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Inside the Guide

Ready to level up your veterinary toxicology game? From activated charcoal to xylitol (and everything in between), this guide is packed with clinical pearls to tackle those toxic terrors. You'll get the scoop on decontamination, antidotes, and all the tools to save the day like the toxin-fighting hero you are.

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Toxins

Emerging Toxins & Updates in Clinical Veterinary Toxicology

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Society is constantly evolving, with each year bringing new trends, from the latest slang among kids to the rapid advancements in technology. As pets are deeply integrated into our lives, they are especially susceptible to the effects of these shifts—and often face increased risks of poisoning. These societal changes can have significant, lasting effects on our veterinary patients, making it crucial for veterinary practitioners to stay informed and adapt to these developments.

Currently, there are several emerging toxins veterinary practitioners should be aware of.

Psychedelic Mushrooms

Due to recent changes in laws, psychedelic mushroom use is on the rise in people (Siegel JS, 2023). Subsequently, in the last 5 years, the ASPCA Animal Poison Control Center (APCC) has seen a 1500% rise in cases of pets being exposed to psychedelic mushrooms or mushroom products, such as gummies. (Tourdot, 2024)

Psilocybin and psilocin are the primary hallucinogenic compounds found in Psilocybe mushrooms. Both are classified as Schedule I controlled substances in the U.S., making possession, use, and distribution illegal, though decriminalization has occurred in certain states and cities. Clinical signs of psilocybin exposure may include altered behavior, ataxia, dilated pupils (mydriasis), vocalization, hyperthermia, tachycardia, and seizures. Symptomatic care is the mainstay of treatment for veterinary patients affected by psilocybin; however, since psilocybin is a serotonin agonist, cyproheptadine, as a serotonin antagonist may be helpful.

Due to the legal complexities surrounding psilocybin, other hallucinogenic mushrooms are emerging in the market, such as Amanita muscaria, Amanita pantherina, and certain species of Clitocybe and Inocybe, which contain compounds like ibotenic acid, muscimol, and muscarine. Ibotenic acid and muscimol can cause nausea, ataxia, disorientation, vocalization, hyperesthesia, tremors, and alternating lethargy and agitation, with rare cases of seizures, respiratory depression, and death. Muscarine exposure can lead to hypersalivation, vomiting, diarrhea, anxiety, bradycardia, hypotension, and dyspnea (Leas EC, 2024) (Tourdot, 2024).

Treatment for muscarine toxicity is symptomatic, with atropine used to manage bradycardia or dyspnea. For ibotenic acid or muscimol exposure, treatment remains symptomatic, but caution is advised when using benzodiazepines due to the risk of additive GABA effects, as muscimol is a GABA agonist.

THC

Like psilocybin, ASPCA APCC has seen a massive increase in THC exposure in the last several years (Tourdot, 2024). Many patients show mild signs of THC toxicity such as ataxia, urinary incontinence, and mild hyperesthesia. However, with the large variety of available products from edibles to vape pens, to waxes, patients can potentially develop more severe signs such as severe CNS depression or coma, significant bradycardia, aspiration pneumonia, or even serotonin signs (hyperactivity, agitation, tachycardia). Symptomatic care remains the primary treatment, although some patients may benefit from lipid emulsion therapy.

Xylazine

Unfortunately, xylazine has made its way into the illicit drug supply. It is usually found as an adulterant to fentanyl (D'Orazio J, 2023). Signs of toxicity are typically an extension of its clinical effects and include CNS depression, ataxia, bradycardia, and hypotension. Xylazine exposure can be suspected in any patient with a suspected illicit drug exposure demonstrating characteristic signs (CNS depression, ataxia, bradycardia, hypotension) that is unresponsive or only partially responsive to naloxone. Reversal of its effects is achieved with atipamezole or yohimbin.

SGLT2 Inhibitors

Sodium-glucose transporter 2 (SGLT2) is a protein on the cell surface in the kidney tubule that helps reclaim glucose from the kidney filtrate. SGLT2 inhibitors are a class of drugs that inhibit this protein, helping to manage diabetes mellitus in humans. In cases of overdoses in dogs and cats, they can lead to diarrhea, lethargy, anorexia, polydipsia, glucosuria, ketonuria, hypokalemia, hypoglycemia, and hyperglycemia. Treatment focuses on monitoring for hypoglycemia and providing symptomatic care (Bogdanffy MS, 2014).

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Clinical Updates

Updates to toxins are not the only changes recently seen in veterinary toxicology. There have been some updates on the clinical side as well.

Tartaric Acid

A 2022 article in the Journal of Veterinary Emergency and Critical Care described several cases of acute kidney injury (AKI) following the ingestion of products containing tartaric acid (Wegenast CA, 2022). Since fruits from Vitis spp. plants are known to have elevated levels of tartaric acid, it is now thought to be the compound responsible for AKI seen in dogs after grape or raisin exposure. In addition to Vitis spp. fruits, tartaric acid is also present in high concentrations in tamarinds, cream of tartar (potassium bitartrate) used in baking, homemade play dough, and some candy or gummy products. While a minimum toxic dose is still unknown, however, exposures of less than 1 per 10 lbs of dog of grapes or raisins or less than 2 per 10 lbs of dog of cooked raisins are generally low risk and are not expected to result in the development of AKI (Tourdot, 2024).

Urine Drug Screens

Urine drug screens are a widely used diagnostic tool in human medicine due to their affordability, availability, and ease of use. Although no tests have been specifically validated for veterinary species, they are increasingly being used in veterinary emergency rooms and clinics as a screening method when an animal shows acute symptoms consistent with illicit drug exposure (JB, 2009). Using a urine drug screen is reasonable to consider when the patient has consistent signs, illicit substances may be in their environment or prescription substances such as opioids, benzodiazepines, barbiturates, or amphetamines may be in the home. A knowledgeable clinician should approach the interpretation of test results in dogs and cats with caution. False negative and false positive test results can occur. A useful rule of thumb is that if the clinical signs don't align with the test results, the test result should be considered unreliable. If a more definitive diagnosis is necessary, consider submitting a sample to a veterinary diagnostic lab for more specific testing.

Extracorporeal Elimination

Although extracorporeal treatments (ECT) have been available for humans for many years, they have become more accessible to veterinary patients in the past decade. Extracorporeal elimination involves drawing blood from the body, processing it to remove the toxic substance, and then returning it to the patient. Common extracorporeal treatments include hemodialysis, hemoperfusion, and therapeutic plasma exchange. Knowing which therapy may be helpful for which toxin may help veterinary practitioners know when it may be helpful to use.

- **Hemodialysis**: Most effective for removing water-soluble substances with a low volume of distribution, low protein binding, and small molecular size. Examples include ethylene glycol, 5-fluorouracil, ethanol, and metaldehyde (Groover J, 2022), (Henry JS, 2023), (Teichmann-Knorrn S, 2020), (Keno LA, 2011).
- **Hemoperfusion**: Best suited for eliminating larger molecular substances with a low volume of distribution and less than 95% protein binding. Examples include amatoxin, baclofen, cannabinoids, ibuprofen, and naproxen (Groover J, 2022) (Tegze JH, 2022), (Culler CA, 2019).
- **Therapeutic Plasma Exchange (TPE, plasmapheresis)**: Most appropriate for substances with a low volume of distribution and high protein binding. An example includes most NSAIDs (Rosenthal MG, 2019).

Ropinirole

Ropinirole, a dopamine agonist initially developed for the treatment of Parkinson's disease, has been repurposed for its emetogenic properties. It is currently marketed as Clevor® for transconjunctival use in dogs. It induces vomiting by binding to dopamine receptors in the chemoreceptor trigger zone. Ropinirole is highly selective for dopamine receptors, primarily D2, in contrast to apomorphine, which also interacts with serotonin, opioid, and alpha-adrenergic receptors to a lesser degree. A 2023 paper in JAVMA showed ropinirole efficacy to be comparable to apomorphine (Rosenstein NA, 2023). Side effects include protracted vomiting, tachycardia, conjunctival hyperemia, protrusion of the nictitans, ocular discharge, and sedation. The administration of metoclopramide is recommended for patients experiencing protracted vomiting and may help alleviate other adverse effects associated with ropinirole (Clevor Prescribing Information).

References

1. Bogdanffy MS, e. a. (2014). Nonclinical safety of the sodium-glucose cotransporter 2 inhibitor empagliflozin. Int J Toxicol, 436-439. (Accessed: https://www.vetoquinolusa.com/clevor-info). Clevor Prescribing Information.

2. Culler CA, V. A. (2019). Successful treatment of a severe cannabinoid toxicity using extracorporeal therapy in a dog. JVECC, 674-679.

3. D'Orazio J, N. L. (2023). Xylazine Adulteration of the Heroin-Fentanyl Drug Supply: A Narrative Review. Ann Intern Med, 1370-1376.

4. Groover J, L. L.-R. (2022). Extracorporeal blood purification in acutely intoxicated veterinary patients: A multicenter retrospective study (2011-2018): 54 cases. JVECC, 34-41.

5. Henry JS, B. S. (2023). Successful treatment of 5-fluorouracil toxicosis with hemodialysis. .JVECC, 388-392.

6. JB, T. (2009). Evaluation of a Human On-site Urine Multidrug Test for Emergency Use With Dogs. JAAHA, 59-66.

7. Keno LA, L. C. (2011). Treatment of accidental ethanol intoxication with hemodialysis in a dog. JVECC, 363-368.

8. Leas EC, e. a. (2024). Need for a Public Health Response to the Unregulated Sales of Amanita muscaria Mushrooms. American Journal of Preventative Medicine, 458-463.

9. Rosenstein NA, J. J. (2023). Rosenstein NA, JohsoRopinirole has similar efficacy to apomorphine for induction of emesis and removal of foreign and toxic gastric material in dogs. JAVMA, 1140-1146.

10. Rosenthal MG, L. M. (2019). Use of therapeutic plasma exchange to treat nonsteroidal anti-inflammatory drug overdose in dogs. JVIM, 596-602.

11. Siegel JS, D. J. (2023). Psychedelics Drug Legislative Reform and legalization in the US. JAMA Psychiatry, 77-83.

12. Tegze JH, P. B. (2022). Amanita mushroom poisoning: efficacy of aggressive treatment in two dogs. Vet Hum Toxicol, 96-99.

13. Teichmann-Knorrn S, D. S. (2020). Retrospective evaluation of the use of hemodialysis in dogs with suspected metaldehyde poisoning (2012-2017): 11 cases. JVECC, 194-201.

14. Tourdot, R. (2024). Tox Trends: Emerging Toxins & Updates in Clinical Veterinary Toxicology. WVMA Zoo School. Wisconsin.

15. Wegenast CA, e. a. (2022). Acute kidney injury in dogs following ingestion of cream of tartar and tamarinds and the connection to tartaric acid as the proposed toxic principle in grapes and raisins. JVECC, 812-816.

Toxins

Food, Glorious Food!

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Allium spp. (n-propyl disulfide)

Onions, garlic, chives, leeks, and shallots are all members of the Allium genus. and contain n-propyl disulfide. The propyl disulfide remains even when the plant is dried, raw, cooked, or pickled. Even onion and garlic powder retain toxicity.[1] On a per weight basis, garlic contains more n-propyl disulfide than onions.

Propyl disulfide, when metabolized, produces free radicals. These free radicals cause oxidative damage to the erythrocyte membrane, leading to hemolysis. While Heinz bodies can be detected within 24 hours, the peak effect of hemolysis is seen at 5 days post exposure.[2]

Since the oxidation occurs at -SH groups on the RBC, cats are more sensitive as they have more -SH groups on their hemoglobin (Cats = 8; Dogs = 4). So how much is too much? For dogs, about 10 g/kg of garlic or 15 g/kg of onion can cause hemolysis and for cats, 1 g/kg of garlic and 5 g/kg of onions is problematic.

Clinical signs include vomiting, inappetence, ataxia, lethargy, recumbency, tachycardia, tachypnea, dyspnea, pale mucus membranes, and hemoglobinuria. Hematology will show anemia, hemoglobinemia, and Heinz bodies.[1,2]

Decontamination includes induction of emesis, and if the recovery of the Allium is poor, administration of activated charcoal. Monitor urine color for 5 days, and PCV as needed. Some animals may need a whole blood or pRBC transfusion and fluids.

Ethanol

Ethanol can be found in alcoholic beverages, liquid medications, cosmetics, hand sanitizers, perfumes, colognes, mouthwashes, food flavorings, and rising raw yeast bread dough. The amount needed to cause intoxication will vary depending on the type of alcohol ingested, as the concentration will vary (200 proof = 100% ethanol) (see Table 1).

Table 1

Percent of ethanol in common alcoholic drinks

- Beer 4 - 12%
- Wine 10 - 14%
- Vodka, gin 40%
- Whiskey 43%
- Grain alcohol 95%

Ethanol is rapidly absorbed by both the oral and dermal route. Peak plasma occurs 30 minutes to 2 hours post exposure. Ethanol is metabolized in the liver (95%) by alcohol dehydrogenase enzyme (ADH) to acetaldehyde and then to acetic acid. The elimination half-life is variable as it is a saturable system.[3]

Clinical signs will vary depending on the amount ingested. Vomiting is common as ethanol is directly irritating to the stomach and high blood ethanol levels stimulate the vomiting reflex. Unfortunately, high blood alcohol also slows the muscles that control the epiglottis, increasing the risk of aspiration. Ataxia, depression, hypotension, tremors, hypoglycemia, acidosis, hypothermia (peripheral vasodilation), coma, respiratory failure, and death can occur.

While blood alcohol content (BAC) is commonly measured in people, it is rarely performed in animals due to turn-around time. An estimate of blood ethanol levels can be performed by dividing the osmol gap by 27. The lowest published oral lethal dose (100% ethanol) is 5.5 ml/kg in the dog and 6 ml/kg in the cat.[3]

Emesis can be induced if it is < 30 minutes since ingestion and the patient is asymptomatic. Activated charcoal is not recommended due to the aspiration risk and the fact that it binds poorly to ethanol. Treatment is supportive and revolves around administration of fluids and optimizing vital signs. Monitor for hypoglycemia, acidosis and hypoxia. If the patient is comatose, pass an endotracheal tube and position the patient to prevent aspiration; a ventilator may be needed. Yohimbine, atipamezole or naloxone can be tried to reverse severe CNS depression or coma, but efficacy is unknown. Hemodialysis can be performed in severe cases.[4]

Most patients recover within 12-24 hours, but cases involving aspiration of gastric contents, co-ingestants, or preexisting disease have a more guarded prognosis.

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Raw Yeast Dough

Raw yeast dough can cause both mechanical and biochemical concerns. Even after ingestion, the yeast continues to metabolize sugars in the dough, producing gas (CO2) and ethanol. This leads to drunk bloated animals.[5]

Clinical signs are the same as ethanol, but there may be accompanying gastric distension. Treatment is the same as ethanol except for decontamination. Emesis can be performed up to 4 hours after ingestion if the patient is asymptomatic. Administration of cold (ice) water can slow down the yeast; warm the patient afterwards. Recovery is frequently within 24-36 hours.[5]

Humulus lupulus (Hops)

Hops (Humulus lupulus) are used in herbal supplements and as a bittering agent when brewing beer. When ingested, hops can cause a malignant hyperthermia-like syndrome in dogs. The toxic principle is unknown.[6]

The typical history is a dog that either ingested unused hops pellets or spent plant material that was in the compost pile. Signs can occur within 3 hours. The dogs become progressively agitated, tachypneic, severely hyperthermic (> 108°F), they may then tremor, seizure, and die within 6 hours.

