Back to the Basics: Approaching Poisonings Correctly, Right from the Start!

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Proper Patient and Toxicity Assessment

When presented with a patient that has had a potential toxin exposure, it is important to make a full assessment of the patient and the toxin before starting treatment. Who, what, when, where, why and how are questions to ask in every toxicity situation. Common things to consider include:

Is the patient stable?

Assessing the patient's vitals and overall health status is often a key factor that is overlooked when presented with a panicked owner and patient. However, many steps that follow are critical in knowing the current condition of the patient.

What is the signalment? (species, breed, age, weight)

When dealing with dogs, certain breeds are at a higher risk for MDR-1 mutation which changes the toxicity severity for numerous medications including ivermectin. Washington State has an excellent website that discusses susceptible breeds and drugs that can be affected by the mutation, http://vcpl.vetmed.wsu.edu/problem-drugs.

Breed conformation may affect the type of decontamination that is recommended or appropriate. Very young or very old animals may have altered toxicity effects. An accurate weight is critical in assessing the degree of toxicity for most ingestions.

What is the current and past medical history including current medications?

Knowing the patient history and current status will help determine what type of therapy the patient can safely receive. If a patient has a history of CHF, administering 2-3x maint. IV fluid rates for a potential renal toxin would likely be inappropriate. Certain medications may interact or worsen toxicity signs depending on the exposure and should be known before starting therapy.

What was the toxin and route of exposure?

Knowing the specific toxin is crucial in many cases. Having a patient present to you that has ingested mouse bait is not a straightforward treatment of vitamin K1. Bromethalin, cholecalciferol and corn cellulose are not treated with vitamin K1. Also, different LAACs will have a different margin of safety and amount required to be ingested before toxicity would be expected.

The route of exposure important in determining the toxicity risk and severity. Was skin exposed to a liquid substance and then the animal licked it off or was it rolled in, walked through, etc.? Is there granular material stuck in the patient's haircoat that may pose a risk if ingested or allowed to remain the haircoat? Many toxins have a different degree of toxicity or treatment needs based on the route of exposure.

How much was the animal exposed to?

Not every toxin exposure will result in signs. It is true that "the dose makes the poison" and jumping to a conclusion that any exposure will require therapy often results in mismanagement and unnecessary stress to the patient, owner and treating veterinarian. While it is also true that there are a few toxins which may result in extremely significant signs at very low doses, i.e. mycotoxins, in general, there is a margin of safety for everything.

What is the time since exposure?

Knowing the time frame plays a large role in determining the type of decontamination that can be done or needs to be done. It also allows you to assess whether or not signs are likely to develop. If an animal has been exposed to a toxin 4 hours prior that would undoubtedly cause signs within a 1-2 hour timeframe yet remains asymptomatic, there is a strong likelihood that a toxic exposure did not occur.

Where did the exposure occur?

Knowing the location of the exposure is helpful at determining other potential confounding factors as well as the potential severity of a product. An animal that has been exposed to a fertilizer used on corn fields will likely have different needs than an animal exposed to a fertilizer placed on a residential yard.

What other factors are involved?

It is important to get the full story, or as much as one is able, in order to put together the most accurate picture as possible. Was the exposure accidental or malicious? Many times, instances arise where a toxin is suspected due to an incident and that becomes the focus instead of the big picture. An example of this is when an owner fertilized the yard 4 days ago and today their dog has started to vomit. The owner is focused on the fertilizer being the culprit but also forgot to mention that he ate the leftover pizza or that there has been company at the house and the dog is often stressed with increased anxiety when this occurs.

Staff safety in handling symptomatic patients

In the midst of urgency when presented with a potential toxicity situation, it is important to remember the safety of staff and take special precautions where needed. Dermal toxins that require decontamination should involve use of personal protective equipment including gloves, glasses or goggles and gown or long sleeves. While this may not be critical for bathing a cat that has had a permethrin product applied, it is very important when dealing with corrosives and hydrocarbons which may be damaging to the skin. Phosphide pesticides produce phosphine gas which, when inhaled, produces asthmatic-like symptoms as well as nausea and headache. The phosphine gas often smells like rotten eggs or garlic. Zinc phosphide used in gopher bait (“peanuts”) is a commonly seen form that is ingested in animals. When inducing emesis, precaution should be taken to ensure that the animal is either outside or in a well-ventilated area of the clinic to minimize inhalation of the gas. It is also important to instruct owners to ensure that the home or vehicle is well-ventilated in the event that the animal has spontaneous vomiting. Animals that have neurologic signs may be more likely to show aggression which may make treatment difficult. Even when animals appear to be stable, caution should be used when handling any animal that may develop neurologic signs as the development of signs may be sudden and unprovoked.

Ideal drugs for toxicity management

While the list of potential toxins to animals is long and covers a wide range of sources, medical management of cases can often be narrowed down to more commonly used drugs. The following are recommended drugs that are ideal to stock in your clinic and always have on hand.

Decontamination needs

Specific discussion of decontamination needs can be found in the Decontamination: It's More than Vomiting!" proceedings.

Ocular

If an animal has been exposed to a chemical that is an irritant or corrosive to the eye, ocular decontamination is warranted. As ocular decontamination should be started as soon as possible, owners should be encouraged to flush the eye at home with tap water. Eye drops should be avoided. Eye was can be used in the clinic in addition to tap water, with saline being the least preferred method.

Dermal

Rinsing product for 15 minutes and bathing with a degreasing dish soap 2-3 times will help to remove product. Burn/wound management should be used as needed.

Inhalation

For minor irritants, fresh air is generally sufficient treatment. Animals with underlying respiratory disease may require more intensive treatment, however. Oxygen therapy is often required for smoke inhalation, carbon monoxide and cyanide toxicity.

Gastrointestinal

Inducing emesis in dogs is performed by using apomorphine or 3% hydrogen peroxide. Apomorphine is a synthetic opioid that stimulates dopamine receptors in the CRTZ and can be given at 0.03mg/kg IV, 0.04mg/kg IM or by crushing ½ tablet for small dogs and 1 tablet for large dogs and placing in the conjunctival sac. Naloxone may be used if excessive sedation occurs without reversing vomiting. 3% hydrogen peroxide is given orally at a dose of 1-2ml/kg (1-2 tsp per 10 pounds). This should be fresh, bubbly and non-expired for effectiveness. Hydrogen peroxide is a gastric irritant and exceeding recommended amounts may result in gastritis with gastric bleeding. Ropinirole has recently been marketed as an emetic in dogs in the form of eye drops under the trade name Clevor®, to be given at a dose of Dose 2.7-5.4 mg/m^2 (average dose 3.75 mg/m^2).

Inducing emesis in cats is best performed by using an *a*-2 adrenergic receptor such as xylazine at 0.44mg/kg IM or dexmedetomidine at 7mcg/kg IM or IV. The sedative effects can be reversed with yohimbine or Anti-Sedan. Hydromorphone at 0.1mg/kg IM or SQ has also shown to have a good response in cats and is more cardiac sparing than an *a*-2 adrenergic agonist. Cats are more sensitive to developing hemorrhagic gastritis with hydrogen peroxide and is often not effective. Apomorphine is also not very effective in cats as the cat vomiting center is mediated by alpha receptors and not dopamine receptors. Apomorphine may cause dysphoria and agitation ("morphine mania") in cats.

The standard dosing of activated charcoal is 1-2g/kg, with 1g/kg being ideal in most situations. A cathartic is recommended to be given with the initial dose to help increase the rate of intestinal evacuation, and is included in many activated charcoal suspensions. Giving repeated doses of activated charcoal without sorbitol is valid for products that undergo enterohepatic recirculation or medications that have extended release properties. Doses are typically repeated every 6-8 hours for up to 24 hours, depending on the toxin. Sodium levels should be monitored and IV or SQ fluids given to minimize the risk of hypernatremia.

Neurologic management

Many toxins cause neurologic signs including agitation, hyperactivity, tremors, seizures, severe CNS depression and obtundation. In most cases, acepromazine at 0.05-0.1mg/kg is ideal for treating most situations of agitation and hyperactivity. This can be given IM or SQ. If given IV, ½ of the dose IV and the other ½ IM or SQ is common. However, there are animals with severe signs where giving the full dose IV would be appropriate. Butorphanol at 0.2-0.4mg/kg IM or SQ is ideal for treating agitation in an animal that may have a low normal blood pressure, be hypotensive, geriatric or where hypotension may develop, as is the case for albuterol and certain marijuana toxicities. Benzodiazepines are RARELY the treatment of choice for agitation and hyperactivity. These are typically contraindicated as the signs are often exacerbated.

