CHAPTER 18

Rodenticides

Rodent poisons are usually added to baits (palatable grain or paste intended to encourage consumption). Safety for animals and humans depends on the toxicity of the agents, concentration of the active ingredient in the bait, the likelihood that a toxic dose will be consumed by non-target species, and bioaccumulation and persistence in body tissues. The first-generation anticoagulants, for example, are reasonably effective against pest rodents and are less toxic than second-generation anticoagulants (see discussion of first- and second-generation anticoagulants in subsection *Coumarins and Indandiones,* following). Rodents are more likely than domestic animals or humans to consume quantities of treated bait that will cause poisoning. However, accidental ingestion by young children or intentional ingestion by individuals with suicidal intent is possible with any poison.

Very small amounts of the extremely toxic rodenticides − **sodium fluoroacetate**, **fluoracetamide, strychnine, crimidine, yellow phosphorus, zinc phosphide** and **thallium sulfate** − can cause severe and even fatal poisoning. **Cholecalciferol** is also a highly toxic agent. The **anticoagulants, indandiones** and **red squill** are less hazardous to humans and domestic animals. Some of the newer anticoagulant compounds, termed "second-generation anticoagulants," may cause human toxicity at a much lower dose than conventional "first-generation anticoagulants"[1,2,3] and can bioaccumulate in the liver.[2]

Yellow phosphorus is not sold in the United States. Zinc phosphide is still registered in the United States and can be found in U.S. retail stores. Thallium sulfate is no longer registered for pesticidal use, but is used by government agencies and in medical diagnostic testing.

Strychnine and sodium fluoroacetate are still used for control of some mammal pests such as coyotes, as is cyanide (see **Chapter 17, *Fumigants*** for cyanide). Only specially trained personnel are allowed to use them.

Crimidine and fluoroacetamide are no longer registered in the United States for use as pesticides. TETS is banned worldwide.

COUMARINS AND INDANDIONES

Toxicology

Anticoagulants (**warfarin** and related compounds, **coumarins** and **indandiones**) are the most commonly used rodenticides in the United States. While there has been a modest decline in the number of exposures in 2008 compared to 1996, from 13,345 to 11,487, they still account for the largest number of reported rodenticide exposures.[4,5] Gastrointestinal absorption of these toxicants is efficient.

Certain agents in this category are referred to as "first-generation" or "second-generation" anticoagulants. "First-generation" anticoagulants, as the name implies, were developed earlier (during World War II), and include hydroxycoumarin derivatives such as warfarin, coumachlor and coumatetralyl. The "second-generation" anticoagulants, sometimes referred to as "superwarfarins," are generally more toxic. These include bromodiolone, brodifacoum and difenacoum.

Coumarins and indandiones depress the hepatic synthesis of vitamin K-dependent blood-clotting factors (II [prothrombin] and VII, IX and X). The antiprothrombin

Coumarins & Indandiones

HIGHLIGHTS

Most commonly used rodenticides in U.S.

Efficient GI absorption

Depress blood clotting and capillary permeability

SIGNS & SYMPTOMS

Bleeding nose/gums, hematuria, melena, eccymoses days after ingestion

For indandiones, headache, confusion, loss of consciousness, seizures

Increase in PT/INR

TREATMENT

Monitor PT/INR

Give Vitamin K_1 upon PT/INR evidence

CONTRAINDICATED

Vitamin K_3 or K_4

effect is best known and is the basis for detection and assessment of clinical poisoning. The agents also increase permeability of capillaries throughout the body, predisposing the animal to widespread internal hemorrhage. This generally occurs in the rodent after several days of warfarin ingestion because of the long half-lives of the vitamin K-dependent clotting factors,[1,2] although lethal hemorrhage may follow smaller doses of the modern, more toxic compounds.[2,3]

To identify potential toxic effects from the coumarins or indandiones, a prothrombin time (PT) is measured. Most laboratories report the PT as being adjusted to the International Normalized Ratio (INR) for patients on anticoagulant medication. Therefore, one may see PT or INR reported by a laboratory. The prolonged prothrombin time (PT/INR) from a toxic dose of coumarins or indandiones may be evident within 24 hours, but usually reaches a maximum in 36-72 hours.[2,6,7] Prolonged PT/INR occurs in response to doses much lower than that necessary to cause hemorrhage. There is concern that the more toxic modern compounds, such as brodifacoum and difenacoum, may cause serious poisoning of non-target mammals, including humans, at much lower dosage. **Brodifacoum**, one of the "second-generation anticoagulants," is much more toxic, partly due to a longer half-life; a dose as low as 1 mg in an adult or 0.014 mg/kg in a child is sufficient to produce toxicity.[2]

