




Cat Toxins are Not Small Dog Toxins

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Just Like....

 A Dog	or Cat	\neq	 Small Human
 A Cat		\neq	 A Small Dog

Feline Exposures

- ◆ 85.8 million owned cats in the US
- ◆ 78 million owned dogs
- ◆ 11% of all APCC cases
 - Dogs = 88%
- ◆ Most common:
 - Insecticides
 - Human medications
 - Plants







I have a present for you.
Hint: it's vomit.



Cats vs Dogs

- ◆ Kinetic differences
 - Chewers (cats) vs gulpers (dogs)
 - CR/XR/SR products
- ◆ Taste
 - No sweet taste buds
- ◆ Dermal exposure = oral exposure



What is so special about cats?

- ◆ More selective eating habits
- ◆ Grooming behavior
- ◆ Concentrated urine
- ◆ Readily vomit (when they want to)



Cats love....

- ◆ Chewable meds
- ◆ Pill pockets



And absolutely nothing that you WANT them to take



Species Differences Metabolism

- ◆ Metabolic processes evolved to allow individual species to handle various components of their diet
 - Cats are true carnivores, and like most animals with more restricted diets, they have fewer biotransformation pathways than those with a more diverse diets, such as herbivores or omnivores
 - This causes issues when cats encounter a xenobiotic that requires a biotransformation pathway they do not possess



Metabolism Phase II Reactions

- ◆ Glucuronidation
 - “Defective” in cats
 - Cats UDP-glucuronosyltransferase encoded by a pseudogene and is dysfunctional
 - Cats don’t effectively glucuronidate phenols, naphthols, morphine, acetaminophen, aspirin, etc.
- ◆ Sulfation
 - Poor in cats



What is so special about cats?

- ◆ Eight reactive sulfhydryl groups on hemoglobin
 - Increased susceptibility of RBC to oxidative damage
 - Forms Heinz bodies and methemoglobinemia
 - Very sensitive to aniline dyes, onions/garlic, acetaminophen, benzocaine
- ◆ Short RBC life span (66-79 d)



Apomorphine

- ◆ Centrally acting emetic
- ◆ May cause a paradoxical reaction in cats
- ◆ Will it induce emesis though?



≠



Inducing Emesis in the Cat

- ◆ Dogs—Chemoreceptor trigger zone (CRTZ) is largely controlled by dopamine receptors. Apomorphine stimulates the CRTZ and often causes emesis
- ◆ Cats—Chemoreceptor trigger zone is largely controlled by α -2 receptors, so apomorphine isn't effective



Emetics in Cats

- ◆ α -2 agonists, like xylazine and dexmedetomidine are used in cats,
- ◆ Xylazine
 - 0.44 mg/kg IM (Plumb)
- ◆ Dexmedetomidine
 - 1-100 mcg/kg have been suggested.
 - 7mcg/kg?

Wiley, JR et al. Evaluation and comparison of xylazine hydrochloride and dexmedetomidine hydrochloride for the induction of emesis in cats: 47 cases (2007-2013). JAVMA. 2016 Apr 15;248(8):923-8.



- ◆ Be prepared to reverse with atipamezole: equivalent volume IM or IV (Plumb)



What about hydrogen peroxide?

- ◆ Effective for use in dogs. May induce emesis in cats.
- ◆ Not recommended for use in cats, due to potential for esophagitis and hemorrhagic gastritis, and necroulcerative gastritis.

◆ Obr, TD; et al. *Necroulcerative hemorrhagic gastritis in a cat secondary to the administration of 3% hydrogen peroxide as an emetic agent.* J Vet Emerg Crit Care (San Antonio). 2017 Sep;27(5):605-608.



What don't we worry about in cats?

- ◆ Xylitol
- ◆ 1 g/kg failed to decrease BG or cause hepatic injury

◆ Jerzsele Á, *Effects of PO Administered Xylitol in Cats.* J Vet Pharmacol Ther. 2018 Jun;41(3):409-414.



What don't we worry about in cats?

