Cycad palms (cycas, zamia)

More commonly known as sago palms, the cycads include *Cycas revoluta, Cycas circinalis,* and *Zamia floridana.* The toxicity of these plants is well known in Southern areas of the country where they are used as common landscape plants. However, the recent development of ‘bonsai’ sized palms has resulted in these plants appearing indoors throughout the country in areas where pet owners and veterinarians may be unfamiliar with their toxicity. Most parts of the plant are toxic, with the seeds containing the highest level of toxic principle (cycasin). Cycasin is hepatotoxic and can also cause gastrointestinal hemorrhage and neurologic signs. Onset of signs may occur as early as a few hours or may be delayed 1-3 days following ingestion. The most common clinical signs include vomiting (+/- blood), diarrhea (+/- blood), weakness, lethargy, ataxia seizures and coma; mortality rates can be high in spite of aggressive treatment. Potential exposure to sago palms should be considered an emergency situation and should managed promptly and aggressively. Treatment should include early decontamination (emesis and activated charcoal with cathartic) if possible. Gastrointestinal protectants should be used as needed. Exposed animals should be closely monitored for at least 24 hours, and fluid therapy using balanced electrolyte solutions should be instituted immediately upon the development of clinical signs. Hypovolemia secondary to massive gastrointestinal fluid and blood losses is possible; blood transfusion may be necessary. Additionally, secondary effects from liver failure, such as hepatic encephalopathy and coagulopathy may develop in severely affected animals. Renal failure has occasionally been reported, most likely as a secondary condition. Clinical laboratory abnormalities include elevations in serum bilirubin, ALT, AST, SAP and WBC; values may not become abnormal until 24 to 48 hours post ingestion. Seizures, if present, generally respond to diazepam. Surviving patients may experience long-term hepatic insufficiency.

Intravenous lipid solutions

(ILS; Intralipid®, Liposyn®) are an emerging treatment modality for emergency medicine. ILS have been used for years as components of total parenteral nutrition (TPN) for critical human and veterinary patients, and had been investigated as a means of drug delivery of certain pharmaceuticals in humans. Originally utilized to attempt to reverse life-threatening cardiotoxicity in humans due to local anesthetic toxicosis, ILS administration has recently been introduced into veterinary emergency medicine where it is showing promise as a means to treat potentially life threatening toxicoses from select xenobiotic exposures. The mechanism of how ILS function as an antidote is not known, but it has been proposed that binding of ILS to lipophilic drugs in the serum reduces free drug available to bind receptors.

Based on animal poison control center experience, favorable results with ILS have been obtained in some cases of toxicosis due to amiodipine, baclofen, benzocaine, bupropion, CCNU, chlorpyrifos, diltiazem, doramectin, endosulfan, ivermectin, moxidectin, minoxidil, marijuana, permethrin, and phenobarbital; note that not all animals in which ILS were utilized responded or made full recoveries. In some instances where full recovery did not occur, response was sometimes seen but animals were euthanized due to financial reasons before full treatment could be completed. In others, there was poor to no response to the ILS, which may relate to the initial dose of the toxicant, other medical issues with the patient, insufficient ILS being used, or other as yet undetermined factors. Some drugs with long half-lives (e.g. calcium channel blockers) have required multiple dosing of lipids, as signs returned after several hours. In theory, ILS should work for any highly lipophilic drug. ILS have the additional advantage of being quite inexpensive to stock (~ $20 for 1 liter); anecdotally, some human hospital pharmacies were reported to over-charge veterinarians as much as $150-200 for a bag of ILS.

ILS have a good safety profile based on years of experience with their use as TPN components. With chronic use, potential side effects have included pyrogenic reactions and lipid overload, which may result in pulmonary compromise; these findings have not been reported with antidotal use of ILS. There have been reports of pancreatitis associated with the antidotal use of ILS in animals; therefore when using multiple doses of ILS, it is recommended that the serum be evaluated for the presence of lipemia prior to dosing and that dosing be suspended until any lipemia has resolved. A few anecdotal reports also exist of hemolysis following the antidotal use of ILS in cats. ILS can alter diagnostic tests due to induction of lipemia. Finally, lipids may interfere with other antidotal therapies (e.g. sedative drugs) that have been previously administered. It should be noted that this therapeutic modality is currently not approved for any species, should be considered experimental (with appropriate informed consent from clients), and should be used only in situations where life-threatening signs not responsive to other therapies are present.

There are several dosing regimens that have been utilized in the management of toxicoses. One regimen utilizes 20% lipid solution with an initial bolus of 1.5 mL/kg administered over 10-20 minutes followed by 0.25 mL/kg/min for 1 hour; repeat dosing can be given at 3-4 hour intervals (or when serum no longer lipemic). Other dosing regimens as well as other information on ILS therapy can be found at www.lipidrescue.org.
Phenylpropanolamine
Phenylpropanolamine (PPA) is a sympathomimetic agent. PPA has been withdrawn from the human market due to an association with increased stroke risk, but it is still used in veterinary medicine for controlling urinary incontinence in dogs. Signs can be seen at therapeutic doses in some dogs, and serious signs appear at doses above 20 mg/kg. Signs include tachycardia, hypertension, panting, agitation, hyperesthesia, piloerection, tremors, seizures, and secondary depression. Bradycardia may result as a reflex from the hypertension, therefore dogs may present either depressed, bradycardic and hypertensive OR agitated, tachycardic and hypertensive. Signs normally start within 30-90 minutes and may continue up to 72 hours, depending on dose. Emesis may be induced if the ingestion was witnessed and within 10-15 minutes. Activated charcoal should be given if no contraindications exist. Heart rate and blood pressure should be closely monitored. Phenothiazines (acepromazine or chlorpromazine) may be used to control agitation, and may also help to lower the blood pressure. Cyproheptadine (1.1 mg/kg QID pm) has been found to be useful in helping to alleviate some of the central nervous system signs due to phenylpropanolamine overdose. Nitroprusside or other pressor agents may be used to manage more severe hypertension. Managing the blood pressure often results in correction of the reflex bradycardia. Atropine is contraindicated in the management of bradycardia as it will worsen the hypertension. Beta-blockers should NOT be used on bradycardic animals as they will worsen the bradycardia. In tachycardic animals very low doses of metoprolol (preferred due to beta-1 selectivity and short half-life) or propranolol may be considered but should be used with caution and only after any CNS signs (agitation, hyperactivity) have been controlled. Over-aggressive use of beta-blockers should be avoided as excessive beta two receptor blockade with concurrent peripheral alpha stimulation could create unopposed alpha stimulation, resulting in a hypertensive crisis. Intravenous fluids are recommended to promote excretion, protect renal function and aid in thermoregulation; fluid rates should be adjusted accordingly in hypertensive animals.