Symptomatic poisoning, with prolonged symptoms due to the long half-lives of second-generation anticoagulants, has been reported even with single exposures; however, these are usually intentional and are large, single dosages.[1] Because of their toxicity in relation to warfarin, patients may require higher dosages of vitamin K and will require longer monitoring of their PT. One patient required vitamin K for several months following discharge.[8] Another was released from the hospital with significant clinical improvement and only slightly elevated coagulation studies after brodifacoum ingestion. Two-and-a-half weeks later, this patient presented in a comatose state and was found to have massive intracranial hemorrhage.[9] In situations of purposeful ingestion, it is difficult to know if the patient is re-exposing himself or herself. Since 1999, individual case reports continue to appear in the medical literature. Nearly all are suicidal ingestions, although there are occasional reports of intentional subacute ingestion or Munchausen by proxy.[10,11,12,13,14,15]

In contrast to the intentional ingestions from suicide attempts, accidental single ingestions are more common, particularly when toddlers ingest a few pellets. The majority of these incidents did not result in significant bleeding, and most patients did not have a prolonged PT/INR.[7,16,17] It should also be noted that beginning June 2011, all rodenticide bait products available for sale on the residential consumer market in the United States must be in the form of blocks (pellets or loose bait no longer allowed) and be contained a tamper-resistant bait station. Also, since 2011, the second generation anticoagulants (brodifacoum, bromadiolone, difenacoum, difethialone) are not allowed in residential consumer products.[18]

Dermal exposure to the long-acting indandiones has also been reported to cause symptomatic bleeding. One 18-year-old patient presented with flank pain and gross hematuria following dermal exposure to 0.106% diphacinone.[19] Another patient had hematuria following exposure to 0.25% chlorophacinone on his torso.[20]

Clinical effects of these agents usually begin several days after ingestion, because of the long half-life of the factors. Primary manifestations include nosebleeds, bleeding gums, hematuria, melena and extensive ecchymoses.[1,2,8,9,21] Patients may also have symptoms of anemia including fatigue and dyspnea on exertion.[21] If the poisoning is severe, the patient may progress to shock and death.

Unlike the coumarin compounds, some indandiones cause symptoms and signs of neurologic and cardiopulmonary injury in laboratory rats. These lead to death before hemorrhage occurs, which may account for the greater toxicity of indandiones in

rodents. In several cases of human poisonings, some of the presenting signs included headache, confusion, loss of consciousness and seizures. These CNS symptoms were found to be related to intracranial hemorrhage.[22,23] One other patient was reported to present in a comatose state. He had severe intra-abdominal bleeding without any intracranial bleeding and eventually recovered.[24]

Confirmation of Poisoning

Coumarin or indandione poisoning results in an increase in PT/INR, the result of reduced plasma prothrombin concentration. This is a reliable test for absorption of physiologically significant doses. Detectable reduction in prothrombin occurs within 24-48 hours of ingestion and persists for 1-3 weeks.[2,6,7] Blood levels of the second-generation anticoagulants can be measured, however the test is not immediately available, nor does it aid in immediate treatment decisions as does the PT or INR.[21]

Treatment of Anticoagulant Toxicosis

If the amount of agent ingested was assuredly no more than a few mouthfuls of coumarin- or indandione-treated bait, or a single mouthful of bait treated with the more toxic brodifacoum or bromadiolone compounds, medical treatment is probably unnecessary. Otherwise:

1. If there is an unknown amount or deliberate ingestion, assess PT/INR at baseline and then daily. While the anticoagulant effects of the coumarins might be noted within 12-24 hours of ingestion, some agents such as brodifacoum may not show an elevation until 48 hours after ingestion, if it does occur.[7] A normal PT/INR 48-72 hours after ingestion makes a significant bleeding event very unlikely.

2. Give phytonadione (vitamin K_1) orally to protect against the anticoagulant effect of these rodenticides, with essentially no risk to the patient. The indication for vitamin K_1 in these patients is laboratory evidence (elevated PT/INR) of excessive anticoagulation after ingestion. It is not recommended empirically after ingestion. On one hand, laboratory evidence may indicate it is not needed. However, most important, vitamin K_1 administration prior to PT/INR elevation may delay the lab abnormalities and the seriousness of the ingestion can be missed.

