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A guidance document for homeowners who suspect that a pet has eaten some Sweeney's Poison Moleworms.

Sweeney's Poison Moleworms contain the active ingredient Bromethalin at a concentration of 0.025% by weight. Each worm weighs 6.5 grams.

Question 1

How much Bromethalin is in 1 Sweeney's Poison Moleworm?

Answer

The concentration of Bromethalin in our product is 0.025% (6.5 grams per worm) X (.00025) =0.001625 grams or **1.625mg of Bromethalin per worm**

Question 2

How much Bromethalin will it take to make a 5 pound (2Kg) dog ill?

Answer

In experimental studies, doses below 1.5 mg/kg were not associated with clinical signs. The minimum dose that may cause sickness in dogs is 1.5 mg per Kg or put simply over 3mg for a 5 pound dog. So a 5 pound dog would have to eat two Sweeney's Poison Moleworms to get sick.

Question 3

What should a homeowner do if it suspects that a dog has eaten a worm or two?

Answer

Take your pet to veterinarian along with this document for guidance.

PEER-REVIEWED

Bromethalin: The other rodenticide

Eric Dunayer, MS, VMD

While most veterinarians are familiar with anticoagulant and cholecalciferol rodent baits, many are unfamiliar with bromethalin-containing baits. Because its name resembles that of the anticoagulant baits bromadiolone and brodifacoum, bromethalin is often mistaken for another anticoagulant bait. Actually, it differs from anticoagulant rodenticides in both its mode of action and treatment.

Available since 1985 to kill rodents resistant to anticoagulants,^{1,2} bromethalin (N-methyl-2,4-dinitro-N-[2,4,6-tribromophenyl]-6-[trifluoromethyl] benzenamine) is marketed in a 0.01% formulation (2.84 mg of

for bait formulations is about 0.54 mg/kg, the minimum lethal dose is 0.45 mg/kg, and 0.75 mg/kg is uniformly fatal.⁴ Based on cases reported to the ASPCA APCC, however, cats have shown signs after ingesting doses of bromethalin as low as 0.24 mg/kg (ASPCA APCC Database: Unpublished data, 1998-2000).

Metabolism

Toxicokinetic information on bromethalin has largely been derived from experimental studies in rats. After ingestion, bromethalin is rapidly absorbed; plasma concentrations peak in about four hours.³ After absorption, bromethalin undergoes N-demethylation in the liver, forming desmethylbromethalin, which is thought to be bromethalin's major toxic metabolite.³ (Guinea pigs do not perform effective N-demethylation of bromethalin, and their oral LD₅₀ for bromethalin is more than 1 g/kg, while their oral LD₅₀ for desmethylbromethalin is 7.5 mg/kg, which is similar to the LD₅₀ for bromethalin in other species.) The body slowly eliminates bromethalin; bromethalin's plasma half-life in rats is about six days.^{2,5} Excretion occurs mainly in bile, and enterohepatic recirculation is suspected.³

Bromethalin's mechanism of action is the uncoupling of oxidative phosphorylation, which leads to decreased cellular ATP production and failure of the Na⁺,K⁺-ATPase pumps. As a result, cells lose their ability to maintain osmotic control, sodium is retained intracellularly, and the cells swell with water. In vitro studies show that bromethalin and its metabolite are potent uncouplers of oxidative phosphorylation, with desmethylbromethalin being about two to three times more potent than bromethalin.⁵ Signs of bromethalin toxicosis are most pronounced in the central nervous system (CNS) because cerebral and spinal cord edema elevates cerebrospinal fluid (CSF) pressures and leads to neurologic dysfunction.¹

Clinical signs

Bromethalin toxicosis in dogs manifests as either a paralytic or convulsant syndrome. Dogs ingesting less

Signs of bromethalin toxicosis are most pronounced in the central nervous system.

bromethalin per ounce of bait) and comes in bait pellets, bars, and place packs.² Bromethalin baits cannot be distinguished from other rodent baits by color or appearance alone.³

Toxicity

In dogs, the oral LD₅₀ for bromethalin in baits is about 2.38 to 5.6 mg/kg, and the reported minimum lethal dose is 2.5 mg/kg.¹ In experimental studies, doses below 1.5 mg/kg were not associated with clinical signs.¹ However, according to ASPCA Animal Poison Control Center (APCC) case records, deaths have been reported in dogs ingesting bromethalin at doses as low as 0.95 to 1.05 mg/kg (ASPCA APCC Database: Unpublished data, 1998-2000).