If the dog is asymptomatic, emesis and activated charcoal with cathartic can be performed. If the dog is symptomatic, start cooling measures (IV fluids, cool water enemas, fans) and administer dantrolene (direct-acting skeletal muscle relaxant). Prognosis is guarded to poor.[6]

Macadamia nuts

Ingestion of macadamia nuts by dogs causes weakness, depression, vomiting, ataxia, tremors, and mild to moderate hyperthermia in dogs. The toxic principle is unknown. Signs can appear within 12 hours. The hind limbs tend to be more involved than the front limbs.[7]

If asymptomatic, emesis can be induced. Most patients will not need hospitalization, but if tremors or hyperthermia are present, fluid therapy and thermoregulation are recommended. Signs can last from 12-48 hours and no long-term effects are expected.

Methylxanthines

Theobromine and caffeine are methylxanthines found in chocolate, coffee, tea, and cola. They cause significant cardiovascular and CNS stimulation. Methylxanthines are typically well absorbed and well distributed, with peak plasma levels reached by 30 – 60 minutes. However, chocolate is more slowly digested/absorbed, and peak effects can be delayed.

The half-life of theobromine in the dog is 17.5 hours, compared to caffeine at 4.5 hours.[8]

The LD^{50} of caffeine and theobromine in the dog is about 100-300 mg/kg. We can begin to see mild GI signs above 20 mg/kg of methylxanthines, cardiotoxic effects above 40 mg/kg, and tremors/seizures above 60 mg/kg.

Different types of chocolate will have different methylxanthine content. To determine the dose, look at the type of chocolate ingested, add the caffeine and theobromine concentration together (either mg/oz or mg/g) to get methylxanthine amount (see Table 2), then divide by the animal's weight.

Table 2. Methylxanthine amounts by type of chocolate

COMPOUND	THEOBROMINE (MG/OZ)	CAFFEINE (MG/OZ)	THEOBROMINE (MG/G)	CAFFEINE (MG/G)
White Chocolate	0.25	0.85	0.008	0.03
Milk Chocolate	58	6	2	0.21
Semi-sweet Chocolate	138	22	5	0.78
Unsweetened Chocolate	393	47	14	1.67
Unsweetened Cocoa Powder	737	70	26	2.5
Cocoa Bean Mulch	255	N/A	9	N/A

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With chocolate ingestion, signs may be delayed up to 12 hours.[8] Initially you can see polydipsia, bloating, vomiting, diarrhea, and restlessness that can progress to hyperactivity, polyuria, tremors, seizures, cardiac arrhythmias, hypertension, hyperthermia, seizure, and coma. Death is due to arrhythmias or respiratory failure.

Methylxanthine treatment includes IV fluid diuresis and monitoring of the HR and rhythm. If the patient is agitated, benzodiazepines or acepromazine can be used. Beta-blockers work well to control tachycardia, and methocarbamol can be used for tremors. Seizures can be controlled with diazepam. Signs may last up to 72 hours in dogs and pancreatitis is a possible sequela.[8]

Dogs are more sensitive to the effects of theobromine than humans or cats, and it has a longer half-life (stays in system longer). Cats are unlikely to consume enough methylxanthines to be a concern as they have no sweet taste buds and do not gorge on food like dogs do.

LD^{50} of theobromine
- Humans 1 g/kg
- Cats 200 mg/kg
- Dogs 100-500 mg/kg

Biological half-life
- Humans ~7 hours
- Cats 7.8 hours
- Dogs 17.5 hours

What about toxicosis in humans? An adult human would need to ingest about 1 pound of milk chocolate per kg body weight or about 0.4 pounds of dark chocolate per kg body weight.

Caffeine is found in coffee beans at 1-2% (10-20 mg/g) and tea at 3-4% (30-40 mg/g) before brewing. A brewed cup of coffee (8 fl. oz) contains 95 mg of caffeine, and a brewed cup of tea (8 fl. oz) contains 26 mg of caffeine. Clinical signs and treatment are just like chocolate, except for a shorter treatment period of time.

Persea americana (avocado)

Avocados contain persin, which is a natural oil-soluble fungicide. Persin is found within the idioblast oil cells. These are common in the skin, leaves ,and flesh of unripe fruit. As the fruit ripens the amount of persin decreases in the flesh.

Since dogs and cats are not big chewers, typically stomach upset or a pit foreign body is seen. Other species can develop severe signs such as noninfectious mastitis and cardiac necrosis.[9]

Prunus spp. (cherries, plums, peaches) and *Malus* spp. (apples)

Pits and seeds of these fruits along with the bark and leaves contain cyanogenic glycosides. Cyanogenic glycosides are cyanide attached to a sugar molecule. They release cyanide when broken apart (chewing, freezing, etc.). Since monogastrics don't chew pits and leaves well, they do not liberate enough cyanide in most cases to cause toxicosis.

Apricot kernels, the almond shaped seed inside of the pit, can be a cyanide issue, as the endocarp has been removed.[10] Apricot kernels are sold as a health food item and/or ground into meal for adding to scrubs or soaps.

Tremorgenic mycotoxins

Penitrem A and roquefortine are common mycotoxins produced from molds (Penicillium spp.) that grow on food. These compounds are tremorgenic and can produce full body muscle tremors in all species. These molds commonly grow on dairy, nuts, and grains. Pets can find these moldy items in the garbage, compost, or in the lawn (fruit/nut trees). The tremorgenic mycotoxins that these molds produce can also cause hyperactivity and seizures within 30 minutes to 2 hours post exposure.[11]

If the pet is asymptomatic and has just ingested the moldy food, emesis can be induced. Administration of activated charcoal should be based on emesis results. Methocarbamol works best for tremor control and benzodiazepines can be used for seizures. Intravenous fluids will help keep the body temperature normal and protect the kidneys from myoglobin.

Vitis spp. (grapes and raisins)

Members of the Vitis spp. have been associated with acute kidney injury in dogs.[12,13] There is no age, breed, or sex predisposition. On histopathology, there is proximal renal tubular degeneration and necrosis with the basement membrane remaining intact. Extensive sloughing of proximal tubule

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epithelium results in extensive necrotic debris within the tubular lumens (obstructive nephropathy). Metastatic mineralization of numerous tissues can occur.

Clinical signs begin with vomiting and/or diarrhea (within 24 hours), followed by depression, dehydration, anorexia, and abdominal pain. Creatinine elevates within 12 hours followed by BUN. In some dogs we can see elevations of calcium, phosphorus, liver enzymes, lipase/amylase, and hyperglycemia.

The toxic component is suspected to be tartaric acid.[14] Tartaric acid is an organic acid found in a variety of plants. Grapes and tamarinds, which have also been associated with AKI, have the highest concentrations. Grapes contain up to 2% tartaric acid, with 0.35-1.1% being more common, while tamarind pulp contains 8-18% tartaric acid. Other fruits such as cherries have 0.008% tartaric acid and raspberries contain 0.009% tartaric acid. Dogs have also developed AKI after ingestion of large amounts of cream of tartar. Cream of tartar is potassium bitartrate (a potassium salt of tartaric acid) that is a by-product of winemaking.

Several early papers demonstrated the renal effects of tartaric acid and its salts as well as the characteristic histopathologic lesions in dogs (extensive necrosis of the convoluted tubules).[15] The amount of tartaric acid in *Vitis* spp. will vary depending on the cultivar of the fruit, growing conditions, ripeness, and environment (see Table 3)

Table 3

Amount of tartaric acid contained in different varieties of grapes vs time to ripeness[16]

Thompson seedless grapes

(most common green grocery grape)

Ripe = 2.05 g/L of tartaric acid

7 weeks previous = 6.55 g/L

Red globe grapes

Ripe = 1.28 g/L

1 week previous = 2.05 g/L

7 weeks = 6.68 g/L

Cotton candy grapes

Ripe = 3.3 g/L

Why dogs? Dogs are uniquely sensitivity to organic acids due to decreased excretion. Dogs are missing OAT-4 (organic acid transporter) that removes tartaric acid from the renal tubular cells and transports it into the urine.[18] The exact mechanism by which tartaric acid causes renal tubular necrosis is unknown, but a related organic acid (maleic acid) causes similar renal lesions in dogs and is thought to selectively inhibit Na-K-ATPase activity and/or deplete ATP in the proximal tubules.[19]

When do we begin to decontaminate? Estimating a worse-case concentration of tartaric acid, emesis

should be induced if more than 1 grape/raisin per 5 kg of dog is ingested (2 per 5 kg if cooked).[14] Thermal decomposition of tartaric acid can explain the observation that cooked grapes and raisins are less toxic, however, the exact temperature and duration of the heating process for full decomposition is unknown. Grape juice, jam, and wine are detartrated and lack nephrotoxicity.

Emesis can be induced up to 8-13 hours post ingestion as tartaric acid delays gastric emptying in dogs.[17] Since tartaric acid causes obstructive nephropathy, is it important to maintain urine output. IV fluids for 48 hours at a diuretic rate is recommended. Renal values should be monitored and if normal at 48 hours, the dog can go home. Oliguric/anuric renal failure can develop within 72 hours of ingestion. Dialyzed dogs had mixed results.

Xylitol

Xylitol is a 5-carbon sugar alcohol in the same family as sorbitol, maltitol, mannitol, and erythritol. However, it is the only one of this group that can cause vomiting, hypoglycemia, and liver necrosis in dogs after ingestion.[20] While xylitol occurs naturally at low levels in many fruits, it can be found in large amounts in sugar-free chewing gums, candy, pudding, high protein peanut butter, toothpaste, quick dissolve and chewable medications, and powdered for baking.

While xylitol is anti-cavity and reduces the severity of ear infections in people, it is not safe for dogs. Xylitol stimulates insulin release for several hours (2.5-7x that of glucose) in the dog, resulting in hypoglycemia at doses of 100 mg/kg or more. Liver necrosis can be seen at doses > 500 mg/kg. It is thought that xylitol uses the pentose phosphate pathway (PPP) instead of the TCA (Kreb's) cycle for metabolism leading to cellular death, but this theory has not been confirmed in dogs.

The onset of clinical signs depends on the form that the xylitol is in. Powdered xylitol, baked goods, quick dissolve medications can all develop signs of hypoglycemia within 15-30 minutes. Other products such as sugar free gum may be delayed for up to 12 hours. Clinical signs include vomiting, depression, weakness, ataxia, seizures, and coma followed by elevations of liver values in 2-24 hours.[20]

Emesis can be induced if our patient is asymptomatic. Activated charcoal does not bind well and is not recommended. Monitor glucose for 12+ hours and feed small frequent meals. If hypoglycemia does develop, dextrose (bolus +/- CRI) should be implemented. A dextrose CRI should automatically be started if the ingestion is over 500 mg/kg. If liver values are rising, monitor coagulation values as a plasma transfusion may be needed. Liver protectants, such as SAMe or acetylcysteine can be used, but it is unknown if they are helpful. Treatment should continue until blood glucose normalizes without supplementation, ALT plateaus, and patient is clinically well.

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References

1. Robertson JE, Christopher, MM, Rogers, QR. Heinz body formation in cats fed baby food containing onion powder. J Am Vet Med Assoc 1998;212(8):1260-1266.

2. Cope RB. Allium poisoning in dogs and cats. Vet Med 2005;100(8):562-566.

3. Wismer T. Ethanol Toxicosis: A Review. Today's Veterinary Practice 2017;7(4):74-76.

4. Keno LA, Langston CE. Treatment of accidental ethanol intoxication with hemodialysis in a dog. J Vet Emerg Crit Care 2011;21(4):363-368.

5. Sobczak B. Bread Dough Toxicosis. Clinician's Brief 2005;Nov:33-34.

6. Becker J, Brutlag AG, Hovda L, Rendahl A, Tart KM. A retrospective evaluation of hops ingestion in 177 dogs (2005-2018). J Vet Emerg Crit Care 2023;33(3);348-353.

7. Hansen SR, Buck WB, Meerdink G, Khan SA. Weakness, tremors, and depression associated with macadamia nuts in dogs. Vet Hum Toxicol 2000:42(1):18-21.

8. Weingart C, Hartmann A, Kohn B. Chocolate ingestion in dogs: 156 events (2015-2019). J Sm Anim Pract 2021;62(11):979-983.

9. Herbert J. Use of intralipid to prevent myocardial necrosis post persin toxicity in an Indian ring neck. Center Vet Ed 2022;307:28-31.

10. Houlton E, Caldwell DJ, Granfone M. Cyanide toxicity secondary to apricot (Prunus armeniaca) kernae meal ingestion in a canine. Toxicon 2024;245:107764.

11. Barker AK, Stahl C, Ensley SM, Jeffery ND. Tremorgenic mycotoxicosis in dogs. Compend Contin Educ Vet 2013;35(2):E2.

12. Eubig PA, Brady MS, Gwaltney-Brant SM, Khan SA, Mazzaferro EM, Morrow CM. Acute renal failure in dogs after the ingestion of grapes or raisins: a retrospective evaluation of 43 dogs (1992–2002). J Vet Intern Med 2005;19:663–674.

13. Croft R, Clementi E, Farmer H, Whalley R, Dunning M, Firth A. Retrospective evaluation of Vitis vinifera ingestion in dogs presented to emergency clinics in the UK (2012-2016): 606 Cases. J Vet Emerg Crit Care 2021;31(1):74-79.

14. Wegenast CA, Meadows ID, Anderson RE, Southard T, Rocio Gonzalez Barrientos C, Wismer TA. Acute kidney injury in dogs following ingestion of cream of tartar and tamarinds and the connection to tartaric acid as the proposed toxic principle in grapes and raisins. J Vet Emerg Crit Care. 2022;32(6):812-816.

15. Underhill FP, Leonard CS, Gross EG, et al. Studies on the metabolism of tartrates. The behavior of tartrate in the organism of the rabbit, dog, rat and guinea pig. J Pharmacol Exp Ther 1931;43(2):359-380.

16. Kliewer MW, Howarth L, Omori M. Concentrations of tartaric acid and malic acids and their salts in Vitis vinifera grapes. Am J Enol Vitic 1976;18:42-54.

17. Blum AL, Hegglin J, Krejs GJ, Largiader F, Sauberli, Schmid P. Gastric emptying of organic acids in the dog. J Physiol 1976;261:285-299.

18. Coyne SR, Landry GM. Tartaric acid induces toxicity in Madin–Darby canine kidney cells, but not human kidney-2 cells in vitro, and is prevented by organic anion transporter inhibition and human OAT-4 transfection. J Vet Emerg Crit Care 2023;33(3):298-304.

19. Zager RA, Johnson ACM, Naito M, Bomsztyk K. Maleate nephrotoxicity: mechanisms of injury correlate with ischemic/hypoxic tubular cell death. Am J Physiol Renal Physiol 2008;294:F187-F197.