Methocarbamol is the drug of choice for tremors that are a result of any toxin. The dosing range is wide at 55-220mg/kg. The preferred route of administration is IV. However, if only tablets are available, they can be crushed, mixed with saline and given rectally. The onset of action will be delayed compared to IV, but remains an acceptable option. Ideally, having a bottle of injectable methocarbamol on hand would be most preferred as signs can be more easily controlled and dosing can be titrated as needed. Benzodiazepines are typically not effective at tremor control and is not recommended.

Seizure control can often require more than one drug of choice. For instances where signs include agitation or hyperactivity, phenobarbital or Keppra is preferred over benzodiazepines as they often exacerbate agitation. In refractory seizure control, propofol or general anesthesia may be needed.

Cerebral edema may occur in cases of bromethalin ingestion and generally requires mannitol therapy in symptomatic cases. Hypoglycemia may develop in numerous instances of toxicity, with the most common being xylitol cases. 50% dextrose solution is imperative to have available for adequate management and control of hypoglycemia.

Renal management

Intravenous fluids may be beneficial for toxins that undergo renal excretion by increasing diuresis of the toxicant. Instances where this is helpful include toxicity of phenobarbital, amphetamines, salicylate, lithium and bromides. Due to NSAIDs being highly protein bound, fluid diuresis serves as a renal protectant.

Specific drugs for renal management needs are rare. In isolated cases, furosemide at 2-4mg/kg IV and mannitol at 1-2g/kg IV have been used to improve diuresis. In general, IV fluids are the treatment of choice for renal management with potential nephrotoxicities including grapes/raisins, NSAIDs and lilies (cats).

Hepatic management

Hepatoprotectants are often needed for toxins that may cause hepatic damage or necrosis. SAM-e containing supplements such as Denosyl® and Denamarin® are generally started after the toxic insult and continued for 2-4 weeks. N-Acetylcysteine is a hepatic detoxifier and used for the acute phase of toxicity.

Cardiac management

Cardiac signs in the poisoned patient typically include changes in heart rate, blood pressure and rhythm. Standard therapies used in other instances of cardiac changes are often used in instances of poisonings as well. It is recommended to review Plumb's or another formulary for more specific dosing instructions, but generally include:

Tachycardia:

Acepromazine: 0.05-0.1mg/kg IV, IM, SQ, used in conjunction w/ agitation +/- hypertension

Butorphanol: 0.2-0.4mg/kg IV, IM, SQ, used in conjunction w/ agitation +/- hypertension

Beta blockers:

Esmolol: 0.25-0.5mg/kg IV over 1-2 mins followed by CRI at 0.01-0.2mg/kg/min

Propranolol: 0.02mg/kg IV over 2-3 mins. Repeat in 20 mins until effect is seen, up to 0.1mg/kg

Metoprolol: 5-50mg TOTAL PO divided q8-12 hours

Bradycardia:

Atropine: 0.02-0.04mg/kg IV

Calcium Gluconate 10%: Reserved for calcium channel blocker toxicities. 0.5-1.5ml/kg IV slowly followed by 0.25-0.35ml/kg/hr CRI. Monitor ECG during administration

Hypertension: Systolic ≥160mmHg (Normal 120mmHg), MAP >130 (Normal 100mmHg)

Acepromazine: 0.02-0.1mg/kg IV, IM, SQ

Amlodipine (arterial vasodilator): Dogs 0.1-0.5mg/kg PO q 12-24 hrs. Cats 0.625-0.125mg PER cat q 12-24 hrs. May take several hours for full effect. DO NOT give if bradycardic.

Beta blockers:

Esmolol 0.25-0.5mg/kg IV over 2-5 mins followed by 10-200mcg/kg/min CRI

Propranolol: 0.02-0.1mg/kg IV q 8-12 hrs. Oral Dogs 0.1-1.0mg/kg q 8-12hrs, Cats 0.25mg PER cat PO q 8-12 hrs

Others include hydralazine, ACE inhibitors, isoflurane

Hypotension: Systolic ≤90mmHg or MAP ≤60mmHg. Normal 80mmHg or MAP 80mmHg

IV fluids: Crystalloids 20ml/kg bolus over 10-15 mins. Repeat 2-3x as needed

Colloids (VetStarch®) 5ml/kg bolus over 15 mins. Repeat 2-3x as needed

Vasopressors: Dopamine, norepinephrine, dobutamine, vasopressin, epinephrine, digoxin

Gastrointestinal management

Toxins that result in gastrointestinal signs are numerous. An anti-emetic such as metoclopramide (Reglan®) at 0.2-.0.5mg/kg IM, SQ, PO, maropitant (Cerenia®) at 1mg/kg SQ or ondansetron (Zofran®) at 0.1-0.2mg/kg SQ, IM, IV is a mainstay for general veterinary care and widely used for treating emesis resulting from GI toxicants. Anti-diarrheals including probiotics, metronidazole and high fiber sources are often needed for treating diarrhea caused by GI toxicants as well. In toxicities where ileus is a concern such as loperamide, metoclopramide has a dual benefit with its anti-emetic and pro-kinetic properties. If GI protectants are needed for potential GI ulceration, a proton pump inhibitor (PPI) is generally preferred with an H2 blocker being used if a PPI is not

available. Sucralfate and a PGE1 analog, such as misoprostol, are frequently used in situations where GI ulceration is of higher risk of occurrence.

Patient management and general follow-up needs

Patient management focuses on symptomatic and supportive care as well as minimizing toxin absorption. Once appropriate decontamination has been performed, home monitoring or continued in hospital care will need to be instituted. For toxins that may cause organ damage such as renal toxins and hepatic toxins, follow-up lab work is generally required following hospitalization or home management. Ingestions that result in hypercalcemia including vitamin D_3, cholecalciferol and calcipotriene often require follow-up therapy and lab work that may last for weeks to months in refractory cases. Thorough and consistent communication with the pet owner is imperative for successful outcomes and should be done for any toxin exposure even if additional hospitalization is not required.

Suggested reading:

Marks S, Kook P, Papick M, Tolbert M, Willard M. ACVIM consensus statement: Support for rational administration of gastrointestinal protectants to dogs and cats. J Vet Intern Med 2018:1-18.
Blackwell's Five-Minute Veterinary Consult Clinical Companion: Small Animal Toxicology 2nd edition.
Peterson and Talcott Small Animal Toxicology 3rd edition.

Decontamination: It's More than Vomiting!

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The goal of decontamination is to inhibit or minimize toxin absorption and to promote excretion or elimination from the body. It also allows us to remove or dilute topical irritants or corrosives. Consider the proper patient assessment as described above to determine if the benefits of decontamination outweigh the risk and whether the exposure will harm the patient. If decontamination is deemed to be warranted, selecting the appropriate method will help ensure successful management of the patient. Types of decontamination include:

Ocular

If an animal has been exposed to a chemical that is considered an irritant or corrosive to the eye, ocular decontamination is warranted. The pH will indicate if it is acidic or alkaline and there are often key words on the bottle such as caution or danger. As ocular decontamination should be started as soon as possible, owners should be encouraged to flush the eye at home with tap water. Eye drops should be avoided. Once in the clinic, a labeled eye wash is ideal, followed by tap water. Saline has not been shown to be beneficial in cases of alkali ocular burns.

If the product is an irritant the eyes should be irrigated for 10-15 minutes at home and monitored for signs of irritation including redness, lacrimation, pawing or rubbing at the eye, squinting or edema. The eyes should be irrigated for 15-20 minutes at home if a corrosive. Corrosive products should also have an additional 15-20 minutes of irrigation performed by a veterinarian followed by a fluorescein stain, topical antibiotic ointment or drops and use of an Elizabethan collar.

Dermal

Dermal decontamination is indicated for exposure to corrosives or irritants, glues or adhesives, gasoline/hydrocarbons and systemically absorbed toxins. This will help prevent oral exposure by self-grooming, remove unwanted substances, minimize paresthesia and reduce the risk of burns.

