Rodenticide ingestion is a common emergency in small animal practice. Several classes of toxicants are used in rodenticides, and multiple agents exist within each class. This article reviews (1) the mechanisms of action of various rodenticides and (2) the treatment of the associated toxicoses.

Most of the common rodenticides are anticoagulants; however, clinicians cannot assume that a patient was exposed to an anticoagulant. Other rodenticides include bromethalin, cholecalciferol, strychnine, and zinc phosphide (TABLE 1). It is important for the veterinary staff to understand that the actions of these rodenticides vary considerably. Proper treatment of the patient requires accurate identification of the toxicant; treatment for the wrong toxicosis could be fatal for the patient.1 When possible, clients should bring the original bait packaging to the veterinary hospital.

In 2007, the American Society for the Prevention of Cruelty to Animals Animal Poison Control Center received approximately 9265 calls related to cases of rodenticide toxicosis. This represents only a small percentage of the actual number of cases. Of the reported cases, 93% were in dogs, 5% in cats, and the remainder in other species, such as birds, horses, pigs, goats, and small mammals. In cases in which the type of rodenticide was identified, 69% involved anticoagulants; 26%, bromethalin; 3%, zinc phosphide; and <1%, cholecalciferol or strychnine.a

Anticoagulants
The original anticoagulant toxicant is warfarin, which is still available commercially, although rodents have developed resistance to it.1,2,3 However, many derivatives of warfarin have been developed and are marketed. Most of the derivatives are more potent or last longer in the body. Derivatives of warfarin include the “first-generation” anticoagulants pindone and valone as well as the “second-generation” anticoagulants brodifacoum, bromadiolone, chlorophacinone, difenacoum, difethialone, and coumafuryl.2 Of these, brodifacoum is the most common in toxicosis cases.2,4

Anticoagulant baits are available in various grain-based forms, including pellets, powders, and paraffin blocks. All are palatable to pets. The toxicant is rapidly absorbed from the gastrointestinal (GI) tract, with peak plasma levels at 12 hours after ingestion.3 In theory, toxicosis can also result from an animal eating a rodent that has consumed the rodenticide. This secondary, or “relay,” toxicosis is rare,2–4 except in rodent-hunting barn cats or birds of prey.4 Geriatric or young patients and patients with preexisting liver disease may be more susceptible to toxicosis.4

The mechanism of action of anticoagulants involves blockage of the enzyme vitamin K1 epoxide reductase, which ultimately results in coagulopathy. Vitamin K1 is a cofactor in the normal coagulation cascade, where it enables activation of clotting factors II, VII, IX, and X. In the process of activating these clotting factors, vitamin K1 is converted to an inactive form. Vitamin K1 epoxide reductase converts it back to the active form so that it can be recycled and used in forming more clotting factors. When this enzyme is blocked, clotting factors cannot be produced. Remaining clotting factors in the body are consumed, resulting in uncontrolled hemorrhage.1–3

Clinical signs of anticoagulant rodenticide toxicosis often are not apparent for 2 to 7 days after ingestion.2–4 Dogs are affected more than cats.2 Clinical signs vary, but all are consequences of hemorrhage. External hemorrhage (e.g., bleeding wounds, epistaxis, hematuria, hematocytia, hemoptyisis, hematemesis, hyphema) is usually easily noted by owners. Internal hemorrhage may be more subtle, resulting in variable signs. Owners may notice dyspnea or coughing (from pulmonary or tracheal hemorrhage), lethargy or weakness (from anemia), neurologic changes (from hemorrhage in the central nervous system), lameness (from

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Rat-Bait Roundup: Rodenticide Toxicoses

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hemarthrosis or hemorrhage into muscles), or pale mucous membranes. Vomiting and anorexia may also be seen.2–4

Diagnosis of anticoagulant rodenticide toxicosis is based on laboratory analysis. A complete blood count generally shows anemia—either regenerative or nonregenerative based on the duration—and thrombocytopenia. A chemistry panel may show hypoproteinemia due to hemorrhage.2 Specific coagulation tests include the activated clotting time (ACT), prothrombin time (PT; also called one-stage prothrombin time [OSPT]), and activated partial thromboplastin time (aPTT) tests.2,3,5 The ACT can be obtained with a cage-side analyzer or with diatomaceous earth blood tubes. The ACT reflects the common coagulation pathway. The PT and aPTT may be obtained using a cage-side analyzer or by submitting blood samples to a reference laboratory. The PT measures the extrinsic pathway of the coagulation cascade, and the aPTT measures the intrinsic pathway. Both are prolonged in cases of anticoagulant rodenticide toxicosis, but the PT becomes abnormal sooner after anticoagulant ingestion.1,2,4 Of the assorted factors in the coagulation cascade, factor VII has the shortest half-life; its absence is revealed by an early prolonged PT.