20. Murphy LA, Dunayer EK. Xylitol Toxicosis in Dogs: An Update. Vet Clin North Am Small Anim Pract 2018;48(6);985-990.

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Toxins

Xylitol Toxicosis in Dogs

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Xylitol is a commonly used sugar substitute that can cause profound hypoglycemia and liver failure in dogs. It is a sugar alcohol derived from hardwood plants and as a byproduct from ethanol production.[1] Because of its sweet taste, slow absorption, and low glycemic index in humans, it is available as 100% xylitol powder for baking and is also frequently found in sugar-free products such as baked goods, gum, chocolate, and other candy, weight-loss protein bars, peanut butter & nut butters, and ice cream. Another common source of xylitol is dietary supplements and human medications. Because xylitol has topical antimicrobial properties and has an ability to impart a cooling sensation, it can be found lurking in toothpaste, mouthwash, dental floss, cosmetics, hair care products, and even clothing.[1]

The xylitol content of various products can be challenging to determine when xylitol is not specifically called out in the nutritional facts, although xylitol will be noted in the ingredient list. Since ingredient contents are listed by weight in descending order, the higher xylitol is on the ingredient list, the higher the xylitol content is in the product. For some products, reporting of sugar alcohols on the nutritional label is voluntary. Other product labels (those that claim to have sugar alcohols) will note the sugar alcohol content (including erythritol, isomalt, maltitol, mannitol, sorbitol, and xylitol) of foods but are not required to list the xylitol content separately.[2] For example, the nutritional label for a particular gum may note that there is 1 gram of sugar alcohol per piece, and may list the ingredients xylitol, sorbitol, gum base, and natural flavors. In this example, the 1 gram of sugar alcohol is divided between xylitol and sorbitol, with more xylitol in the product compared to sorbitol. For specific xylitol information, it can sometimes be useful to contact the manufacturer of the product to obtain the amount present.

Dogs are the species most susceptible to xylitol toxicosis. Other species, such as ruminants and rabbits, have demonstrated increased insulin release when administered xylitol intravenously (IV) without significant clinical signs.[3] In one small study, cats did not develop hypoglycemia or liver effects despite oral exposure up to 1000 mg xylitol/kg body weight.[4] Xylitol does not cause significant insulin release in humans, rats, or horses. In dogs, oral ingestions of 100 mg/kg can result in hypoglycemia and 500 mg/kg may result in hepatic necrosis.[3]

MECHANISM OF ACTION

After ingestion, xylitol reaches peak plasma concentrations in dogs within 30 minutes. It is metabolized primarily in the liver to D-xylulose, then via the pentose-phosphate pathway to glucose, glycogen and lactate, with glucose as the predominant metabolite. In dogs, xylitol stimulates a greater insulin surge compared to an equal amount of glucose, leading to hypoglycemia. This insulin surge increases in a dose-dependent manner.[1,3] In other words, the higher the amount of xylitol ingested, the greater the insulin surge.

The exact mechanism by which xylitol causes hepatotoxicity is not completely known but may be due to cellular death from ATP depletion as xylitol is metabolized by the pentose-phosphate pathway rather than the citric acid cycle.[5] Another possible theory is that the generation of reactive oxygen species during xylitol metabolism causes hepatocellular damage.

CLINICAL SIGNS

The onset of clinical signs can vary depending on the type of xylitol-containing product ingested. Powdered xylitol, mints, fast-dissolve medications, and other foods or substances that rapidly disintegrate can result in clinical signs of hypoglycemia within as little as 30 minutes, while products like gum disintegrate slowly when not chewed and can result in signs of hypoglycemia being delayed by up to 12 hours.[3] The most common signs reported with xylitol exposure are vomiting, lethargy and weakness.[3] Depression and seizures have also been reported, typically due to hypoglycemia. Hypoglycemia is a frequent blood chemistry change, although hyperglycemia has also been reported. Hyperglycemia is thought to be due the Somogyi phenomenon (rebound hyperglycemia) from high insulin levels.[6] Additional blood chemistry findings include hypokalemia, hypophosphatemia, hyperphosphatemia, and elevated liver enzymes, particularly elevated alanine aminotransferase (ALT). Liver enzyme elevations may be seen within 4-24 hours of large exposures over 500 mg/kg and have been seen even without changes in the blood glucose.[3] Coagulopathies (as measured by the prothrombin and partial thromboplastin times) have been reported with severe liver enzyme elevations.[3] Thrombocytopenia has also been rarely reported.[3,7]

Continued on page 20

TREATMENT

The decision to induce vomiting in a dog exposed to xylitol depends on the amount and form ingested, how long ago the exposure was, and the dog's presenting blood glucose on arrival at the hospital. Exposures to some forms of xylitol (such as 100% xylitol products, mints, or fast-dissolve medications/ supplements) should not have emesis induced because they are unlikely to be recovered in the vomit since they are rapidly absorbed.[3] Certain varieties of gum may also have a high xylitol content in the outer coating of the gum which is absorbed faster than the gum base, lowering the effectiveness of emesis. Ingestions of xylitol over 100 mg/kg body weight, or if the amount of xylitol is unknown, should have emesis considered if the dog has not vomited prior to arriving at the hospital, has no contraindications for emesis, and the exposure was recent (less than one hour).[3] Keep in mind that signs of hypoglycemia such as weakness can develop quickly and may lead to aspiration should they be seen while the patient is vomiting.

Activated charcoal is not recommended for xylitol exposures. Activated charcoal is an adsorbent, meaning that it binds to particles within the digested tract. In vitro studies have shown that xylitol does not bind well to activated charcoal.8 Additionally, since xylitol is readily and rapidly absorbed from the digested tract, activated charcoal is unlikely to be effective.

Dogs that have ingested a toxic amount of xylitol should be monitored closely for at least 12-24 hours after exposure. Baseline bloodwork on presentation should include blood glucose and electrolytes (potassium and phosphorus). Those patients that ingest an unknown amount of xylitol or ingest over 500 mg/kg body weight should also have initial liver enzymes and a complete blood count (CBC) including platelet count evaluated.[3,7] The blood glucose should be monitored every 2-3 hours, potentially more frequently for severely affected dogs. Hypoglycemia is expected within 12 hours of ingestion, and if it develops and persists, monitoring beyond 12 hours may be necessary.[3] The electrolytes should be reassessed in 8-12 hours to determine if supplementation is necessary. After baseline liver values have been determined, they should be monitored at 12, 24 and 48 hours post ingestion.[3] Longer monitoring may be needed if liver enzymes remain elevated. Coagulation parameters such as the prothrombin and partial thromboplastin time should also be monitored if liver enzymes are substantially elevated. The CBC may be reassessed 24 hours after exposure for evidence of thrombocytopenia, although this is rarely reported.

Supportive care for dogs that have ingested a toxic amount of xylitol includes fluid therapy and potentially hepatoprotectants.[3] An IV catheter should be placed if the dog is at risk for hypoglycemia. Hypoglycemia can be treated with an intravenous dextrose bolus followed by a continuous rate infusion of 2.5-5% dextrose peripherally and continued until hypoglycemia resolves. Dextrose fluids may also support the liver and should be administered for at least 12 hours (or until hypoglycemia resolves if present) if the

patient is at risk for hepatotoxicity. Additionally, hepatoprotectants such as s-adenosyl-L-methionine (SAMe) (20 mg/kg/day), milk thistle (50 mg/kg/day), and/or 5% n-acetylcysteine (NAC) (initial dosage of 140 mg/kg by mouth or IV through a bacteriostatic filter followed by 70 mg/kg every 6 hours for up to 7 additional treatments) can be considered.[3] Their effectiveness at preventing and treating liver damage from xylitol has not been determined.

Additional treatment for xylitol exposures includes nutritional support and symptomatic care. Patients exposed to xylitol should be fed meals every 2-3 hours for 12 hours or until hypoglycemia resolves.[3] If a dog has evidence of hepatic damage and coagulopathy, vitamin K1 (1.5-2.5 mg/kg orally twice daily with food) and potentially fresh frozen plasma transfusions should be considered. Electrolyte disturbances such as hypokalemia, hypophosphatemia and hyperphosphatemia are usually transient, but may require supplementation if severe alterations are seen.

PROGNOSIS

Hospitalization for dogs exposed to a toxic amount of xylitol may be needed for 1-3 days, potentially longer depending on the response to treatment. With prompt and effective treatment, the prognosis after xylitol exposure in dogs is generally good. Early decontamination (when possible) and management of hypoglycemia is key. For dogs that develop mild to moderate liver enzyme elevations and mild coagulopathies the prognosis can be good as well if treated aggressively. When dogs develop severely elevated liver enzymes suggestive of hepatic necrosis, severe coagulopathies, and/or repeated episodes of hypoglycemia, the prognosis may be more guarded, although some of these more severely affected patients can recover successfully.[3]

1. DuHadway MR, Sharp CR, Meyers KE, and Koenigshof AM. Retrospective evaluation of xylitol ingestion in dogs: 192 cases (2007-2012). JVECC 2015, 25(5):646-654.

2. Code of Federal Regulations, Title 21, Chapter I, Subchapter B, Part 101, Subpart A, Section 101.9 https://www.ecfr.gov/current/title-21/chapter-I/subchapter-B/part-101/subpart-A/section-101.9 accessed 2/23/2023.

3. Murphy LA, Dunayer EK. Xylitol Toxicosis in Dogs An Update. Vet Clin Small Anim 2018, 48(6):985-990.

4. Jerzsele A, Karancsi Z, Paszti-Gere E, et al. Effects of p.o. administered xylitol in cats. J Vet Pharmacol Ther. 2018, 41(3):409-414.

5. Xia Z, He Y, Yu J. Experimental acute toxicity of xylitol in dogs. J Vet Pharmacol Ther. 2009, 32:465-469.

6. Piscitelli, CM, Dunayer, EK, Aumann, M. Xylitol Toxicity in dogs. Compendium. 2010, February: E1-E4.

7. Dunayer EK, Gwaltney-Brant SM. Acute hepatic failure and coagulopathy associated with xylitol ingestion in eight dogs. JAVMA. 2006, 229(7):1113-1117.

8. Cope RB. A screening study of xylitol binding in vitro to activated charcoal. Vet Hum Toxicol. 2004, 46:336-7

Toxins

Top Poisons That Kill

WEBINAR HIGHLIGHTS

Justine Lee, DVM, DACVECC, DABT
Director of Medicine / Founder, VETgirl

In this VETgirl Webinar "TOP POISONS THAT KILL" on December 18, 2024, Dr. Justine Lee, DACVECC, DABT reviews the top 5 poisons that have a high fatality rate, including isoniazid, 5-FU, ethylene glycol, organophosphates/carbamates, and bifenthrin. If you see any of these, you want to read on to make sure you're aware of these top poisoning fatalities! In case you missed the webinar, watch it again HERE or read the cliff notes below!

Each year, the ASPCA Animal Poison Control Center manages hundreds of thousands of poisoning calls. The majority of toxicants affecting dogs and cats do not kill acutely[1] – it takes several days before end-stage effects from toxicosis occur (e.g., anuric renal failure, acute hepatic necrosis, etc.). Likewise, only a smaller percentage of toxicants result in acute death.[1] In this lecture, we will review the mechanism of toxicosis, clinical signs, and overall treatment of the deadly and most unusual drug overdoses seen in dogs and cats. The reader is advised to contact the ASPCA Animal Poison Control Center (888-426-4435) for lifesaving, 24/7 advice as needed.

ISONIAZID

Isoniazid (commonly known as INH) is a human medication used for tuberculosis. While it is used in veterinary medicine to treat Mycobacterium or Actinomyces, it has a narrow margin of safetyw in dogs and cats.[2,3] This drug works by blocking the synthesis of mycolic acid. INH depletes the CNS of pyridoxine and also decreases levels of GABA within the brain. Many assume that since this is an "antibiotic" that it is safe; however, when accidentally ingested in dogs (and rarely, cats), it can result in severe CNS signs (e.g., tremors, refractory seizures,

coma, death). The LD^{50} in dogs is estimated to be as low as 50 mg/kg;[2,3] at this same dose, seizures can be seen. One 300 mg tablet can result in severe poisoning in a 10-pound dog. Other clinical signs include GI signs (e.g., hypersalivating, vomiting, diarrhea), acid-base disturbances (e.g., metabolic acidosis), hyperthermia (secondary to tremors or seizures), and organ injury (e.g., hepatic injury, acute kidney injury, etc.). Due to the rapid onset of clinical signs, it is often too late to decontaminate the patient. Gastric lavage under anesthesia may be necessary. Treatment also includes IV fluids, antiemetics, anticonvulsants, muscle relaxants, supportive care, and the antidote pyridoxine hydrochloride (typically available as 100 mg/ml) (Dose: suggested dose of 71 mg/kg IV, diluted to 5-10%, slow over 30-60 minutes).[2,3] Clinicopathologic monitoring should include a biochemistry panel and recheck hepatic panel 3-5 days later.

5-FLUOROURACIL (5-FU)

The most life-threatening topical toxin to dogs and cats is 5-fluorouracil (5-FU). 5-FU, commonly known by the brand names Efudex®, Carac®, Adrucil®, and Fluoroplex®, is a prescription anti-neoplastic medication that is often used for treatment of actinic keratosis or superficial basal cell carcinoma in humans. It is commonly sold in low concentration products (e.g., 0.5-5%), and works by inhibiting DNA and RNA synthesis and production, resulting in programmed cell death.[4-7] While IV administration of 5-FU is occasionally used as a chemotherapeutic agent in dogs (e.g., for mammary gland tumor, etc.), it is not recommended for use in cats. Decades ago, topical 5-FU was used in cats for the treatment of squamous cell carcinoma; however, it resulted in severe toxicosis and death due to its narrow margin of safety. Clinical signs of 5-FU toxicosis can often be seen within 30 minutes up to 6 hours; death has been reported as early as 7 hours.[4-7] Clinical signs include acute GI signs (e.g., hypersalivation, anorexia, vomiting, abdominal pain, diarrhea, bloody diarrhea, etc.), CNS signs (e.g., ataxia, tremors, seizures), and bone marrow suppression (e.g., anemia, leukopenia, thrombocytopenia).[4-7] The lowest reported toxic (oral) dose in dogs is 6 mg/kg, while the minimal reported lethal dose is 20 mg/kg. One case report did have a dog survive ingestion of 46 mg/kg of 5-FU.[4-7] That said, the prognosis with 5-FU toxicosis is typically grave in cats and guarded in dogs (with a reported survival in dogs of approximately 25%). Death typically occurs due to secondary complications from the 5-FU such as sepsis (due to leukopenia), increased intracranial pressure (due to persistent seizures), intracranial hemorrhage (due to severe thrombocytopenia), or DIC (due to severe seizures). Unfortunately, most patients present with severe clinical signs, where it is too late to perform decontamination. Therefore, treatment should be aimed at symptomatic supportive care, anti-convulsant therapy, anti-emetics, anti-diarrheals, IV fluids (to help maintain perfusion), thermoregulation, broad-spectrum antibiotics, clinicopathologic monitoring, and symptomatic supportive care. If the patient is able to survive the acute crisis, clinicopathologic monitoring is necessary every 3-4 days thereafter for 2-3 weeks, until bone marrow function returns to normal.[4-7]

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ETHYLENE GLYCOL (EG)

Accidental or malicious poisoning with ethylene glycol (EG) is common, as the public is generally well aware of its toxic nature. Sources of EG include automotive antifreeze (radiator coolant, which typically contains 95% EG), windshield deicing agents, motor oils, hydraulic brake fluid, developer solutions, paints, solvents, etc.[8,9] As little as 4.4 ml/kg can result in severe acute kidney injury (AKI) in canine patients, while as little as 1.4 ml/kg can result in AKI in feline patients (based on high concentration EG products).[8,9] Ethylene glycol is metabolized by the body to highly poisonous metabolites (including glycoaldehyde, glycolic acid, and oxalic acid), which lead to severe AKI secondary to development of calcium oxalate crystalluria.[8,9]

Three stages of ethylene glycol poisoning:

1. **Stage 1:** This occurs within 30 minutes to 12 hours and looks similar to alcohol poisoning. Signs of ataxia, hypersalivating, vomiting, seizuring, and polyuria/polydipsia are seen.[8,9]

2. **Stage 2:** This occurs within 12-24 hours post-exposure,8 and clinical signs seem to "resolve" to the pet owner; however, during this time frame, severe internal injury is still occurring. Signs of ataxia may seem to improve during this stage, but signs of dehydration, tachycardia, and tachypnea may be seen.