Irritant products generally have a caution statement on the label and result in mild redness and irritation. Rinsing product off or bathing with a degreasing dish soap is generally effective treatment. Vitamin E oil may also provide relief in situations where paresthesia is present. Corrosive products are alkaline or acidic in nature and generally have a danger statement on the label. These products result in chemical burns to the skin. Rinsing product for 15 minutes and bathing with a degreasing dish soap 2-3 times will help to remove product. Burn/wound management should be used as needed.

Glues and adhesives are typically non-toxic. They adhere to the eyelid, teeth, skin and fur. Certain types can be loosened with oil. The affected fur can be clipped if the animal is bothered to help avoid self-mutilation. Otherwise, if the affected area is not problematic, no therapy is generally necessary, and the product should wear off with time.

Gasoline and hydrocarbons are typically not seriously toxic. They may cause defatting of the skin resulting in cracking, secondary infections and chemical irritant contact dermatitis. Bathing 2-3 times with a degreasing dish soap is generally adequate therapy. There is a small risk for aspiration if oral exposure occurs and if inhaled, CNS depression may develop.

Systemically absorbed toxins do not generally cause dermal damage, however, result in systemic signs. These include tea tree oil, topical pain creams, estrogen creams, pyrethrin products (cats), psoriasis cream and 5-FU. Bathing 2-3 times in a degreasing dish soap will help to minimize absorption depending on the timing since exposure.

Inhalation

Toxins that may require respiratory decontamination include concentrates or corrosives, including bleach and ammonia mixtures, as well as smoke inhalation and carbon monoxide. A simple yet important aspect of inhalation decontamination is to remove the animal from the source of exposure. For minor irritants, fresh air is generally sufficient treatment. Animals with underlying respiratory disease may

require more intensive treatment.Oxygen therapy is often required for smoke inhalation, carbon monoxide, and cyanide toxicity.

Birds are very sensitive to inhalants, and fragrances, Teflon, and regular respiratory irritants may cause significant concern. The animal should be removed from the source, be given humidified oxygen, and offered heat support and fluids.

Gastrointestinal

Emesis

Emesis is by far the most common method of gastrointestinal decontamination. Approximately 49% (range of 9-75%) of stomach contents are recovered less than 30 minutes after ingestion. 17-62% is recovered 1 hour after ingestion. These ranges often make emesis success or failure difficult to assess, particularly when the ingestion is suspected but not known or when the number of items ingested is unknown as is often the case when an animal chews up a bottle of medication or eats a handful of raisins. If emesis is unproductive, it does not guarantee that the ingestion did not happen as emesis does not fully empty the stomach of its contents.

In many cases, there is a window of opportunity of only 1-2 hours for a positive return on emesis. However, there are certain toxins that can have successful emesis for up to 6 hours post ingestion. These include grapes, raisins, chocolate, xylitol containing gum, bezoars, massive ingestions and drugs that decrease gastric emptying (opioids, salicylates, anticholinergics and tricyclic antidepressants).

Inducing emesis in dogs is performed by using apomorphine or 3% hydrogen peroxide. Apomorphine is a dopaminergic receptor agonist drug that stimulates dopamine-2 receptors in the CRTZ and can be given at 0.03mg/kg IV, 0.04mg/kg IM or by crushing ½ tablet for small dogs and 1 tablet for large dogs and placing in the conjunctival sac. Naloxone may be used if excessive sedation occurs without reversing vomiting. 3% hydrogen peroxide is given orally at a dose of 1-2ml/kg (1-2 tsp per 10 pounds). This should be fresh, bubbly and non-expired for effectiveness. Hydrogen peroxide is a gastric irritant and exceeding recommended amounts may result in gastritis with gastric bleeding. Ropinirole has recently been marketed as an emetic in dogs in the form of eye drops under the trade name Clevor®, to be given at a dose of Dose 2.7-5.4 mg/m^2 (average dose 3.75 mg/m^2).

Inducing emesis in cats is best performed by using an *a*-2 adrenergic receptor agonist drug such as xylazine at 0.44mg/kg IM or dexmedetomidine at 7mcg/kg IM or IV. The sedative effects can be reversed with yohimbine or atipamezole. These drugs are approx. 50% effective in cats, may cause excessive sedation and, in rare cases, cause cardiovascular collapse. These are not generally recommended for older or disease compromised cats. Hyrdomorphone at 0.1mg/kg IM or SQ has also shown to have a good response in cats and is more cardiac sparing than an *a*-2 adrenergic agonist. Cats are more sensitive to developing hemorrhagic gastritis with hydrogen peroxide and is often not effective, therefore, not recommended. Apomorphine is also not very effective in cats as the cat CRTZ is mediated by alpha receptors and not dopamine receptors. Apomorphine may cause dysphoria and agitation ("morphine mania") in cats.

Products used in the past that should NOT be used to induce emesis include salt, syrup of ipecac, digital manipulation, liquid dish soap, raw eggs, Tabasco, or mustard. Salt toxicity, gastric irritation, nerve damage or aspiration may occur when other methods are used.

Emesis should not be induced in symptomatic animals, those that have already vomited to bile/clear, or those with a history of aspiration pneumonia or at risk for such due to laryngeal paralysis or megaesophagus. Examples of toxicity ingestions that should not have emesis induced include sharp/dangerous objects that may cause more trauma to the esophagus or enter the soft palate, corrosive agents (alkaline batteries, disc batteries, alkaline substances with a pH >11, acidic substances with a pH < 3) that may cause chemical burns to the esophagus and GIT, or hydrocarbons (gasoline, kerosene, motor oil) that present a moderate aspiration risk.

Caution should be taken if inducing emesis in brachycephalic breeds, young animals (less than 3 months of age), geriatric pets (greater than 10-12 years of age), animals with a history of heart disease,

seizures, recent surgery or those that have a non-toxic ingestion. Species that do not vomit include rabbits, ruminants (sheep, cattle, llama, goat), horses, birds and several rodents including chinchillas, rats and gerbils. Other decontamination methods will be needed for these species.

Gastric lavage

Gastric lavage may or may not be more effective at removing gastric contents. Often the more forceful contractions of the gastric muscles during emesis are more effective at removing contents than passive flow from lavage. This is a viable option for those species that do not vomit, symptomatic patients with a large ingestion, a large amount of stomach contents or where emesis was unsuccessful. It also may be helpful with potentially fatal ingestions including calcium channel blockers, beta blockers, baclofen, and metaldehyde.

Safe performance of gastric lavage requires sedation, intubation, and endotracheal insufflation. The animal should be in right lateral recumbency with the head tilted down at an approximately 20-degree angle. The stomach tube should be measured to the last rib, passed in to the stomach, and flushed with 5-10ml/kg warm water. The stomach should be agitated and then aspirated or allow for gravity to drain stomach contents. Once adequate removal of stomach contents is achieved, activated charcoal can be given. Caution should be used, however, as it is not uncommon for regurgitation to occur and the risk of aspiration is high. If activated charcoal is given, an anti-emetic, head elevation and continued intubation for as long as animal will tolerate until they can protect their airway should also be done.

Risks that are associated with gastric lavage include aspiration pneumonia, the need for general anesthesia, esophageal or gastric rupture and electrolyte imbalances. There are numerous contraindications to performing gastric lavage. These include hydrocarbon ingestions due to the high aspiration risk, corrosives, recent surgery (pending location), unstable patients, and those at a risk for bleeding or injury.

Activated charcoal and cathartics

Activated charcoal binds to many toxins in the GI tract by physical contact and weak covalent forces. Charcoal is a black powder composed of partially decomposed cellulose of soft wood. Activated charcoal is produced by heating common charcoal in the presence of a gas which creates numerous internal pores to trap chemicals within the activated charcoal. This process results in a highly porous material with an enormous surface area relative to its weight. The adsorptive capacity of activated charcoal is a function of its binding surface area. There is limited data regarding the benefit of activated charcoal with many toxins and one must weigh the risk vs. benefit when considering its use.

Benefits of activated charcoal include that it is readily available, relatively inexpensive, decreased absorption of 25-30% when administration is delayed, and beneficial use a wide number of toxins. Activated charcoal can be given with food to aid in administration without decreasing effectiveness. Drawbacks of activated charcoal use include difficulty of administration, potential vomiting after administration, potential diarrhea, binding to therapeutic medications, the unknown benefit with many toxins, and most importantly, the risk of hypernatremia. Hypernatremia may occur with any dose of activated charcoal, with an increasing risk as the number of doses increase.