- ◆ Avocado
 - Toxicosis has not been reported in cats
 - Likely not digesting and masticating well enough to release persin



What don't we worry about in cats?

- ◆ Macadamia nuts
 - In dogs, hind end weakness, tremors, hyperthermia
 - Toxicosis has only been reported in dogs and not in cats

• Gwaltney-Brant, S. *Macadamia Nuts*. *Small Animal Toxicology* 3rd ed. Elsevier, 2013: 625.



What do they just not often get into?

- ◆ Ant bait stations
- ◆ Rodenticides
- ◆ Cannabis-containing edibles



Specific Toxins for Cats



Glo Jewelry

- ◆ Dibutyl phthalate
- ◆ Unpleasant taste
- ◆ Not systemically toxic
- ◆ Clinical signs:
 - Typically very dramatic
 - Drooling, hyperactivity, head shaking, mydriasis, vocalizing



This tastes terrible!
Life just isn't worth living anymore



Glo Jewelry

- ◆ Decontamination & Treatment:
 - Taste treat (milk, tuna juice)
 - Place cat in a dark room to find any areas that they glow
 - Wipe off any glowing areas with a damp cloth to prevent re-exposure




Note: this decontamination method does not work well in GMO cats



Potpourri

- ◆ Liquid potpourri
- ◆ Cats are especially sensitive
- ◆ Local injury resembles alkaline corrosive injury
- ◆ Do not induce emesis or give activated charcoal



Potpourri Clinical Signs

- ◆ Corrosive injury (ulcers)
 - Oral cavity
 - Tongue
 - Esophagus
 - Skin
- ◆ Hyperthermia
- ◆ Depression
- ◆ Pain
- ◆ Dysphagia
- ◆ Anorexia



Knocking over the Christmas tree doesn't seem so bad now, does it?



Corrosive Agents Treatment

- ◆ Immediate dilution with milk
- ◆ Sucralfate slurries
- ◆ Proton Pump Inhibitors
- ◆ IV fluids





Corrosive Agents Treatment

- ◆ Pain medication
 - Opioids
 - "Magic Mouthwash"
- ◆ Antibiotics
- ◆ Soft food
- ◆ Gastrostomy tube
- ◆ Steroids—controversial




Acetaminophen

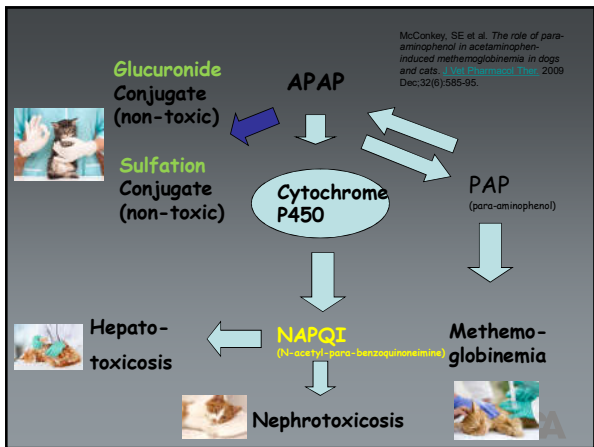
- ◆ Analgesic, antipyretic, mild anti-inflammatory
- ◆ Exact mechanism of action is unknown
 - Believed to block production of prostaglandins from arachidonic acid by inhibiting COX-3
- ◆ Forms:
 - Tablets: 80-650 mg
 - Liquid: 32-100 mg/ml



Acetaminophen Kinetics

- ◆ Rapidly absorbed from the GI tract
- ◆ Peak plasma levels
 - **10-60 minutes** for regular products
 - 60-120 min for extended release forms
- ◆ Uniformly distributed into most body tissues
 - Highest concentration in the peri-portal zone of the liver and renal medulla





Acetaminophen

- ◆ There is no safe acetaminophen dose for cats
 - Deficient in glucuronyl transferase
 - 10 mg/kg has produced signs of toxicity
- Ferrets are as sensitive as cats



Acetaminophen Methemoglobinemia

- ◆ Mucous membranes appear muddy or brown in color
 - Accompanied by tachycardia, tachypnea, weakness, and lethargy