3. **Stage 3:** In cats, this stage occurs 12-24 hours after ethylene glycol exposure.[8,9] In dogs, this stage occurs 36-72 hours post-ingestion.[8] During this stage, severe AKI occurs secondary to calcium oxalate crystalluria. Severe anorexia, depression, hypersalivation, uremic halitosis, coma, vomiting, and seizures may be seen.

Any patient suspected of EG toxicosis should have an EG blood test, venous blood gas, and urinalysis performed. Evidence of a positive EG test, metabolic acidosis, elevated anion gap, and presence of calcium oxalate crystalluria is consistent with EG toxicosis, and prompt therapy is indicated. Be aware that EG testing is only accurate within approximately the first 24 hours, as false negatives may be found thereafter due to complete metabolism of the EG to its more toxic metabolites. With EG testing, keep in mind that the toxic metabolites of EG are not typically detected on routine EG testing – only ethylene glycol itself. On veterinary specific EG tests, rare false positives for EG may be from other drugs such as propylene glycol, sorbitol, mannitol, alcohol, etc.

Treatment for EG toxicosis includes antidote therapy, aggressive IV fluid therapy, monitoring urine output and clinicopathologic parameters, anti-emetic therapy, and symptomatic supportive care. The antidote, fomepizole (also known as 4-MP), is expensive but lifesaving when administered to dogs within the first 8-12 hours of ingestion. In cats, the antidote must be administered within 3 hours of ingestion to be effective.[8-9] Dosing for 4-MP is significantly different between dogs and cats. For dogs, the dose of 4-MP is: 20 mg/kg, IV, first dose; 15 mg/kg at 12 hours; 15 mg/kg at 24 hours; 5 mg/kg at 36 hours. For cats, the dose of 4-MP is: 125 mg/kg, IV, first dose; 31.25 mg/kg IV at 12 hours; 31.25 mg/kg IV at 24 hours; 31.25 mg/kg at 36 hours.

Ethanol can also be used as an antidote if fomepizole is not available, as it competes with alcohol dehydrogenase, thereby preventing metabolism of EG into its more toxic metabolites. A 7% of ethanol is made by removing 175 ml from a 1L bag of saline and adding 175 ml of an 80-proof vodka. If 190 proof grain alcohol is available, a 7% solution can be made by removing 74ml from a 1L bag of saline and adding 74 ml of the grain alcohol. Remember to use only "clear" alcohols on patients (e.g., grain alcohol, vodka, etc.). The dose of ethanol in dogs and cats is a loading dose of 8.6 ml/kg (600 mg/kg) 7% ethanol slow IV then continue with a CRI of 1.43 ml/kg/hr (100 mg/kg/hour) IV as a CRI for 24-36 hours. Regardless, antidote therapy must be started immediately to ensure good outcome. Once a patient has already developed azotemia, the prognosis is generally poor to grave without hemodialysis. EG toxicosis should be suspected in any patient with unexplained neurologic signs, metabolic acidosis or an elevated anion gap ((Na+ + K+) – (Bicarb + Cl-) >25). Any combination of these signs should prompt the administration of an EG blood test. The detection of calcium monohydrate oxalate crystalluria is virtually diagnostic for EG toxicosis. Be aware that ethylene glycol testing is only accurate within approximately the first 24 hours, as false negatives may be found thereafter due to complete metabolism of the EG to its more toxic metabolites. On veterinary specific EG tests, rare false positives for EG may be from other drugs such as propylene glycol, sorbitol, mannitol, alcohol, etc.

ORGANOPHOSPHATES/ CARBAMATES

Thankfully, carbamates and OPs are rarely seen now; the acutely seizing patient is rarely a result of this toxicosis nowadays. That's likely a result of the Environmental Protection Agency (EPA) removing many of these dangerous insecticides off the market (replacing them with pyrethrins and pyrethroids instead). However, some products (particularly rose or plant fertilizer/insecticide combination products, cattle ear tags, etc.) still exist.[10-11] Add to the fact that gardeners often mix these dangerous chemicals with additional bone or blood meal (which is highly palatable to pets), thus resulting in increased ingestion of the toxin. Carbamates and OPs work by competitively inhibiting acetylcholinesterase and pseudocholinesterase (e.g., the enzymes that breaks down acetylcholine), which prevents the breakdown of acetylcholine (AcH), resulting in too much AcH and stimulation of sympathetic, parasympathetic, and peripheral nervous systems. This results in AcH accumulation at nerve junctions, resulting in severe clinical "SLUDGE" signs (e.g., salivation, lacrimation, urination, defecation, gastrointestinal).

Some carbamates and OPs have various levels of

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toxicosis (e.g., ranging from low to very high), depending on the active ingredient. Clinical signs can be seen as early as 30-60 minutes, and typically are seen within 6 hours (but rarely seen > 12 hours). By the time patients present to the veterinary clinic, it is typically too late to decontaminate safely. Clinical signs include severe GI signs (e.g., hypersalivation, vomiting, diarrhea), cardiovascular signs (e.g., tachycardia, bradycardia, pallor, shock), CNS signs (e.g., agitation, sedation, mydriasis or miosis, tremors, seizures, coma), and respiratory signs (e.g., tachypnea, dyspnea, hypoxemia). Death may occur due to fluid accumulation with the bronchi, or secondary to disseminated intravascular coagulation (DIC) secondary to hyperthermia from tremors and seizure activity. Very rarely, intermediate syndrome can be seen with OP toxicosis, where clinical signs are seen > 24-72 hours after onset of acute signs; these signs can last up to 7-14 days and include signs of neuromuscular weakness, ventroflexion of the neck, cranial nerve deficits, and even death from respiratory depression and hypoventilation.[10-11]

Treatment includes aggressive decontamination (e.g., gastric lavage with an inflated endotracheal tube, administration of activated charcoal with a cathartic), fluid therapy, anti-emetics (e.g., maropitant), muscle relaxants (e.g., methocarbamol), anticonvulsants (e.g., phenobarbital, diazepam, levetiracetam, etc.), thermoregulation, electrocardiogram, blood pressure monitoring, and symptomatic supportive care. Most importantly, aggressive use of the antidote atropine or 2-PAM (which is rarely available from human medical facilities) is warranted. Atropine, an anticholinergic, blocks the neurotransmitter acetylcholine in the central and peripheral nervous systems. Atropine competes with AcH at the post-ganglionic parasympathetic sites (and hence is called an antiparasympathetic or parasympatholytic drug).[10-11] It is also called an antimuscarinic as it antagonizes the muscarine-like actions of AcH.[10-11] It is used for the treatment of SLUDGE signs from organophosphate or carbamate toxicity. With OP toxicosis, atropine should be given despite the tachycardiac; higher doses are often necessary. Doses for atropine are higher than anesthetic doses for bradycardia and range from 0.1-0.5 mg/kg IV or IM as needed.

BIFENTHRIN

Bifenthrin is a synthetic derivative of pyrethroids and is commonly found in household insect sprays and insecticides (e.g., permethrin, cypermethrin, cyphenothrin, etc.). Bifenthrin in dogs causes the same clinical signs as permethrin in cats and can be quite profound as compared to other pyrethrins/pyrethroids; rarely, it can result in fatality[12] Due to a cat's altered liver glucuronidation metabolism, cats are significantly more sensitive to pyrethrins than dogs. While a precise toxic dose for cats is not well established, products containing greater than a 5-10% concentration of pyrethrins may lead to systemic toxicosis. The diluted amount found in household insect sprays and topical flea sprays and shampoos is typically < 1%. Toxicosis from exposure to these products is highly unlikely. The application of canine spot-on pyrethrin/pyrethroid based insecticides (typically ~40-50% concentration) to cats is the primary cause of feline pyrethrin toxicosis. Cats that groom dogs following recent spot-on applications are also at high risk for toxicosis; ideally, pets should be separated until the spot-on product has completely dried on the dog to prevent cat exposure.

Signs of systemic toxicosis of pyrethroid toxicosis in cats include GI signs (e.g., hypersalivation, vomiting, nausea), CNS signs (e.g., disorientation, weakness, hyperexcitability, tremors, seizures) and respiratory signs (e.g., tachypnea, dyspnea). Tremors are extremely responsive to methocarbamol (22-220 mg/kg IV PRN to effect), a centrally acting muscle relaxant, although oral absorption of methocarbamol is often slower in onset of action. In general, tremors are less responsive to benzodiazepines (e.g., diazepam). Seizures may be controlled with anticonvulsants (phenobarbital, 4-16 mg/kg IV PRN to effect) or general gas anesthesia. Dermal decontamination is crucial but should be performed after stabilization. This should be performed with a liquid dish detergent (e.g., Dawn, Palmolive) or follicular flushing shampoo. Supportive care including the monitoring and maintenance of hydration, body temperature and blood glucose levels are necessary. Signs may persist for 1-4 days, depending on the animal. The prognosis is excellent with aggressive dermal decontamination and treatment.

Conclusion

Pet owners should be appropriately educated on how to pet-proof the house and be trained on what common human medications can be toxic to pets. Pet owners should also be appropriately educated on crate training to help minimize toxin exposure. When in doubt, the ASPCA Animal Poison Control Center should be consulted for toxic ingestions that veterinarians are unaware of.

References

1. Swirski AL, Pearl DL, Berke O, O'Sullivan TL. Companion animal exposures to potentially poisonous substances reported to a national poison control center in the United States in 2015 through 2014. J Am Vet Med Assoc 2020;257(5):517-530.

2. Villar D, Knight MK, Holding J, et al. Treatment of acute isoniazid overdose in dogs. Vet Hum Toxicol 1995;37(5):473-7.

3. Schmid DR, Lee JA, Wismer TA, et al. Isoniazid toxicosis in dogs: 137 cases (2004-2014). J Am Vet Med Assoc 2017;251(6).

4. Powell LL. 5-Fluorouracil. The Five-Minute Veterinary Consult Clinical Companion: Small Animal Toxicology. Ames, IO: Wiley-Blackwell. pp. 164-169.

5. Dorman DC, Coddington KA, Richardson RC. 5-Fluorouracil toxicosis in the dog. J Vet Intern Med 1990;4:254-257.

6. Sayre RS, Barr JW, Bailey EM. Accidental and experimentally induced 5-fluorouracil toxicity in dogs. J Vet Emerg Crit Care 2012;22:545-549.

7. Friedenberg SC, Brooks AC, Monnig AA, Cooper ES. Successful treatment of a dog with massive 5-fluorouracil toxicosis. J Vet Emerg Crit Care 2013;23:643-647.

8. Khan SA, Schell MM, Trammel HL, et al. Ethylene glycol exposures managed by the ASPCA National Animal Poison Control Center from July 1995 to December 1997. Vet Hum Toxicol 1999;41:403-406.

9. Grauer GF, Thrall MA, Henre BA, Hjelle JJ. Comparison of the effects of ethanol and 4-methylpyrazole on the pharmacokinetics and toxicity of ethylene glycol in the dog. Toxicol Lett 1987;35(2-3):307-14.

10. Klainbart S, Grabernik M, Kelmer E, et al. Clinical manifestations, laboratory findings, treatment and outcome of acute organophosphate or carbamate in toxication in 102 dogs: A retrospective study. Vet J 2019;251: doi: 10.1016/j.tvjl.2019.105349. Epub 2019 Jul 31.

11. Askoan VR, Kerl ME, Evans T, Harmon M. Organophosphate intoxication in 2 dogs from ingestion of cattle ear tags. J Vet Emerg Crit Care 2019;4:424-430.

12. Buchweitz JP, Mader D, Lehner AF. Bifenthrin fatality in a canine: A case report with postmortem concentrations. J Anal Toxicol 2019;43(1):72-78.

NOTE: When in doubt, all drug dosages should be confirmed and cross-referenced with a veterinary drug reference guide.

Spring Plants

When The Best Laid Plants Go Awry: Handling Common Spring Plant Exposures in Dogs and Cats

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As the shadows of winter give way to the sunrays of spring, we start to see whispers of green emerge from the earth. Then the dog gets let out, tramples them, rips them out of the ground, and eats them. Companion animal exposures to these plants are very common. A basic familiarity with the most common spring-blooming plants is a helpful tool for any veterinary medical professional[1-4]

It is worth noting that many plants are toxic, however, this does not necessarily mean an exposure is going to be life-threatening. When presented with a patient after a plant exposure, first take a thorough medical and exposure history, perform a physical examination, and then determine the actual risk for the patient before determining what treatments, if any, are indicated. Be sure the plant in question has been properly identified with its scientific name, as many different plants can share a common name, such as "lily." Assistance with plant identification can be found at community garden centers, poison control hotlines, and reputable social media groups. If the plant in question was part of a home or commercial landscape, then also determine if any fertilizers or pesticides were used alongside it. During the physical examination, be sure to look for evidence of pollen or other plant material on the haircoat, in the teeth, or in the vomitus.

Unfortunately, the question of "how much plant material is too much?" does not come with a standard answer. The answer to this question is complicated by many factors including the time of year, the part of the plant ingested, the health of the plant, the soil quality, the species of animal involved, and knowledge gaps in the scientific literature. If after taking a complete history and performing a physical examination, an accurate risk assessment cannot be determined, it is reasonable to perform decontamination (only if there is minimal risk of doing so) and then to monitor the patient closely for the development of clinical signs.

Plants that Target the Gastrointestinal System

Ornamental Bulbs and Rhizomes

Common ornamental bulbs and rhizomes include Crocus spp., Iris spp., *Hyacinthus* spp., *Tulipa* spp., *Narcissus* spp., *Clivia* spp., *Hippeastrum* spp., and *Galanthus nivalis*. These plants contain a variety of alkaloids that irritate the gastrointestinal tract. All parts of the plants are considered toxic, however, the highest concentration of alkaloids is within the bulb. Larger exposures to the toxic alkaloids (primarily bulb ingestion) can cause CNS signs such as depression, ataxia, and tremors. Seizures are rare but possible. Ingestion of the densely fibrous bulbs can also cause gastrointestinal obstruction in some patients. In most cases, signs will develop within a few hours. In healthy patients, exposures to plant foliage usually do not require decontamination. The risk is for mild to moderate vomiting, diarrhea, and lethargy. Patients can be monitored for signs and treated symptomatically with antiemetics, fluid therapy, and a bland diet. Exposures to plant bulbs are more likely to result in CNS signs or foreign body obstruction (FBO). In these cases, induction of emesis can be performed. If most or all of the plant material is recovered, then the patient can be given an antiemetic and monitored for ongoing signs. Activated charcoal administration is usually not needed, although if emesis is unsuccessful and bulb material was ingested it could be considered. More severe gastrointestinal signs may require IV fluid therapy, antacids, sucralfate, or exploratory laparotomy for suspected FBO. Mild tremors and seizures can be treated with benzodiazepines while more severe tremoring can be managed with methocarbamol.

