

## DOC WHAT DID HE GET INTO? EMERGENCY APPROACH TO INTOXICATIONS

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### Introduction

Malicious or accidental exposure to a toxin often presents a diagnostic and therapeutic challenge for the veterinary practitioner. The majority of intoxications occur when an animal ingests or is exposed to toxins in its home environment. The majority of intoxications occur when an animal accidentally ingests or is inadvertently administered prescription or over-the-counter medications meant for human use. Veterinary medications, too, can be toxic if ingested or applied to the wrong species, age of animal or in higher-than recommended doses. Some breeds of dog with genetic mutations are particularly sensitive to compounds used in everyday practice for most dogs. Pesticides, fertilizers, rodenticides and products that contain ethylene glycol continue to top lists of ingested toxins despite being known intoxicants for animals.

When the dose and type of toxin are known, in some cases the treatment may be somewhat easier. In the cases of toxin ingestion, the goals of gastric decontamination are to first remove the substance from the stomach and then to prevent further absorption, when possible. Next, methods to hasten the elimination from the body should be considered. In many cases, treatment is largely supportive and empiric, treating abnormal clinical signs and not the specific toxin itself. The type of decontamination strategy will depend on the neurologic status of the patient at the time of presentation and the nature of the substance ingested.

### Gastric Decontamination

Induction of emesis (canine - apomorphine 0.02-0.04 mg/kg IV; feline dexmedetomidine 7-10 mcg/kg/IM or xylazine 0.36-0.64 mg/kg IM)) should be attempted for compounds that are ingested within 2 hours, are not quickly absorbed and are not caustic or petroleum based. Emesis does not eliminate or empty all gastric contents, however, so administration of activated charcoal may be recommended to bind with residual toxin within the gastrointestinal tract to prevent absorption or hasten elimination.

Orogastric lavage should be performed in any patient that does not vomit after induction of emesis, or in patients that do not have an intact gag reflex and cannot protect their airway, (i.e. severely obtunded, seizures, or comatose). It is dangerous to perform orogastric lavage in patients without a cuffed endotracheal tube in place, due to the risk of creating iatrogenic aspiration pneumonia. In rare cases, the patient can have an orogastric and endotracheal tubes placed without additional sedation. Peri anesthetic monitoring should include pulse oximetry, invasive or noninvasive blood pressure, ECG, and capnometry. The cuff on the endotracheal tube should be securely inflated, to prevent the aspiration of gastric contents into the trachea and lungs.

After endotracheal intubation, measure an orogastric tube from the tip of the nose to the last rib, then place a piece of tape to mark that spot. Lubricate the tube with sterile lubricant then pass the tube through a roll of 2 inch white tape or a mouth gag. Lavage the stomach with warmed tap water, alternating between instilling warm water then allowing the contents of the stomach to flow from the stomach via orogastric tube into a separate bucket. Save a sample of the gastric contents if needed for lateral analysis. Lavage the stomach until the fluid runs clear. Following instillation of activated charcoal, remove the tube by kinking it and then removing it quickly to prevent leakage of anything in the tube into the trachea. Wake the patient up slowly and leave the endotracheal tube in place for as long as possible to protect the animal's airway.

### Activated Charcoal and Cholestyramine

Activated charcoal is an adsorbent that binds with compounds in the gastrointestinal tract. It has the benefits of not being systemically absorbed and can help prevent recirculation of substances that undergo enterohepatic recirculation if administered as multiple doses (1-2 g/kg PO Q6h). Because administration of activated charcoal can be messy, mixing the gel or suspension in food can be an easier and better tolerated method of administering it in an awake and compliant patient. Studies have demonstrated that the adsorptive capacity of activated charcoal is diminished when mixed with food, however does not appear to affect clinical efficacy. Activated charcoal should be considered in animals when induction of emesis may be contraindicated but the patient is still alert and able to swallow safely.

Cholestyramine is a resin that, when administered *per os*, binds with bile in the gastrointestinal tract to help eliminate some toxins that undergo enterohepatic recirculation. Its use (0-3 – 1 g/kg PO Q6-8h x 3-5 days) should be considered in cases of cholecalciferol, anticoagulant rodenticide, beta-blocker, digitalis derivatives, NSAIDs and phenobarbital ingestion/intoxication.