The proteins induced by vitamin K antagonism/absence (PIVKA) test may also be performed. This test is available as an in-house kit or may be submitted to a reference laboratory. It measures the presence of dysfunctional clotting factors,3 but it is not specific for rodenticide toxicosis. Similar PIVKA test results may also be obtained in cases of liver disease, malnutrition, and malabsorption.1

Occasionally, toxicologic studies may be necessary to document the presence of the toxicant. Reference laboratories can perform assays on serum, blood, or liver tissue to detect and quantify the exact toxicant.3 In general, this is necessary only in cases that may involve a criminal investigation. The treatment of anticoagulant rodenticide toxicosis depends on the time from ingestion to presentation to the veterinary hospital and on the presence of clinical signs of coagulopathy. In cases of recent ingestion (within 2 to 4 hours), standard decontamination measures (i.e., induction of emesis and administration of activated charcoal with a cathartic) should be taken2–5 (TABLE 2). Overaggressive use of activated charcoal can have adverse effects, such as hypernatremia. Steps should be taken to monitor and prevent adverse reactions from activated charcoal use. At the clinician’s discretion, vitamin K1 may be dispensed as a prophylaxis. If vitamin K1 is not dispensed, a PT test should be performed 72 hours after ingestion.2,5

If the patient is hemorrhaging, treatment must be more aggressive. The goals of treatment are to give activated clotting factors, replace lost red blood cells, and administer vitamin K1. Transfusions of fresh whole blood or thawed, fresh-frozen plasma deliver clotting factors. Fresh-frozen plasma is administered at 6 to 10 mL/kg and whole blood at 12 to 20 mL/kg.2,3 If the patient is significantly anemic from blood loss, either fresh whole blood or stored packed red blood cells should be administered.

A hemorrhaging patient should be hospitalized and may require adjunctive therapy, such as oxygen administration, IV fluids, antibiotics, therapeutic centesis, or analgesics. The prognosis varies depending on the location of the hemorrhage.3,4

In a bleeding patient, vitamin K1 should be administered subcutaneously or orally.4 Subcutaneous vitamin K1 injections have a higher risk of anaphylactic reaction, so oral administration is preferred if not contraindicated (e.g., in a vomiting or comatose patient).4 The dose of vitamin K1 for a hemorrhaging or asymptomatic patient depends on the specific anticoagulant and the amount ingested. For first-

<table>
<thead>
<tr>
<th>Toxicant</th>
<th>Bait Concentration</th>
<th>LD₅₀, Toxic Dose (dog; mg/kg)</th>
<th>LD₅₀, Toxic Dose (cat; mg/kg)</th>
<th>Toxic Amount of Bait for a 10-lb dog</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>0.025%</td>
<td>20–300</td>
<td>5–30</td>
<td>13 oz</td>
</tr>
<tr>
<td>Diphacinone</td>
<td>0.005%</td>
<td>0.9–8</td>
<td>15</td>
<td>3 oz</td>
</tr>
<tr>
<td>Brodifacoum</td>
<td>0.005%</td>
<td>0.2–4</td>
<td>25</td>
<td>0.6 oz</td>
</tr>
<tr>
<td>Bromadiolone</td>
<td>0.005%</td>
<td>11–15</td>
<td>&gt;25</td>
<td>35 oz</td>
</tr>
<tr>
<td>Bromethalin</td>
<td>0.01%</td>
<td>3.7</td>
<td>0.54</td>
<td>NA</td>
</tr>
<tr>
<td>Cholecalciferol</td>
<td>0.075%</td>
<td>1.5–8.0</td>
<td>NA</td>
<td>0.25 tbsp</td>
</tr>
<tr>
<td>Strychnine</td>
<td>0.5%–1.0%</td>
<td>0.5–1.2</td>
<td>2.0</td>
<td>NA</td>
</tr>
<tr>
<td>Zinc phosphide</td>
<td>0.5%–10%</td>
<td>20–40</td>
<td>20–40</td>
<td>1 tbsp</td>
</tr>
</tbody>
</table>

*Toxic doses represent the LD₅₀ (lethal dose, 50%; i.e., the dose at which 50% of exposed animals will die). Toxicosis may occur at much lower doses. NA = not available.
generation anticoagulants, a vitamin K1 dosage of 2.5 mg/kg/day for 7 to 14 days is generally sufficient. Treating the effects of second-generation anticoagulants may require a vitamin K1 dosage of 5 mg/kg/day for 30 days or more. Bioavailability is increased by giving oral vitamin K1 with a fatty meal such as canned food.