There are numerous situations where activated charcoal use should be avoided based on the status of the animal. These include animals that are symptomatic, particularly with neurologic signs as aspiration risks are increased, animals with dehydration, current hypernatremia, hypovolemic shock, decreased GI motility/ileus, recent GI surgery and protracted vomiting. Activated charcoal should be avoided in instances where the risk of aspiration pneumonia is higher, including an unprotected airway, decreased level of consciousness, excessive sedation or agitation and when having to force feed. Activated charcoal should also be avoided in situations where endoscopy or abdominal surgery of the GI tract may be needed, concerns of a gastric or intestinal obstruction and ingestions where there is an increased risk of aspiration pneumonia, such as with caustic substances and hydrocarbons. Contraindications to activated charcoal use in general include exposures that occurred > 2 hours after ingestion unless enterohepatic recirculation occurs, or extended release formula medication was

ingested, alcohols (ethanol and ethylene glycol), xylitol, heavy metals, salt, paintball and non-toxic ingestions.

Cathartics are helpful at gastrointestinal decontamination for numerous reasons including accelerated speed of drug transit through the GIT, decreased time for toxin absorption, and decreased time for desorption of toxin from the activated charcoal. Sorbitol, a hexahydric sugar alcohol, is frequently combined in activated charcoal formulations at a dose of 3ml/kg PO of a 70% solution. Magnesium based cathartics (magnesium hydroxide, magnesium oxide, magnesium sulfate) should be used with caution in cats due to their increased risk of serum and brain magnesium levels. Hypermagnesemia displayed as hypotonia, ECG changes, altered mental status and respiratory failure may occur. It is also recommended to avoid magnesium-based cathartics in bromethalin toxicities due to potential similar clinical signs if hypermagnesemia were to occur. Magnesium hydroxide is often used in cases of mild iron toxicity due to its ability to precipitate binding of iron in the GIT to insoluble iron hydroxide.

The standard dosing of activated charcoal is 1-2g/kg, with 1g/kg being ideal in most situations. A cathartic is recommended to be given with the initial dose to help increase the rate of intestinal evacuation. Repeated doses of activated charcoal without sorbitol is valid for products that undergo enterohepatic recirculation or medications that have extended release properties. Doses are typically repeated every 6-8 hours for up to 24 hours, depending on the toxin. Sodium levels should be monitored and IV or SQ fluids given to minimize the risk of hypernatremia.

Whole bowel irrigation

Whole bowel irrigation (WBI) is rarely used in veterinary medicine. Situations when WBI may be helpful include enteric coated medications, iron ingestion, sustained or extended release medications and ingestions of packets of medications. WBI is performed using a nasoesophageal or nasogastric tube and administering 25-40ml/kg PEG-ES solution orally followed by a continuous oral infusion of 0.5ml/kg per hour until there is radiographic clearance or clear feces are present. Contraindications for WBI are like that of activated charcoal administration.

Endoscopy and surgical removal

Endoscopy may be indicated for ingestions of objects in situations where emesis would not be safe either due to the object size/shape or risk of oral/esophageal injury, such as ingestions of coins, non-leaking batteries, patches (fentanyl, lidocaine), bottles/plastic and metals. Endoscopy may also be warranted in evaluating injury to the esophagus and stomach. Negative aspects to endoscopy include the status of the animal if symptomatic, cost, equipment access and the need for general anesthesia.

When an animal is unable to vomit or if an object is not able to be removed endoscopically, surgery may be necessary for a successful outcome. Examples of this include leaking batteries, bread dough, a large number of objects and medication bezoars. Occasionally, surgery is required for removal of substances that do not pose a toxicity concern, however, a foreign body/obstruction concern. Sharp objects and large foreign bodies may require surgical removal. Gorilla Glue® has expansive properties and while toxicity is not seen, can form a hard, rock-like substance that encompasses the diameter of the stomach.

Suggested Reading:

Blackwell's Five-Minute Veterinary Consult Clinical Companion: Small Animal Toxicology 2nd edition.

Peterson and Talcott Small Animal Toxicology 3rd edition.

Niedzwecki, AH, et al. Effects of oral 3% hydrogen peroxide used as an emetic on the gastroduodenal mucosa of healthy dogs. JVECC, 2016; 0:1-7.

Willey, JL, et. Al. Evaluation and comparison of xylazine hydrochloride and dexmedetomidine hydrochloride for the induction of emesis in cats: 47 cases (2007-2013). JAVMA, 2016; 248:923-928.

Thawley, VJ. Assessment of dexmedetomidine and other agents for emesis induction in cats: 43 cases (2009-2014). JAVMA, 2015; 247:1415-1418.

FROM THE PLANTER TO THE CARPET: TOXIC PLANTS

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INTRODUCTION

For curious dogs or cats, it's difficult to resist the allure of plants. While many plants are simple gastrointestinal irritants, some have the potential to cause life-threatening toxicosis. Therefore, it is essential for technicians and veterinarians to be familiar with common plants that have the potential to cause severe toxicosis in dogs and cats.

LILIES

Plant name: Lily (*Lilium spp.* and *Hemerocallis spp*.)
Other common name(s): Easter lily, tiger lily, Japanese show lily, stargazer lily, rubrum lily, day lily
Species of concern: Cats only
Toxic dose: 1-2 leaves or petals, ingestion of the pollen from the fur or water from the vase
Toxic portion of plant: All, even the pollen
Onset/duration of clinical signs: Usually 6-12 hours post exposure.
Clinical signs: Early onset vomiting, depression, anorexia. Acute anuric renal failure in 1-3 days. Azotemia, epithelial cats (12-18 hrs post ingestion) proteinuria, and glucosuria. Pancreatitis is a rare sequela.
Treatment: No antidote. Induce emesis within 1-2 hrs after ingestion (xylazine is preferred in cats) followed by one dose of activated charcoal. IV crystalloid therapy at 2-3 times maintenance for 48 hrs. If oliguric, a furosemide CRI (1-2 mg/kg/hr) and mannitol bolus (1-2 g/kg) in well hydrated patients may be used. Gastrointestinal protectants as needed. Peritoneal or hemodialysis has been successful.
Prognosis: Good if treated early and aggressively; poor if treatment is delayed 18-24 hr or anuria has developed.

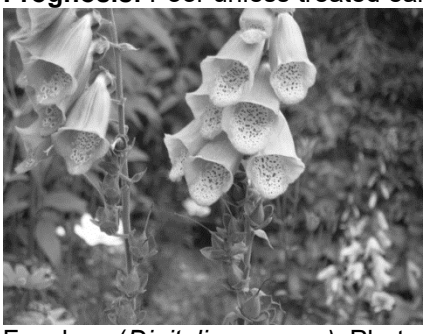
Asiatic hybrid lily (*Lillium spp.)* Photo courtesy of Tyne K Hovda, Pet Poison Helpline.

INSOLUBLE CALCIUM OXALATES

Plant names: Anthurium, flamingo flower (*Anthurium* spp.), Arrowhead vine (*Syngonium* spp.), Caladium (*Caladium* spp.), Calla lily (*Zantedeschia* spp.), Dumbcane (*Dieffenbachia* spp.), Peace lily (*Spathiphyllum* spp.), Philodendron, sweetheart vine (*Philodendron* spp.), Pothos, Hunter's robe, Devil's ivy (*Epipremnum* spp.), Umbrella plant (*Schefflera actinophylla*)
Other common name(s): Calla lily, Philodendron, Peace lily
Species of concern: All
Toxic dose: Varies with the plant. In general, a small ingestion can cause clinical signs.
Toxic portion of plant: All
Onset/duration of clinical signs: Onset rapid to within a few hours, lasting up to 24 hrs after ingestion.
Clinical signs/MOA: These plants contain insoluble calcium oxalate crystals (raphides) that are released from the plant (idioblasts) when chewed. Signs include oral irritation (salivation, redness, pawing), v/d, anorexia. Oropharyngeal swelling and dermal/eye irritation can occur, though rare.
Treatment: Dilute with water or milk, antiemetic, SQ fluids, GI protectants as needed.