### **Intravenous Lipid**

Intravenous lipid emulsion (Intralipid®, 20%) is a newer method of treating lipophilic or cardiotoxic substances. The exact mechanisms of action of how lipids aid in toxin/drug removal is not well-understood. In some instances, the lipid acts as a “lipid sink” where upon entry into the bloodstream, the lipid sequesters a lipophilic compound and does not allow it to act on target receptors to exert potentially toxic effects. For cardiotoxic substances such as lidocaine or calcium channel blockers, the lipid may alter myocardial cell metabolism to prevent toxicity. More recent thought is that the lipid acts as a “shuttle” which scavenges plasma molecules of a toxic substance from target tissues where the toxin is stored then transports the substance to a site of metabolism or excretion. More than two dozen case reports exist in the veterinary literature at this time describing the use of lipid for treatment of ivermectin, moxidectin, baclofen, amphetamines, calcium channel blockers, tremorgenic mycotoxin, permethrin and marijuana toxicity. Intralipid® should be administered at a dose of 1.5 ml/kg IV over one minute, then 0.25 ml/kg/min for 30-120 minutes. The dose can be repeated in 6 hours if the serum is no longer lipemic at that time. Potential risks and adverse sequelae of lipid administration can be pancreatitis, corneal lipid deposition, hyperlipidemia and facial pruritus.

### **Supportive Care**

Intravenous fluid therapy should be considered for several reasons. First, IV fluids should be performed to help maintain hydration and maintain normal cardiovascular status of the patient. Some toxins such as paintball ingestion or even administration of activated charcoal can cause a cathartic diarrhea leading to a free water deficit and hypernatremia. Affected patients are prone to dehydration without supportive care. Secondly, intravenous fluids can aid in diuresis and hasten elimination of the compound from circulation. A rule of thumb is to provide 2 – 3 times calculated maintenance fluid volumes for the patient, provided that there is no evidence of intravascular or interstitial fluid volume overload such as the development of tachypnea, pulmonary crackles, or chemosis.

Specific antidotes can be administered in some cases if the toxin is known. Irrespective of whether the toxin is known or can be reversed with an antidote, supportive care measures should be implemented to maintain the patient's hydration status, heart rate, blood pressure, respiratory function, body temperature, and urine output. Since many toxins can cause cardiac and respiratory depression, respiratory monitoring including arterial blood gas analyses, pulse oximetry and capnometry should be performed to make sure the patient is oxygenating and ventilating adequately. In severely obtunded patients, passive range of motion exercises and frequent turning should be performed to prevent disuse atrophy, peripheral edema, decubital ulcers, and positional atelectasis. The mechanisms of action, clinical signs of intoxication, decontamination and therapies for newer infrequently encountered toxins will be discussed.

### **Specific Toxins**

**Macadamia nuts** Macadamia nuts can cause clinical signs of vomiting, diarrhea, ataxia, tremors, and ascending paralysis in some dogs. The toxic principle is unknown. Treatment is supportive in nature. Following gastric decontamination, intravenous fluids, methocarbamol to treat tremors and prevent hyperthermia, and antiemetics should be administered to nausea and vomiting. In experimental cases, all dogs made a complete recovery within 72 - 96 hours of ingestion.

**Paintballs** Paintballs are gelatin capsules that contain multiple colors of paint in a sorbitol or glycerol carrier. The sugars are osmotically active, and can cause a sudden onset of neurologic or gastrointestinal signs including ataxia, seizures, and diarrhea. The loss of water in excess of solute can result in hypernatremia, a free water deficit, and increased serum osmolality. Clinical signs of paintball ingestion can include ataxia, tremors, hyperesthesia, seizures, and severe diarrhea. Treatment largely consists of orogastric lavage and administering warm water enemas to help speed the movement of the paintballs through the gastrointestinal tract. Administration of activated charcoal (usually in a propylene glycol carrier) is contraindicated, as the compound's cathartic actions will pull more fluid into the gastrointestinal tract. Baseline electrolytes should be obtained, then carefully monitored. If severe hypernatremia develops, hypotonic solutions such as 0.45% NaCl + 2.5% dextrose

or 5% dextrose in water can be administered after calculating the patient's free water deficit. Because of the large volume of fluid loss, IV fluid rates may seem excessive, but will be necessary to normalize acid-base, electrolyte and hydration status. In most cases, these patients can survive with prompt recognition of the problem at hand, careful electrolyte monitoring, and aggressive decontamination strategies and intravenous fluid support.

**Baclofen/Carisoprodol** Baclofen and carisoprodol are centrally-acting GABA agonist muscle relaxants. Clinical signs of vomiting, ataxia, vocalization, hypoventilation, seizure and death can occur after ingestion of very low doses. Treatment consists of gastric decontamination strategies, and supportive care to control seizures and maintain adequate ventilation. Cyproheptadine, a serotonin antagonist, is sometimes helpful in controlling dysphoria. Flumazenil, a GABA antagonist, is actually contraindicated, as it may cause worsening of clinical signs. Supplemental oxygen or mechanical ventilation may be required in cases of hypoventilation and respiratory failure.

