Rodenticide Poisoning: Introduction

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Many poisons have been used against rodent pests. Farm animals, pets, and wildlife often gain access to these poisons via the baits or the poisoned rodents or by malicious intent. This discussion covers the most commonly used rodenticides. Strychnine poisoning (*Strychnine Poisoning: Introduction*) is discussed separately.

Anticoagulant Rodenticides (Warfarin and Congeners):

Potentially dangerous to all mammals and birds, anticoagulant rodenticides are the most frequent cause of poisoning in pets. Pets and wildlife may be poisoned directly from baits or indirectly by consumption of poisoned rodents. Intoxications in domestic animals have resulted from contamination of feed with anticoagulant concentrate, malicious use of these chemicals, and feed mixed in equipment used to prepare rodent bait.

All anticoagulants have the basic coumarin or indanedione nucleus. The "first-generation" anticoagulants (warfarin, pindone, coumafuryl, coumachlor, isovaleryl indanedione, and others less frequently used) require multiple feedings to result in toxicity. The "intermediate" anticoagulants (chlorophacinone and in particular diphacinone) require fewer feedings than

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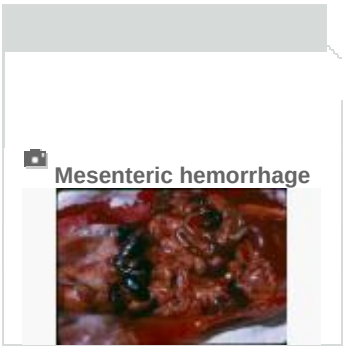
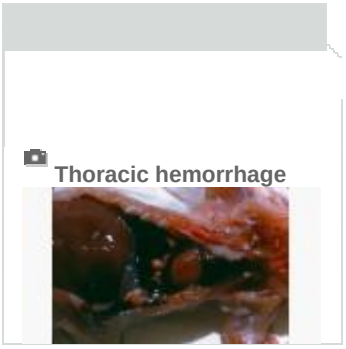
"first-generation" chemicals, and thus are more toxic to nontarget species. The "second-generation" anticoagulants (brodifacoum and bromadiolone) are highly toxic to nontarget species (dogs, cats, and potentially livestock) after a single feeding.





The anticoagulants antagonize vitamin K, which interferes with the normal synthesis of coagulation proteins (factors I, II, VII, IX, and X) in the liver; thus, adequate amounts are not available to convert prothrombin into thrombin. A latent period, dependent on species, dose, and activity, is required, during which clotting factors already present are used up. New products have a longer biologic half-life and therefore prolonged effects (which require prolonged treatment). For example, the half-life in canine plasma of warfarin is 15 hr, diphacinone is 5 days, and bromadiolone is 6 days, with maximum effects estimated at 12-15 days. Brodifacoum may continue to be detectable in serum for up to 24 days.

Clinical signs generally reflect some manifestation of hemorrhage, including anemia, hematomas, melena, hemothorax, hyphema, epistaxis, hemoptysis, and hematuria. Signs dependent on hemorrhage, such as weakness, ataxia, colic, and polypnea, may be seen. Depression and anorexia occur in all species even before bleeding occurs.

Anticoagulant rodenticide toxicosis is usually diagnosed based on history of ingestion of the substance. Differential diagnoses when massive hemorrhage is encountered include disseminated intravascular coagulation, congenital factor deficiencies, von Willebrand's disease, platelet deficiencies, and canine ehrlichiosis. A prolonged prothrombin, partial thromboplastin, or thrombin time in the presence of normal fibrinogen, fibrin degradation

products, and platelet counts is strongly suggestive of anticoagulant rodenticide toxicosis, as is a positive therapeutic response to vitamin K_1.