   CAUTION: ***Phytonadione, specifically, is required. Neither vitamin K_3 (menadione, Hykinone) nor vitamin K_4 (menadiol) is an antidote for these anticoagulants. These need to be metabolized by the liver to active vitamin K, and with the potential of significant bleeding, liver function may be impaired. They were not effective as antidotes in prior poisonings.***[22,25]

3. If possible, administer vitamin K_1 by mouth. While vitamin K_1 can be given orally, subcutaneously (SC), intramuscularly (IM) and intravenously (IV), oral use is preferred because of its good adverse event profile. Anaphylactoid reactions resulting in death have been reported via the IV route; therefore, IVs should be restricted to those patients who are critically ill and cannot take it by any other route. IM or SC use can result in significant hematoma in anti-coagulated patients and, again, use of these routes should be reserved for those patients unable to take Vitamin K_1 orally.

Coumarins & Indandiones
COMMERCIAL PRODUCTS

Anticoagulants

brodifacoum (Havoc, Talon)

bromadiolone (Contrac, Maki)

coumachlor

coumatetralyl

difenacoum

difethialone

warfarin (Cov-R-Tox, Liqua-Tox)

Indandiones

chlorophacinone (Rozol)

diphacinone (diphacin, Ditrac, Ramik, Tomcat)

pivalyn (Pival)

radione

4. Begin dosing with vitamin K_1. Dosing can be variable and may depend on the level of anticoagulation and the agent ingested. The usual starting dose is:

Dosage of Vitamin K_1

- ***Adults: 10-50 mg orally, 2-4 times per day***
- ***Children: 5-10 mg (or 0.4 mg/kg/dose) orally, 2-4 times per day***

5. Monitor PT/INR for response to vitamin K_1 and, once declining, doses can be decreased accordingly. Patients who ingest large amounts, particularly of the superwarfarin compounds, will likely have a very prolonged period of decreased prothrombin activity. Patients may need to be treated for as long as 3 or 4 months.[8,9]

6. With ingestions of certain agents such as the second-generation anticoagulants, very large doses of vitamin K_1, between 100 mg up to 400 mg, have been needed initially to reverse the anticoagulation.[6,26] These large doses may be required from weeks to months, depending on the extent of the ingestion and anticoagulation. Monitor patients closely to assure that they are taking the vitamin K_1 and not deliberately re-exposing themselves.

7. Give patients who present with active bleeding fresh frozen plasma or whole blood, while also receiving vitamin K_1. This will temporize the bleeding until the vitamin K_1 has time to replenish the missing factors.

INORGANIC RODENTICIDES

Toxicology

Yellow phosphorus is a corrosive agent that damages all tissues it contacts, including skin and the gastrointestinal epithelium. A similar compound, **white phosphorus**, is used as an explosive agent in ammunition and fireworks, and some recent reports of toxicity have been from this source.[27,28] The skin is subject to severe burns from white phosporus, which can be third degree and require grafting.[27]

Initial symptoms of yellow phosphorus ingestion usually reflect mucosal injury and occur a few minutes to 24 hours following ingestion. The first symptoms include severe vomiting and burning pain in the throat, chest and abdomen. The emesis may be bloody (either red, brown or black)[29] and on occasion may have a garlic smell.[30,31,32] In some cases, central nervous system signs such as lethargy, restlessness and irritability are the earliest symptoms followed by symptoms of gastrointestinal injury. Shock and cardiopulmonary arrest leading to death may occur within hours in severe ingestions.[31]

If the patient survives the initial toxic effects, there may be a second stage, characterized by a period of apparent improvement that can last a few hours or days, although this is not always the case.[29] In severe poisoning, a third stage of toxicity then ensues with systemic signs indicating severe injury to the liver, myocardium and brain. Nausea and vomiting recur. There is a severe toxic hepatitis with elevated liver transaminases, and jaundice with elevation in both total and direct bilirubin levels.[29,32,33] Neutropenia has also been reported.[34] Hypovolemic shock and toxic myocarditis may develop. Brain injury is manifested by convulsions, delirium and coma. The coma may result from hyperammonemia due to severe hepatic failure.[32,33] Anuric renal failure

commonly develops because of shock and the toxic effects of phosphorus products and accumulating bilirubin on renal tubules. The mortality rate of phosphorous poisonings may be as high as 50 percent.[29]

