropriately administering it)!
2. In dogs ingesting LAACs chronically, there is the risk of potential accumulation within the body. Any “second” exposure should be prophylatically treated with oral Vitamin K1 therapy for the appropriate duration of time.
3. Vitamin K1 should not be administered intramuscularly (IM) or IV. If you suspect a patient is coagulopathic, administer into a vascular muscle bed (IM) can result in a large hematoma within the muscle. Also, IV administration of Vitamin K1 can result in anaphylactic shock. Rather, critically ill, actively bleeding dogs should be stabilized with frozen plasma (FP) or fresh frozen plasma (FFP) concurrently.

CARDIAC MEDICATIONS

Certain cardiac medications include broad categories such as calcium channel blockers, beta blockers, and angiotensin-converting enzyme (or “ACE”) inhibitors. These medications are commonly used in both human and veterinary medicine to treat underlying cardiac disease or hypertension. Each category of cardiac medication has different margins of safety. Calcium channel blocker and beta-blocker toxicosis should be treated aggressively, as these two categories of medications have a narrow margin of safety. Toxicosis of these agents can result in myocardial failure, severe bradycardiac, and hypotension; untreated, cardiac output becomes reduced, and secondary severe hypoperfusion and ARF can potentially develop.11-13 With ACE-inhibitors, severe overdoses can cause hypotension, dizziness, weakness, and hypotension. In general, there is a wider margin of safety with ACE-inhibitors, which are typically considered much safer. Pets ingesting small amounts of ACE-inhibitors can potentially be monitored at home, unless they have underlying disease (e.g., kidney failure, cardiac disease, etc.). With ACE-inhibitors, ingestions > 10-20X a therapeutic dose are generally considered toxic, and can result in severe clinical symptoms (e.g., hypotension).13 Treatment for any cardiac medication includes decontamination (e.g.,

emesis induction, gastric lavage, activated charcoal administration), blood pressure monitoring, aggressive IV fluid therapy if hypotension is detected, and blood work monitoring. With severe toxicosis, the use of high-dose insulin therapy or intravenous lipid emulsion may be warranted as a potential antidote for calcium channel blocker toxicosis.11

CONCLUSION

Pet owners should be appropriately educated on how to pet-proof the house, and be trained on what common household products and kitchen items are poisonous. Pet owners should also be appropriately educated on crate training to help minimize toxin exposure. Once a pet is exposed to a toxicant, it is imperative to determine if emesis is appropriate, and to understand when it may be contraindicated (e.g., symptomatic patient, delayed time since exposure, hydrocarbons, etc.). Knowledge of the underlying mechanism of action, the pharmacokinetics (including absorption, distribution, metabolism, and excretion), and the toxic dose of the toxicant are imperative in determining appropriate decontamination and therapy for the patient.

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