SOLUBLE OXALATES CONTAINING PLANTS
Plant names: Common or garden rhubarb (*Rheum rhabarbarum*), Shamrock plant (*Oxalis* spp.), Sour Star Fruit (*Averrhoa carambola*)
Other common name(s): Rhubarb, Shamrock, Star Fruit
Species of concern: All
Toxic dose: Varies with the plant.
Toxic portion of plant: Varies. Leaves of rhubarb are toxic but not the stalk. All parts of shamrock and sour star fruit are toxic.
Onset/duration of clinical signs: Onset rapid to within a few hours, lasting several days after ingestion.
Clinical signs/MOA: Oxalic acid/oxalate salts cause GI irritation, bind Ca which leads to hypocalcemia & CaOx renal damage
Clinical signs: Lethargy, vomiting, anorexia, hypocalcemia, tetany, CaOx crystalluria, ARF
Treatment: Emesis, activated charcoal w/sorbitol, IV fluids for 48hrs, antiemetic, monitor renal enzymes/UA daily for 72hrs & hospitalize on IV fluids for 48hrs

CARDIAC GLYCOSIDES
Plant names: Foxglove (*Digitalis lannata and D. purpuea),* Oleander (*Nerium oleander)*, Lily of the Valley (*Convallaria majalis),* Kalanchoe (*Kalanchoe spp.)*
Other common name(s): Yellow Oleander, Lucky Nut, Be-Still Tree
Species of concern: All
Toxic dose: Varies with the plant. In general, just a few seeds or leaves (fresh or dried) are concerning.
Toxic portion of plant: All
Onset/duration of clinical signs: 45 min to a few hours after ingestion.
Clinical signs/MOA: These plants contain cardiac glycosides, similar to digoxin, and interfere with the Na/K pump mediated by ATPase. This results in an increase in intracellular sodium and a decrease in intracellular potassium with a resultant loss of myocardial function due to a decreased resting membrane potential. Common signs include salivation, vomiting, diarrhea and abdominal pain within 45 min as well as hyperkalemia and bradycardia with 1st, 2nd or 3rd degree AV block, ventricular arrhythmias, and asystole. Weakness and depression often precede cardiac abnormalities. Some, such as kalanchoe, may also cause neurological signs and mydriasis.
Treatment: Early emesis and activated charcoal (repeated q 4-6 hrs for 2-3 doses). ECG monitoring x 24 hrs if symptomatic. Judicious use of IV crystalloids. Atropine (0.02-0.04 mg/kg IV, IM, SQ) for bradycardia. Antiemetics such as maropitant, 1 mg/kg SQ q 24 h (not labeled for cats). Lidocaine or procainamide for persistent tachycardia (rare). A temporary pacemaker and digoxin-specific Fab fragments (Digibind®, 1-2 vials needed, ~$600/vial) have been used successfully in dogs.
Prognosis: Poor unless treated early and aggressively.



Foxglove (*Digitalis purpuea).* Photo courtesy of Tyne K Hovda, Pet Poison Helpline.

GRAYANOTOXINS
Plant name: Rhododendrons and azaleas (*Rhododendron spp.)*, Laurels (*Kalmia spp.)*
Other common name(s): Mountain Laurel, Sheep Laurel
Species of concern: All
Toxic dose: Ingestion of 0.2 % of animal's body weight. An adult human can eat 3 leaves/flowers without developing clinical signs.
Toxic portion of plant: All.
Onset/duration of clinical signs: Rapid (1-2 hrs), rarely delayed up to 12 hrs.

Clinical signs: These plants contain grayanotoxin glycosides which bind to sodium channels, increase their permeability and result in prolonged depolarization of cardiac muscle. Gastrointestinal signs such as hypersalivation, vomiting, diarrhea and abdominal pain predominate. Cardiac signs such as bradycardia or tachycardia, arrythymias, and hypotension may also occur. Rarely, CNS signs such as tremors, seizures, and coma can occur.
Treatment: No antidote. Early emesis and activated charcoal (repeated q 4-6 hrs for 2-3 doses). ECG and blood pressure monitoring x 24 hrs if symptomatic. Judicious use of IV crystalloids. Atropine (0.02-0.04 mg/kg IV, IM, SQ) for bradycardia. Antiemetics such as maropitant, 1 mg/kg SQ q 24 h (not labeled for cats). Lidocaine or procainamide for persistent tachycardia (rare).
Prognosis: Good with early intervention.

SAGO PALM
Plant name: Sago or cycad palm (*Cycas spp., Macrozamia spp, Zamias spp.)*
Other common name(s): Leatherleaf palm and Japanese fern palm. These are not true palms. Grown outdoors in warm areas, houseplants in cool areas.
Species of concern: Dogs
Toxic dose: 1-2 seeds are fatal in a medium sized dog. A “few bites” can cause poisoning.
Toxic portion of plant: All, especially the seeds, contain cycasin and other toxins.
Onset/duration of clinical signs: Variable (hours to days)
Clinical signs: Common signs include vomiting and diarrhea (+/- blood), lethargy, depression within hours. Acute, severe hepatic necrosis develops in -2-3 days. CNS signs (weakness, coma, seizures) are possible and may be related to liver failure.
Treatment: Induction of emesis and multiple doses of activated charcoal (q 4-6 hrs for 2-3 doses), IV fluids with dextrose, B vitamins and colloids as needed. Hepato protectants such as SAMe (load at 40 mg/kg/day PO for 3-4 days, then 20 mg/kg/day x 2 weeks) and/or silymarin (20-50 mg/kg daily PO). Broad spectrum antibiotics if liver necrosis. Diazepam (0.25-0.5 mg/kg IV PRN) for seizures. GI protectants as needed.
Prognosis: Good if treated prior to the onset of liver failure.

Suggested reading:

Toxic Plants of North America, 2nd ed. Burrows/Tyrl (2013)

Blackwell’s Five-Minute Veterinary Consult Clinical Companion: Small Animal Toxicology 2nd edition.

Peterson and Talcott Small Animal Toxicology 3rd edition.

Handbook of Toxic Plants of North America, Burrows/Tyrl (2006)

A Guide to Poisonous House and Garden Plants, Knight (2006)

Common Psychiatric Pharmaceutical Poisonings

Renee D Schmid, DVM, DABVT, DABT – Pet Poison Helpline Bloomington, MN

Nearly half of the exposures managed by Pet Poison Helpline are to human drugs. Here we will discuss the most common prescription psychiatric exposures: Anti-depressants, ADHD treatments, and more. For each of these, we will review clinical signs of toxicity, diagnostics, and treatment.

Amphetamines and Methylphenidate

Prescription stimulants are commonly prescribed for treatment of attention deficit disorder in children and adults, narcolepsy, and sometimes weight loss. Common amphetamine drug brands include Adderall®, Dexedrine®, Desoxyn®, Dyanavel®, Dextrostat®, Evekeo® and Vyvanse®. Methylphenidate (Ritalin® and Concerta®) and dexmethylphenidate (Focalin®) are also commonly prescribed CNS stimulants. Novel formulations of these drugs are appearing on the market. Adzenys® XR-ODT is an extended release amphetamine in an orally disintegrating tablet designed to make administration easier for children or other people who have difficulty swallowing pills, and Daytrana® is a transdermal patch designed to deliver methylphenidate throughout the day. Fruit-flavored chews and solutions are also available. These stimulant drugs may come in immediate-release or an extended or sustained release formulation, as indicated by the letters XR, SR, ER, LA, or CD in the trade name.

While the range of toxicity varies amongst these drugs, clinical signs typically begin near a dosage of 1 mg/kg in dogs. Immediate-release drugs are rapidly absorbed, and clinical signs can develop 20-30 minutes after ingestion. Sustained-release products and transdermal patches (if swallowed whole) may result in a slower onset of action as well as a prolonged duration of clinical signs. Signs of intoxication involve CNS over-stimulation and excessive sympathomimetic effects such as agitation, vocalization, hyperactivity, hypertension, head bobbing, mydriasis, hyperthermia, tachycardia, tremors, and seizures.

Treatment is primarily symptomatic and supportive. Emesis should only be performed on asymptomatic animals and needs to be done promptly due to the rapid onset of clinical signs. Activated charcoal may be helpful, especially with sustained release products. Ingested patches may need to be retrieved by emesis, gastric lavage, or endoscopy. Maintaining control of agitation, hyperthermia, tachycardia, and tremors are key elements in these cases. Acepromazine (0.05-0.1+ mg/kg IV, IM, SQ) or chlorpromazine (0.5-1 mg/kg IV or IM) can be successfully used to achieve sedation and can be additionally beneficial in reducing heart rate, temperature, and blood pressure in agitated patients. It is recommended to start at the low end of the dosage range for sedatives and increase as needed. Some animals may require larger dosages than are listed here. Additionally, serotonin syndrome may occur and can be treated with cyproheptadine 1.1 mg/kg in dogs or 2-4 mgs total per cat orally or crushed into a slurry and delivered rectally. Benzodiazepines are typically avoided as they tend to result in paradoxical increased CNS excitement in these patients. Other commonly used interventions include injectable methocarbamol for tremors, injectable beta-blockers for tachycardia refractory to sedation, and IV fluids. Prognosis is generally good with prompt and aggressive treatment, though prolonged care may be needed, especially in large overdoses of extended release drugs.

