VETgirl HEPATOTOXICANT TABLE

ASPCA® Animal Poison Control Center (888) 426-4435

TOXIN	SOURCE	MECHANISM OF ACTION	CLINICAL SIGNS	CLIN PATH	TOX TEST	TREATMENT	PROGNOSIS
Mothballs	Paradichlorobenzene (PDB) *(NOTE: Make sure to differentiate from naphthalene)*	Organochlorine insecticide	Vomiting, abdominal pain, liver and kidney damage	Hemolytic anemia Hemolysis Methemoglobinemia (rare in dogs and cats; reported in humans)		• Prompt GI decontamination • Fluid administration to induce diuresis • Symptomatic response to adverse signs • Supportive care of vital functions • Seizure control with parenteral benzodiazepines	Organochlorine insecticide with an LD_{50} of approximately 500 mg/kg
NSAIDs	Carprofen Deracoxib	Inhibit PG synthesis → mostly GI and renal effects, reported liver effects as well (chronic)	DOG DOSES: > 20 mg/kg: vomiting, GI ulcers > 40 mg/kg: AKI Idiosyncratic liver toxicity (1.4 cases out of 10,000)	↑↑↑ ALT GI and AKI related findings: • anemia • hypoproteinemia • azotemia • hyperphosphatemia, etc.		• Immediate discontinuation • Treatment for hepatic failure • Hepatoprotectants (SAMe or NAC)	DOG DOSES: Hepatotoxicity, when observed, typically develops with **chronic** dosing (e.g., 5-30 days of chronic use; median 19 days)
Acetaminophen (APAP)	Analgesic and antipyretic derived from paracetamol (*Note: Not an NSAID)*	Metabolized to NAPQI, binds to macromolecules and causes lipid peroxidation of membranes; induces direct cell injury and death leading to hepatic necrosis Oxidative damage in cats, resulting in metHb, Heinz body formation	DOG: GI signs, CNS depression, hepatotoxicity (icterus, coagulopathy); metHb can occur at higher doses (cyanosis, dyspnea) but not as common as in cats CAT: Respiratory distress, hypoxemia, cyanosis, edema of face and paws, metHb	↑↑ LES (AST thought to be most sensitive) MetHb, Heinz bodies, chocolate-brown appearance to blood	Plasma, urine or tissue	NAC replenishes glutathione, provides sulfur and will directly bind NAPQI Others: • Vitamin C • SAMe • IV Fluids Methylene blue has been described, but not recommended, especially in the cat (due to Heinz body formation)	DOGS: 100 mg/kg hepatotoxicity; 200 mg/kg methemoglobinemia CATS/FERRETS: 10 mg/kg methemoglobinemia KCS can occur in dogs after even therapeutic doses
Xylitol	Sweetener in sugar-free products, such as chewing gum and baking products	Induces hypoglycemia by stimulating insulin secretion from the pancreas of dogs Hepatic necrosis thought to be from decrease ATP production (xylitol uses pentose phosphate pathway instead of TCA [Kreb's] cycle)	Clinical signs develop in as short a time as 30 to 60 minutes Weakness, ataxia, collapse, and seizures from hypoglycemia may last 12 to 24 hrs, perhaps caused by the slow xylitol release from the ingested formulations and its absorption Liver injury (within 24 hrs), including signs of melena, hepatic encelopathy, hemorrhage	Hypoglycemia, ↑↑ LES, DIC, coagulopathy		• Stat BG and treatment for hypoglycemia; emesis if recent ingestion and normoglycemic • Activated charcoal not indicated • Fluid support and glucose support (dextrose can correct hypoglycemia and is liver supportive by providing ATP) even in the face of euglycemia • Response from clinical effects is usually rapid and within 12 to 24 hrs • Recheck liver values at 24 and 48 hrs to evaluate for liver involvement • SAMe for 1-2 weeks if hepatotoxic dose ingested	> 0.1 g/kg → hypoglycemia > 0.5 g/kg → acute hepatic necrosis