Zinc phosphide is much less corrosive to skin and mucous membranes than yellow phosphorus. Both zinc phosphide and aluminum phosphide (often used as a fumigant) can be very toxic following ingestion, although zinc phosphide ingestion is relatively less common than its aluminum counterpart.[35] In terms of toxicity following ingestion, phosphine is thought to be released from the metal phosphide following contact with fluids in the GT tract.[35] While the emetic effect of zinc released in the gut may provide a measure of protection for humans, fatal ingestion of zinc phosphide has been reported.[36,37] Nausea and vomiting, agitation, chills, chest tightness, dyspnea and cough may progress to pulmonary edema. These symptoms, as well as systemic toxicity, may be delayed or present after initial benign exam. Patients face many of the same systemic toxicities encountered with yellow phosphorous, including hepatic failure with jaundice and hemorrhage, delirium, convulsions and coma (from toxic encephalopathy); tetany from hypocalcemia and anuria from renal tubular damage. Ventricular arrhythmias from cardiomyopathy and shock also occur and are another common cause of death.[30,38] Severe hypoglycemia has also been reported, which is also thought to be of hepatic origin by inhibition of glycogenolysis and gluconeogenesis.[38,39] (Conversely, hyperglycemia has been reported following ingestion of the fumigant aluminum phosphide.)[40] Inhalation of phosphine gas from improper use of phosphide rodenticides has resulted in pulmonary edema, myocardial injury and multisystem involvement.[41] For more information about the effects of phosphine gas poisoning, see the section on aluminum phosphide in **Chapter 17, *Fumigants***.

Thallium sulfate is well absorbed from the gut and across the skin. It exhibits a very large volume of distribution and is distributed chiefly to the kidney and liver, both of which participate in thallium excretion. Most blood-borne thallium is in the red cells. Thallium is thought to exert its toxic effects by competing with intracellular potassium and interfering with intracellular enzyme reactions.[42] Elimination half-life from blood in the adult human is about 1.9 days. Most authors report the LD_{50} in humans to be between 10-15 mg/kg.[43]

Unlike other inorganic rodenticides such as yellow phosphorous and zinc phosphide, thallium poisoning tends to have a more insidious onset with a wide variety of toxic manifestations. The gastrointestinal, central nervous, cardiovascular, renal and integumentary systems are prominently affected by toxic intakes of thallium. Early symptoms include abdominal pain, nausea, vomiting, bloody diarrhea, stomatitis, salivation and ileus. Elevated liver enzymes may occur, indicating tissue damage. Proteinuria and hematuria may also occur. Other patients experience signs of central nervous system toxicity including headache, lethargy, muscle weakness or even paralysis, loss of deep tendon reflexes, paresthesias, tremor, ptosis and ataxia. These signs and symptoms usually occur several days to more than a week after exposure.[42,43,44] Extremely painful paresthesias, either in the presence or absence of gastrointestinal signs, may be the primary presenting complaint.[42,45,46,47] Myoclonic movements, convulsions, delirium and coma reflect more severe neurologic involvement.

Cardiovascular effects include hypotension, due at least in part to a toxic myocardiopathy, myocardial ischemia and ventricular arrhythmias.[48] Hypertension occurs later and is probably a result of peripheral arterial vasoconstriction. Patients may also develop alveolar edema and hyaline membrane formation in the lungs, consistent with a diagnosis of Acute Respiratory Distress Syndrome.[48] Death from thallium poisoning may be caused by respiratory failure or cardiovascular collapse.[47,48] Absorption of nonlethal doses of thallium has caused protracted, painful neuropathies and paresis, optic nerve atrophy, persistent ataxia, dementia, seizures and coma.[45]

Phosphorus

HIGHLIGHTS

Phosphorus poisonings are often fatal

SIGNS & SYMPTOMS

Yellow phosphorus usually causes mucosal injury, emesis, burning throat

TREATMENT

Decontaminate skin using PPE

Supportive treatment

Monitor urine albuman, glucose, sediment

Monitor serum alkaline phosphatase, LDH, ALT, AST, prothrombin time, bilirubin

CONTRAINDICATED

Emesis induction

Potassium permanganate lavage

Zinc Phosphide
HIGHLIGHTS

Less corrosive than yellow phosphorus

Can be very toxic following ingestion

SIGNS & SYMPTOMS

Nausea, vomiting, agitation, chills, cough

TREATMENT

Supportive treatment

Control airway

Consider GI decontamination

Alopecia is a fairly consistent feature of thallium poisoning that may be helpful in diagnosing a case of chronic poisoning. Since it occurs 2 weeks or more after the onset of acute symptoms, it is not diagnostically helpful early in the presentation.[42,43,45,49]

Confirmation of Poisoning

Phosphorus and phosphides sometimes impart a foul rotten fish odor to vomitus, feces, and the breath. Luminescence of vomitus or feces is an occasional feature of phosphorus ingestion. Hyperphosphatemia and hypocalcemia occur in some cases but are not consistent findings.

