You've Gotta Be Kitten Me: Cat Toxins
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Introduction

The American Veterinary Medical Association estimated in 2019 there were 58 million owned cats and 76 million owned dogs in the United States. Despite cats being close to dog numbers in the US, only about 9% of the calls to the ASPCA Animal Poison Control Center were regarding cats. The most common reported exposures in cats were insecticides, human medications, and plants.

Species Differences

There is a common adage in veterinary medicine that cats are not just small dogs. This wisdom holds especially true for toxicology. Cats can have an increased sensitivity to toxins due to differences in metabolism, kinetics, individual tastes, grooming habits, and red blood cells. Because cats are obligate carnivores, they have evolved with fewer biotransformation pathways than herbivores and omnivores. The problem arises when they encounter a xenobiotic that they do not possess a biotransformation pathway. Cats have a UDP-glucuronosyltransferase encoded by a pseudogene, thus glucuronidation pathways are dysfunctional in cats. This defective glucuronidation pathway prevents cats from glucuronidating a range of agents, including phenols, naphthols, morphine, acetaminophen, and aspirin. Cats also are poor sulfators and have difficulty metabolizing xenobiotics that require sulfation.
In addition to facing some challenges with metabolism of xenobiotics, species differences in red blood cells also put cats at higher risk from certain xenobiotics. Cats have eight sulfhydryl groups on their hemoglobin, which increases the susceptibility to oxidative damage, such as methemoglobinemia and Heinz body anemia. They also have a short red blood cell life span.

Decontamination/Emesis

Emesis is mediated by dopamine receptors in the chemoreceptor trigger zone in dogs. Apomorphine can induce emesis in dogs by stimulating these dopamine receptors. In cats, however, emesis is mediated by alpha-2 receptors in the chemoreceptor trigger zone. Therefore, apomorphine is not effective for inducing emesis in cats. Alpha-2 agonists, such as xylazine and dexmedetomidine, are recommended for the induction of emesis. Depression can be seen secondary to the administration of an alpha-2 agonist in cats. Because this would make emesis unsafe, due to the risk of aspiration in a depressed patient that is not adequately able to protect her airway, an IV catheter should always be placed in cats that have these medications administered to them and atipamezole should be given, if depression should occur.

Hydrogen peroxide is not recommended for use in cats, due to the potential for esophagitis and necroulcerative gastritis to develop as a sequela.

Toxins of Less Concern for Cats

Some substances that we are concerned about producing toxicosis in other species do not cause significant concerns for toxicosis in cats. For example, Xylitol failed to induce hypoglycemia or hepatotoxicity in cats. Similarly, there are no reports of avocado toxicosis in cats, likely due to deficiency in mastication and digestion of the avocado thorough enough to release the persin. Macadamia nuts have not been shown to cause neurologic signs in cats, as they do in dogs. Cats very infrequently reported to have ingested ant bait stations, rodenticide, and cannabis containing edibles (though they will ingest plant material) to the ASPCA Animal Poison Control Center.

Cat Toxins

Glo Jewelry

Cats seem to be inordinately fascinated with glo jewelry containing dibutyl phthalate. When they chew on and puncture the glow sticks, the bitter taste of the dibutyl phthalate causes an often intense taste reaction. Owners may show significant concern for the abnormal behaviors that their cats exhibit, but this is not a life threatening toxicosis. Treatment is quite simple in these cases, give a taste treat to dilute out the bitter taste and examine the cat in a dark room, removing any of the glowing substance from the hair coat with a damp cloth, preventing re-exposure.

Potpourri

Liquid potpourri contains a combination of essential oils and cationic detergents. Cats seem to be both particularly sensitive and likely to ingest liquid potpourri. Oral and dermal exposures are most common and can cause corrosive injury to the oral cavity, tongue, skin, and esophagus, as well as hyperthermia, anorexia, dysphagia, and depression. Diagnostics include CBC in hyperthermic patients. Decontamination includes thorough bathing in cats that have dermal exposures, dilution with water or dairy products in cats with oral exposures, and thorough flushing for cats with ocular exposures. Induction of emesis and administration of activated charcoal are contraindicated in pets with exposure to caustic substances. Treatments are symptomatic and supportive and include: gastroprotectants, pain control, broad spectrum antibiotics, nutritional support, and fluid diuresis.

Acetaminophen

Acetaminophen (APAP) is an analgesic and antipyretic. In dogs, 75% of the dose of APAP undergoes glucuronidation and 10-20% undergoes sulfation. However, because cats are deficient in glucuronyl transferase, only 1% of the dose undergoes glucuronidation and 90% of the dose undergoes sulfation. When sulfate is depleted in cats, the start to make the toxic metabolite para-aminophenol (PAP). PAP is responsible for methemoglobinemia in dogs and cats. PAP is excreted two closely related enzymes N-acetyltransferase 1 and N-acetyltransferase 2 (NAT 1 and NAT 2). Cats only have NAT1. Another metabolite, N-acetyl-para-benzoquinoneimine (NAPQI) leads hepatotoxicity. Hepatotoxicity is possible but not commonly seen with acetaminophen toxicosis in cats. Acetaminophen levels in cats peak 30 minutes post ingestion, so while emesis and activated charcoal would be effective if enacted early enough in the course of intoxication, this is typically not feasible. Any exposure to acetaminophen in cats should be considered potentially toxic. Cats should be monitored for 12 hours for the development of methemoglobinemia. Treatment consists of the administration of N-acetylcysteine. Acetylcysteine is a precursor of glutathione synthesis and can be oxidized to provide organic sulfate needed to metabolize APAP through the sulfation pathway. Liver values should be monitored for 48 hours in cats with significant acetaminophen overdoses. Intravenous fluids are recommended in symptomatic cats. Cimetidine is contraindicated in the treatment of acetaminophen toxicosis in cats, as it will increase the risk of methemoglobinemia. Rarely, facial and paw edema can be seen. This edema does not respond to corticosteroids or antihistamines, but it does resolve on its own.