Wisteria spp.

Wisteria spp. contain lectin (a glycoprotein) and wisterin (a glycoside) in all parts of the plant although they are concentrated in the seeds and pods. Ingestion of plant material will usually result in mild to severe gastroenteritis depending on the quantity and parts of plant material ingested. Patients that ingest foliage or flowers can usually be monitored for gastrointestinal signs and treated symptomatically if they develop. Patients that ingest the seed pods can have emesis induced and then be treated with an antiemetic. Rarely, patients may need hospitalized care with IV fluids, antacids, sucralfate, antidiarrheals, and nutritional support.

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Plants that target the Cardiovascular System

Rhododendron spp. and *Kalmia spp.*

The primary toxic components of these common ornamental plants are grayanotoxins. Grayanotoxins are found in all parts of the plant including the nectar, which means that honey derived from these plants can also be toxic. Grayanotoxins bind and slow down the opening and closing of sodium channels, resulting in more persistent depolarization. Thus, the excitable membranes of myocytes and neurons are most sensitive to these toxins. Affected patients will usually develop hypersalivation and/or vomiting within 30 minutes. Bradycardia, hypotension, lethargy, weakness, ataxia, disorientation or agitation, tremors, and dyspnea may occur within 6 hours. Signs may last 24 – 72 hours. Decontamination by induction of emesis and/or administration of activated charcoal is recommended if more than a mouthful of plant material is ingested. An antiemetic can be administered, and patients should then be monitored closely for development of further signs and treated symptomatically. If cardiovascular signs develop, the patient should be started on non-calcium-containing IV fluid therapy and serum potassium should be monitored as hypokalemia can exacerbate signs. Atropine can be given as needed for bradycardia. Benzodiazepines can be used for tremors or seizures (rare).

Helleborus spp. and *Convallaria spp.*

Hellebore are popular perennials that bloom in very early spring. They contain protoanemonin and saponins that serve to irritate the gastrointestinal mucosa. Vomiting, diarrhea, anorexia, and colic are common. More concerningly, these plants contain bufadienolides, which are digitalis-like glycosides (cardenolides).[5]

Convallaria spp. contain a vast array of potent cardenolides. Similar to *Helleborus spp*., initial signs are usually gastrointestinal in nature but can quickly progress to cardiovascular instability. For both *Helleborus spp.* and *Convallaria spp*., all parts of the plant are toxic, but the roots and rhizomes are the most toxic.[6]

Cardenolides inhibit the sodium-potassium-ATPase pump on cell membranes. This results in increased intracellular sodium. Excess sodium ions are exchanged for calcium via the sodium-calcium exchanger. The resultant increase in intracellular calcium slows conduction and increases contractility.[7] Patients typically develop bradyarrhythmias and hypotension. Hyperkalemia, tachyarrhythmias and ventricular fibrillation are also possible. Signs typically start within 24 hours of exposure although they may be delayed out to 3 days. GI signs are usually seen first. When appropriate, patients ingesting more than a mouthful of these plants can have emesis induced. An antiemetic can then be administered. If emesis is unsuccessful or only partially successful, a single dose of activated charcoal can be administered. Patients should be monitored for a minimum of 24 hours for the development of cardiovascular signs. For exposures to large amounts of plant material, continuous ECG monitoring is ideal. If cardiovascular signs develop, serum potassium levels should be monitored closely. The patient can be started on non-calcium-containing IV fluids. Atropine or

glycopyrrolate can be used for bradyarrhythmias. Ventricular arrhythmias can be treated with lidocaine or phenytoin. Insulin and dextrose are recommended for severe hyperkalemia. Refractory arrhythmias can be treated with digoxin immune Fab (Digibind®), a digoxin-specific antibody derived from immunized sheep, that works rapidly and can be life-saving in the most severe cases.[8]

Plants that target the Central Nervous System

Brunfelsia spp.

Brunfelsia spp. are common ornamental shrubs found in the southern United States. They contain several potent compounds that contribute to their toxicity. Most notably is brunfelsamidine, which causes tremors and seizures. Affected patients typically display vomiting, diarrhea, ataxia, tremors, and seizures. Cardiac arrhythmias are also possible.[10]

Patients may appear hyperesthetic, disoriented or agitated. Severely affected patients may suffer hyperthermia, DIC, rhabdomyolysis, and death. Any exposed patient should be evaluated and treated. Patients will show signs within 12 hours of exposure. Decontamination must be approached with caution, as neurologic patients are at increased risk of suffering complications such as aspiration pneumonia. If a large amount of plant material was ingested and the patient is already neurologic, intubation and administration of a single dose of activated charcoal with sorbitol via orogastric tube can be considered. Gastric lavage could also be attempted, but recovery of plant material may be limited. Serial water enemas every 6-8 hours may also help hasten the elimination of plant material. Tremors can be controlled with methocarbamol and seizures may be controlled with benzodiazepines, levetiracetam, or phenobarbital. The patient should be placed on an intravenous balanced crystalloid fluid and monitored closely for complications such as hyperthermia, rhabdomyolysis, acidosis, and DIC. Severe signs may last several days with minor tremors potentially continuing for several weeks.

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Plants that target the kidneys

Lilium spp. and *Hemerocallis spp.*

Although these plants typically won't bloom until summer in most climates, we do start to see *Lilium* spp. (particularly the Easter lily, *Lilium longiflorum*) in spring floral arrangements. Much of what makes these plants particularly toxic remains a mystery although the toxin appears to be water-soluble. Cats are the only species known to exhibit signs of toxicity. Clinical signs manifest initially as vomiting and lethargy. Within 48 hours, signs can progress to anorexia, polyuria, polydipsia, acute kidney injury, oliguria or anuria, and death. Any exposure, including dermal exposures to pollen, should be considered to put the patient at risk of AKI. If a large amount of plant material was ingested, then emesis can be induced. If there was a dermal exposure, then the patient should be bathed with mild dish soap. The patient should be then placed on a diuretic rate of an intravenous balanced crystalloid fluid for 48 hours. Renal function should be monitored closely, and any signs may be treated symptomatically. Patients that receive prompt fluid diuresis have an excellent prognosis.[12] Patients whose treatment is delayed or who develop oliguria have a poor prognosis.

1. Lieske CL. Spring-blooming bulbs: A year-round problem. In: Veterinary Medicine. August 2002: pp 580-588

2. Burrows GE and Tyrl RJ. Toxic Plants of North America 2nd ed. 2013. John Wiley & Sons Inc. pp 629

3. Burrows GE and Tyrl RJ. Toxic Plants of North America 2nd ed, 437, John Wiley & Sons Inc. 2013.

4. Manhart IO, DeClementi C, and Guenther CL. Mountain laurel toxicosis in a dog. Journal of Veterinary Emergency and Critical Care 23(1) 2013, pp 77-81

5. Burrows GE and Tyrl RJ. Toxic Plants of North America 2nd ed, 1014 John Wiley & Sons Inc. 2013.

6. Burrows GE and Tyrl RJ. Toxic Plants of North America 2nd ed, 763-764. John Wiley & Sons Inc. 2013.

7. Galey FD. "Cardiac Glycosides" In Clinical Veterinary Toxicology, edited by Konnie H Plumlee, 386-387. Mosby Inc, 2004.

8. Zoltani CK. "Cardiovascular Toxicity" In Veterinary Toxicology 3rd ed, Edited by Ramesh C. Gupta, 229. Elsevier Inc. 2018.

9. 9 Burrows GE and Tyrl RJ. Toxic Plants of North America 2nd ed, 1135. John Wiley & Sons Inc. 2013.

10. 10 Clipsham R. Brunfelisa australis (Yesterday, Today, And tomorrow Tree) and Solanum Poisoning in a Dog. J Am Anim Hosp Assoc 2012; 48:139-144

11. 1 Rumbeiha WK, Francis JA et al. A comprehensive study of Easter lily poisoning in cats. J Vet Diagn Invest 2004; 16:527-541

12. 2 Bennett AJ, Reineke EL. Outcome following gastrointestinal tract decontamination and intravenous fluid diuresis in cats with known lily ingestion: 25 cases (2001-2010). J Am.Vet Med Assoc 2013; 242:1110-1116.

Toxic Spring Plants Chart

Dangerous to animals if ingested

Convallaria spp.
Lily of the Valley

Crocus vernus
Spring Crocus

Galanthus nivalis
Snowdrop

Helleborus spp.
Hellebore, Lenten rose

Hemerocallis spp.
Day lily

Hippeastrum spp.
Fire lily

Hyacinthus spp.
Hyacinth

Iris vernus
Iris

Kalmia latifolia
Mountain laurel

Tulipa spp.
Tulip

Narcissus spp.
Daffodil, Paperwhite

Rhododendron spp.
Rhododendron, Azalea, Rosebay, Great laurel

Brunfelsia spp.
Yesterday Today and Tomorrow Plant, Kiss-me-quick, Lady of the Night, Morning-noon-night

Lilium spp.
Easter lily, Asiatic lily, Stargazer lily, Tiger lily, Casablanca lily

Decontamination

What Do I Need to Know About Activated Charcoal?

Justine Lee, DVM, DACVECC, DABT
Director of Medicine / Founder, VETgirl

Ah, activated charcoal (AC). The product veterinary technicians hate to give, understandably!

But, before you reach for that bottle of activated charcoal, what do you need to know?

First, before you administer activated charcoal, make sure to do the following:

1. Get an appropriate history
2. Triage the patient
3. Perform a thorough physical exam
4. Ask yourself if decontamination is appropriate*
5. Ask yourself if giving AC is appropriate

**For example, if the dog is already profusely vomiting, it's too late to induce emesis. If the product doesn't bind to charcoal, then it's not worth giving AC!*

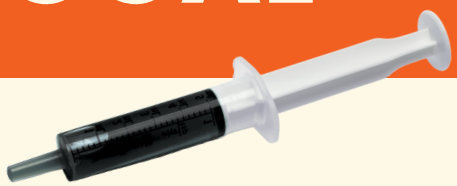
When should you NOT give activated charcoal (e.g., contraindications of activated charcoal)

Before administering AC and a cathartic, it is imperative to consider whether or not the patient has a contraindication for its administration. Activated charcoal should not be given to the poisoned patient when the toxicant does not reliably bind to AC. Examples of toxicants that do not absorb reliably to AC include:

- ethylene glycol
- alcohols (e.g., methanol, ethanol) sugar alcohols (e.g., xylitol)
- heavy metals
- hydrocarbons
- corrosive/causative substances
- things on the periodic table

Another contraindication for administering AC includes severe sedation, decreased gag reflex (who have an increased risk of aspiration pneumonia), or intestinal obstruction. Contraindications for administration of AC with a cathartic include

When should you use ACTIVATED CHARCOAL?



IS THE PET STABLE?

(Signs of instability include seizure, coma, depression, loss of gag reflex, risk for aspiration.)

YES

Will charcoal bind the toxin?

YES

Are signs expected to be life-threatening?

YES

Check hydration & serum sodium.

NORMAL

Give charcoal.

ABNORMAL

Treat dehydration, lower sodium. Once completed, reconsider if charcoal should be given.

NO

Treat clinical signs, consider treatment options, or antidote, if indicated.

NO

Treat clinical signs.

Scan the QR code for more information on activated charcoal.
aspcapro.org/poison

ASPCA™

For expert toxicology advice, contact the Animal Poison Control Center at **888.426.4435**

**A consultation fee may apply.*

hypernatremia, dehydration, and salt toxicosis (e.g., salt, ice melts, homemade play dough), as fluid loss through the intestinal tract can result in excessive free water loss and severe, secondary hypernatremia.

Other contraindications for AC include:

- endoscopy (which would obscure visualization)
- abdominal surgery of the GI tract
- gastric or intestinal obstruction
- gastrointestinal hemorrhage or perforation (due to pathology, caustic injury, etc.)
- recent surgery
- late-stage presentation with clinical signs already present
- dehydration
- lack of borborgymi/ileus
- hypernatremia
- hypovolemic shock
- compromised airway (risk for aspiration pneumonia)
- ingestion of a caustic substance or hydrocarbon (due to increased risk for aspiration pneumonia)
- unprotected airways that are at risk for aspiration pneumonia (e.g., a depressed state of consciousness, excessive sedation)*

** Ideally, protect the airway with an inflated endotracheal tube (ETT) if the patient is being gavaged.*

How and when should I give activated charcoal?

When administering AC, it should ideally be given within < 5 minutes of ingestion to be most effective. In veterinary medicine, this is almost impossible due to driving time (to the clinic), lapsed time since ingestion, time to triage, and the amount of

time it takes to physically deliver AC (e.g., syringe feeding, orogastric tube). As a result, administration of AC is often delayed for up to an hour or more. As time since ingestion is often unknown (e.g., pet owner coming home from work to find their pet poisoned), decontamination (including emesis and administration of AC) is often a relatively benign course of action, provided the patient is not already symptomatic.

Can I give activated charcoal even if the patient ingested the toxicant hours ago?

As always, when administering any drug, it is important that benefits outweigh the risks, and that complications be prevented when possible. In veterinary medicine, administration of AC with a cathartic as long as 6 hours out may still be beneficial with certain types of toxicosis.

When can you give activated charcoal in a delayed manner? In the following situations:

- If the product has delayed release [e.g., extended release (XR) or sustained release (SR)]
- If the product undergoes enterohepatic recirculation (see multi-dose AC below)
- If there are financial limitations that prevent hospitalization

Does human medicine give activated charcoal?

While human medicine has moved away from administration of AC with poisoned patients, the aggressive use of AC in veterinary medicine is still warranted, as this is often our last line of defense when it comes to adequately decontaminating our patients. Certain modalities of therapy—e.g., antidotes [such as fomepizole, pralidoxime chloride (2-PAM), digoxin-specific antibody fragments], plasmapheresis, hemodialysis, mechanical ventilation— along with financial limitations of pet owners, limit our ability to treat poisoned pets aggressively as compared to human medicine. As a result, the continued use of AC in veterinary medicine is still warranted as a first line of defense therapy.

What dose of activated charcoal should I use in my veterinary patients?

Current recommended dosing for single dose AC is 1–5 g of AC/kg with a cathartic (e.g., sorbitol) to promote transit time through the GI tract. I personally use lower than this – I start with 2 g/kg of AC for the first dose. If I'm giving multiple doses of AC (see below), I'll drop to 1 g/kg of AC for additional doses (and make sure to avoid the use of cathartics with the additional doses, to help minimize the risk of hypernaremia). I typically don't give more than 2-3 total doses of charcoal to a patient.

When should I reach for multiple doses of activated charcoal?

Human studies have found that multi-dose AC significantly decreases the serum half-life of certain drugs, including antidepressants, theophylline, digitoxin, and phenobarbital. While veterinary studies are lacking, there is likely an added benefit from using multi-dose AC, provided the patient is well hydrated and monitored appropriately. Certain situations or toxicities, including drugs that undergo enterohepatic recirculation; drugs that diffuse from the systemic circulation back into the intestinal tract down the concentration gradient; or ingestion of SR, XR, or long-acting (LA) release products will require multi-dose administration of AC. Keep in mind that when administering multiple doses of AC to a patient, the additional doses ideally should not contain a cathartic (e.g., sorbitol), due to increased risks for dehydration and secondary hypernatremia. Current recommended dosing for multiple doses of AC is 1–2 g of AC without a cathartic /kg of body weight, PO q 6 hours for 2-3 more doses.