Guanfacine and Clonidine

Guanfacine is a centrally active drug with alpha 2-adrenergic agonist properties used for treatment of ADHD. It is not a stimulant, and the mechanism of action in treating ADHD is unknown. It can be used alone for treatment or in combination with other stimulants. Common brand names for this drug are Intuniv®, an extended release formulation, and Tenex®, an immediate release form of the drug. Clonidine is another similar alpha 2-adrenergic agonist drug sometimes used off-label to treat ADHD, autism, and Tourette's Syndrome. Both clonidine and guanfacine were originally used as antihypertensive agents, and clonidine is also sometimes prescribed as a sleep aid, especially for children with sleep disturbances associated with ADHD or the stimulants prescribed to treat ADHD. Clonidine is now being used in dogs for certain behavioral conditions including phobias and separation anxiety.
Overdose of guanfacine and clonidine can result in clinical signs including depression, sedation, ataxia, vomiting, bradycardia, hypotension, and potentially seizures and tremors. Signs can develop at low

doses, and these drugs have a narrow margin of safety in pets. Signs are expected within 4 hours of exposure and can last 24-72 hours.
Asymptomatic patients may be induced to vomit and then given one dose of activated charcoal. In symptomatic patients, atipamezole, while not a true antidote, can be used to reverse signs of toxicity with these drugs and is typically dosed at 50 mcg/kg IM. Atipamezole will need to be re-dosed frequently as it typically lasts only 2-3 hours, while the effects of clonidine and guanfacine can have a duration of 24 hours or longer. IV fluids are warranted to maintain hydration, increase perfusion, and support blood pressure. Vital signs, especially heart rate and blood pressure, should be monitored frequently. If seizures occur, they can be treated with standard anticonvulsants.

Atomoxetine
Atomoxetine (Strattera™) is a non-stimulant SNRI (selective norepinephrine reuptake inhibitor) used as a second line treatment drug for ADHD. At low doses, signs of anorexia, sedation or agitation have been reported with potential for hypertension, tachycardia, and possibly tremors at higher doses. Signs usually develop within a few hours and can last 12-24 h. Cats and pets with liver disease are thought to be more sensitive to the effects of this drug.

With recent ingestion, induce emesis and then give one dose of activated charcoal. Treatment is symptomatic and supportive if signs develop with anti-emetics for nausea/vomiting, sedation for agitation, beta blockers if persistent tachycardia develops, and methocarbamol for tremors.

SSRI Antidepressants
Prescription antidepressants drugs routinely rank amongst the most commonly prescribed medications in the US and are increasingly used in veterinary medicine for a variety of behavioral disorders, including separation anxiety, storm phobias, inappropriate urine marking, stereotypic behaviors, and psychogenic alopecia. Common SSRIs include fluoxetine, citalopram (Celexa®), escitalopram (Lexapro®), paroxetine (Paxil®), and sertraline (Zoloft®). These drugs may come as either an immediate release or extended release formulation.

Selective serotonin reuptake inhibitors block the reuptake of serotonin in the presynaptic membrane, which results in an increased concentration of serotonin in the CNS. The range of toxicity varies depending on the drug and species. Small overdoses of SSRIs typically result in sedation or agitation, hypersalivation, vomiting, mydriasis, and tremors. Larger overdoses may cause tremors, seizures, nystagmus, dysphoria, vocalization, aggressive behavior, ataxia, and, bradycardia. As the degree of overdose increases, so does the risk for the development of serotonin syndrome, a toxidrome characterized by central nervous, autonomic, and neurobehavioral signs including agitation, vocalization, vomiting, diarrhea, muscle rigidity, increased reflexes, tremors, hyperthermia, hypertension, and transient blindness.

Treatment of SSRI overdoses is largely supportive and symptomatic. Appropriate decontamination with early emesis and activated charcoal is recommended if aspiration risk is low. Cyproheptadine, a serotonin antagonist, is useful in reducing the severity of signs, especially vocalization and dysphoria and is dosed at 1.1 mg/kg in dogs and 2-4 mg total dose per cat q 4-6 hours either orally or crushed into a slurry and delivered rectally. Agitation may be treated with acepromazine (0.05-0.2 mg/kg, IV, IM, or SQ PRN) or chlorpromazine (0.5-1 mg/kg, IV or IM PRN) starting at the low end of the dosage range and increasing as needed. Some animals may require larger dosages than are listed here. Benzodiazepines are typically avoided as they tend to result in paradoxical increased CNS excitement in these patients. Additional treatments include methocarbamol for tremors (55-220 mg/kg, IV slowly and to effect), IV fluids for thermal cooling and to maintain hydration and adequate perfusion, and beta-blockers (e.g., propranolol 0.02-0.06 mg/kg, slowly IV) for tachycardia and hypertension that is not corrected following appropriate sedation.

Overdoses of other antidepressants such as duloxetine (Cymbalta®), a SNRI, and venlafaxine (Effexor®), a bicyclic antidepressant, are clinically similar to SSRI overdoses. Cats seem particularly drawn to Effexor capsules and will readily ingest them. Treatment is similar to SSRI overdoses but more focus on sedation may be needed.

Tricyclic Antidepressants

Tricyclic antidepressants are another class of antidepressants used in human medicine as well as veterinary medicine for separation anxiety, other behavior conditions, excessive grooming or feather plucking, urinary conditions, pruritus, and neuropathic pain. Common tricyclic antidepressants include amitriptyline, clomipramine (Clomicalm®), nortriptyline, and doxepin.

These drugs have a narrow margin of safety, and anticholinergic effects can develop with overdose. Signs of toxicity may include constipation, urine retention, mydriasis, sedation vs agitation, disorientation, ataxia, arrhythmias, tachycardia, hypertension, vomiting, serotonin signs, and seizures. Treatment is similar to SSRI overdoses with decontamination, IV fluids, sedation if agitation develops, cyproheptadine if serotonin syndrome develops, antiemetics for vomiting and nausea, methocarbamol for tremors, and anticonvulsants if seizures develop. Close monitoring of vital signs, especially cardiovascular monitoring, is warranted Many tricyclic antidepressants are fat soluble, so treatment with intravenous lipids may be helpful in cases of severe toxicity.

Benzodiazepines and Non-Benzodiazepine Sleep Aids

Benzodiazepines are commonly used as anxiolytics, anticonvulsants, muscle relaxants and sedatives/hypnotics. Non-benzodiazepine hypnotics are typically used as sleep aids in human medicine. Although the two groups have different pharmacological profiles, both exert their effects through the inhibitory neurotransmitter gamma-amino butyric acid (GABA) and have similar clinical effects and treatment regimens. Common benzodiazepines used in veterinary medicine include alprazolam (Xanax®), diazepam (Valium®), lorazepam (Ativan®), midazolam (Versed®), and zolazepam found in combination with tiletamine as the dissociative agent (Telazol®). Other benzodiazepines used in human medicine include clonazepam (Klonopin®), oxazepam (Serax®), and temazepam (Restoril®). Common Non-benzodiazepine hypnotics include zolpidem (Ambien®), eszopiclone (Lunesta®), and zaleplon (Sonata®).

Both families of drugs have a relatively wide margin of safety, and fatality is unlikely to occur with acute overdose. Chronic oral use of diazepam in cats, however, can result in hepatic failure and should be avoided. Following ingestion, clinical signs of acute intoxication typically develop rapidly within 30-60 minutes and commonly include sedation vs paradoxical CNS stimulation (agitation), ataxia, confusion, and vomiting.

