Aspirin
Aspirin (acetylsalicylic acid, ASA) is the salicylate ester of acetic acid and is a weak acid derived from phenol. It is available as tablets and capsules (65, 81, 325, and 500 mg), powders, effervescent tablets and oral liquid preparations. Aspirin reduces pain and inflammation by reducing prostaglandin and thromboxane synthesis through inhibition of cyclooxygenase. At very high doses, aspirin and other salicylates uncouple oxidative phosphorylation leading to decreased ATP production. Salicylates also affect platelet aggregation.

Aspirin is rapidly absorbed from the stomach and proximal small intestine. Aspirin is metabolized in the liver and excreted through the urine. The elimination half life increases with the dose. Cats are deficient in glucuronyl transferase and have prolonged excretion due to decreased metabolism. Elimination is also slower in neonates and geriatric animals.

Signs may include vomiting (+/- blood), hyperpnea, respiratory alkalosis, metabolic acidosis, gastric hemorrhage, central lobular liver necrosis, and bleeding diathesis. Fever and seizures may be seen due to the uncoupling of oxidative phosphorylation. Renal insufficiency is uncommon with salicylate toxicoses.

Emesis can be performed in the asymptomatic animal, unless contraindicated. Activated charcoal adsorbs aspirin and repeated doses may be used with large ingestions. A cathartic should be used, unless the animal is dehydrated or has diarrhea. Liver values, glucose, acid base status and electrolytes should be monitored. Maintain hydration and start GI protectants (sucralfate, H2 blockers, +/- misoprostol, +/- omeprazole). Gastric protectants should be continued for 5 - 7 days; longer in the symptomatic patient. Antiemetics should be used to control vomiting. Alkalization of the urine results in ion trapping of salicylate in the kidney tubule and increases its secretion. Ion trapping should only be used in cases where the acid base balance can be monitored. Assisted ventilation and supplemental oxygen may be required if the animal is comatose. Seizures should be treated with diazepam. Fluids, whole blood, and electrolytes may be needed to control hypotension and hemorrhage, manage acute bleeding ulcers, and correct electrolyte abnormalities. Acid-base imbalances should be corrected. Hyperpyrexia should be treated conservatively as aggressive cooling (ice baths or cold water enemas) may result in hypothermia. Prognosis is good if the animal is treated promptly and appropriately. The development of hepatic necrosis is considered to have a poor prognosis. With hepatic damage, treatment may need to be continued for weeks.

Other Salicylates
Salicylates are found in many products. Bismuth subsalicylate (Pepto-Bismol®, Kaopectate®) contains 9 mg of salicylate in 1 ml (2 tablespoons = 325 mg aspirin). Topically applied salicylates (arthritis, psoriasis, teething, wart removal) can be absorbed through the skin and cause systemic problems. Oil of wintergreen is used as a flavoring for candy and contains approximately 98% methyl salicylate.

**Acetaminophen**

Acetaminophen (Tylenol®, non-aspirin pain reliever, APAP) is a synthetic non-opiate derivative of p-aminophenol. Acetaminophen is rapidly and almost completely absorbed from the GI tract. Peak plasma levels are seen at 10-60 minutes (60-120 min for extended release). Two major conjugation pathways are used to metabolize APAP by most species (P-450 metabolism followed by glucuronidation or sulfation). APAP-induced hepatotoxicity is due to the formation of the oxidative metabolite, N-acetyl-para-benzoquinoneimine (NAPQI). Glutathione can conjugate and neutralize NAPQI, but when glutathione stores are depleted, NAPQI binds to sulfhydryl groups on the hepatic cell membrane and damages the lipid layer. Another metabolite, PAP (para-aminophenol), appears to be responsible for methemoglobinemia and Heinz body formation.

Methemoglobin values increase within 2-4 hours, followed by Heinz body formation. Clinical signs include depression, icterus, vomiting, hypothermia, methemoglobinemia, facial or paw edema, death, dyspnea, and hepatic necrosis. Liver necrosis is less common in cats than in dogs. Clinical signs of methemoglobinemia may last 3-4 days. Hepatic injury may not resolve for several weeks. Early decontamination is most beneficial. Emesis is usually unrewarding. Activated charcoal adsorbs APAP and a cathartic should also be used, unless the animal is dehydrated or has diarrhea. Monitor liver values and for the presence of methemoglobinemia. ALT, AST and bilirubin may rise within 24 hours after ingestion and peak within 48 to 72 hours.