When in doubt, contact the ASPCA Animal Poison Control Center (888) 426-4435 for more life-saving information!

References available upon request.

Decontamination

The Use of Cholestyramine for the Veterinary Poisoned Patient

Justine Lee, DVM, DACVECC, DABT
Director of Medicine / Founder, VETgirl

In this VETgirl online veterinary continuing education blog, we review the use of cholestyramine in the veterinary poisoned patient. If you contact the ASPCA Animal Poison Control Center (888) 426-4435, their veterinary toxicology staff may recommend cholestyramine as part of decontamination. But what exactly is it? Is it the same thing as activated charcoal and do I really need to get it?

Cholestyramine is a bile acid sequestrant and anti-lipemic agent. Cholestyramine works by combining with the bile acids in the intestines and forming an insoluble complex that is then excreted in the feces. This results in "partial removal of the bile acids from the enterohepatic circulation by preventing their absorption."

What toxicants should I use it for in the veterinary poisoned patient?

Cholestyramine is thought to help bind bile in the gut as an effective decontaminant method for certain toxicants such as:

- *Blue green algae (microcystins)*
- *Vitamin D (cholecalciferol)*
- *Anticoagulant rodenticides (although we'll rarely see these anymore, as they have been transitioned out by cholecalciferol and bromethalin in the United States)*
- *Beta blockers*
- *Dgitalis/digitoxin*
- *Certain NSAIDs (e.g., piroxicam, diclofenac, naproxen, ibuprofen)*
- *Phenobarbital*
- *Tetracyclines*
- *Methotrexate*
- *Phenytoin*
- *Sago palm (Cycad palm)*

The use of cholestyramine has recently been utilized more in veterinary decontamination. According to the ASPCA Animal Poison Control Center (APCC), it is thought to "decrease the body burden of vitamin D3" as cholecalciferol undergoes enterohepatic recirculation with bile acids. Note that the efficacy has not been well documented in clinical practice, however.

Where do I get it?

You can purchase cholestyramine from human pharmacies or even veterinary supply companies. It isn't very expensive, and if you're an emergency clinic or specialty clinic, you should have this in stock (IMO, specifically for Vitamin D3 toxicosis).

What's the dose in veterinary medicine?

Current recommended doses of cholestyramine from the ASPCA APCC are: 0.3–0.5 g/kg, dissolved in liquid and administered orally every 6–8 hours for 3–5 days, depending on the initial dose of cholecalciferol ingested. Other resources have a higher dose at: 0.3-1 g/kg TID X 4 days or 1-2 g/dog BID, 1 g/cat BID. Contraindications for the use of cholestyramine include patients with complete biliary obstruction and hypersensitivity to cholestyramine. With chronic administration, Vitamin K1 should be supplemented to prevent secondary depletion.

When in doubt, contact the ASPCA Animal Poison Control Center (888) 426-4435 for more life-saving information!

References available upon request.

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PODCASTS

- Intravenous Lipid Emulsion Therapy for the Management of Toxicities in Dogs and Cats
- Tartaric acid as the proposed toxic principle in grapes and raisins
- Dexmedetomidine versus xylazine as an emetic in cats
- Intravenous Lipid Emulsion with Lidocaine Toxicity in Cats
- Toxicology mistakes to avoid in your poisoned patients!
- Intravenous lipid emulsion (ILE) with ivermectin toxicity in dogs : Getting the skinny on using fat!

BLOGS

- Intravenous Lipid Emulsion Therapy for the Management of Toxicities in Dogs and Cats
- How to Treat Cocaine Toxicity in Dogs
- Baclofen toxicity in dogs and cats
- NSAID toxicity in dogs and cats
- Can I use hydrogen peroxide in the canine poisoned patient?
- The use of cholestyramine for the veterinary poisoned patient
- Marijuana toxicity in dogs: Part 1
- Marijuana toxicity in dogs: Part 2
- Learning with veterinary toxicologist, Dr. Tina Wismer ...
- 5-FU toxicosis in a dog
- Top 5 poisons to induce emesis in the veterinary poisoned patient
- Grape and raisin toxicity
- Activated charcoal: To give or not to give?

WEBINARS/ VIDEOS

- All You Need to Know About Veterinary Antidotes
- Top Poisons That Kill
- ILE Therapy in Baclofen Toxicity
- How to perform gastric lavage
- Top 10 Human Medications Poisonous to Dogs and Cats
- Large Animals and Toxic Plants – Which are problems?
- Top 5 Emergencies You Will See in the ER - Part 1
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Antidotes

Antidotes in Veterinary Medicine

Justine Lee, DVM, DACVECC, DABT
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In the poisoned veterinary patient, treatment should be aimed at decontamination and symptomatic supportive care. If an antidote is available, it should be promptly initiated if available, safe, and financially feasible.[1] An antidote is defined as "any compound that is used to counteract the effects of a toxicant."[2] The goal of an antidote is to interfere with the ADME of a toxicant and eliminate or reduce the adverse effects of the toxicant.[2] Antidotes can be classified into several board categories,[3,4] based on the mechanism by which they work or are protective. These include the following:

- Chemical antidotes
- Functional antidotes
- Pharmacological or physiological antidotes

Unfortunately, in veterinary medicine, there is "little economic incentive for pharmaceutical companies to seek approval for antidotal medications with only a small projected market;"[1] hence, there is a paucity of antidotes available. The use of antidotes is generally considered extra-label in veterinary medicine [Animal Medicinal Drug Use Act (AMDUCA) of 1994],[5,6] and pet owners should be made aware of this. As there are thousands of "antidotes" out there, this lecture will only focus on the most common or important 10-12 used in veterinary medicine. When in doubt, the ASPCA Animal Poison Control Center should be consulted as needed.

CHEMICAL ANTIDOTES

Chemical antidotes work directly on the toxicant;[3,4] these specific antidotes bind to the toxicant to "yield an innocuous compound that is excreted from the body."[3] Chemical antidotes work by affecting how the toxicant works or interacts directly with the compound.[2] Chemical antidotes can either "decrease the toxicity of the agent or increase its excretion"[1] and work by binding with the toxicant to product a non-harmful compound that is then later excreted by the body.[3] Examples of chemical antidotes include antivenins, chelating agents and immunologic agents such as F(ab') fragments [e.g., digoxin-specific F(ab') fragments].

Antivenins

Antivenins work by neutralizing venom antigens via passive immunization with venom antigen-specific immunoglobulins (from horse, sheep) that have been hyper-immunized with the

venom(s) of a given species.[7] The use of antidote therapy can be considered with venomous snake and black widow spider bites to help prevent or help treat coagulopathy, paralysis, and thrombocytopenia;[3,8] however, they will not help with tissue necrosis.[3] Depending on the type, certain antivenins may be difficult to secure or find. The National Animal Poison Control Center (888-426-4435) or any Regional Poison Control Center (800-222-1222) may have additional resources that can enable the location of an appropriate antivenom.

There are **three USDA-approved veterinary antivenins** available against North American pit vipers including the following types:

- Antivenin (Crotalidae) Polyvalent (Equine origin) (ACP); lyophilized IgG preparation; (Antivenin™; Boehringer Ingelheim Vetmedica, Inc., St. Joseph, MO); canine indication.
- Antivenin Crotalidae Polyvalent (Equine origin); liquid plasma preparation; (Rattler Antivenin™; Mg Biologics, Ames, IA); canine and equine indication.**
- Antivenin Polyvalent Crotalidae (F(ab')2 (Equine origin); liquid injectable preparation; (VenomVet™; MT Venom, LLC, Canoga Park, CA); use indication species not specified.

There are **two FDA-approved human antivenin** products:

- Antivenin (Crotalidae) Polyvalent Immune Fab (Ovine origin); lyophilized preparation; (CroFab®; BTG International, West Conshohocken, PA)
- Crotalidae Immune F(ab')2 (Equine origin); lyophilized preparation; (Anavip®; Rare Disease Therapeutics, Inc., Franklin, TN)

The benefit of using an antivenin that contains F(ab) components of the immunoglobulin molecule is that it has lower risk of allergic reaction and allows for faster reconstitution and has a greater volume of distribution. However, its use is off label since it is for humans, and it is expensive, and the risks of administration may outweigh the potential benefits.

Continued on page 44

The use of IV antivenin should be considered early in the treatment of envenomation (ideally within 6 hours).[3,7,8] Depending on the type of antivenin used, several vials may be necessary, which can be cost-prohibitive. The patient should be monitored carefully during administration of antivenins, as serum sickness, anaphylactic, or anaphylactoid reactions can occur, particularly if the patient has received antivenin previously.

Immunologic agents/ Fab (Digibind, DigiFab)

The use of digoxin immune Fab fragments can be used for life-threatening cardiac glycoside toxicosis (e.g., cardiac glycoside-containing plants, digoxin, Bufo toad); however, its use is typically limited to life-threatening cardiac arrhythmias where traditional antiarrhythmic therapy has failed. ds-Fab moieties work by "binding free digitalis glycoside molecules in the extracellular fluid as well as those already bound to sodium-potassium ATPase."[9] It has been reported to successfully treat toxicosis and is commercially available as 2 ds-Fab products: DigiFab (Protherics, Inc., Nashville, TN, USA) and Digibind (GlaxoSmithKline, Parma, Italy]. Antidigitoxin Fab fragments have a higher affinity for digoxin.4 Each bottle of Digibind contains 38 mg of Fab, which will bind to 0.6 mg of digoxin or digitoxin.[4] Each vial of DigiFab contains 40 mg of Fab, which will bind approximately 0.5 mg digoxin.[10] The FDA information for DigiFab is available here.

Digoxin immune Fab fragments may be cost prohibitive ($500/bottle) and can be obtained from a human hospital. Little evidence or animal studies have been used to establish the veterinary dose; however, published doses include:[3,4,9]

- If the serum digoxin level is available, the number of vials should be based on the serum digoxin level (ng/mL) X body weight (in kilograms)/100.

Unfortunately, in the veterinary patient, it is rare to obtain a timely serum digoxin concentration. For this reason, the general recommendation is to administer 1-2 vials (slowly over 30 minutes, using a 0.22-micron filter if possible) and reassess the patient.[3,4]

Enzyme inhibitors

Fomepizole (also known as 4-MP), is a competitive inhibitor of alcohol dehydrogenase. It is preferred over ethanol in dogs as it does not result in CNS depression, diuresis, and hyperosmolality. In cats, it is the antidote of choice if used within 3 hours, as the survival with ethanol is much worse in comparison to fomepizole. While expensive, it is lifesaving when administered to dogs within the first 8-12 hours of ingestion; some sources say that it can be effective as late as 36-hours post-exposure.[11-13] In cats, the antidote must be administered within 3 hours of ingestion to be effective.[3,4,11] Dosing for 4-MP is significantly different between dogs and cats:

- Dogs: 4-MP 20 mg/kg, IV, first dose (over 15-30 minutes); 15 mg/kg at 12 hours; 15 mg/kg at 24 hours; 5 mg/kg at 36 hours. 5 mg/kg IV can be given every 12 hours until the EG test is negative.
- Cats: 4-MP 125 mg/kg, IV, first dose; 31.25 mg/kg IV at 12 hours; 31.25 mg/kg IV at 24 hours; 31.25 mg/kg at 36 hours.

PHARMACOLOGICAL ANTIDOTES

Pharmacological antidotes (often called physiological antidotes) work by directly antagonizing the toxicant.[3,4] These types of antidotes work by directly working on the receptor site, by preventing formation of toxic metabolites, by restoring normal physiological function, or by assisting with more rapid elimination of the toxicant from the body.[1,3,4] Examples include reversal agents (e.g., naloxone for opioids, atipamezole for alpha-adrenergic agonists, flumazenil for benzodiazepines), n-acetylcysteine (e.g., acetaminophen), pralidoxime for OP toxicosis, etc.

- **Atipamezole** is an alpha-adrenergic antagonist that reverses medetomidine and dexmedetomidine. It can be used off-label to also reverse other drugs such as xylazine, clonidine, bromonidine, tizanidine, and amitraz.4 It has a very short half-life (e.g., 2-3 hours) and may need to be re-dosed if necessary.
- **Atropine** is an anticholinergic that competes with acetylcholine at the post-ganglionic parasympathetic sites (and hence is called an antiparasympathetic or parasympatholytic drug).[4,7] It is also called an antimuscarinic as it antagonizes the muscarine-like actions of AcH.[4,7] It is used for the treatment of SLUDGE signs from organophosphate or carbamate toxicity. With OP toxicosis, atropine should be given despite the tachycardiac; higher doses are often necessary.
- **Ethanol** can be used as an antidote for ethylene glycol toxicosis, if fomepizole is not available. Ethanol competes with alcohol dehydrogenase, thereby preventing metabolism of ethylene glycol into its more toxic metabolites. Only clear ethanol should be used (e.g., grain alcohol, vodka).
  - A 7% of ethanol is made by removing 175 ml from a 1L bag of saline and adding 175 ml of an 80-proof vodka. If 190 proof grain alcohol is available, a 7% solution can be made by removing 74 ml from a 1L bag of saline and adding 74 ml of the grain alcohol.
  - Dose: loading dose of 8.6 ml/kg (600 mg/kg) 7% ethanol slow IV then continue with a CRI of 1.43 ml/kg/hr (100 mg/kg/hour), IV as a CRI for 24-36 hours.

Continued on page 46

- **Flumazenil** (Romazicon™) is the reversal agent for benzodiazepine overdoses as it competitively antagonizes the benzodiazepine receptor site. It is an imidazobenzodiazepine derivative that rapidly displaces benzodiazepines from the receptor, reversing its effect within minutes.[4] It is very short-acting (e.g., 1-2 hours) and can be expensive. The author generally only uses this for severe respiratory depression or marked CNS signs.
- **N-acetylcysteine** (NAC) is the primary antidote for the treatment of acetaminophen/paracetamol toxicosis. NAC provides an available source of intracellular glutathione, and also is thought to have additional hepatoprotective effects including anti-inflammatory activity, enhanced mitochondrial energy metabolism, and improved oxygen delivery with liver injury.[14,15] Specifically with acetaminophen, toxicosis occurs when glucuronidation and sulfation pathways are depleted; this results in toxic metabolites building up and secondary oxidative injury occurring.[14,15] With acetaminophen toxicosis, NAC is used to limit the formation of the toxic metabolite NAPQI by providing additional glutathione substrate. While NAC can be safely used as a hepatoprotecant with hepatotoxicants, there is a paucity of veterinary literature on the outcome with its use. That said, it is considered benign and safe. When dosing, the author recommends parenteral administration to allow for continued administration of activated charcoal (as some limited enterohepatic recirculation occurs with acetaminophen toxicosis). When administering NAC by any route, it must be diluted, as it is corrosive or irritating. If NAC is not available, S-adenosyl-methionine (SAMe) can be also given as a glutathione source with any hepatotoxicant.[14-17]
- **Naloxone** is a pure opioid antagonist and can be used for the reversal of opioid overdose. It has a rapid onset of action (1-5 minutes) but short duration of action (1.5 hours).[3] Repeated doses are often necessary. It will not reverse respiratory depression from buprenorphine; much higher doses are often necessary to reverse buprenorphine.