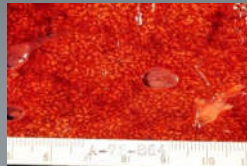
Acetaminophen Liver necrosis

- ◆ NAPQI binds to sulfhydryl groups on cell membranes
 - Cell necrosis
- ◆ Central lobular necrosis
 - Most common
 - Higher concentration of cytochrome P-450 and associated enzymes



Acetaminophen Liver necrosis

- ◆ Depletion of glutathione reserves leads to hepatotoxicity
 - If glutathione is present, it can conjugate and neutralize the NAPQI
- ◆ Liver necrosis is less common with cats than with dogs
 - Hepatic necrosis has a poor prognosis



Acetaminophen Other Clinical Signs

- ◆ Depression
- ◆ Facial or paw edema
- ◆ Hypothermia
- ◆ Vomiting
- ◆ Death



Photos: Robert Russon, DVM



Acetaminophen Diagnosis

- ◆ Exposure history
- ◆ Clinical signs
- ◆ Quantitative acetaminophen plasma levels can confirm exposure
 - Available at human hospitals
 - 4 hours post exposure
 - However, this is NOT sensitive enough for cats



I'm not impressed with your "advanced diagnostics"



Acetaminophen Decontamination

- ◆ Early decontamination is most beneficial
 - Emesis
 - Activated charcoal and cathartic
 - Monitor for methemoglobinemia for 12 hours
 - In cats, methemoglobin values start to increase within 2-4 hours, followed by Heinz body formation



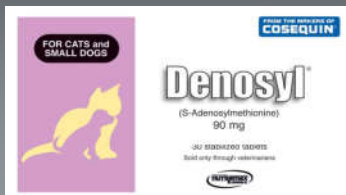
Acetaminophen

- ◆ Monitor liver values
 - ALT, AST and bilirubin may rise within 24 hours
 - If values are normal at 48 hours, no problems expected
 - Rare to see hepatotoxicity in cats



Treatment

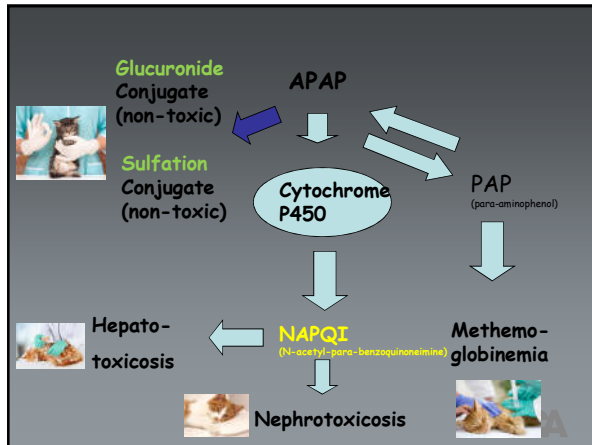
- ◆ S-adenosylmethionine (SAME, Denosyl®)
 - 20 mg/kg/day



Acetaminophen: Treatment

- ◆ N-acetylcysteine (Mucomyst®)
 - Precursor in the synthesis of glutathione
 - Works in a couple of important ways
 1. Can be oxidized to organic sulfate needed for the sulfation pathway
 2. Provides an alternate substrate for conjugation to reduce the extent of liver injury or methemoglobinemia





Treatment

- ◆ NAC is available in 10% and 20% solutions
- ◆ Loading dose: 140 mg/kg
 - Dilute to 5% concentration in 5% Dextrose or sterile water
 - Alternative loading dose
 - 280 mg/kg at high doses
- ◆ 70 mg/kg QID for 7 treatments
 - 12 to 17 doses



Thank you so much for saving my life. I'll happily take the NAC and won't try to kill you or your techs. Said no cat ever.