Symptomatic patients need initial stabilization, including oxygen if dyspneic. Treatment involves replenishing the glutathione stores and converting methemoglobin back to hemoglobin. N-acetylcysteine (Mucomyst®, NAC) is a precursor in the synthesis of glutathione and can be oxidized to organic sulfate, providing sulfhydryl groups that bind with APAP metabolites to enhance elimination. An initial oral loading dose of 140 mg/kg (dilute to 5% in dextrose or sterile water) is given, followed by 70 mg/kg PO QID for 7 treatments, or longer if still symptomatic. Fluid therapy is used to correct dehydration and for maintenance needs, not for diuresis. Whole blood transfusion may be necessary to increase oxygen carrying capacity, but cats must be monitored for volume overload. Ascorbic acid provides a reserve system for the reduction of methemoglobin back to hemoglobin; however, ascorbic acid has questionable efficacy and may irritate the stomach. Cimetidine is an inhibitor of cytochrome p-450 oxidation system but takes several days to become effective and should be avoided in cats. It has now been demonstrated that cimetidine blocks one of the only pathways that cats have to convert methemoglobin back to hemoglobin. For hepatic injury, s-adenosylmethionine (SAME, Denosyl-SD4®) at 20 mg/kg/day shows a positive effect for treatment of APAP toxicosis.
Prognosis is good if the animal is treated promptly. Animals with severe signs of methemoglobinemia or with hepatic damage have poor to guarded prognosis.

**Ibuprofen**

Ibuprofen (Motrin®, Advil®, etc.) is a nonsteroidal anti-inflammatory agent. Ibuprofen inhibits prostaglandin synthesis by blocking the conversion of arachidonic acid to various prostaglandins. Ibuprofen decreases secretion of the protective mucous layer in the stomach and small intestine and causes vasoconstriction in gastric mucosa. Ibuprofen inhibits renal blood flow, glomerular filtration rate, tubular ion transport, renin release and water homeostasis. Ibuprofen may also affect platelet aggregation and possibly hepatic function. Serious hepatotoxicosis is not a common problem with ibuprofen. Absorption of ibuprofen is rapid (0.1 to 1.5 h). Plasma half life in the dog has been reported to be 2-2.5 hours, but the elimination half life is considerably longer. Ibuprofen is metabolized in the liver and undergoes significant enterohepatic recirculation before being excreted in the urine. The onset of GI upset is generally within the first 2-6 hours after ingestion, with GI hemorrhage and ulceration occurring 12 hours to 4 days post ingestion. Renal failure often occurs within the first 12 hours after massive exposure to an NSAID but may be delayed for 3-5 days.

Emesis can be performed in the asymptomatic animal. Activated charcoal adsorbs ibuprofen and a cathartic should also be used, unless the animal is dehydrated or has diarrhea. GI protectants are very important. A combination of misoprostal, H2 blockers, sucralfate and omeprazole can be used to manage and/or prevent gastric ulcers. Animals should be started on IV fluids at twice maintenance for 48 hours if renal failure is expected. Monitor BUN, creatinine, and urine specific gravity (baseline level, 24, 48, and 72 h). Acid-base disturbances are rare and usually transient. Fluids, whole blood, inotropic agents, and electrolytes should be given to control hypotension and hemorrhage, maintain renal function, and correct electrolyte abnormalities. Assisted ventilation and supplemental oxygen may be required if animal is comatose. Prognosis is good if the animal is treated promptly and appropriately. Gastrointestinal ulceration usually responds to therapy. Acute renal insufficiency resulting from ibuprofen administration has been considered reversible.