Cats are much more sensitive to bromethalin than dogs. Based on experimental studies, in cats the LD₅₀

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than the LD₅₀ but more than the minimum toxic dose develop signs of a paralytic syndrome one to four days after ingestion, beginning with hindlimb weakness and ataxia. As the syndrome progresses, depression, tremors, hyperreflexive hindlimb paralysis, loss of deep pain, and decreased conscious proprioception may develop. Other signs include vomiting, anorexia, nystagmus, anisocoria, opisthotonos, Schiff-Sherrington syndrome, seizures, and coma. The signs may progress for one or two weeks. Death may be due to respiratory failure. Signs may take several weeks to resolve in animals recovering from bromethalin poisoning.¹

Dogs ingesting doses exceeding the LD₅₀ exhibit a convulsant syndrome. The onset of signs generally occurs four to 36 hours after ingestion and includes hyperexcitability, hyperthermia, tremors, and focal and generalized motor seizures that may be sound- or light-induced.¹

Cats appear to develop the paralytic syndrome regardless of the dose ingested. In addition to the signs seen in dogs, cats may show abdominal distention due to ileus and an inability to urinate as well as increased urethral tone indicative of upper motor neuron bladder paralysis. In the final phases of

the toxicosis, cats may show a decerebrate posture.⁴

Diagnosis

Without a history of bait ingestion, it may be difficult to diagnose bromethalin toxicosis because there are no pathognomonic clinical laboratory abnormalities in dogs or cats.^{1,4} A postmortem diagnosis can be made by finding characteristic CNS lesions and bromethalin in body tissues. Microscopically, CNS changes include mild to moderate cerebral edema and white-matter spongiosis from widespread myelin vacuolization. There is no evidence of inflammation.⁵⁻⁷ Changes occur in the optic nerves but not in the peripheral nervous system.^{3,6,7} The highest concentrations of bromethalin are found in fat, the liver, the kidneys, and the brain.⁶

Differential diagnoses for the convulsant presentation of a bromethalin toxicosis may include infectious CNS diseases such as rabies as well as metaldehyde, strychnine, zinc phosphide, and ethylene glycol intoxication. Differential diagnoses for the paralytic presentation are spinal cord or CNS trauma, neoplasia, intervertebral disk disease, rabies, ionophore (e.g. monensin) toxicosis, and coonhound paralysis (idiopathic polyradiculoneuritis).

Treatment and prognosis

The best treatment for bromethalin ingestion is early, aggressive decontamination. Emesis or gastric lavage to reduce the ingested dose may be the most useful treatment. But emesis should not be induced in symptomatic animals. Multiple doses of activated charcoal, even hours after ingestion, have been suggested be-

cause bromethalin and its metabolite appear to undergo enterohepatic recirculation.⁸ While this regimen may delay the onset and reduce the magnitude of signs in dogs, multiple doses of activated charcoal may not be as beneficial in cats.⁴ The ASPCA APCC's recommendation to induce emesis or administer activated charcoal is based on the potential dose ingested and time since ingestion (*Table 1*). If you are not sure how much was ingested, treat at the most aggressive level.