Thallium can be measured in the serum, whole blood, urine and hair. The most reliable method for diagnosis is considered a 24-hour urine excretion. Values in non-exposed individuals have been reported to be less than 10 µg/liter per 24 hours.[43,46,47,48,49,50] Urinary excretion in the range of 10-20 mg/ liter indicates severe poisoning.[46,47,48,50] Hair analysis is likely to be useful only in establishing protracted prior absorption. Normal serum concentrations are less than 2 micrograms per liter.[47,50] Whole blood thallium levels greater than 100 micrograms/dL indicate poisoning.[51]

Treatment of Yellow Phosphorus Toxicosis

1. Brush or scrape non-adherent phosphorus from the skin. Wash skin burns with copious amounts of water. Make sure all particles of phosphorus have been removed. If burned area is infected, cover with an antimicrobial cream.

2. Take special care to prevent your and other healthcare personnel's exposure when treating a patient poisoned by yellow phosphorus. While this is true of most pesticide poisonings, with a yellow phosphorus poisoning, personal protection, as outlined in **Chapter 3, *General Principles***, must be worn to avoid secondary contamination and burns from phosphorous particles in the patient's bodily fluids.

3. Provide supportive, symptomatic treatment. Poisonings by ingested yellow phosphorus are extremely difficult to manage. Control of airway must be established prior to considering gastrointestinal decontamination as described in **Chapter 3**.

4. Do not induce emesis. Lavage with potassium permanganate solution had historically been recommended in the management of phosphorus ingestion; however, there is not sufficient evidence for its efficacy. It is not recommend it because of the corrosive nature of yellow phosphorus.

5. Treat patients with shock in an intensive care unit.

6. Monitor urine albumin, glucose and sediment to detect early renal injury. Extracorporeal hemodialysis will be required if acute renal failure occurs, but it does not enhance excretion of phosphorus. Monitor ECG to detect myocardial impairment.

7. Monitor serum alkaline phosphatase, LDH, ALT, AST, prothrombin time and bilirubin to evaluate liver damage. Administer Aquamephyton^{R} (vitamin K_1) if prothrombin level declines.

8. Administer parenteral pain medication for pain from burns.

Treatment of Poisoning by Zinc Phosphide

1. Provide supportive, symptomatic treatment in an intensive care setting. There is no specific antidote for the treatment of phosphine exposure, and poisonings by ingestion are extremely difficult to manage.

2. Establish control of airway before considering gastrointestinal decontamination as described in **Chapter 3**, ***General Principles***.

   CAUTION: ***Highly toxic phosphine gas may evolve from emesis, lavage fluid and feces of victims of these poisons. The patient's room should be well ventilated. Persons attending the patient must wear gloves to avoid contact with the phosphorus. Air purifying or supplied-air respiratory equipment should be worn by healthcare providers if available.***

3. See the section on treatment of aluminum phosphide poisoning in **Chapter 17, *Fumigants*** for specific therapy for phosphine gas.

Treatment of Thallium Sulfate Toxicosis

1. If thallium sulfate was swallowed less than an hour prior, consider gastrointestinal decontamination as outlined in **Chapter 3** ***General Principles***. Multiple doses of activated charcoal may be helpful in increasing thallium elimination.[46]

2. Give electrolyte and glucose solutions by intravenous infusion to support urinary excretion of thallium by diuresis. Monitor fluid balance carefully to ensure that fluid overload does not occur. If shock develops, treat the patient in an intensive care unit.