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Metaldehyde	Known as a molluscicide, used for the control of slugs and snails (although recently replaced by less toxic iron phosphate)	Results in the disruption of the GABAergic system Monoamine oxidase, 5-hydroxytryptamine, and norepinephrine may also be involved in the toxic mechanism	May be seen as soon as 30 minutes after ingestion but typically occur within 3 to 5 hrs GI (vomiting, diarrhea) and CNS (hyperesthesia, incoordination, hyperthermia, seizures) signs Liver damage and cirrhosis may occur 2-3 days after exposure Death from respiratory failure may occur within 4-24 hrs after exposure	Acidosis, liver value abnormalities	Characteristic odor of formaldehyde may be present in the stomach contents along with bait material No consistent and pathognomonic gross or histological lesions occur in metaldehyde poisoned animals	• Decontamination, if appropriate • Gastric lavage with inflated ETT should be performed if the patient is symptomatic and evidence of pellets still in stomach on radiograph; administration of 1 dose of charcoal if gastric lavage performed • Stabilization of vital signs, IV fluids, anti-emetics, acid-base monitoring, methocarbamol/anticonvulsant therapy, respiratory and CV system monitoring, supportive care	Acute median LD values are 210 to 600 mg/kg for dogs and 207 mg/kg for cats Prognosis is good if survival is > 24 hrs from ingestion with early treatment
Copper	Coins, feeds, solutions, wire, jewelry, food	Breeds that are homozygous for a recessive gene (Bedlington Terrier, Skye Terrier, West Highland White Terriers, Labrador Retrievers, Doberman Pinschers) have excessive copper storage in the liver	Lethargy, anorexia, vomiting, weight loss, jaundice		Quantitative hepatic copper values; genetic testing (some breeds)	• Chelation with penicillamine or trientine • Supportive care for other derangements	Increasing zinc in diet can aid in prevention
Benzodiazapines (oral) **CATS ONLY**	Oral diazepam (valium) and alprazolam (not seen with parenteral administration); typically seen with chronic oral dosing	Acute hepatic necrosis in 5-11 days of oral treatment	Sedation, malaise, ataxia, jaundice	Markedly ↑↑↑ ALT ↑ T-bili, PT/PTT			
Amatoxin Mushrooms	*Amanita* spp., *Galerina* spp., *Conocybe* spp., *Lepiota* spp.	Inhibit DNA and RNA transcription and protein synthesis; bind to actin filaments, deform cytoskeleton → hepatocyte death	Develop GI signs within 6-24 hrs "False" recovery period, followed by fulminant liver failure and AKI in 36-48 hrs	↑↑ Liver enzymes within 48-72 hrs	Centrilobular hemorrhagic necrosis	• Decontamination (emesis and AC if < 2 hrs post ingestion) • IV fluids, sequester amatoxin bile in gallbladder with octreotide CRI, NPO), ultrasound-guided bile aspiration	Alpha amanitin LD_{50} (human) = 0.1 mg/kg Easily found in one mushroom
Blue-Green Algae	Cyanobacteria Hepatotoxins (*Microcystis* spp., *Nodularia* spp., *Oscillatoria* spp. most common; *Anabaena* spp. less often) Can also contain neurotoxins	Microcystin binds to protein phosphatase in cytoskeleton, disorganization of actin leads to cellular collapse, intrahepatic hemorrhage, death	Death in hrs to days with hepatotoxin GI (e.g., vomiting/diarrhea), CNS (e.g., weakness, ataxia, tremors, seizures), cardiac (e.g., collapse, pallor, tachycardia, respiratory failure, hemorrhagic and hypovolemic shock) Very acute clinical signs with neurotoxin (death can occur in minutes to hrs) – CNS signs and SLUDGE-like signs	↑↑ Liver enzymes within a few to 24 hrs; ↑↑ PT/PTT; anemia	Diffuse hepatic necrosis	• Decontamination is often too late – gastric lavage +/- activated charcoal, bathe (use protective gear) • PCV/TS/BG • Baseline Chem, CBC PT/PTT	Toxic dose – 50-11,000 mcg/kg Prognosis – often grave