In human medicine, more physicians are taking a "watch and wait" approach toward first-time, unintentional ingestion of anticoagulant rodenticides in pediatric patients. The physicians are neither monitoring coagulation status nor prescribing vitamin K1. If veterinary clients have consulted with a human poison control center before calling a veterinarian, they may not fully appreciate the dangers of anticoagulant ingestion in dogs and cats.

In 2008, the Environmental Protection Agency passed regulations prohibiting the sale of the anticoagulants brodifacoum, bromadiolone, difenacoum, and difethialone to private consumers. These anticoagulants are still available to pest-control services. Because of the regulations, veterinary clinics may see a higher percentage of nonanticoagulant toxicosis cases, particularly involving bromethalin.

**Bromethalin**
Bromethalin may be incorrectly assumed to be an anticoagulant because its name is similar to brodifacoum and bromadiolone, but it is a wholly different toxicant. Bromethalin interferes with oxidative phosphorylation and ATP production in the brain, resulting in cerebral edema and elevated cerebrospinal fluid pressure. Cats are particularly sensitive to bromethalin, developing toxicosis after ingestion of 0.24 mg/kg, or <0.5 oz of bait. Patients with acute toxicosis from ingesting a large amount of bromethalin may present with seizures, hyperexcitability, hyperthermia, and severe muscle tremors. Seizures may be precipitated by bright light or loud noises, resembling seizures induced by strychnine (see below). Acute bromethalin toxicosis is generally rapidly fatal. Ingestion of smaller amounts of toxicant can lead to chronic, progressive neurologic dysfunction within 1 to 2 weeks. Signs may include hindlimb weakness or paralysis, ataxia, loss of deep pain perception, coma, and seizures.

Bromethalin is rapidly absorbed after ingestion, so induction of emesis is useful only within the first 4 hours of ingestion. Induction of emesis is contraindicated if the patient is stuporous or having seizures. In a stuporous patient, sedation and gastric lavage may be performed. The toxicant is metabolized by the liver and excreted in the bile; however, it undergoes enterohepatic recirculation, meaning that it is reabsorbed by the intestine from the bile. Because of this recirculation, activated charcoal must be administered multiple times (e.g., q4–8h for up to 2 days). If a patient is showing clinical neurologic signs, supportive treatment (i.e., administration of mannitol, furosemide, and/or dexamethasone) may be attempted to reduce cerebral edema. Seizures may be controlled with phenobarbital or diazepam. However, the prognosis is poor.

**Cholecalciferol**
Cholecalciferol, or vitamin D3, increases calcium absorption from the intestines, bone, and urine as well as phosphorus reabsorption from bone. This results in an increase in serum calcium and phosphorus. Hypercalcemia can lead to weakness, GI signs, and renal tubular necrosis. A calcium × phosphorus (Ca × P) product exceeding 60 to 70 results in mineralization of soft tissues, including the kidneys, heart, major vessels, lungs, and stomach.

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**TABLE 2** **Drugs and Doses for Gastrointestinal Decontamination of Dogs and Cats**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Emetics</strong></td>
<td></td>
</tr>
<tr>
<td>Hydrogen peroxide (3%)</td>
<td>1–2 mL/kg</td>
</tr>
<tr>
<td>Apomorphine</td>
<td>0.03–0.04 mg/kg IV, 0.04–0.08 mg/kg IM, or crushed tablet in conjunctival sac (dogs)</td>
</tr>
<tr>
<td>Xylazine</td>
<td>0.44–1.1 mg/kg IM (cats)</td>
</tr>
<tr>
<td><strong>Adsorbent</strong></td>
<td></td>
</tr>
<tr>
<td>Activated charcoal</td>
<td>1–4 g/kg (mixed with 50–250 mL water if powdered charcoal is used)</td>
</tr>
<tr>
<td><strong>Cathartics</strong></td>
<td></td>
</tr>
<tr>
<td>Sodium sulfate or magnesium sulfate (epsom salt)</td>
<td>250 mg/kg</td>
</tr>
<tr>
<td>Sorbitol (70%)</td>
<td>1–2 mL/kg</td>
</tr>
</tbody>
</table>

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4. For example, if a patient has a serum calcium concentration of 15.8 mg/dL and a serum phosphorus concentration of 8.4 mg/dL, the Ca × P product is 15.8 × 8.4 = 132.7.
mineralization leads to acute renal failure, which may be fatal. Signs of toxicosis (e.g., anorexia, polyuria, polydipsia, lethargy, excessive salivation, vomiting) may develop within 12 to 36 hours. Young animals, cats, animals on a high-calcium or high-phosphorus diet, and animals with preexisting kidney disease are more susceptible to toxicosis.

