TOXINS AND POISONING

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Toxic exposure or ingestion is a very common presenting complaint in both small animal emergency medicine and general practice. It is extremely important to have the client bring the original container and label with them to the hospital so that the toxic substance can be identified. It is also important to note that not all toxin exposure is via ingestion. Animals can also experience contact and inhaled toxicities, although ingestion is by far the most common route of exposure.

A history should be taken on all patients with possible toxin exposure prior to instituting treatment. Your history should include the following:

- What product was ingested, including the active ingredient?
- How much was ingested (minimum and maximal exposures)?
- The time the product was ingested (or time range)?
- Is the pet showing any clinical signs?
- Does the pet have any other medical problems?
- Was anything given at home (ie. Hydrogen peroxide, food...)?

Once it has been determined the pet has experienced a toxic exposure, decontamination should be your first goal. The goal of decontamination is to minimize further absorption from the body and to promote elimination.

Oral Decontamination

Oral decontamination typically involves emesis induction. Emesis may not be recommended in all situations and should be advised based upon the length of time since ingestion, the substance ingested, current clinical signs and concurrent medical problems. The induction of emesis is typically only recommended if the exposure was less than 1-2 hours prior to presentation and the patient is neurologically appropriate. Emesis should not be performed if a caustic or volatile substance has been ingested, the patient is neurologically inappropriate or they suffer from an underlying disease process that makes them at increased risks for aspiration pneumonia (ie. laryngeal paralysis).

The most common agent used in veterinary hospitals to induce vomiting is apomorphine (in dogs) and xylazine (in cats). Apomorphine works by directly stimulating the chemoreceptor trigger zone (CRTZ) in dogs. Apomorphine is not recommended for cats due to its ineffectiveness. Apomorphine is available in an injectable solution or as a table that can be placed subconjunctivally. Patients may become overly sedate with this medication and naloxone can be administered to reverse the sedation effects but this will not reverse the emetic effect. Xylazine is a centrally mediated alpha$_2$-adrenergic agonist that can induce emesis in cats. The induction of emesis is unpredictable in cats and xylazine can lead to profound sedation. Yohimbine can be used to reverse these sedative effects. If yohimbine is not available atipamezole may be used for reversal at a dose of 1 mg per 10 mg of xylazine administered.

Doses:

Apomorphine (canine): 0.02-0.05 mg/kg IV	Naloxone: 0.01-0.04 mg/kg IV
Xylazine (feline): 0.44-1.1 mg/kg IM, SQ	Yohimbine: 0.1 mg/kg IV, IM

Gastric lavage can also be performed, but this requires general anesthesia and is more labor intensive. Patient must be intubated during gastric lavage to prevent aspiration. Activated charcoal can also be administered during gastric lavage but these patients must be closely monitored as aspiration can occur.

Activated charcoal

Activated charcoal is a carbonaceous substance that has a large surface area that can bind and adsorb a number of toxins. Not all compounds are equally adsorbed and therefore charcoal should only be administered to patients that have ingested a toxin that readily binds to activated charcoal. Charcoal is not effective in binding large poorly water soluble organic compounds and it is not effective in binding metals, caustic substances or very small molecules such as xylitol or ethylene glycol.

Activated charcoal can be obtained with or without sorbitol, a cathartic that is used to decrease gastrointestinal transit time. The risks and benefits of administering charcoal must be evaluated for every patient. If multiple doses of charcoal are required only the first dose should contain sorbitol. High doses of activated charcoal may cause hypernatremia and hyperosmolar syndromes. Therefore it is important to evaluate a patient's electrolyte status prior to repeat doses of charcoal. Activated charcoal should be administered at 1-5 g/kg for first dose then 1-2 g/kg (without sorbitol) for subsequent doses. Please note that the doses listed on the Toxiban bottles are higher than those currently recommended by Animal Poison Control.

Intravenous Lipid Emulsion Therapy

Intravenous lipid emulsion (ILE) therapy has been used in both human and veterinary medicine to aid in the treatment of lipophilic drug toxicities. ILE is thought to act as a lipid sink were

lipophilic compounds are contained within the lipid high vascular space decreasing the volume of “active” free drug. ILE may also help increase cardiac performance by increasing intracellular calcium concentrations and providing monocytes with energy sources. Possible side effects of ILE therapy include fat emboli, fat overload syndrome, pancreatitis, worsening of acute respiratory distress syndrome (ARDS) and coagulopathy. The most commonly reported dose of 20% ILE therapy is 1.5 - 4 ml/kg bolus over 1 minute, then a constant rate infusion (CRI) of 0.25 ml/kg/min for 30 – 60 minutes (extrapolated from human literature).