FUNCTIONAL ANTIDOTES

- **Functional antidotes** lessen the severity of the clinical signs of the toxicant. Functional antidotes do not directly interact with the toxicant itself. An example of functional antidotes includes cyproheptadine (e.g., serotonin syndrome), calcitonin (e.g., hypercalcemia), bisphosphates (hypercalcemia), intravenous lipid emulsion (ILE) (e.g., fat soluble toxicant exposure), and methocarbamol (e.g., toxicants resulting in tremors).
- **Bisphosphates** (e.g., pamidronate) are used as an antidote for hypercalcemia secondary to cholecalciferol toxicosis. It lowers calcium levels by binding to hydroxyapatite crystals within the bone. Bisphosphates impede osteoclast activity and induce osteoclast apoptosis.[7] As it is now generic, it is much more cost effective and readily available. Calcium levels should be monitored every 12- hours; if persistent hypercalcemia is evident, additional dosing can be used 3-7 days after the initial dose. Calcitonin can

also be considered. It is preferred by some toxicologists over the use of calcitonin as it has longer lasting effects.[4]

- **Calcitonin** can be used to treat hypercalcemia secondary to cholecalciferol toxicosis. It is an osteoclast inhibiting hormone that acts directly on bone by inhibiting osteoclastic bone resorption.[7] Calcitonin also reduces tubular reabsorption of calcium (along with phosphate, potassium, sodium, magnesium, and chloride), and promote renal excretion.[7] It must be given parenterally, as it is destroyed in the gut after oral administration.[7] It can be used when a bisphosphate is not readily available or in conjunction with treatment.
- **Cyproheptadine** (Periactin™) is a serotonin antagonist and antihistamine (H1 blocker). Cyproheptadine competes with histamine for sites on H1-receptor sites. Formerly used as an appetite stimulant in cats, it is now used to treat serotonin syndrome (e.g., agitation, hyperesthesia, tremors, seizures) secondary to SSRI antidepressant and amphetamine toxicosis.
- **Intravenous lipid emulsion** (ILE) For more information on ILE, please see an appropriate veterinary reference book for more information.
- **S-adenosyl-methionine** (SAMe) acts as a methyl donor, while also donating an aminopropyl group to be a source of polyamines.[7] SAMe also generates sulfur containing compounds necessary for conjugation reactions used in detoxification within the liver and as a precursor for glutathione.[7] Exogenous SAMe

increases liver and RBC glutathione levels and/or prevents its depletion.[7] It is also an inhibitor of apoptosis within the hepatocyte. It should be given on an empty stomach, as the presence of food can significantly reduce the amount absorbed. It is commonly used as a benign, safe hepatoprotectant with toxicants such as Amanita spp. poisoning, blue-green algae, xylitol, acetaminophen, etc.[14-17]

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Limitations of antidotes

There are several limitations of the use of antidotes in veterinary medicine. Unfortunately, some are cost prohibitive, including 4-MP (e.g., fomepizole), which is currently several thousand per bottle (unless compounded). Likewise, F(ab') crotalid antivenin therapy can cost close to $1,000/bottle. Certain antidotes have limited to no availability; the antidote for botulism (antitoxin) is only available through the Centers for Disease Control and Prevention (CDC). Lastly, keep in mind that the cost versus benefit analysis must be considered for the patient. Adverse effects can rarely be seen with antidotes and can result in rare but potentially deadly complications. The pet owner should be made aware of the extra label use – along with the rare complications – that can occur with the use of antidotes in the veterinary patient.

Conclusion

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. Keep in mind that as very few toxicants have a readily available antidote, treatment should always be aimed at symptomatic supportive care. When in doubt, if the veterinary professional is unaware of how to treat a specific toxicant, the ASPCA Animal Poison Control Center should be consulted for life-saving care.

References

1. DeClementi C. Prevention and treatment of poisoning. In: Gupta RC, ed. Veterinary Toxicology: Basic and Clinical Principles, 1st ed. New York: Academic Press, 2007:1139-1158

2. Gwaltney-Brant SM, Lee JA, Fernandez AF. Drugs used to treat toxicosis. Kirk & Bonagura's Current Veterinary Therapy XVI, 2019. Pending publication.

3. Hovda LH. Antidotes and other useful drugs. In: Hovda L, Brutlag A, Poppenga R, Peterson K, eds. Blackwell's Five-Minute Veterinary Consult Clinical Companion: Small Animal Toxicology, 2nd ed Iowa City Wiley-Blackwell, 2016, pp. 36-48.

4. Gwaltney-Brandt S. Newer antidotal therapies. CVC, 2010. Accessed http://veterinarycalendar.dvm360.com/newer-antidotal-therapies-proceedings-0?id=&sk=&date=&pageID=3

5. Bright SJ, Post LO: Veterinary antidotes and availability: an update, Center for Veterinary Medicine, US Food and Drug Administration. Available at: http://www.abvt.org/public/docs/antidoteupdate08.pdf, 2008. Accessed Jan 15, 2018.

6. American Board of Veterinary Toxicology: Review of veterinary antidotes. Available at: http://www.abvt.org/public/docs/reviewofveterinaryantidotes.pdf. Accessed Jan 15, 2018.

7. Peterson, M. Snake Envenomation in Small Animal Critical Care Medicine by Silverstein, D.C. and Hopper, K. Saunebar Inc. 2009, pg. 399-404.

8. Plumb's Veterinary Drug Handbook, 7th edition. Wiley-Blackwell, 2011.

9. Pao-Franco A, Hammond TN, Weatherton LK, et al. Successful use of digoxin-specific immune Fab in the treatment of severe Nerium oleander toxicosis in a dog. J Vet Emerg Crit 2017;27(5):596-604.

10. FDA, DigiFab label. Accessed https://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/FractionatedPlasmaProducts/ucm117624.pdf

11. Connally HE, Hamar DW, Thrall MA. Inhibition of canine and feline alcohol dehydrogenase activity by fomepizole. Am J Vet Res 2000;61:450-455.

12. Connally HE, Thrall MA, Forney SD, et al. Safety and efficacy of 4-methylpyrazole for treatment of suspected or confirmed ethylene glycol intoxication in dogs: 107 cases (1983-1993). J Am Vet Med Assoc 1996;209(11):1880-18803.

13. Grauer GF, Thrall MA, Henre BA, et al. Comparison of the effects of ethanol and 4-methylpyrazole on the pharmacokinetics and toxicity of ethylene glycol in the dog. Toxicol Lett 1987;35(2-3):307-314.

14. Johnson SE. Updates on hepatoprotective therapies. Proceedings, CVC, Accessed: http://veterinarycalendar.dvm360.com/update-hepatoprotective-therapies-proceedings?id=&sk=&date=&pageID=2

15. Babski DM, Koenig A. Acetaminophen. In: Osweiler G, Hovda L, Brutlag A, Lee JA, eds. Blackwell's Five-Minute Veterinary Consult Clinical Companion: Small Animal Toxicology, 1st Ed. Iowa City: Wiley-Blackwell, 2010, pp. 687-695.

16. Webb CB, Twedt DC, Fettman MJ, et al. S-adenosylmethionine (SAMe) in a feline acetaminophen model of oxidative injury. J Feline Med Surg 2003;5(2):69-75.

17. Wallace KP, Center SA, Hickford FH, et al. S-adenosyl-L-methionine (SAMe) for the treatment of acetaminophen toxicity in a dog. J Am Anim Hosp Assoc 2002;38(3):246-54.=

Footnotes

a. Personal communication, the ASPCA Animal Poison Control Center

b. Loftin E. Toxicities in the ER. Available at: https://www.dovelewis.org/pdf/events/Erika_toxins.pdf.

Abbreviations

ADME = absorption, distribution, metabolism and excretion

VETgirl NEPHROTOXICANT TABLE

TOXIN	SOURCE	MECHANISM OF ACTION	CLINICAL SIGNS
Cholecalciferol/ Vitamin D_3 Products	Rodenticides OTC or Prescription Vitamin D_3 Psoriasis creams (calcipotriene) e.g. Dovonex®, Calcitrene®, Sorilux®	Hypercalcemia: Vitamin D precursor of activated Vit D_3 leading to calcium reabsorption from kidneys, bone and GI tract	Signs result from hypercalcemia: depression, lethargy, weakness, anore vomiting, malaise, hematemesis, PU/P uremic halitosis, constipation, melena dehydration AKI usually 2-3d post-exposure due to soft tissue mineralization of renal tubu
Ethylene Glycol (EG)	Antifreeze (95% EG), Windshield de-icing agents, motor oils, hydraulic brake fluid, developer solutions, paints, some industrial solvents	Alcohol dehydrogenase (ADH) converts EG to glycoaldehyde and organic acids (glycolic acid and oxalic acid) –> calcium oxalate crystalluria –> AKI	**Stage 1 (0.5-12h):** Signs similar to alcohol poisoning – ataxia, hypersalivation, nausea, vomiti seizures, PU/PD, metabolic acidosis **Stage 2 (12-24h):** Signs seem to “resolve” from Stage 1 but severe internal injury – dehydratio tachycardia and tachypnea **Stage 3** **(12-24h in CATS and 36-72h in DOGS** Severe AKI, severe anorexia, lethargy, hypersalivation, uremic halitosis, coma depression, vomiting and seizures

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	CLIN PATH FINDINGS	TOX TEST	TREATMENT	PROGNOSIS
exia, PD, , o ules	Hypercalcemia Hyperphosphatemia Azotemia Metabolic acidosis	Serum parathyroid hormone (iPTH) – will be suppressed and low Total Ca^{++} and iCa^{++}– elevated $25(OH)D_3$ and $1,25(OH)_2D_3$ levels elevated	If no hypercalcemia, conservative treatment but aggressive decontamination: • emesis • activated charcoal • cholestyramine Limited fluid therapy Clinpath monitoring q24h x 2-3d: • SDMA • BUN/creatinine • Ca/Phosphorous • iCa^{++} If hypercalcemia present, then calciuresis tx: • hospitalization • IV fluids (0.9% NaCl) • furosemide • prednisone • zoledronic acid • calcitonin (hard to find) • pamidronate	**>0.1-0.5 mg/kg** can result in clinical signs and hypercalcemia, respectively LD_{50} 85 mg/kg (dog) Minimum acute toxic dose in dogs of calcipotriene is 37 µg/kg BW
ing, on, **S):** , a,	High osmolal gap seen as early as 1 hour after ingestion High anion gap and normochloremic acidosis w/in 3 hours of ingestion Chemistry changes: • low iCa^{++} • hypoglycemia • hyperphosphatemia • azotemia Calcium monohydrate crystals in the urine may present as early as 3-6 hours from ingestion and is considered "diagnostic"	EG or metabolites are only accurate within 24h of ingestion Cats can have false negative results Rare false positives for EG with propylene glycol, sorbitol, mannitol, alcohol, etc. Woods lamp on vomitus, paws, mouth as many products will fluoresce	**Fomepizole (4-MP antidote)** is the therapy of choice in which EG ingestion is suggested, and data supports use of higher doses of fomepizole in cats suspected of ingestion DOGS: 4-MP – 20 mg/kg IV 1st dose; 15 mg/kg at 12h; 15 mg/kg at 24h; 5 mg/kg at 36h CATS: 4-MP – 125 mg/kg IV 1st dose; 31.25 mg/kg at 12h; 31.25 mg/kg at 24h; 31.25 mg/kg IV at 36h 7% ethanol solution can be used if 4-MP unavailable (remove 175mls from 1L bag of saline and add 175ml of 80-proof vodka OR remove 74mls from 1L bag of saline and add 74mls of 190-proof grain alcohol) – use only "clear" alcohols • loading dose 8.6 ml/kg (600 mg/kg) 7% ethanol slowly IV • follow with CRI of 1.43 ml/kg/hr (100 mg/kg/hr) IV for 24-36h	• Excellent - dogs treated by 5 hours following ingestion • Good - cats treated by 3 hours following ingestion • Grave without hemodialysis – azotemic patients The minimum lethal dose of undiluted EG is 4.2 - 6.6 ml/kg in the dog and 1.5 ml/kg in the cat. DOGS: 4.4 ml/kg –> AKI CATS: 1.4 ml/kg –> AKI

VETgirl NEPHROTOXICANT TABLE

TOXIN	SOURCE	MECHANISM OF ACTION	CLINICAL SIGNS	CLIN PATH FINDI
NSAIDs	Cats and certain dog breeds (e.g. German Shepherds anecdotally) are more sensitive and need to GI signs secondary to GI ulceration (vomiting, diarrhea, melena, hematemesis, etc.) is more comm			
	Ibuprofen (Advil®, Bufren®, certain types of Motrin®)	Competitive inhibition of prostaglandin (PG) synthesis –> mostly GI and AKI	Anorexia, vomiting, hematemesis, diarrhea, melena, abdominal pain, lethargy, malaise, uremic halitosis, GI ulceration dehydration, renal effects, CNS effects	Anemia Azotemia Liver changes possible based or dose and type of NSAID
	Carprofen (Rimadyl®)	Competitive inhibition of PG synthesis –> mostly GI and renal effects, reported liver effects as well		
	Deracoxib (Deramaxx®)	Competitive inhibition of PG synthesis –> mostly GI and renal effects		
	Firocoxib (Previcox®)	Competitive inhibition of PG synthesis –> mostly GI and renal effects		
	Naproxen sodium (Aleve®, certain types of Motrin®, Buproxen®, Naprofex®)	Competitive inhibition of PG synthesis –> mostly GI and renal effects		

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NGS	TOX TEST	TREATMENT	PROGNOSIS
o be treated aggressively. With cats, severe AKI is more commonly seen clinically and with dogs, only seen initially, followed by secondary AKI.			
n	N/A	• GI decontamination • Activated charcoal – multiple doses • IV fluid therapy for diuresis • GI protectants 7-10 days Chemistry – Baseline, then as needed up to 48 hours	DOG DOSES: **16-50 mg/kg** – GI signs **50-100 mg/kg** – severe GI signs **100-250 mg/kg** - GI and renal **>300 mg/kg** – fatalities **>400 mg/kg** – CNS signs (coma, ataxia, seizures) CATS DOSES: **>5 mg/kg** – GI signs **>20 mg/kg** - renal **>200 mg/kg** – CNS signs
		• GI decontamination • Activated charcoal – multiple doses • IV fluid therapy for diuresis • GI protectants 7-10 days Chemistry – Baseline, then as needed up to 48 hours	DOG DOSES: **Any dose** – vomiting **>20 mg/kg** – GI signs **>40 mg/kg** – renal CATS DOSES: **>4.4 mg/kg**
		• Emesis and activated charcoal X 1 (binds well to charcoal) • IV fluid therapy for diuresis • GI protectants 7-10 days Chemistry – Baseline, then as needed up to 48 hours	DOG DOSES: **>15 mg/kg** – GI issues **>30 mg/kg** – potential renal
		Tablets rapidly dissolve, emesis may not be helpful unless ingestion was very recent • Single dose of activated charcoal • IV fluid therapy for diuresis • GI protectants 7-10 days Chemistry – Baseline, then as needed up to 48 hours	DOG DOSES: **>25 mg/kg** – vomiting, GI ulcers **>50 mg/kg** – renal
		Decontaminate: • activated charcoal – multiple doses T½ (dog) is 74 hours, as the drug undergoes extensive enterohepatic recirculation Due to the prolonged half life, fluids need to be continued for at least 72 hours GI protectants for 7-14 days Recommend monitoring electrolytes, especially sodium	DOG DOSES: **>5 mg/kg/day for 7 days** – ulcerative gastritis **>10 – 25 mg/kg** - renal

VETgirl NEPHROTOXICANT TABLE

TOXIN	SOURCE	MECHANISM OF ACTION	CLINICAL SIGNS
Grapes and Raisins	*Vitis spp.* **NOT** grapeseed extract	Active ingredient, tartaric acid, was discovered by ASPCA APCC as primary causative agent. Dogs are more sensitive as they do not excrete organic acids well. Thompson seedless grapes (most common green grocery grape) Ripe = 2.05 g/L of tartaric acid Red globe grapes Ripe = 1.28 g/L of tartaric acid Cotton candy grapes Ripe = 3.3 g/L of tartaric acid	Vomiting, inappetence, diarrhea, letha anorexia, abdominal pain, uremic bre and subsequent oliguria and anuria (48-72h post-ingestion)
True Lilies	*Lilium spp.* (Easter lily, stargazer lily, tiger lily and other Asiatic hybrid lilies) *Hemerocallis spp.* (some species of day lilies) Peace, Peruvian, Calla lilies, lily of the valley are not "true" lilies are therefore, not nephrotoxic	CATS only Ingestion of leaves, petals, pollen or vase water	Vomiting, depression, anorexia Anuric AKI in 1-3d

NOTE: When in doubt, all drug dosages and treatment advice should be confirmed and cross-referenced with a r
When in doubt, the ASPCA Animal Poison Control Center at (888) 426-4435 should be consulted as needed.