In cases of recent ingestion of cholecalciferol-containing rodenticides, standard GI decontamination is recommended. This involves induction of emesis followed by administration of activated charcoal and a cathartic. Activated charcoal should be administered q6–8h for 48 hours because of enterohepatic recirculation of the toxicant. A baseline serum chemistry panel should be obtained. Hypercalcemia may be accompanied by azotemia, hyperkalemia, and hyperphosphatemia if renal failure is present. Calcium, phosphorus, blood urea nitrogen, and creatinine levels should be rechecked every 24 hours for 4 to 6 days. If the serum calcium level begins increasing, treatment to lower it should be initiated. IV 0.9% sodium chloride diuresis, furosemide, and prednisone increase calcium excretion into the urine. If these measures are not sufficient to decrease the serum calcium level, a bisphosphonate drug such as pamidronate may also be used. Pamidronate is administered as a slow IV infusion and blocks calcium resorption from bone.

If the patient is treated promptly before signs develop, the prognosis is good. However, if cholecalciferol toxicosis is not diagnosed until acute renal failure is present, the prognosis is poor.

Strychnine

Strychnine and zinc phosphide are restricted-use chemicals, meaning they are only available to professional pest-control services. However, toxicosis caused by these chemicals may occasionally be seen in general small animal practice. Strychnine is very rapidly absorbed after ingestion. The toxicant blocks glycine, an inhibitory (relaxing) neurotransmitter in the central nervous system, resulting in overstimulation. Signs (e.g., muscle spasms, hyperextension of the limbs and neck, convulsions, hyperthermia, seizures) may develop within 10 to 120 minutes after ingestion. Seizures may be precipitated by touch, bright light, or loud noises. The respiratory muscles are also affected, leading to respiratory failure and death. Treatment of strychnine toxicosis must be initiated rapidly. Induction of emesis is generally contraindicated because affected animals are usually already symptomatic. The patient may instead be sedated and intubated for gastric lavage and administration of activated charcoal. Convulsions may be controlled with pentobarbital, diazepam, methocarbamol, or general anesthesia. IV fluids should be administered to maintain renal perfusion, and the patient should be kept in a quiet, dimly lit room. The prognosis with strychnine toxicosis is poor because of the rapid onset of clinical signs.

Zinc Phosphide

After ingestion, zinc phosphide is rapidly converted by the acidic (pH: 1 to 3) environment of the stomach into phosphine gas. This gas is highly toxic to the patient and to clients or veterinary personnel who are exposed as the patient exhales. The gas is said to smell like garlic or rotting fish and is also spontaneously flammable. Species that are unable to vomit (e.g., rabbits, rodents) are more susceptible to toxicosis.

If the patient is asymptomatic, emesis may be induced. Emesis should be induced in a veterinary hospital using apomorphine, as hydrogen peroxide increases the liberation of phosphine gas. To decrease stomach acidity, the client may be instructed to administer an over-the-counter antacid such as magnesium hydroxide, aluminum hydrox-
ide, or calcium carbonate.\textsuperscript{13,14} Clients should be advised to administer an antacid only if it will not delay the animal’s transport to the veterinary clinic.

Treatment in the hospital may include sedation for gastric lavage; administration of IV fluids, oxygen, analgesia, gastroprotectants, and hepatoprotectants; mechanical ventilation; and control of seizures.\textsuperscript{3,14} Lavaging with 0.5% sodium bicarbonate may decrease phosphine production by increasing the pH of the stomach.\textsuperscript{2,14} It is important not to use water for lavage because it increases the liberation of phosphine gas. Ensure there is adequate ventilation around the patient.\textsuperscript{13} The prognosis is poor if the patient is symptomatic.\textsuperscript{3,14}

Humans exposed to phosphine gas from an affected patient may experience chest pain, lung irritation, coughing, and dizziness.\textsuperscript{13} The toxic level of phosphine gas in humans is below the threshold at which the odor is detectable; therefore, a lack of odor does not imply safety.\textsuperscript{13,14} Exposed persons should move to fresh air immediately.\textsuperscript{15} If a person has difficulty breathing, call 911.

**Conclusion**

As anticoagulant rodenticides are phased out after the recently passed regulations, veterinary clinics may see a higher percentage of nonanticoagulant toxicosis cases involving the four other classes of rodenticides, which have vastly different toxic spectrums. Clinicians cannot identify the type of rodenticide by the owner’s description (e.g., “blue-green pellets”) because the products may appear similar. It is imperative to identify the active ingredient. The prognosis varies by the type of rodenticide, the amount ingested, and the time from ingestion to presentation.

**References**