3. Control seizures and myoclonic jerking as outlined in **Chapter 3**.

4. Consider hemodialysis. It has been used on victims of severe poisoning.[46,50]

5. Use potassium ferric ferrocyanide (Prussian blue) orally to enhance fecal excretion of thallium by exchange of potassium for thallium in the gut. It is available in the United States as an insoluble preparation, primarily for the purposes of radioactive thallium and radioactive cesium poisoning.[53] However, Prussian blue therapy has often been reported as a therapy in rodenticide poisonings.[42,46,50,43]

Dosage of Prussian Blue

- ***Adults and adolescents over 13: 3 grams orally, 3 times a day.[53] Unfortunately, there is no established pediatric dosage by weight. The only available guidance for dosage by weight is from two adult cases that reported using a dosage of 250 mg/kg/day.[42,54]***

Several methods for chelating and/or accelerating disposition of thallium have been tested and found either relatively ineffective or hazardous. Chelating agents are not recommended in thallium poisoning. While potassium chloride has been recommended, it has been reported to increase toxicity to the brain[45,48] and has not been shown to increase elimination in some cases.[52]

Thallium Sulfate

HIGHLIGHTS

Well absorbed from gut, across skin

Distributed chiefly to kidney, liver

SIGNS & SYMPTOMS

Wide variety of symptoms

Alopecia in chronic cases

TREATMENT

Consider GI decontamination

IV electrolytes, glucose

Administer Prussian Blue

CONTRAINDICATED

Chelating agents

Potassium chloride

SEVERE MULTIORGAN METABOLIC TOXICANTS

Toxicology

Sodium fluoroacetate and **fluoroacetamide** are readily absorbed by the gut but only to a limited extent across skin. The toxic mechanism is distinct from that of fluoride salts. Three molecules of fluoroacetate or fluoroacetamide are combined in the liver to form a molecule of fluorocitrate, which poisons critical enzymes of the tricarboxylic acid (Krebs) cycle, blocking cellular respiration. The heart, brain and kidneys are the organs most prominently affected. The effect on the heart is to cause arrhythmias, progressing to ventricular fibrillation, which is a common cause of death. Metabolic acidosis, shock, electrolyte imbalance and respiratory distress are all signs of a poor prognostic. Neurotoxicity is expressed as violent tonic-clonic convulsions, spasms and rigor, sometimes not occurring until hours after ingestion.[55]

Strychnine is a natural toxin (nux vomica) that causes violent convulsions by direct excitatory action on the cells of the central nervous system, chiefly the spinal cord. Death is caused by convulsive-induced muscle spasms of the diaphragm and thoracic intercostals, resulting in impaired respiration.[56,57] The severe seizures can cause rhabdomyolysis, and the released myoglobin can result in renal failure. Other symptoms may include muscle stiffness, pain and hyperreflexia. Patients are generally conscious and oriented between seizures, which can be helpful in making the diagnosis in an unknown seizure event.[56,57] Since strychnine is rapidly absorbed and distributed, the onset of symptoms is usually within 15-20 minutes of ingestion. Strychnine is detoxified in the liver. Residence half-life is about 10 hours in humans. The lethal dose in adults is reported to be between 50 and 100 mg, although as little as 15 mg can kill a child.[58]

Crimidine is a synthetic chlorinated pyrimidine compound that inhibits pyridoxine (vitamin B_6). In adequate dosage, it causes violent convulsions similar to those produced by strychnine. Cases of human poisoning are very rare, though one is presented in the Belgian literature.[59]

Tetramethylenedisulfotetramine (TETS) is a tasteless and odorless convulsant rodenticide that is highly toxic, with an estimated human adult lethal dose of about 7-10 mg. It works by antagonizing g-amino butyricacid (GABA). It has been banned worldwide since 1984. Unfortunately, it is still available through illegal means and has been used in mass poisonings in the past. A recent case in the United States reported refractory seizures in a 15-month-old after playing with a white powder for rodent control that the parents had purchased in China and brought with them to New York City. Seizures began within 15 minutes of exposure and became refractory. She required intubation and mechanical ventilation for 3 days. Following recovery from the acute seizures, she was noted to have persistent neurological problems including cortical blindness, absence seizures and severe developmental delays. Eventually, through gas chromatography/mass spectrometry after testing negative for the other well known convulsant rodenticides and bromethalin, the powder was identified as TETS.[60]

Confirmation of Poisoning

Strychnine and crimidine can both be detected in the blood using high performance thin layer chromatography.[61] For strychnine detection in small samples (as little as 0.1 mL), another method using liquid chromatography with photodiode-array detection has been described.[57,61] Strychnine levels that exceed 1 mg/L may be lethal, although one patient survived a blood concentration of 4.73 mg/L.[57,62,63,64] Because of the infrequency of crimidine poisoning, human blood levels are not well known. These tests are likely to be only available at specialized laboratories.

Treatment of Sodium Fluoroacetate and Fluoroacetamide Toxicosis

Poisonings with these compounds have occurred almost entirely as a result of accidental and suicidal ingestions.