Nephrotoxic Lilies

Ingestion of true lilies or nephrotoxic lilies illustrate very succinctly that the risk of toxicosis of a substance to cats must be considered separately from the risk to dogs. While dogs may develop mild gastrointestinal upset after the ingestion of a true lily, cats are at risk of developing acute kidney injury. The mortality rate for cats ingesting *Lilium longiflorum* and not receiving prompt, aggressive treatment is reported at anywhere from 50-100%.

All parts of the lily are considered toxic. The toxin is unidentified but is present in the water-soluble fraction of plant extract. Cases of nephrotoxicity have been documented from cats ingesting or chewing on any part of the plant, licking pollen off their faces, or drinking water from a vase that has contained lilies. Decontamination may be helpful, but given that the toxic principle is water soluble, even recovery of the ingested plant material would not eliminate the need for fluid diuresis. Nephrotoxic lilies cause degeneration and necrosis of the proximal renal tubules. Sloughing of renal tubular epithelial cells results in tubular blockage and anuric renal failure. Fluid diuresis, monitoring renal values, urinalysis, and electrolytes are indicated in all cases of cats exposed to nephrotoxic lilies. Antiemetics should be considered in cats that are vomiting. Prognosis is good if treatment is instituted within 18 hours post exposure prior to the onset of acute kidney injury. Prognosis is guarded to poor for cats with oliguric or anuric renal failure, but in some cases, peritoneal dialysis or hemodialysis for several weeks may allow the renal tubules to regenerate and cats may regain normal renal function.

There are two hurdles to timely and appropriate treatment of true lily toxicosis. The first is the correct identification of the lily. The scientific name of the plant should always be obtained, as there are numerous plants that have the word 'lily' in their common name and not all of them are nephrotoxic to cats. True lilies include plants from one of the following two genera: *Lilium* and *Hemerocallis*. Common nephrotoxic lilies include: Daylily (*Hemerocallis spp.*), Asiatic lily (*Lilium aratum* and *Lilium speciousum*), Easter lily (*Lilium Longiflorum*), and Japanese lily (*Lilium speciousum*). This is not to say that there may not be other toxic concerns with other plants with 'lily' in their common name (such as Lily of the Valley (Convallaria majalis), which is not nephrotoxic, but does contain cardiac glycosides, which can cause life threatening clinical signs). The second hurdle to timely and appropriate treatment of true lily toxicosis is client education. In a study by Slater and Gwaltney-Brant, only about 27% of owners whose cats were exposed to a nephrotoxic lily reported that they knew that they were toxic prior to their cat's exposure. While lily exposures happen year-round, we do notice a spike in calls in on the Easter and Valentine's Day holidays and the days or weeks thereafter.

Venlafaxine

Venlafaxine is a selective serotonin and norepinephrine reuptake inhibitor. Venlafaxine is used as an antidepressant. Cats are highly attracted to the capsules, and venlafaxine is one of the most common medication exposures in cats. Even low doses (2-3 mg/kg) can cause signs of serotonin syndrome in cats (mydriasis, vomiting, tremors, tachycardia, ataxia, agitation, and hypertension). Decontamination for asymptomatic cats with a recent venlafaxine exposure consists of emesis and activated charcoal. Repeated doses of activated charcoal can be considered in cats exposed to an extended release product. Treatment is symptomatic and supportive. Intravenous fluids should be considered for symptomatic cats. Acepromazine and/or cyproheptadine is helpful for agitation, especially if serotonin syndrome is also present. Methocarbamol should be considered for tremors and beta blockers for tachycardia in a calm cat. Signs with the extended release products can last up to 72 hours. Intravenous lipid emulsion has been shown to decrease plasma levels and decrease treatment time.

Concentrated Permethrin Products

Permethrin is a type I pyrethroid which effects sodium channels in nerve endings. Cats are more sensitive to the effects of permethrin, though there are low concentration permethrin products (typically less than 1%) that are labeled for the use on or around cats. Cats are typically exposed to high concentration permethrin products in one of two ways: the product is applied to them by the pet owner or they are in close contact with or groom a dog in the household while the product has not yet dried. Clinical signs of permethrin toxicosis include: erythema at the application site, muscle tremors, hypersalivation, depression, gastrointestinal upset, seizures, and death. The onset of clinical signs can occur anywhere from a few hours to up to 48 hours post exposure. Cats with high concentration permethrin products applied to them should be bathed with a liquid dishwashing detergent. Generalized muscle tremors are typically controlled with methocarbamol +/- diazepam or midazolam. Benzodiazepines can be used to treat seizure, if present. Intravenous fluids are typically indicated to help maintain normal hydration status. The use of intravenous lipid emulsion has been reported to be effective but can be associated with complications.

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