Vitamin K_1 is antidotal. Recommended dosages vary from 0.25-2.5 mg/kg in warfarin (coumarin) exposure, to 2.5-5 mg/kg in the case of long-acting rodenticide intoxication (diphacinone, brodifacoum, bromadiolone). Vitamin K_1 is administered SC (with the smallest possible needle to minimize hemorrhage) in several locations to speed absorption. IV administration of vitamin K_1 is contraindicated, as anaphylaxis may occasionally result. The oral form of K_1 may be used daily after the first day, commonly at the same level as the loading dose (divided BID). Fresh or frozen plasma (9 mL/kg) or whole blood (20 mL/kg) IV is required to replace needed clotting factors and RBC if bleeding is severe. One week of vitamin K_1 treatment is usually sufficient for first-generation anticoagulants. For intermediate and second-generation anticoagulants or if anticoagulant type is unknown, treatment should continue for 2-4 wk to control longterm effects. Administration of oral vitamin K_1 with a fat-containing ration, such as canned dog food, increases its bioavailability 4-5 times as compared with vitamin K_1 given PO alone.

Coagulation should be monitored weekly until values remain normal for 5-6 days after cessation of therapy. Vitamin K_3 given as a feed supplement is ineffective in the treatment of anticoagulant rodenticide toxicosis. Additional supportive therapy may be indicated, including thoracocentesis (to relieve dyspnea due to hemothorax) and supplemental oxygen if needed.

ANTU (α-Naphthylthiourea):

ANTU causes local gastric irritation; when absorbed, it increases permeability of the lung capillaries in all animals, although species variability in dose response is marked. Properties of ANTU, when compared with those of warfarin, have led to near abandonment of its use. Dogs and pigs are occasionally poisoned; ruminants are resistant. Animals with an empty stomach readily vomit after ingestion of ANTU; however, food in the stomach decreases the stimulation to vomit, and fatal quantities may be absorbed. Signs include vomiting, hypersalivation, coughing, and dyspnea. Animals prefer to sit. Severe pulmonary edema, moist rales, and cyanosis are present. Dependent signs include weakness; ataxia; rapid, weak pulse; and subnormal temperature. Death from hypoxia may occur within 2-4 hr of ingestion, while animals that survive 12 hr may recover.

The lesions are suggestive. The most striking findings are pulmonary edema and hydrothorax. Hyperemia of the tracheal mucosa; mild to moderate gastroenteritis; marked hyperemia of the kidneys; and a pale, mottled liver are found in most cases. Tissue for chemical analysis must be obtained within 24 hr.

Emetics should be used only if respiratory distress is not evident. Prognosis is grave when severe respiratory signs occur. Agents providing sulfhydryl groups, eg, n-amyl mercaptan, sodium thiosulfate (10% solution), or n-acetylcysteine are beneficial. Positive-pressure oxygen therapy, an osmotic diuretic (eg, mannitol), and atropine (0.02-0.25 mg/kg) may relieve the

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pulmonary edema.

Bromethalin:

This nonanticoagulant, single-dose rodenticide is a neurotoxin that appears to uncouple oxidative phosphorylation in the CNS. CSF pressure increases, which places pressure on nerve axons and results in decreased conduction of nerve impulses, paralysis, and death. In dogs, a dose of 1.67 mg/kg is toxic, and 2.5 mg/kg (25 g of bait/kg body wt) is lethal.

Bromethalin can cause either an acute or a chronic syndrome. The acute effects follow consumption of ≥5 mg/kg bromethalin. Signs, which include hyperexcitability, muscle tremors, grand mal seizures, hindlimb hyperreflexia, CNS depression, and death, may appear ~10 hr after ingestion. Chronic effects are seen with lower dosages and may appear 24-86 hr after ingestion. This syndrome is characterized by vomiting, depression, ataxia, tremors, and lateral recumbency. The effects may be reversible if exposure to bromethalin is discontinued. Bromethalin toxicosis should be considered when cerebral edema or posterior paralysis is present.

Treatment should be directed at blocking absorption from the gut and reducing cerebral edema. Use of mannitol as an osmotic diuretic and corticosteroids have been suggested but have shown little effect in dogs poisoned by bromethalin. Use of activated charcoal for several days may improve the recovery rate.