1. If the patient is seen within an hour of exposure and is not convulsing, consider gastrointestinal decontamination as outlined in **Chapter 3,** ***General Principles***. If the victim is already convulsing, control the seizures before undertaking gastric lavage and catharsis.

2. Control seizures as outlined in **Chapter 3**. Seizure activity from these compounds may be so severe that doses necessary for seizure control may paralyze respiration. For this reason, as well as severe cardiac toxicity, these patients should be managed in a critical care environment, with pulmonary ventilation supported mechanically. This has the added advantage of protecting the airway from aspiration of regurgitated gastric contents.

3. Treat patients in an intensive care unit, with special attention to fluids, electrolytes and cardiovascular monitoring.

4. Give calcium gluconate (10% solution) slowly, intravenously to relieve hypocalcemia. Take care to avoid extravasation.

Dosage of Calcium Gluconate
supplied as 100 mg/mL (10% solution)

- ***Adults and children over 12 years: 10 mL of 10% solution, given slowly, intravenously. Repeat as necessary.***
- ***Children under 12 years: 200-500 mg/kg/24 hr divided Q6 hour. For cardiac arrest, 100/kg/dose. Repeat dosage as needed.***

Antidotal efficacy of glycerol monacetate and ethanol, observed in animals, has not been substantiated in humans. These therapies are not recommended in humans.

Treatment of Strychnine, Crimidine or TETS Toxicosis

Strychnine and crimidine cause violent convulsions shortly following ingestion of toxic doses. Both poisons are probably well adsorbed by charcoal.

1. Control seizures as outlined in **Chapter 3**, ***General Principles***. Because of the severity of toxicity from this poison, patients should be treated in an intensive care unit setting if available. If seen within an hour of ingestion and the patient is conscious and not convulsing, consider gastrointestinal decontamination with charcoal. If seizures have already begun, they should be controlled prior to attempting decontamination.

2. Administer intravenous fluids to support excretion of absorbed toxicants. Inclusion of sodium bicarbonate in the infusion fluid counteracts metabolic acidosis generated by convulsions caused by strychnine.[64,65,66,67,68]

3. Avoid hemodialysis and hemoperfusion. Their effectiveness has not been tested.

Severe Multiorgan Metabolic Toxicant
HIGHLIGHTS

Sodium fluoroacetate/ fluoroacetamide readily absorbed by gut

Strychnine acts on CNS

Crimidine inhibits Vitamin B_6

TETS antagonizes GABA

TETS banned worldwide

SIGNS & SYMPTOMS

Sodium Fluoroacetate/ Fluoroacetamide

Blocks cellular respiration

Affects heart, brain, kidneys

Heart arrhythmia

Strychnine/Crimidine

Violent convulsions

TETS

Seizures

TREATMENT

Sodium Fluoroacetate/ Fluoroacetamide

Control seizures

Decontaminate GI tract as appropriate

Monitor fluids, electrolytes, cardiovascular

IV calcium gluconate

Strychnine/Crimidine

Control seizures

Decontaminate GI tract as appropriate

IV fluids with sodium bicarbonate

Consider pyridoxine

TETS

Supportive treatment

4. Consider administering pyridoxine. Because of the mechanism of crimidine toxicity, pyridoxine (vitamin B_6) has been suggested for seizures due to this convulsant, though there are no humans reports of its use.[69]

5. Provide supportive treatment of TETS poisoning. The patient will likely require intensive care in order to survive.

MISCELLANEOUS RODENTICIDES

Red squill and cholecalciferol are no longer registered as rodenticides. Bromethalin is widely used and is available in the form of bait stations and loose pellets.

Toxicology

Red squill is an ancient rodenticide, consisting of the inner portions of a small cabbage plant grown in eastern Mediterranean countries. The toxic properties are probably due to cardioactive glycosides. For several reasons, mammals other than rodents are unlikely to be poisoned: (1) red squill is an intense nauseant, so animals that vomit (rodents do not) are unlikely to retain the poison; (2) the glycoside is not efficiently absorbed from the gut; and (3) absorbed glycoside is rapidly excreted. Injection of the glycosides leads to effects typical of digitalis: alterations in cardiac impulse conduction and arrhythmias.