Treatment of acute ingestions consists of appropriate decontamination and supportive care. If necessary, the reversal agent or antidote, flumazenil, can be used but is rarely needed as these drugs are typically well tolerated. In symptomatic animals, monitor the body temperature and blood pressure and provide thermoregulation. IV crystalloids can be used as needed to maintain perfusion, treat hypotension, and correct dehydration. In cases of paradoxical stimulatory signs, additional benzodiazepines should *not* be administered as they will exacerbate the clinical signs. Instead, acepromazine (0.05-0.2 mg/kg IV, IM or SQ PRN) or butorphanol (0.1-0.5 mg/kg IV, IM, or SQ PRN) can be used. The reversal agent flumazenil (0.01 mg/kg, IV to effect PRN) is the antidote for benzodiazepine overdoses but is only necessary in rare cases of severe CNS or respiratory depression.

Lithium

Lithium carbonate and lithium citrate are used to treat bipolar disorder and as an adjunct to other antidepressants in humans, and its mechanism of action is not well understood. It has recently been tried as a treatment of anemia and neutropenia in dogs with bone marrow suppression, though with questionable efficacy. Lithium is a cation that competes with sodium, potassium, calcium, and magnesium at cellular sites, so animals with renal disease, dehydration, and sodium depletion can be more sensitive to this drug.

Acute overdoses of this drug are typically well tolerated with only mild vomiting, anorexia, and lethargy expected. Chronic overdose, which occurs rarely in pets, can be more serious, and signs may include lethargy, muscle rigidity, tremors, seizures, hypotension, arrhythmias, and bradycardia.

Emesis may be induced with recent ingestion. Activated charcoal is not effective at binding lithium. IV fluids can increase elimination of lithium, and 0.9% NaCl may be more effective at enhancing renal

excretion. Treatment is otherwise symptomatic and supportive with antiemetics for vomiting, anticonvulsants for seizures, and methocarbamol for tremors and muscle rigidity.

Lamotrigine

Lamotrigine (Lamictal®) is a phenyltriazine anticonvulsant that is also used to treat bipolar disorder in humans. Overdose of this drug can result in vomiting, lethargy vs hyperactivity, ataxia, weakness, tremors, seizures, hypokalemia, and acidosis. Arrhythmias, hypotension, and rare hepatotoxicity are also possible. This drug is rapidly absorbed with onset of action in most cases within 4 hours, and signs can last 24-48 hours.

Treatment of acute ingestions consists of appropriate decontamination and supportive care. Intravenous fluid may aid elimination and is also used for hydration and perfusion. Close monitoring of heart rate, EKG, and blood pressure are warranted. Ventricular arrhythmias may be treated with lidocaine or procainamide if needed. Antiemetics are used as needed for vomiting, and diazepam and/or phenobarbital if seizure activity develops. Very depressed or comatose patients may need monitoring of respirations and blood gas, and some dogs require ventilatory support.

Antipsychotics

Antipsychotic drugs are used in human medicine to treat bipolar disorder, schizophrenia, and other psychiatric and neurologic conditions in humans. Common drugs in this class include olanzapine (Zyprexa®), risperidone (Risperdal®), aripiprazole (Abilify®), and ziprasidone (Geodon®). Signs of toxicity with these drugs include agitation or lethargy, hyperesthesia, vomiting, diarrhea, hypotension, tachycardia, ataxia, vocalization and aggression, serotonin syndrome, and arrhythmias. Olanzapine can cause fluctuations between sedation and agitation. Animal studies of risperidone have shown that induction of emesis with apomorphine can be inhibited by this drug and may not be productive. It is also important to note that the “discmelt” version of Abilify® may contain xylitol.

These drugs are quickly absorbed with rapid onset of signs, and signs typically last approximately 24 hours in dogs. Treatment of acute ingestions consists of appropriate decontamination with emesis only in asymptomatic patients and activated charcoal only if low risk of aspiration. IV fluids are used for hydration and perfusion. Treatment is supportive with close monitoring of vital signs and blood pressure in symptomatic pets. Sedation is warranted in agitated pets, and if serotonin syndrome develops, cyproheptadine 1.1 mg/kg orally or rectally may be administered every 6-8 hours as needed. Tremors can be treated with methocarbamol and seizures with standard anticonvulsants.

Suggested Reading

- Blackwell’s Five-Minute Veterinary Consult Clinical Companion: Small Animal Toxicology 2nd edition.
- Peterson and Talcott Small Animal Toxicology 3rd edition.
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- Thomas DE, et al. Retrospective evaluation of toxicosis from selective serotonin reuptake inhibitor antidepressants: 313 dogs (2005-2010). J Vet Emerg Crit Care22:674-81, 2012.

Know When to Feast and When to Fret - Foods Toxic to Pets

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Chocolate

The main toxic components of chocolate are two types of methylxanthines: theobromine and caffeine. Methylxanthines cause an increase in cAMP due to inhibition of cellular phosphodiesterase, stimulate the release of catecholamines from the adrenal medulla, cause competitive inhibition of adenosine, and increase intracellular calcium levels, which ultimately results in cerebral vasoconstriction, increased cardiac muscle contractility, and CNS stimulation. Theobromine is slowly absorbed by dogs and may take up to 10 hours before peak plasma levels are reached. The half-life of theobromine is also longer in dogs at 17.5 hours.

When assessing the toxicity of chocolate, it is important to remember that darker chocolates such as cocoa powder, unsweetened chocolate, and higher cocoa content dark chocolates contain more theobromine and are therefore more toxic to pets. Milk chocolate contains less theobromine and is better tolerated, and white chocolate contains minimal theobromine with minimal risk of toxicity. With chocolate ingestions, it is also important to get a good history to rule-out other potentially toxic co-ingestions such as marijuana, xylitol, macadamia nuts, alcohol, and raisins.

Theobromine toxicity will typically result in mild GI upset and excitement starting around 20mg/kg, moderate signs with potential for tachycardia at 40mg/kg, and potential for tremors and seizures at 60mg/kg. Due to the slow absorption of chocolate, induction of emesis is often rewarding even 6 hours after ingestion. Due to enterohepatic recirculation, multiple doses of activated charcoal are warranted, and IV fluids can help with excretion, as well as hydration and perfusion. Frequent walks or urinary bladder catheterization can keep the bladder empty to prevent reabsorption of metabolites in the urine. Treatment is otherwise symptomatic and supportive with close monitoring of vital signs, antiemetics for vomiting, sedation for agitation, beta blockers for sustained tachycardia, antiarrhythmics as needed, and anticonvulsants if seizures occur. Due to the prolonged half-life of theobromine, severely affected animals may remain symptomatic up to several days after ingestion.

Caffeine

Caffeine toxicity is possible when pets consume foods or drinks high in caffeine such as coffee, tea, and energy drinks; when they ingest caffeine pills or supplements that contain caffeine; and sometimes in novel forms, such as caffeine gum for alertness. Caffeine is rapidly absorbed, reaches peak plasma levels within 30-60 minutes, and has a half-life of 4 hours. Most common signs with overdose of caffeine include vomiting, diarrhea, CNS excitation, cardiac stimulation, hypokalemia, and hypertension. Mild signs are expected at 15 mg/kg of caffeine, moderate signs at 25 mg/kg, and severe CNS and cardiovascular signs at 50 mg/kg.

Treatment of caffeine toxicity is similar to chocolate toxicity. As caffeine is rapidly absorbed, emesis is generally not recommended in symptomatic patients, especially those as risk of aspiration. Due to enterohepatic recirculation of caffeine, multiple doses of activated charcoal can be useful, and IV fluids can help with excretion, as well as hydration and perfusion. Frequent walks or urinary bladder catheterization can keep the bladder empty to prevent reabsorption of metabolites in the urine. Treatment is otherwise symptomatic and supportive with close monitoring of vital signs, antiemetics for vomiting, sedation for agitation, beta blockers for sustained tachycardia, antiarrhythmics as needed, and anticonvulsants if seizures occur. Potassium should be monitored in cases of caffeine toxicity and may need to be supplemented in IV fluids if hypokalemia develops.

Xylitol

Xylitol is an increasingly popular, naturally-occurring sugar alcohol used as a sugar free sweetener in low calorie, sugar free, diabetic, and diet foods. It may be used alone as a sweetener in foods or in combination with other sweeteners such as aspartame, sugar, and/or other sugar alcohols. Xylitol is most

commonly ingested as an ingredient in sugar free gums and other premade foods but is also available in a powdered form for baking at home.