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Cholecalciferol:

Although this rodenticide was introduced with claims that it was less toxic to nontarget species than to rodents, clinical experience has shown that rodenticides containing cholecalciferol are a significant health threat to dogs and cats. Cholecalciferol produces hypercalcemia, which results in systemic calcification of soft tissue, leading to renal failure, cardiac abnormalities, hypertension, CNS depression, and GI upset.

Signs generally develop within 18-36 hr of ingestion and can include depression, anorexia, polyuria, and polydipsia. As serum calcium concentrations increase, clinical signs become more severe. Serum calcium concentrations >16 mg/dL are not uncommon. GI smooth muscle excitability decreases and is manifest by anorexia, vomiting, and constipation. Hematemesis and hemorrhagic diarrhea may develop as a result of dystrophic calcification of the GI tract and should not lead to a misdiagnosis of anticoagulant rodenticide toxicosis. Loss of renal concentrating ability is a direct result of hypercalcemia. As hypercalcemia persists, mineralization of the kidneys results in progressive renal insufficiency.

Diagnosis is based on history of ingestion, clinical signs, and hypercalcemia (*see also Hypercalcemia in Dogs and Cats: Overview*). Other causes of hypercalcemia, such as hyperparathyroidism, normal juvenile hypercalcemia, paraneoplastic hypercalcemia, hemoconcentration (hyperproteinemia), and diffuse osteoporosis should be ruled out. Gross lesions associated with hypercalcemia include pitted, mottled kidneys; diffuse hemorrhage of the GI mucosa; and roughened, raised plaques on the great vessels and on the surface of the lungs and abdominal viscera.

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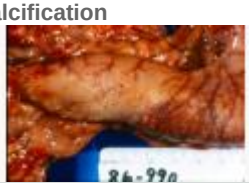
Cholecalciferol, histopathologic calcification

Cholecalciferol, serosal calcification



Recommended therapy includes gastric evacuation, generally followed by administration of activated charcoal at 2-8 g/kg body wt in a water slurry. Calciuresis is accomplished with 0.9% sodium chloride solution and administration of furosemide (initial bolus of 5 mg/kg, IV, followed by a constant rate IV infusion of 5 mg/kg/hr) and corticosteroids (prednisolone, 1-2 mg/kg, BID). Furosemide and prednisolone should be continued for 2-4 wk, and the serum calcium concentration monitored at 24 hr, 48 hr, and 2 wk after cessation of treatment. Additionally, calcitonin may be used at 4-6 IU/kg, SC, every 2-3 hr, until the serum calcium stabilizes at <12 mg/dL. The IV use of calcium chelators such as Na-EDTA has been used in severe cases, but this use is experimental and requires close monitoring of blood calcium to prevent hypocalcemia. The dose of prednisolone should be tapered if it is administered for >2 wk to prevent acute adrenocortical insufficiency. Continuous peritoneal dialysis may be considered if the animal is in renal failure. A low-calcium diet should be provided in all cases of significant exposure to cholecalciferol rodenticides.

Recently, pamidronate disodium, a specific inhibitor of bone resorption used for the treatment of hypercalcemia of malignancy and Paget's disease in humans, has shown promise in the treatment of cholecalciferol toxicosis in dogs. It is given slowly IV at 1.3-2.0 mg/kg in saline solution over 2-4 hr. Two infusions are given 4 days apart. Pamidronate disodium has a long-lasting inhibitory action on bone resorption, thus requiring only limited infusions. Total serum calcium and BUN should be monitored 2 and 4 days after the last infusion.

Metaldehyde:

This polymer of acetaldehyde is used as a snail or slug bait, to which dogs and livestock may be exposed. (*See also* METALDEHYDE POISONING, *Metaldehyde Poisoning: Introduction*.) Toxic effects are due to absorption of limited acetaldehyde from metaldehyde hydrolysis in the stomach, but primarily to the metaldehyde itself. Signs range from salivation and vomiting to anxiety and incoordination with muscle tremors, fasciculations, and hyperesthesia leading to continuous muscle spasms, prostration, and death. Generally, the muscle spasms are not initiated by external stimuli, but excessive muscular activity is common, often producing high body temperatures. Differential diagnoses include strychnine poisoning and anticholinesterase insecticide toxicity. The finding of metaldehyde bait or pellets in the vomitus and the possible odor of acetaldehyde from stomach contents or on the animal's breath may assist in diagnosis.