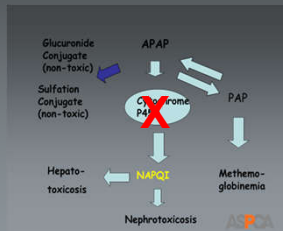
Treatment

- ◆ IV fluids
 - Support in symptomatic doses
 - Protect kidneys with very high doses
- ◆ Ascorbic acid ??
 - Helps with reduction of methemoglobin back to hemoglobin
 - Questionable efficacy, may irritate the stomach
- ◆ Methemoglobinemia
 - Oxygen, NAC

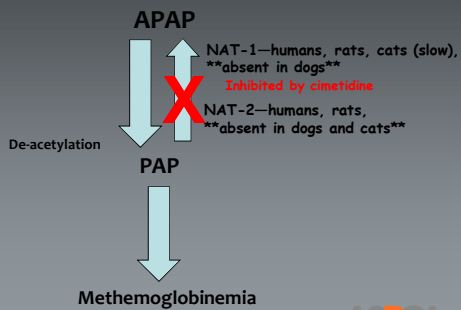


What about Cimetidine?

- ◆ Cimetidine
 - Inhibits cytochrome p-450 oxidation system





NOT for use in cats






Prognosis

- ◆ Good, if treated promptly
 - Severe signs of methemoglobinemia or hepatic damage have poor to guarded prognosis
- ◆ Clinical signs of methemoglobinemia may last 3-4 days
- ◆ Hepatic injury may not resolve for several weeks, or may have permanent dysfunction




Nephrotoxic Lilies in Cats

- ◆ Unidentified water soluble toxic principle
- ◆ Necrosis of proximal renal tubular epithelial cells
 - Sloughing into lumen, blocks lumen
 - Basement membrane remains intact
- ◆ Nephrotoxicity has only been documented in cats
 - *Hemerocallis* sp. can cause blindness in cattle





Client Education is Still Important

- ◆ Sixty nine percent of cat owners said they could recognize a lily and 27% knew that lilies were toxic prior to their cats' exposures
- ◆ Slater MR and S Gwaltney-Brant. *Exposure circumstances and outcomes of 48 households with 57 cats exposed to toxic lily species.* *J Am Anim Hosp Assoc.* 2011 Nov-Dec;47(6):386-90.



- ◆ Nephrotoxic or “True” Lilies:
- ◆ Daylily (*Hemerocallis spp.*)
- ◆ Asiatic lily (*Lilium aratum* and *L. speciosum*)
- ◆ Easter lily (*L. Longiflorum*)
- ◆ Japanese lily (*L. speciosum*)

◆ Many plants are called lilies but we do not have the concern for renal failure in cats. Always make sure that that scientific name starts with the word ‘*Lilium*’ or ‘*Hemerocallis*’



Asiatic Lily



Daylily







Nephrotoxic Lilies Clinical Signs

- ◆ Initial signs include vomiting, diarrhea, and lethargy.
- ◆ Signs progress to anorexia, depression, dehydration, isosthenuria, and acute renal failure
- ◆ Pancreatitis can also be seen

◆ Rumbelha, WR, et al. A comprehensive study of Easter lily poisoning in cats. J Vet Diagn Invest. 2004 Nov;16(6):527-41.



Nephrotoxic Lilies Bloodwork Changes

- ◆ BUN, creatinine, phosphorus, and potassium elevations are typically seen within 24-72 hours
- ◆ Creatinine is often disproportionately elevated when compared to BUN



Nephrotoxic Lily Risk

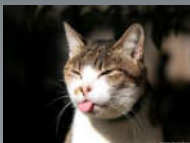
- ◆ Acute Renal Failure in cats has been seen from exposure to:
 - Leaves
 - Flowers
 - Pollen
 - Water that plant material or flowers have been sitting in
- ◆ Any exposure should be taken seriously



Nephrotoxic Lilies Decontamination

- ◆ Decontamination and treatment are designed prevent renal tubular obstruction from necrosis and sloughing of epithelial cells.