**Selective serotonin reuptake inhibitors (SSRI)** A toxicity that is becoming more and more frequent is the ingestion of a class of drug called selective serotonin reuptake inhibitors, most commonly prescribed for depression, obsessive-compulsive disorder, and anxiety in humans. The most common drugs that we see in this class include Prozac (fluoxetine), Paxil (paroxetine), Zoloft (sertraline), and Luvox (fluvoxamine). Accumulation of serotonin can cause "Serotonin Syndrome", characterized by trembling, seizures, hyperthermia, ptialism or hypersalivation, cramping or abdominal pain, vomiting and diarrhea. Other clinical signs of SSRI intoxication include depression, tremors, bradycardia or tachyarrhythmias, and anorexia. Treatment of suspected SSRI intoxication involves gastric decontamination and symptomatic treatment of other clinical signs if they occur. Seizures can be treated with intravenous diazepam (0.5 – 1 mg/kg IV). Tachyarrhythmias can also be treated according to type. Methocarbamol (55 – 220 mg/kg IV to effect, not to exceed 330 mg/kg/day), a skeletal muscle relaxant, can be used to control muscle tremors. Cyproheptadine (1 mg/kg), a serotonin antagonist, can be dissolved in water and administered per rectum. Any animal that has ingested an SSRI should be promptly treated and carefully observed for at least 72 hours for side effects.

**Rodenticides** Bromethalin is an uncoupler of oxidative phosphorylation that is contained in newer rodenticide compounds. Bromethalin often resembles other forms of rodenticides, and cannot be distinguished by color and texture alone. In dogs, the LD50 is approximately 1.0 mg/kg; in cats, half this dose can be lethal. Sublethal doses can cause a paralytic syndrome within 1 – 4 days of ingestion. Clinical signs include vomiting, ataxia, ascending paralysis, hyperreflexia, loss of conscious proprioception and deep pain, and severe tremors, seizures, coma, and death. If a lethal dose is ingested, early signs of exposure can occur within 10 hours of ingestion, and are associated with hyperexcitability, and seizures. Clinical signs can continue to progress over 1 – 2 weeks after exposure. During this time, treatment largely consists of supportive care to control tremors (methocarbamol 55 – 220 mg/kg IV to effect), hyperthermia, cerebral edema (mannitol 1 g/kg IV, followed 20 minutes later by furosemide 1 mg/kg IV), and dehydration (with intravenous crystalloid fluids) should occur. In some cases, hypoventilation occurs, requiring mechanical ventilation. Clinical signs of coma can be severe and last for 14 days. If an animal presents to you immediately after ingestion, vomiting should be induced, followed by doses of activated charcoal administered every 8 hours for 2 days, as this compound is thought to undergo enterohepatic recirculation.

**Xylitol** Xylitol is a sugar alcohol that, when ingested by humans, does not cause a significant increase in blood glucose. In dogs, xylitol causes a massive rapid and dose-dependent release of insulin from pancreatic beta-cells. After ingestion, clinically significant hypoglycemia followed by signs of vomiting, weakness, ataxia, mental depression, hypokalemia, seizures, and coma can develop. Clinical signs associated with xylitol ingestion can develop within 30 minutes of ingestion, and can last for more than 12 hours, even with aggressive treatment. Even in dogs that do not become hypoglycemic, there is a risk of acute hepatic failure within 72 hours of xylitol ingestion. N-acetylcysteine (Mucomyst 140 mg/kg IV, followed by 70 mg/kg IV Q6h, total of 7 doses) with S-adenosyl methionine can be administered to help support the liver during initial stages of therapy.

Treatment of known xylitol ingestion should be treated as with any other toxin ingestion, including induction of emesis or orogastric lavage, followed by administration of activated charcoal. It remains unknown at this time whether activated charcoal actually delays or prevents the absorption of xylitol from the canine gastrointestinal tract. Blood glucose concentrations should be analyzed and maintained with supplemental dextrose as a constant rate infusion (2.5 – 5%) until normoglycemia can be maintained with multiple frequent small meals.

Hypokalemia may develop as it is driven intracellularly by the actions of insulin. Hypokalemia should be treated with supplemental potassium chloride by infusion, not to exceed 0.5 mEq/kg/hour. Unless clinical signs associated with hepatic failure observed, prognosis is generally good with aggressive gastric decontamination and supportive care.

### **Cannabinoids**

Legalization of marijuana and marijuana derivatives for medical and recreational use has been associated with an exponential increase in the incidence of clinical signs of intoxication in dogs. Concomitant with the increased risk of exposure to cannabinoids is the increased potency and use of THC containing edible products available. Clinical signs of marijuana/THC toxicity can occur within minutes (inhalation) to 1-2 hours (ingestion), and include CNS depression, ataxia, mydriasis, urinary incontinence/dribbling, agitation, hyperesthesia, increased sensitivity to motion or noise, bradycardia and either hyper-or hypothermia. Rarely, respiratory and cardiac arrest have been reported in cases following ingestion of THC containing baked goods. Treatment of THC intoxication is largely supportive with administration of intravenous fluids to maintain hydration, ambient rewarming for hypothermia, and oxygen if hypoventilation occurs. Intravenous lipid emulsion has been used with variable success, but should be considered for extremely small patients who have been exposed to large amounts of THC or in patients who are comatose.

### **References/Suggested Reading**

Available upon request