Treatment is most effective if initiated early. Further toxicant absorption should be prevented by induced emesis, gastric lavage, and oral dosing with activated charcoal. Hyperesthesia and muscle activity may be controlled with diazepam at 2-5 mg, IV, or light barbiturate anesthesia and muscle relaxants as needed. IV fluid therapy with lactated Ringer's solution or 5% glucose should be aggressive to promote toxin excretion and to combat dehydration and the acidosis induced by the excessive muscle activity. Continuous supportive care is important. Prognosis is heavily determined by the exposure dose, but if death does not occur earlier, animals poisoned by metaldehyde may show clinical improvement 24-36 hr after initial onset of signs. Top

Phosphorus:

In its white (or yellow) form, phosphorus is hazardous to all domestic animals and is locally corrosive and hepatotoxic when absorbed. Phosphorus is infrequently used as a rodenticide today, but dogs occasionally become exposed through ingestion of fireworks that contain white phosphorus. The onset of signs of poisoning is sudden. Early signs include vomiting, severe diarrhea (often hemorrhagic), colic, and a garlic-like odor to the breath. Apparent recovery can occur up to 4 days after ingestion, but additional signs of acute liver damage may develop, including hemorrhages, abdominal pain, and icterus. Hepatic encephalopathy is followed by convulsions and death. Lesions include severe gastroenteritis; fatty liver; multiple hemorrhages; and black, tarry blood that fails to clot. Body tissues and fluids may be phosphorescent, and the gastric contents have a garlic odor. Death is due to hepatic and renal failure.

Prognosis is grave unless treatment is instituted early. A 1% solution of copper sulfate is an effective emetic and also forms a nonabsorbable copper phosphide complex. Gastric lavage with a 0.01-0.1% potassium permanganate solution or a 0.2-0.4% copper sulfate solution should be followed by activated charcoal adsorbent and 30 min later by a saline cathartic. Any fat in the diet must be avoided for 3-4 days or longer because fats favor additional absorption of phosphorus. Mineral oil orally has been recommended because it dissolves phosphorus and prevents absorption. Top

Red Squill:

This rodenticide is a cardiac glycoside derived from the plant *Urginea maritima* . It is of limited current use. Because rats are incapable of vomiting, red squill is more toxic to that species. It is unpalatable to domestic animals but, when eaten, usually induces vomiting in dogs and cats. Large quantities are required for toxicity in farm animals. It is considered relatively safe, but dogs, cats, and pigs have been poisoned. Signs are vomiting, ataxia, and hyperesthesia followed by paralysis, depression, or convulsions. Bradycardia and cardiac arrhythmias may end in cardiac arrest. The clinical course seldom is longer than 24-36 hr.

Treatment consists of supportive therapy and evacuation of the GI tract using gastric lavage and saline cathartics. Atropine sulfate SC at 6- to 8-hr intervals may prevent cardiac arrest. Phenytoin at 35 mg/kg, TID, should be given to dogs to suppress arrhythmias.

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Sodium Monofluoroacetate (1080):

1080 is a colorless, odorless, tasteless, water-soluble chemical that is highly toxic (0.1-8 mg/kg) to all animals, including humans. Its use is restricted to certain commercial applications. Fluoroacetate is metabolized to fluorocitrate, which blocks the tricarboxylic acid cycle—a mechanism necessary for cellular energy production. It causes toxic effects by overstimulating the CNS, resulting in death by convulsions, and by causing alteration of cardiac function that results in myocardial depression, cardiac arrhythmias, ventricular fibrillation, and circulatory collapse. CNS stimulation is the main effect in dogs, while the cardiac effects predominate in horses, sheep, goats, and chickens. Pigs and cats appear about equally affected by both.