Marijuana & synthetic cannabinoids
Marijuana is composed of the dried leaves, stems, seeds and flowers of Cannabis sativa. Although there are many cannabinoids in marijuana, the major active component is delta-9-tetrahydrocannabinol (THC). The concentration of THC in a given marijuana plant will vary with the strain of plant as well as environmental conditions such as adequate pH, water, soil type, nutrition, etc. Pets can be exposed when they ingest the dried plant material (fresh plant is much less toxic), inhale the smoke of burning marijuana (sometimes intentionally blown into their faces by humans), or ingest food products into which the marijuana has been incorporated (e.g. marijuana brownies). Marijuana butter has become a popular means of introducing the drug into food; due to its highly lipophilic nature, THC becomes concentrated in the butter. Exposure of pets to the plant material or smoke is rarely fatal, but ingestion of marijuana butter has resulted in canine fatalities. Signs can vary depending on the type and amount of THC ingested. Lower levels of exposure can result in CNS depression with hyperesthesia, ataxia, hypermetria, urinary incontinence, tremors, mydriasis, hypothermia, bradycardia, and hypersalivation. More severe intoxications may result in agitation, hyperthermia, tachycardia, anxiety/apprehension, vocalization, nystagmus, seizures, stupor, coma and death. Treatment is symptomatic. Benzodiazepines are generally helpful for CNS stimulation, while thermoregulation and minimizing sensory stimuli is recommended for CNS depression. Activated charcoal with cathartic can be used if it can be administered safely; induction of emesis is generally contraindicated in animals showing more than mild CNS depression. Intravenous lipid infusions have anecdotally been used with success in marijuana cases, although the author knows of at least one case where lipid infusion resulted in seizure in a dog that had previously received diazepam for severe agitation and tremors; it was assumed that the lipid may have interfered with the diazepam. The popularity of synthetic cannabinoids has grown over the last several years. These products, variously known as “Spice,” “K-2,” “Skunk,” or “Black Mamba,” are potent cannabinoid receptor agonists and have been associated with ‘bad trips,’ rhabdomyolysis and renal injury in humans.

Venlafaxine
Venlafaxine (Effexor®) is a bicyclic antidepressant that is a potent serotonin and noradrenaline reuptake inhibitor as well as a weak dopamine reuptake inhibitor. It is available as both immediate release and extended release medications. While it is rare for cats to willingly ingest medications, cats seem to readily eat venlafaxine, and appear particularly attracted to the extended-release capsules. Doses as low as 2-3 mg/kg can cause signs of serotonin syndrome. Mydriasis, vomiting, tachypnea, tachycardia, ataxia and agitation are the most common signs. Treatment would consist of emesis in asymptomatic individuals. Activated charcoal can be administered with a repeated dose in 4-6 hours if an extended release formulation was involved. Heart rate and blood pressure should be monitored. Acepromazine may be used for the agitation, and cyproheptadine (2-4 mg per cat, PO or rectally) may be useful in antagonizing the serotonin effects. With ingestion of the extended release medication, cats can be symptomatic for up to 72 hours. Venlafaxine is lipid soluble, so ILS may help to decrease plasma levels and decrease treatment time. Liposyn, or any other 20% lipid solution, can be given through a peripheral catheter. A bolus of 1.5 ml/kg is given, followed by 0.25 ml/kg/min for 30-60 minutes. This is repeated in four hours if the serum is clear. As an aside, venlafaxine will cause a false positive reaction for PCP on the OTC urine drug tests.
**Xylitol**

Xylitol is a sugar alcohol used in sugar-free products such as gums and candies as well as for baking. In dogs, xylitol causes a rapid, dose-dependant insulin release followed by potentially significant hypoglycemia. Signs can include vomiting, weakness, ataxia, depression, hypokalemia, seizures, and coma. Some dogs have developed elevated liver enzymes following ingestion of xylitol. Some of these dogs have gone on to develop severely elevated liver enzymes, bilirubinemia, and coagulation abnormalities. Signs can develop within 30 minutes. Emesis performed after signs develop increases the risk of complications associated with vomiting such as aspiration. Activated charcoal does not appreciably bind xylitol. Frequent small meals or oral sugar supplementation may be used to manage dogs not showing signs. If clinical signs of hypoglycemia develop, a bolus of IV dextrose followed by dextrose CRI should be used to control moderate to severe hypoglycemia. Hypokalemia, likely secondary to insulin-induced movement of potassium into cells, should be treated if significant. Treatment should continue until blood glucose normalizes which may take 24 hours or longer. The use of liver protectants such as SAM-e may be helpful. Prognosis is generally good; however if elevated liver enzymes, bilirubinemia, and coagulation abnormalities develop, the prognosis is guarded.