**Selective Serotonin Reuptake Inhibitors (SSRIs)**

Selective serotonin reuptake inhibitors (SSRIs) all differ structurally, but have the same ability to inhibit presynaptic neuronal reuptake of serotonin. Drugs in this class include fluoxetine (Prozac®), paroxetine (Paxil®), sertraline (Zoloft®), fluvoxamine (Luvox®), citalopram (Celexa®) and escitalopram (Lexapro®). They have little to no effect on non-serotonin neurotransmitters and thus have less anticholinergic, sedative and cardiovascular side effects than other types of antidepressants. The most common signs of overdose are depression, vomiting, anorexia, ataxia, muscle tremors, arrhythmia (tachycardia and bradycardia are possible), and hypertension. The term serotonin syndrome has been used to describe multiple signs associated with severe SSRI toxicosis, including agitation, tremors, tachycardia, and hyperthermia. Other less common signs include diarrhea, salivation, mydriasis, seizures, nystagmus, and coma.
Emesis should only be attempted with recent exposures, assuming that the patient is asymptomatic. Gastric lavage may be considered if large numbers of pills were ingested. Activated charcoal with a cathartic should be administered and may be effective several hours after exposure. Treatment consists of monitoring vital signs closely, controlling clinical signs and providing appropriate supportive care. Diuresis does not enhance excretion because SSRIs are highly protein bound, but fluid therapy should be considered to help support blood pressure and maintain renal function. Diazepam can be used to control seizures, and treatment of CNS signs may also help in the control of some of the other signs such as tachycardia, hypertension, and hyperthermia. Propranolol may be used to counter tachycardia. Cyproheptadine, in addition to being an antihistamine and an appetite stimulant, is a non-selective serotonin reuptake inhibitor. Chlorpromazine or acepromazine can be used in addition to cyproheptadine to treat agitation.

**Amphetamines and related compounds**

Amphetamines can be found in both prescription ADHD and weight loss medications (Ritalin®, Adderall®, Vyvanse®, Concerta®), as well as illicit substances (methamphetamine, crack). Pseudoephedrine is found in cold and allergy medications. Amphetamines and pseudoephedrine are sympathomimetic alkaloids. They stimulate alpha- and beta-adrenergic receptors, causing the release of endogenous catecholamines at synapses in the brain and heart. This stimulation causes peripheral vasoconstriction and cardiac stimulation resulting in hypertension, tachycardia, ataxia, agitation, tremors, and seizures.

Asymptomatic animals may have emesis induced and activated charcoal administered. Fluid therapy is important to enhance elimination and maintain CV stability. Agitation, hyperactivity, and tremors tend to respond best to phenothiazines. Diazepam can worsen dysphoria. Because part of the syndrome is related to serotonin excess, cyproheptadine has been used to manage some of the CNS effects. If tachycardia persists, propranolol may be used. Signs may last up to 48-72 hrs in severe cases.

**Albuterol**

Albuterol (Proventil®, Ventolin®) is a synthetic sympathomimetic amine with primarily beta-2 receptor agonist properties. It is used most commonly for the treatment of asthma. Albuterol binds to beta-2 receptors on the surface of the smooth muscle cells in many different tissues as well as in skeletal muscle, liver and cardiac tissue. Binding to the receptor initiates the conversion of ATP to cyclic AMP, which mediates a variety of intercellular responses resulting in smooth muscle relaxation, increased skeletal muscle contractility and an intracellular shift of potassium. Overdoses of albuterol may lead to effects of beta-1 stimulation, including increased inotropic and chronotropic effects on the heart.

Dogs are usually exposed by chewing on inhalers but there are also solutions, syrups, powders, tablets, and extended release tablets available. When inhalers are punctured, dogs get an inhalation plus an oral exposure. This leads to a quick onset of signs and prolonged
duration signs. When inhaled, signs can begin in five minutes. Ingestions usually have a lag time of 30 minutes before clinical signs start. In dogs, signs generally resolve within 12 hours except for certain individuals who may experience signs for up to 48 hours. The most common signs seen are tachycardia, vomiting, depression, tachypnea, hyperactivity, muscle tremors, hypokalemia, and weakness. Rarely, death has been reported.

Decontamination is not advised for inhaler, solution or syrup exposure due to rapid absorption and onset of actions. Emesis (if within minutes of ingestion) and activated charcoal are advised with tablet ingestion only (especially extended relief tablets). Vital signs, heart rate and rhythm, and serum potassium levels should be monitored closely for at least the first 12 hours post-exposure and longer if clinical signs persist.