A characteristic lag phase of ≥30 min after ingestion occurs before the onset of nervousness and restlessness. Marked depression and weakness follow in all species except dogs and pigs. Affected animals rapidly become prostrate, and the pulse is weak and 2-3 times normal rate. Death is due to cardiac failure. Usually, dogs and pigs rapidly develop tetanic convulsions similar to those of strychnine poisoning. Many exhibit severe pain. Vomiting is prominent in pigs. Dogs usually have urinary and fecal incontinence and exhibit frenzied running. The course is rapid; affected animals die within hours after signs appear. Few animals that develop marked signs recover. Congestion of organs, cyanosis, subepicardial hemorrhages, and a heart stopped in diastole are common necropsy findings.

Emetics are contraindicated if clinical signs are present. Gastric lavage and adsorbents (activated charcoal, 0.5 g/kg) are recommended. Prognosis is grave if clinical signs are severe. Barbiturates are preferred for controlling seizures. Glyceryl monoacetate (monacetin) has been used with inconsistent results as a competitive antagonist of fluoroacetate. The recommended dose is 0.55 mL/kg, IM, or IV in 5 parts of sterile saline solution, every 30 min for several hours.

The danger of secondary poisoning due to ingestion of rodents killed with 1080 is high and has led to restrictions in its use (and use of fluoroacetamide) in the USA. Only certified, insured exterminators can purchase 1080, and a black dye must be mixed with it for identification.

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Sodium Fluoroacetamide (1081):

1081 causes signs similar to those of 1080 (*see* above) and requires the same treatment.

Thallium Sulfate:

This general cellular poison can affect all species of animals. It has been banned for use as a rodenticide. Onset of clinical signs may be delayed 1-3 days and, although all body systems are affected, the most prominent signs are of the GI, respiratory, integumentary, and nervous systems. Signs include gastroenteritis (occasionally hemorrhagic), abdominal pain, dyspnea, blindness, fever, conjunctivitis, gingivitis, and tremors or seizures. After 4-5 days and an apparent recovery, or after repeated small doses, a chronic dermatitis characterized by alopecia, erythema, and hyperkeratosis occurs. Necrosis of many tissues is a common necropsy finding.

Treatment of the acute phase of thallium poisoning includes emetics, gastric lavage with a 1% sodium iodide solution, and IV administration of 10% sodium iodide. Diphenylthiocarbazone (dithizone, 70 mg/kg, PO, TID) is antidotal but must be given within 24 hr of exposure. At the same time and for 14 days thereafter, Prussian blue 100 mg/kg should be given BID in oral aqueous suspension to stop enterohepatic recirculation of the thallium and to enhance its excretion in the feces. Symptomatic treatment of the diarrhea and convulsions is needed with particular attention to fluid and electrolyte balance, nutrient needs, prevention of secondary infection, and good nursing care.

Zinc Phosphide and Aluminum Phosphide:

Zinc phosphide has been used extensively around farms and barns because affected rats tend to die in the open. Toxicity is due to liberation of phosphine gas at the acid pH in the stomach. The gas results in direct GI tract irritation along with cardiovascular collapse. The toxic dose is ~40 mg/kg, and onset is rapid in animals with a full stomach. Clinical signs include vomiting, abdominal pain, and aimless running and howling, followed by depression, dyspnea, and convulsions (which may resemble those seen in strychnine or fluoroacetate poisoning). Death is due to respiratory arrest. The odor of acetylene is present in vomitus or stomach contents. Less frequent lesions include visceral congestion and pulmonary edema. Diagnosis is based on history of exposure to zinc phosphide, suggestive clinical signs, and detection of zinc phosphide in stomach contents. Zinc levels in the blood, liver, and kidneys may be increased. Treatment must include supportive therapy, calcium gluconate, and appropriate fluids to reduce acidosis. Sodium bicarbonate (in cattle, 2-4 L of 5%), PO, to neutralize stomach acidity is recommended.

Note: The previous information was taken from the Merck veterinary handbook (Feb 2013). Please consult the handbook for more current information.