Abbreviations: AC: Activated charcoal; AKI: Acute kidney injury; BW: blood work; CNS: central nervous system; G

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	CLIN PATH FINDINGS	TOX TEST	TREATMENT	PROGNOSIS
argy, ath,	Clinpath changes consistent w/ AKI: • hypercalcemia and hyperphosphatemia initially • azotemia may develop in 24h	N/A	Aggressive gastrointestinal decontamination: • emesis induction (even delayed several hours post-ingestion) • Decontaminate if more than 1 grape or raisin/10 lb (5 kg) of dog, or 2 raisins/10 lb (5 kg) if cooked (cookies, bread, bagels) Aggressive IV fluid therapy for up to 72h post-ingestion Anti-emetics BP and UOP monitoring Serial BW monitoring (q12-24h) Asymptomatic patients monitor BW q24h then 48-72h post-ingestion Hemodialysis or peritoneal dialysis in severe cases	• Excellent – no signs of AKI • Fair to poor – with AKI
	Severe azotemia Urinalysis: • epithelial casts (12-18h post ingestion) • proteinuria • glucosuria	N/A	Aggressive decontamination: • emesis • activated charcoal X 1 GI support: • antiemetics • H_2 blockers or proton pump inhibitors if azotemic IV fluid therapy Clin path monitoring q24h x 2-3d UOP monitoring for 48h Hemodialysis if anuric Symptomatic & supportive care	• Fair to good, if tx is early and aggressive • Grave, if anuric or oliguric kidney injury

reference guide such as *Plumb's Veterinary Drug Handbook* or a veterinary toxicology resource.

GI: gastrointestinal; OTC: over-the-counter; UOP: urine output

VETgirl HEPATOTOXICANT TABLE

TOXIN	SOURCE	MECHANISM OF ACTION	CLINICAL SIGNS
Mothballs	Paradichlorobenzene (PDB) *(NOTE: Make sure to differentiate from naphthalene)*	Organochlorine insecticide	Vomiting, abdominal pain, tremors, seizures, and liver and kidney dama
NSAIDs	Human NSAIDs Veterinary NSAIDs	Inhibit PG synthesis → mostly GI and renal effects, reported liver effects as well (chronic)	DOG DOSES: > 20 mg/kg: vomiting, GI ulcers > 40 mg/kg: renal toxicity Idiosyncratic liver toxicity (1.4 cases of 10,000)
Acetaminophen (APAP)	Analgesic and antipyretic derived from paracetamol *(Note: Not an NSAID)*	Metabolized to NAPQI, binds to macromolecules and causes lipid peroxidation of membranes; induces direct cell injury and death leading to hepatic necrosis Oxidative damage in cats, resulting in metHb, Heinz body formation	DOG: GI signs, CNS depression, hepatotoxicity (icterus, coagulopath metHb can occur but not as commo as cats at at higher doses (cyanosis dyspnea) CAT: Respiratory distress, hypoxemia, cyanosis, edema of face and paws
Xylitol	Sweetener in sugar-free products, such as chewing gum and baking products	Induces hypoglycemia by stimulating insulin secretion from the pancreas of dogs Hepatic necrosis thought to be from decrease ATP production (xylitol uses pentose phosphate pathway instead of TCA [Kreb's] cycle	Clinical signs develop in as short a t as 30 to 60 minutes Weakness, ataxia, collapse, and seizures from hypoglycemia may las 12 to 24 hours, perhaps caused by t slow xylitol release from the ingeste formulations and its absorption Liver injury (within 24 hours), includi signs of melena, hepatic encelopath hemorrhage

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	CLIN PATH	TOX TEST	TREATMENT	PROGNOSIS
	Hemolytic anemia Hemolysis Methemoglobinemia (rare in dogs and cats; reported in humans)		• Prompt GI decontamination • Fluid administration to induce diuresis • Symptomatic response to adverse signs • Supportive care of vital functions • Seizure control with parenteral benzodiazepines	Organochlorine insecticide with an LD_{50} of approximately 500 mg/kg
	↑↑↑ ALT GI and AKI related findings: • anemia • hypoproteinemia • azotemia • hyperphosphatemia, etc.		• Immediate discontinuation • Treatment for hepatic failure • Hepatoprotectants (SAMe or NAC)	DOG DOSES: Hepatotoxicity, when observed, typically develops with **chronic** dosing (e.g., 5-30 days of chronic use; median 19 days)
	↑↑ LES (AST thought to be most sensitive) MetHb, Heinz bodies, chocolate-brown appearance to blood	Plasma, urine or tissue	NAC replenishes glutathione, provides sulfur and will directly bind NAPQI Others: • Vitamin C • SAMe • IV Fluids Methylene blue has been described, but not recommended, especially in the cat (due to Heinz body formation)	DOGS: 100 mg/kg hepatotoxicity; 200 mg/kg methemoglobinemia CATS/FERRETS: 10 mg/kg methemoglobinemia KCS can occur in dogs after even therapeutic doses
	Hypoglycemia, ↑↑ LES, DIC, coagulopathy		• Stat BG and treatment for hypoglycemia; emesis if recent ingestion and normoglycemic • Activated charcoal not indicated • Fluid support and glucose support (dextrose can correct hypoglycemia and is liver supportive by providing ATP) even in the face of euglycemia • Response from clinical effects is usually rapid and within 12 to 24 hrs • Recheck liver values at 24 and 48 hrs to evaluate for liver involvement • SAMe for 1-2 weeks if hepatotoxic dose ingested	> 0.1 g/kg → hypoglycemia > 0.5 g/kg → acute hepatic necrosis

VETgirl HEPATOTOXICANT TABLE

TOXIN	SOURCE	MECHANISM OF ACTION	CLINICAL SIGNS
Metaldehyde	Known as a molluscicide, used for the control of slugs and snails (although recently replaced by less toxic iron phosphate)	Results in the disruption of the GABAergic system Monoamine oxidase, 5-hydroxytryptamine, and norepinephrine may also be involved in the toxic mechanism	May be seen as soon as 30 minutes after ingestion but typically occur w 3 to 5 hours Clinical signs include GI (vomiting, diarrhea) and CNS (hyperesthesia, incoordination, hyperthermia, seizur Liver damage and cirrhosis may occ 2-3 days after exposure Death from respiratory failure may occur within 4-24 hours after exposu
Copper	Coins, feeds, solutions, wire, jewelry, food	Breeds that are homozygous for a recessive gene (Bedlington Terrier, Skye Terrier, West Highland White Terriers, Labrador Retrievers, Doberman Pinschers) have excessive copper storage in the liver	Lethargy, anorexia, vomiting, weight loss, jaundice
Benzodiazapines (oral)	Oral diazepam (valium) and alprazolam in CATS (not seen with parenteral administration); typically seen with chronic oral dosing	Acute hepatic necrosis in 5-11 days of oral treatment	Sedation, malaise, ataxia, jaundice
Amatoxin Mushrooms	*Amanita* spp., *Galerina* spp., *Conocybe* spp., *Lepiota* spp.	Inhibit DNA and RNA transcription and protein synthesis; bind to actin filaments, deform cytoskeleton → hepatocyte death	Develop GI signs within 6-24 hours "False" recovery period, followed by fulminant liver failure and AKI in 36- hours
Blue-Green Algae	Cyanobacteria Hepatotoxins (*Microcystis* spp., *Nodularia* spp., *Oscillatoria* spp. most common; *Anabaena* spp. less often) Can also contain neurotoxins	Microcystin binds to protein phosphatase in cytoskeleton, disorganization of actin leads to cellular collapse, intrahepatic hemorrhage, death	Death in hours to days with hepatot GI (e.g., vomiting/diarrhea), CNS (e.g., weakness, ataxia, tremors, seizures), cardiac (e.g., collapse, pallor, tachycardia, respiratory failur hemorrhagic and hypovolemic shoc Very acute clinical signs with neurot (death can occur in minutes to hours CNS signs and SLUDGE-like signs

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	CLIN PATH	TOX TEST	TREATMENT	PROGNOSIS
ithin res) cur ure	Acidosis, liver value abnormalities	Characteristic odor of formaldehyde may be present in the stomach contents along with bait material No consistent and pathognomonic gross or histological lesions occur in metaldehyde poisoned animals	• Decontamination, if appropriate • Gastric lavage with inflated ETT should be performed if the patient is symptomatic and evidence of pellets still in stomach on radiograph; administration of 1 dose of charcoal if gastric lavage performed • Stabilization of vital signs, IV fluids, anti-emetics, acid-base monitoring, methocarbamol/anticonvulsant therapy, respiratory and CV system monitoring, supportive care	Acute median LD values are 210 to 600 mg/kg for dogs and 207 mg/kg for cats Prognosis is good if survival is > 24 hours from ingestion with early treatment
		Quantitative hepatic copper values; genetic testing (some breeds)	• Chelation with penicillamine or trientine • Supportive care for other derangements	Increasing zinc in diet can aid in prevention
	Markedly increased ALT Increased T-bili, PT/PTT			
y 48	↑↑ Liver enzymes within 48-72 h	Centrilobular hemorrhagic necrosis	• Decontamination (emesis and AC if < 2 h post ingestion) • IV fluids, sequester amatoxin bile in gallbladder with octreotide CRI, NPO), ultrasound-guided bile aspiration	Alpha amanitin LD_{50} (human) = 0.1 mg/kg Easily found in one mushroom
oxin e, k) oxin s) –	↑↑ Liver enzymes within a few to 24 h; elevated PT/PTT; anemia	Diffuse hepatic necrosis	• Decontamination is often too late – gastric lavage +/- activated charcoal, bathe (use protective gear) • PCV/TS/BG • Baseline Chem, CBC PT/PTT	Toxic dose – 50-11,000 mcg/kg Prognosis – often grave

VETgirl HEPATOTOXICANT TABLE

TOXIN	SOURCE	MECHANISM OF ACTION	CLINICAL SIGNS
Sago Palm	Cycads (*Cycas* spp., *Macrozamia* spp.) (SE, South central or tropical areas of US usually) but can be found as bonsai household plant	All parts of the plant are poisonous, but seeds contain largest amount of toxin	GI signs (vomiting, diarrhea) within 1 minutes to several hours, CNS signs (lethargy, seizures) (48-72 hours), liver failure (24-72 hours)
Iron	Multivitamins, iron supplements, fertilizers, snail/slug bait	When serum iron exceeds the binding capacity of transferrin and ferritin, free iron causes lipid peroxidation and damage to liver, heart and brain Iron is also caustic to the GI mucosa	GI signs (e.g., vomiting, hematemesi melena, diarrhea) within 0.5-6 hours liver failure 12-24 hours later With large doses can see hypovoler shock, coagulopathy and acidosis
Aflatoxins	Mycotoxin (mold) found in corn, peanuts, cottonseed, rice and potatoes	Metabolized into reactive epoxide, binds to hepatocytes Large acute exposures = hepatic necrosis; smaller chronic exposures = neoplasia	Vomiting, anorexia, lethargy, icterus, coagulopathy
Aspirin	Pain medication	Hepatotoxicity thought to be from inhibition of mitochondrial function	GI (e.g., anorexia, vomiting, melena, stomach ulcers), lethargy, icterus
Lectins (toxalbumins)	Castor bean *(Ricinus communis)*, Precatory bean *(Abrus precatorius)*, Black locust (*Robinia* spp.), Mistletoe *(Phoradendron)*	Stops cellular protein synthesis in multiple organs	GI (e.g., anorexia, vomiting), lethargy anorexia, icterus, weakness, tremors death
Essential oils	Pennyroyal oil, melaleuca (tea tree) oil	Unknown	Vomiting, lethargy, ataxia, hind limb weakness, icterus
Veterinary drugs associated with hepatotoxicity (albeit rare)	isoniazid, ketoconazole, lomustine, methimazole, melarsomine, mitotane, sulfonamides, trazodone, zonisamide		

Abbreviations: AKI: acute kidney injury; CNS: central nervous system; DIC: disseminated intravascular coagulatio
PTT: partial thromboplastin time

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	CLIN PATH	TOX TEST	TREATMENT	PROGNOSIS
5 s	↑↑ Liver enzymes (24-72 h)	Centrolobular and mid-zonal coagulative hepatic necrosis	• Baseline bloodwork, PT/PTT • PCV/TS/BG/liver panel q 24 hours x 2-3 days	1-2 seeds can lead to severe signs Grave prognosis once hepatoxicity seen
is, ; mic	↑↑ Liver enzymes; elevated PT/PTT if liver necrosis	Serum iron levels; chelate warranted if iron > 400 mcg/dl)	• MgOH can be given while iron is still in the GI tract • Emesis if appropriate. Activated charcoal does not bind and should not be used • Other treatment includes antiemetics, GI protectants/antacids, hepatoprotectants, deferoxamine (chelator), supportive care, blood work monitoring	Toxicity dependent on amount of elemental iron 20-50 mg/kg = GI signs 50-80 mg/kg = GI ulcers > 80 mg/kg = liver and other systemic effects
,	↑↑ Liver enzymes; elevated PT/PTT	Acute – diffuse hepatic necrosis Chronic – fatty liver	Fluid therapy, anti-emetics, blood work monitoring, hepatoprotectants, symptomatic and supportive care	
	↑↑ Liver enzymes	Centrilobular hepatic necrosis	Fluids, anti-emetics, antacids, gastroprotectants, hepatoprotectants	Dogs > 400 mg/kg for liver effects
y, s,	↑↑ Liver enzymes		Fluids, anti-emetics, symptomatic and supportive, hepatoprotectants	All parts of plants are toxic. Seeds are most toxic part of *Ricinus* and *Abrus*. Seeds must be chewed to release the toxin.
	↑↑ Liver enzymes		Symptomatic and supportive (fluids, hepatoprotectants)	Usually associated with application of 100% oil to open wound, ear canal or oral ingestion
			• Discontinuation of drug • Hepatoprotectants • Symptomatic supportive care	

n; GI: gastrointestinal; LD: lethal dose; LES: liver enzymes; NAC: N-acetylcystine; PT: prothrombin;

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