Propranolol or other non-selective beta blockers should be administered if heart rates greater than 160 to 180 bpm are observed. Propranolol slows the heart rate, has direct myocardial depressant effects and helps normalize serum potassium levels. Potassium may be supplemented as needed and should be considered if serum potassium levels fall below 2.5 mEq/l. Animals with known or underlying cardiac disease may be at risk for decompensation and sudden death. Agitation can be treated with diazepam or low dose acepromazine. Prognosis in most cases is very good.

**Calcium Channel Blockers (CCB)**

Calcium channel blockers (verapamil, diltiazem, nifedipine, etc.) slow the activity of the SA pacemaker as well as conduction through the AV node. They also cause frequency-dependent channel blockade in the AV node so that it is effective in slowing supraventricular arrhythmias. Calcium channel blockers reduce total peripheral resistance, blood pressure, and cardiac afterload. They can also cause negative inotropic effects, but this is rarely of clinical significance.

Calcium channel blockers have a low margin of safety, causing hypotension and dysrhythmias. Bradycardia is the most common arrhythmias although others are possible. Hyperglycemia, hyperkalemia, hypokalemia, and hypocalcemia are possible. Standard decontamination practices should be performed in cases of significant exposure. Any dose exceeding the therapeutic dose should be monitored for cardiovascular signs and electrolyte abnormalities. Fluid replacement and calcium administration may help correct blood pressure and conduction abnormalities. Atropine and isoproterenol may be used for bradyarrhythmias and may be more effective following calcium administration. If hypotension persists, insulin/dextrose, norepinephrine, neosynephrine, dopamine, dobutamine, or amrinone can be tried. The newest treatment is intralipids. Prognosis is dependent on dosage and response to therapy.

**Baclofen**

Baclofen is a centrally acting skeletal muscle relaxant that mimics γ-aminobutyric acid (GABA) within the spinal cord and causes a flaccid paralysis of skeletal muscles. At oral therapeutic levels, baclofen has virtually no CNS effects due to its poor ability to cross the
blood brain barrier, but in overdose situations, CNS effects are common. The most common clinical signs of toxicosis are vomiting, ataxia and vocalization/disorientation, but the most life threatening signs are dyspnea, respiratory arrest and seizures. Dyspnea and respiratory arrest are secondary to paralysis of the diaphragm and intercostal muscles.

The onset of clinical signs varies in dogs with signs occurring anywhere from 15 minutes to 7 hours post exposure (average of 1.9 hr). Duration of clinical signs vary from several hours to several days. Signs can continue long after serum baclofen levels have returned to normal due to the slow clearance from the CNS. Dog doses as low as 1.3 mg/kg can cause vomiting, depression and vocalizing. There are no established lethal doses in animals, but per the APCC data base, deaths in dogs have occurred at doses as low as 8 mg/kg.

Due to the rapid onset of clinical signs, emesis should be considered in only the asymptomatic, recently exposed patient. Gastric lavage may be considered with large ingestions, but care must be taken to ensure that anesthesia does not compound CNS depression. Short acting induction agents such as propofol or pentothal followed by inhalent anesthesia with a protected airway is preferred. All asymptomatic cases should receive activated charcoal with a cathartic. Avoid magnesium-based cathartics (Epsom salts), as they may worsen CNS depression. Exposed animals should be monitored for 12 hours for development of clinical signs.

Ventilatory support is a prime concern and endotracheal intubation and positive pressure mechanical ventilatory support may be needed for an extended time in severe cases. Diazepam is the drug of choice for centrally acting skeletal muscle relaxant-induced seizures. Propofol or isoflurane may be considered in cases that are refractory to diazepam. Long acting barbiturates or other agents that produce profound or prolonged CNS depression should be used with care. Cyproheptadine (1.1 mg/kg PO or rectally) has been used successfully to reduce the vocalization/disorientation seen in some animals. Fluid diuresis is used to enhance elimination and maintain blood pressure. Intralipids have been used successfully in early intoxications. The use of CNS respiratory stimulants are of questionable value and experimental studies have failed to consistently produce positive outcomes when flumazenil was used and have potential to cause serious adverse effects (seizures). Prognosis is variable, and can depend on the availability of ventilatory support for depressed patients. Prognosis is more guarded if seizures develop.