Listed below are several compounds that are responsive to ILE therapy.

- Macrocyclic lactones (ivermectin, moxidectin)
- Lidocaine and Bupivacaine
- Pyrethrins
- Calcium channel blockers (Verapamil, diltiazem, amlodipine)
- Tetrahydrocannabinol (THC)
- Baclofen
- Naproxen
- Metaldehyde
- Diazepam
- Nicotine
- Cyclosporine
- Digoxin
- Vinblastine

Dermal Decontamination

Animals can also develop toxicities secondary to dermal exposures. If a dermal toxicity is suspected the patient should be bathed with a mild detergent soap such as Dawn dish soap.

There are very few reversal agents or antidotes for toxicities. When such an antidote exists it should be administered. If no antidote exists, once decontamination has been accomplished the focus of treatment is typically symptomatic and supportive care. Below we will discuss some common veterinary toxicities.

Non-steroidal anti-inflammatory drugs (NSAIDs)

NSAIDs inhibit cyclooxygenase (COX) which is a key enzyme in the production of prostaglandins. Prostaglandins are important in a number of homeostatic functions including maintaining renal blood flow, gastric and intestinal mucous production and normal platelet function. NSAID toxicity can lead to a variety of clinical signs including gastrointestinal ulcerations, acute kidney injury, neurologic dysfunction, hepatic injury and platelet dysfunction. The toxic dose for NSAIDs varies based upon species and the product ingested; therefore animal

poison control should ideally be consulted in all NSAID toxicities to determine the margin of safety, product half-life and recommended treatments.

Gastrointestinal decontamination is typically recommended if ingestion was within 2-4 hours of presentation. Many NSAIDs undergo enterohepatic circulation and therefore multiple doses of activated charcoal (every 6-8 hours) may be recommended. The goal of treatment is prevention of gastric and renal injury. Treatment with misoprostol, proton pump inhibitors (omeprazole or pantoprazole) and sucralfate is recommended for 10-14 days post toxicity to help prevent NSAID induced ulcerations. Fluid diuresis for at least 48 hours is recommended if a renal toxic dose is ingested to help prevent acute kidney injury. The patient's renal values should be monitored at least every 24 hours during this treatment period. Should acute renal failure develop hemodialysis may be necessary.

Xylitol

Xylitol is a sugar-free sweetener that is found in many foods and gums. Xylitol stimulates insulin release in dogs, resulting in hypoglycemia. Ingestion may also cause acute hepatic necrosis at higher doses. Activated charcoal has limited benefit in these patients as it does not readily bind xylitol and toxicosis can occur in as little as 15 - 30 minutes post-ingestion. Emesis is recommended if ingestion is recent. Patients ingesting a toxic dose should be hospitalized for 12 - 24 hours for monitoring. Baseline liver values should be obtained and rechecked every 24 hours for 3 days. The blood glucose should be monitored every 1 - 4 hours for 12 - 24 hours post ingestion. If hypoglycemia is noted a bolus of 50% dextrose diluted (1:2 with 0.9% NaCl) should be administered over 1 - 2 minutes followed by a constant rate infusion of 2.5 - 5% dextrose.

Hypoglycemia has been reported following ingestion of > 0.1 g/kg xylitol while acute hepatic necrosis has been reported in animals ingesting > 0.5 g/kg. A typical stick of gum contains 0.3 - 0.4 grams of xylitol. Other products contain varying amounts of xylitol. Clinical signs of xylitol toxicity include lethargy, weakness, collapse, seizure activity or signs of liver failure.

Grapes and Raisins

Grape and raisin toxicities have been associated with the development of acute kidney injury. The exact mechanism of toxicity and toxic dose for grape/raisin ingestion is unknown. Treatment involves decontamination and aggressive fluid diuresis for 48 - 72 hours. Grapes and raisins can stay in the stomach for prolonged periods of time and therefore emesis induction should be performed if ingestion was within 6 hours. One dose of activated charcoal should be administered once emesis has been completed and an antiemetic has been administered. Renal values should be monitored at least every 24 hours for 3 days and urine output should be closely monitored. If oliguria or anuria develops, hemodialysis or peritoneal dialysis may be necessary.

Clinical signs associated with grape/raisin ingestion vary over the course of the disease. Gastrointestinal signs can be seen within 12 - 24 hours of ingestion and azotemia can be seen within 24 hours. Oliguria/ anuria typically do not develop until 48-72 hours post ingestion.

Rodenticides

Rodenticides are manufactured from a number of different active ingredients. Therefore it is essential clients bring the packaging of the ingested product with them to the hospital. The most common rodenticides are anticoagulant rodenticides and bromethalin containing products.