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Sago Palm	Cycads (*Cycas* spp., *Macrozamia* spp.) (SE, South central or tropical areas of US usually) but can be found as bonsai household plant	All parts of the plant are poisonous, but seeds contain largest amount of toxin	GI signs (vomiting, diarrhea) within 15 minutes to several hrs, CNS signs (lethargy, seizures) (48-72 hrs), liver failure (24-72 hrs)	↑↑ Liver enzymes (24-72 hrs)	Centrolobular and mid-zonal coagulative hepatic necrosis	• Baseline bloodwork, PT/PTT • PCV/TS/BG/liver panel q 24 hrs x 2-3 days	1-2 seeds can lead to severe signs Grave prognosis once hepatoxicity seen
Iron	Multivitamins, iron supplements, fertilizers, snail/slug bait	When serum iron exceeds the binding capacity of transferrin and ferritin, free iron causes lipid peroxidation and damage to liver, heart and brain Iron is also caustic to the GI mucosa	GI signs (e.g., vomiting, hematemesis, melena, diarrhea) within 0.5-6 hrs; liver failure 12-24 hrs later With large doses can see hypovolemic shock, coagulopathy and acidosis	↑↑ Liver enzymes; ↑↑ PT/PTT if liver necrosis	Serum iron levels; chelate warranted if iron > 400 mcg/dl)	• MgOH can be given while iron is still in the GI tract • Emesis if appropriate. Activated charcoal does not bind and should not be used • Other treatment includes antiemetics, GI protectants/antacids, hepatoprotectants, deferoxamine (chelator), supportive care, blood work monitoring	Toxicity dependent on amount of elemental iron 20-50 mg/kg = GI signs 50-80 mg/kg = GI ulcers > 80 mg/kg = liver and other systemic effects
Aflatoxins	Mycotoxin (mold) found in corn, peanuts, cottonseed, rice and potatoes	Metabolized into reactive epoxide, binds to hepatocytes Large acute exposures = hepatic necrosis; smaller chronic exposures = neoplasia	Vomiting, anorexia, lethargy, icterus, coagulopathy	↑↑ Liver enzymes; ↑↑ PT/PTT	Acute – diffuse hepatic necrosis Chronic – fatty liver	Fluid therapy, anti-emetics, blood work monitoring, hepatoprotectants, symptomatic and supportive care	
Aspirin	NSAID pain medication	Hepatotoxicity thought to be from inhibition of mitochondrial function	GI (e.g., anorexia, vomiting, melena, stomach ulcers), lethargy, icterus	↑↑ Liver enzymes	Centrilobular hepatic necrosis	Fluids, anti-emetics, antacids, gastroprotectants, hepatoprotectants	Dogs > 400 mg/kg for liver effects
Lectins (toxalbumins)	Castor bean *(Ricinus communis)*, Precatory bean *(Abrus precatorius)*, Black locust (*Robinia* spp.), Mistletoe *(Phoradendron)*	Stops cellular protein synthesis in multiple organs	GI (e.g., anorexia, vomiting), lethargy, anorexia, icterus, weakness, tremors, death	↑↑ Liver enzymes		Fluids, anti-emetics, symptomatic and supportive, hepatoprotectants	All parts of plants are toxic. Seeds are most toxic part of *Ricinus* and *Abrus*. Seeds must be chewed to release the toxin.
Essential oils	Pennyroyal oil, melaleuca (tea tree) oil	Unknown	Vomiting, lethargy, ataxia, hind limb weakness, icterus	↑↑ Liver enzymes		Symptomatic and supportive (fluids, hepatoprotectants)	Usually associated with application of 100% oil to open wound, ear canal or oral ingestion
Veterinary drugs associated with hepatotoxicity (albeit rare)	isoniazid, ketoconazole, lomustine, methimazole, melarsomine, mitotane, sulfonamides, trazodone, zonisamide					• Discontinuation of drug • Hepatoprotectants • Symptomatic supportive care	

Abbreviations: AKI: acute kidney injury; CNS: central nervous system; DIC: disseminated intravascular coagulation; GI: gastrointestinal; LD: lethal dose; LES: liver enzymes; Meth: methemoglobin; NAC: N-acetylcystine; PT: prothrombin; PTT: partial thromboplastin time