- ◆ Decontamination



Nephrotoxic Lilies Treatment

- ◆ IV fluid diuresis for 48 hours
- ◆ Monitor renal values daily for 72 hours



Nephrotoxic Lilies Treatment

- ◆ Regeneration of damaged tubules?
 - Determine if the basement membrane is intact





Prognosis

- ◆ In cases where aggressive, prompt treatment is started, the prognosis is excellent
- ◆ Treatment is most effective when started less than 18 hours post-exposure
- ◆ Some anuric patients have had renal function restored after long-term peritoneal or hemodialysis

◆ Bennett AJ, Reineke EL. Outcome following gastrointestinal tract decontamination and intravenous fluid diuresis in cats with known lily ingestion: 25 cases (2001-2010). *JAVMA* 2013 Apr 15;242(8):1110-6.

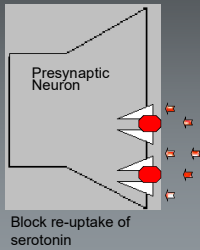


Venlafaxine (Effexor®)

- ◆ Bicyclic antidepressant
 - available as both an immediate release and extended release medication
- ◆ Potent serotonin and noradrenaline reuptake inhibitor
- ◆ Cats **love** the capsules



Selective Serotonin Reuptake Inhibitors (SSRI)



Venlafaxine

- ◆ 2-3 mg/kg can cause signs of serotonin syndrome
 - Mydriasis
 - Vomiting
 - Tremors
 - Tachycardia
 - Ataxia
 - Agitation



Venlafaxine Decontamination

- ◆ Emesis?
- ◆ Activated charcoal
 - Repeated in 4-6 hours if extended release
- ◆ Monitor HR and BP



Venlafaxine Treatment

- ◆ Fluids
- ◆ Agitation and/or serotonin syndrome
 - Acepromazine
 - Cyproheptadine (2-4 mg per cat, PO or rectally)
- ◆ Tremors
 - Methocarbamol
- ◆ Tachycardia
 - Beta blockers



Treatment

- ◆ Intralipids (ILE)
 - Decrease plasma levels and decrease treatment time
 - 20% lipid solution (peripheral catheter)
 - Bolus of 1.5 ml/kg is given, followed by 0.25 ml/kg/min for 30-60 minutes
 - Repeat in four hours if the serum is clear (no lipemia present) and sign recur



Concentrated Permethrin and Cats

- ◆ Feline toxicity
 - Accidentally applied to cats
 - Cats that groom or engage in close physical contact with recently treated dogs



Concentrated Permethrin and Cats

- ◆ Clinical signs
 - Muscle tremors
 - Seizures
 - Hypersalivation
 - Depression
 - Vomiting
 - Anorexia
 - Death



Feline Permethrin Toxicosis

- ◆ Onset of clinical signs
 - As fast as 2-4 hours post-exposure, but can be delayed up to 24 hours
- ◆ Treatment:
 - Bathe entire cat with liquid dish washing detergent
 - **Methocarbamol**
 - IV fluids
 - Thermoregulation
 - Diazepam or midazolam



Intralipids?

- ◆ Has shown to improve clinical signs in some studies
 - ◆ Potential sequelae:
 - Lipemia
 - Corneal lipidosis
 - Fat overload syndrome
 - ◆ May partially bind methocarbamol (Log p 0.61)
-
- ◆ Peacock RE, et al. A randomized, controlled clinical trial of intravenous lipid emulsion as an adjunctive treatment for permethrin toxicosis in cats. JVECCS (San Antonio). 2015 Sep-Oct;25(5):597-605.
 - ◆ Seitz MA and JM Burkitt-Creedon. Persistent gross lipemia and suspected corneal lipidosis following intravenous lipid therapy in a cat with permethrin toxicosis. JVECCS (San Antonio). 2016 Nov;26(6):804-808.



Feline Permethrin Toxicosis

- ◆ Prognosis:
 - Usually good for mildly tremoring cats
- ◆ Treatment duration:
 - Normally 24 hours, but a few cases have needed 48 - 72 hours to resolve



Questions?

C 16. Mental break time. This is your last regular (non-final) test of the year. You deserve an easy question. What is 1 + 1?

- a. Not this one
- b. Still not this one
- c. 2
- d. You've gone too far, go back to C.