Anticoagulant rodenticides inhibit the activity of vitamin K epoxide reductase which converts vitamin K epoxide to its active reduced form which is necessary for activation of clotting factors II, VII, IX and X. Ingestion of anticoagulant rodenticide prevents formation of these clotting factors leading to coagulopathy and clinical bleeding. Most animals have 3-7 days worth of circulating clotting factors and therefore clinical signs of coagulopathy do not occur until these factors have been utilized. Factor VII has the shortest half-life of all the Vitamin K dependent factors and because of this the prothrombin time (PT) will become prolonged first. Prolongation of the PT can be seen in as little as 24 - 48 hours post ingestion, while active bleeding is typically not seen for 3 - 5 days post ingestion.

Vomiting should be induced in any patient presenting for acute rodenticide ingestion and activated charcoal should be administered. Multiple doses of activated charcoal are recommended for bromethalin ingestion, but is unnecessary for anticoagulant rodenticides. For acute toxicities prior to the onset of clinical signs, Vitamin K1 therapy (2.5 - 5 mg/kg/day) can be administered for 14-30 days depending on the active ingredient within the anticoagulant rodenticide. A PT should be rechecked 48 hours after the last dose of vitamin K1 to ensure no further treatment is needed. Alternatively a PT can be checked 48 - 72 hours after initial ingestion. If the PT is normal at this time further therapy is not warranted. If the PT is prolonged Vitamin K1 therapy should be instituted. If this route is elected the client should be warned about the risk of bleeding. If an animal presents for active bleeding secondary to rodenticide exposure and is confirmed to be coagulopathic via clotting tests, inpatient therapy will be required. This involves administration of fresh frozen plasma, frozen plasma or whole blood transfusions in addition to Vitamin K1.

Bromethalin is a neurotoxic rodenticide that uncouples oxidative phosphorylation in the mitochondria of the central nervous system resulting in cerebral edema and demyelination of the long nerves. Bromethalin is readily absorbed from the GI tract and there is no antidote. Clinical signs can appear in as little as 2 hours, but can take up to 96 hours to develop with low-dose exposures. Decontamination should be performed as soon as possible and activated charcoal should be administered. Depending on the dose of bromethalin ingested charcoal may need to be repeated every 8 hours for up to 48 hours. If neurologic signs develop treatment is symptomatic

and neurologic recovery may occur over days to weeks. If clinical signs are severe the prognosis for recovery is very poor.

Lilies

Lilies within the genera *Lilium* and *Hemerocallis* may cause acute renal failure in cats when ingested. All parts of the plant including the pollen are toxic to cats and as little as 1-2 leaves can cause renal failure. Clinical signs of lily ingestion can develop within hours of ingestion and anuric renal failure can be seen in 1-3 days. Signs of toxicity include vomiting, diarrhea, anorexia, depression and abdominal pain/discomfort. Treatment for lily ingestion includes gastrointestinal decontamination, activated charcoal administration, intravenous fluid diuresis for 48 - 72 hours, antiemetics and close monitoring of renal values. Hemodialysis and peritoneal dialysis have been performed in cats who develop anuria/oliguria secondary to lily toxicosis. Prognosis is good if treatment is implemented early. Once anuria has developed the prognosis is grave without dialysis but is favorable with hemodialysis.

Pyrethrins and Pyrethroids

Pyrethrins are commonly found in household insect sprays and topical insecticides including monthly flea and tick prevention. Cats have altered glucuronidation making them more sensitive to pyrethrin than dogs. The exact feline toxic dose is unknown but concentrations more than 5-10% may lead to systemic toxicosis. Many feline products contain <1% pyrethrin while most canine products can contain concentrations up to 40-50%. In this author's experience most feline exposures are secondary to dog products being placed on cats or cats grooming dogs who received a topical pyrethrin.

Clinical signs of pyrethrin toxicosis include hypersalivation, vomiting, tremors, disorientation, weakness, seizures and respiratory symptoms. If pyrethrin toxicity is suspected the patient should be immediately washed with a gentle dish detergent such as dawn dish soap. Severe tremors should be treated with injectable methocarbamol (22 - 220 mg/kg IV PRN up to 330 mg/kg/day to effect). If tremors are mild oral methocarbamol can be used. These patients can also develop hyperthermia secondary to their muscle tremors and therefore their temperatures should be closely monitored. If seizure activity occurs phenobarbital (2 - 4 mg/kg IV PRN) should be administered. Clinical signs can persist for 1 - 4 days depending on the amount of exposure. The overall prognosis for Pyrethrin toxicity is excellent with early treatment.

Toxicities are very common in veterinary medicine and prompt decontamination and supportive care can great decrease the likelihood of clinical signs developing.

References:

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