Xylitol is known to increase insulin release from the pancreas of dogs, which can result in hypoglycemia if ingested at doses of 0.1 g/kg and above. Elevated liver enzymes and liver necrosis may occur with large ingestions of > 0.5 g/kg xylitol. Cats are not considered to be sensitive to xylitol.

Xylitol is rapidly absorbed by the stomach and upper GI tract when ingested by dogs. It is safest to verify normoglycemia before inducing emesis, and activated charcoal is not indicated as it does not reliably bind to xylitol. If a hypoglycemic dose has been ingested, monitor blood glucose for at least 8 hours with the plan to supplement 2.5-5% dextrose as needed if hypoglycemia develops.

In dogs that have ingested a potentially hepatotoxic dose of xylitol, preemptive dextrose supplementation for 24-48 hours is thought to help mitigate liver toxicity. Treatment with liver protectants, such as SAM-e and N-acetylcysteine, are warranted in patients consuming hepatotoxic doses of xylitol. Liver enzymes are monitored every 12-24 hours for at least 48-72 hours or until they have normalized or at least plateaued. In cases of hepatic necrosis, secondary coagulopathy is possible, so coagulation monitoring and transfusion may needed.

Grapes and Raisins

Grapes, raisins, sultanas, and *Vitus spp.* currants (marketed as Zante currants) have been shown to cause renal failure in dogs. *Ribus spp.* currants are in the gooseberry family and do not cause renal toxicity in dogs. The toxicity risk to cats and ferrets is unknown, however considered lower risk with only rare anecdotal reports of toxicity. The mechanism of toxicity is unknown and is considered to be idiosyncratic. Grape seed extract appears to be safe and has not been shown to cause renal injury.

Vomiting is often an early sign of grape and raisin toxicity in dogs and usually develops within 24 hours of ingestion. 24-48 hours after ingestion, signs progress to lethargy, continued vomiting, inappetence and possible abdominal pain. Azotemia may occur within 24 hours of ingestion. Untreated, anuria and oliguria may be seen within 48-72 hours of ingestion. Decontamination is central in prevention of grape and raisin toxicity in dogs. As grapes are slowly absorbed, emesis can be performed up to 6 hours after ingestion followed by one dose of activated charcoal. Baseline lab work to assess current renal function, anti-emetics, and IV fluids for 48 hours are important components to therapy. Renal function should be monitored daily during hospitalization, and if azotemia occurs, IV fluids are continued for 24-48 hours after values have either returned to normal or stabilized. Prognosis is good in patients that are treated early and aggressively.

Onions and Garlic

Foods from the *Allium* species include onions, garlic, shallots, chives, scallions, and leeks, and if ingested in sufficient quantity by cats and dogs, they can result in oxidative hemolysis and anemia. For onions, ingestions > 5 g/kg in cats and 15-30 g/kg in dogs are considered toxic. Garlic is more potent, and doses of >1 g/kg is considered toxic for cats and > 5 g/kg is considered toxic to dogs. Clinical signs of toxicity include vomiting, diarrhea, lethargy, depression, abdominal pain, diarrhea, pallor, tachycardia, tachypnea, and icterus. Signs may develop within 1-2 days with a large acute exposure or up to several days with smaller exposures.

When toxic quantities of onions or garlic are consumed, treatment involves early induction of emesis and then one dose of activated charcoal. Baseline blood work should be checked with the plan to continue to monitor the PCV/CBC until it has normalized if anemia develops. Anemia typically resolves 10-14 days after ingestion. Any gastrointestinal signs can be treated supportively with fluids, anti-emetics, anti-diarrheals, and bland diet as needed. Antioxidants such as ascorbic acid, Vitamin E, and NAC have not been proven to provide any protective effects.

Macadamia Nuts

Ingestion of macadamia nuts by dogs can cause signs including vomiting, diarrhea, pancreatitis, lethargy, hyperthermia, weakness, tremors, lameness, and ataxia. Approximately 1 nut/kg body weight is considered toxic to dogs. Signs are usually self-limiting and typically resolve within 24-48 hours. This is a poorly understood toxicity, and dogs seem to be the only species sensitive to macadamia nuts.

Treatment involves early decontamination by inducing emesis and then one dose of activated charcoal for patients that have recently ingested a toxic amount of these nuts. For symptomatic patients, treatment is supportive with antiemetics if vomiting or nausea develop, fluids as needed for hydration, nursing care, supportive treatment if pancreatitis develops, thermoregulation, analgesia for lameness or joint stiffness, and methocarbamol if tremors develop. Prognosis is excellent with this toxicity and a full recovery is expected.

Unbaked Yeast Bread Dough

Rising, uncooked yeast dough is another category of potentially toxic food and would include any yeast dough to make bread, rolls, buns, or pizza. Dogs will readily eat entire loaves of rising bread dough, and unfortunately a dog's warm, dark stomach is an ideal environment for yeast to ferment, which results in production of both gas and ethanol (alcohol). When ingested, the dough rapidly expands in the stomach, gas is produced by the yeast, and dangerous distension of the dog's stomach can result. The alcohol produced by the yeast can also cause dogs to develop ethanol toxicity with signs including hypoglycemia, ataxia, weakness, and lethargy.

With recent ingestion in an asymptomatic patient, emesis can be induced to remove the dough. If the dough is not recovered with emesis, gastric lavage with cold water can also be attempted. Activated charcoal is not indicated and is not considered helpful for this toxicity.

Symptomatic patients should be hospitalized for monitoring and may need serial radiographs to assess passage of dough. In rare cases, surgical removal of the dough may be necessary. Intravenous fluids can be given for hydration and perfusion, and dextrose supplementation may be needed if hypoglycemia from ethanol toxicity develops. Vitals should be monitored closely and heat support may be needed for hypothermic patients. Metabolic acidosis can develop and is treated with IV fluids and potentially sodium bicarbonate if severe.

Alcohol

Pets, especially dogs, will readily drink unattended glasses of beer, wine, and other alcoholic beverages if given the opportunity. Dogs can also develop alcohol toxicity after eating alcohol-soaked desserts, like rum balls or cakes soaked in rum or bourbon. Ethanol can cause depression, weakness, ataxia, GI signs, and potentially hypoglycemia, hypothermia, acidosis with higher doses. Onset of signs is rapid as ethanol is rapidly absorbed.

Ethanol is rapidly absorbed, so emesis induction is rarely rewarding. Induction of vomiting should be avoided in symptomatic patients due to risk of aspiration. Activated charcoal does not bind to alcohol and is not indicated. Treatment is symptomatic and supportive with intravenous fluids for hydration and perfusion with dextrose supplementation if hypoglycemia develops. Vitals should be monitored closely and heat support may be needed for hypothermic patients. Metabolic acidosis can develop and is treated with IV fluids and potentially sodium bicarbonate if severe. Naloxone has been used with variable results to reverse CNS depression and may be redosed as needed if effective. Antiemetics may be given for nausea and vomiting. Prognosis is good, especially with early and appropriate treatment.

Avocado

Avocado is primarily toxic to birds, and all parts of *Persea americana* (fruit, pits, leaves, and stems) are considered toxic in affected species. Signs of avocado toxicity in birds include agitation, feather-pulling, fluffed feathers, lethargy, anorexia respiratory distress, pulmonary edema, respiratory collapse, pericardial effusion, cardiac arrhythmias, and sudden death. Avocado toxicity has also been reported in rabbits with cases of non-infectious mastitis and agalactia reported in nursing rabbits, and cardiac arrhythmias,

submandibular edema, respiratory distress, and sudden death developing in rabbits after ingestion of leaves. In dogs and cats, avocado may cause mild GI upset, rare pancreatitis, and if the pit is ingested whole, there may be concern for gastrointestinal obstruction.

Immediate care is indicated for birds that ingest avocado. Crop lavage followed by one dose of activated charcoal can be administered to asymptomatic birds. Recently exposed and asymptomatic rabbits can also be given one dose of activated charcoal (they cannot be induced to vomit). Treatment is symptomatic and supportive with oxygen, nutritional support, and diuretics for pulmonary edema. If mastitis develops, it is non-infectious, so antibiotics are not typically required. Warm compresses and analgesia can be helpful. Prognosis is poor once cardiac or respiratory symptoms occur in birds and rabbits.

Suggested Reading

- Blackwell's Five-Minute Veterinary Consult Clinical Companion: Small Animal Toxicology 2nd edition.
- Peterson and Talcott Small Animal Toxicology 3rd edition.
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