Cholecalciferol is the activated form of vitamin D (vitamin D_3). Although it is registered for use as a rodenticide, most toxic exposures from vitamin D result from over supplementation or ingestion of multivitamins. Cholecalciferol's toxic effect is probably a combination of actions on the liver, kidneys and possibly the myocardium, the last two toxicities being the result of hypercalcemia. Symptoms and signs of vitamin D-induced hypercalcemia in humans are fatigue, weakness, headache and nausea.[70] Polyuria, polydipsia, nephrocalcinosis, hypertension and proteinuria may result from acute renal tubular injury by hypercalcemia.[71,72] The rodenticide form of cholecalciferol has been implicated in numerous poisonings of domestic animals, however, there are no reports in the published medical literature of toxicity.

Bromethalin is a neurotoxin that works by uncoupling oxidative phosphorylation, thus depleting adenosine triphosphate (ATP). The resultant loss of ATP results in disruption of the sodium/potassium channels causing cerebral edema and eventually increased intracranial pressure.[73] Human poisonings are rare, although there is one reported fatality in the medical literature. Symptoms mirror what may be found in animal poisonings (dog and cat), which include mental status changes, stupor, coma, and cerebral edema.[74,75,76,77] Although not reported in these case examples, seizures may also occur. Treatment for bromethalin poisoning is supportive as outlined in the **Chapter 3, *General Principles***. There are no known antidotes.

Confirmation of Poisoning

Cholecalciferol intoxication is indicated by an elevated concentration of calcium (chiefly the unbound fraction) in the serum. There are no generally available tests for the other rodenticides or their biotransformation products.

Treatment of Red Squill Toxicosis

Red squill is unlikely to cause poisoning unless ingested at substantial dosage. The problem is usually self-correcting because of its intense emetic effect. If, for some

reason, the squill is retained, consider gastrointestinal decontamination as outlined in **Chapter 3, *General Principles***. Monitor cardiac status electrocardiographically.

Treatment of Cholecalciferol Toxicosis

Cholecalciferol at high dosage may cause severe poisoning and death. Human poisonings from its use as a rodenticide have not been reported, but vitamin D overdosage has occurred under clinical circumstances. Treatment is directed at limiting gastrointestinal absorption, accelerating excretion and counteracting the hypercalcemic effect.

1. If cholecalciferol has been ingested within an hour prior to treatment consider gastric decontamination as outlined in **Chapter 3, *General Principles***. Repeated administration of charcoal at half or more the initial dosage every 2-4 hours may be beneficial.

2. Administer intravenous fluids (normal saline or 5% glucose) at moderate rates to support excretory mechanisms and excretion. Monitor fluid balance to avoid overload, and measure serum electrolytes periodically. Measure total and ionized calcium levels in the blood 24 hours after cholecalciferol ingestion to determine severity of toxic effect. Monitor urine for protein, red and white cells to assess renal injury. Patients should be managed in an intensive care unit setting with nephrological consultation if possible.

3. Consider using prednisone and similar glucocorticoids to reduce elevated blood calcium levels. Although prednisone and glucocorticoids have not been tested in cholecalciferol overdosage, it is possible that they would be beneficial.

Dosage of Prednisone and Glucocorticoids

- ***Approximately 1 mg per kilogram per day, to a maximum of 20 mg per day***

4. Consider administering calcitonin (salmon calcitonin, Calcimar). It is a logical antidote for cholecalciferol actions, but has only very limited use in human poisoning.[78] Calcium gluconate for intravenous injection should be immediately available if indications of hypocalcemia (carpopedal spasm, cardiac arrhythmias) appear.

Dosage of Calcitonin

- ***In other conditions, the usual dosage is 4 International Units per kg body weight every 12 hours, by intramuscular or subcutaneous injection, continued for 2-5 days. The dose may be doubled if calcium-lowering effect is not sufficient. Consult package insert for additional directions and warnings.***

5. Consider administering cholestryamine. It appears to be effective in the treatment of Vitamin D toxicity in animals[79] but has seen very limited use in humans.[80,81]

Miscellaneous Rodenticides

HIGHLIGHTS

Red squill toxicity probably due to cardioactive glycosideds

Cholecalciferol is activated form of vitamin D_3

Bromethalin depletes ATP, disrupting sodium/potassium channels

SIGNS & SYMPTOMS

Cholecalciferol
Fatigue, weakness, headache, nausea

Bromethalin
Mental changes, stupor, coma, cerebral edema

TREATMENT

Red Squill
Consider GI decontamination if no emesis

ECG monitoring

Cholecalciferol
Consider GI decontamination as appropriate

IV fluids

Consider prednisone

Consider calcitonin

Consider cholestryamine

Bromethalin
Supportive; no known antidote

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