Since the signs of bromethalin intoxication result from cerebral edema and elevated CSF pressure, treatment with corticosteroids and osmotic agents intended to reduce cerebral edema would seem to be indicated. Initial studies in rats showed that corticosteroids and osmotic agents help treat bromethalin-induced cerebral edema.⁵ Unfortunately, the clinical

TABLE 1 The ASPCA APCC's Decontamination Recommendations for Bromethalin Ingestion

Time Since Exposure	Dose Ingested*	Action
Dogs		
< 4 hours	0.1–0.49 mg/kg	Emesis or one dose of activated charcoal
> 4 hours	0.1–0.49 mg/kg	One dose of activated charcoal
< 4 hours	0.5–0.75 mg/kg	Emesis and three doses of activated charcoal over 24 hours
> 4 hours	0.5–0.75 mg/kg	Three doses of activated charcoal over 24 hours
< 4 hours	> 0.75 mg/kg	Emesis and three doses of activated charcoal a day for 48 hours
> 4 hours	> 0.75 mg/kg	Three doses of activated charcoal a day for 48 hours
Cats		
< 4 hours	0.05–0.1 mg/kg	Emesis or one dose of activated charcoal
> 4 hours	0.05–0.1 mg/kg	One dose of activated charcoal
< 4 hours	0.1–0.3 mg/kg	Emesis and three doses of activated charcoal over 24 hours
> 4 hours	0.1–0.3 mg/kg	Three doses of activated charcoal over 24 hours
< 4 hours	> 0.3 mg/kg	Emesis and three doses of activated charcoal a day for 48 hours
> 4 hours	> 0.3 mg/kg	Three doses of activated charcoal a day for 48 hours

*Note: 1 oz 0.01% bromethalin bait contains 2.84 mg of bromethalin.

Continued

use of these agents in dogs and cats has proved ineffective. In dogs, these agents may initially lower the CSF pressure, but stopping treatment returns CSF pressure to pretreatment levels quickly. Further, the use of these agents has little effect on the progression of signs.⁸ In cats, no effect on the onset or progression of signs was seen with these treatments.⁴ The failure of treatments intended to reduce cerebral edema may be due to the accumulation of fluid within myelin sheaths since it may be more difficult to mobilize the edema from these locations.³

One study indicated that *Ginkgo biloba* might effectively treat bromethalin-induced cerebral edema. Rats given 100 mg/kg of a commercial *G. biloba* preparation at the same time that they were given bromethalin exhibited significantly less cerebral edema than the untreated controls.⁹ However, since these rats were euthanized about 48 hours after dosing, the treatment's long-term efficacy and its potential usefulness after the onset of signs are unknown.

Once signs of a bromethalin toxicosis appear, offer symptomatic and supportive treatment, including seizure control, nutritional support, and basic nursing care for recumbent animals. Mild signs such as hindlimb weakness may resolve with time. Animals with paralysis or seizures generally have a poor to grave prognosis for survival.^{3,4,8}

Conclusion

Bromethalin ingestion can cause potentially life-threatening signs in dogs and cats. Prompt, aggressive decontamination remains the most effective treatment. Management of any rodenticide toxicosis depends on the type and amount of bait ingested. Because a rodenticide's active ingredient cannot be determined from the bait's physical appearance, veterinary staff should identify an ingested rodenticide from the package's label to ensure proper treatment. Instruct clients to bring the product's package to the veterinary clinic along with their pets.

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BROMETHALIN — It's Not What You Think

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Bromethalin is a rodenticide that is commonly mistaken for a second-generation anticoagulant, such as brodifacoum or bromadiolone, although it is actually a neurotoxin. Bromethalin is sometimes considered safer for use around dogs than second-generation anticoagulant rodenticides because a larger amount of bait must be ingested before signs develop. However, if signs do develop, they are extremely difficult to treat effectively.

MECHANISM OF ACTION

Bromethalin is thought to uncouple oxidative phosphorylation in mitochondria, resulting in decreased ATP generation. With decreased ATP, there is too little energy available to maintain sodium (Na⁺) and potassium (K⁺) ion channel pumps. This leads to fluid accumulation within myelin sheaths and vacuolation of the nervous system, resulting in nerve conduction impairment, paresis, paralysis, and death.¹

TOXICITY

The oral LD₅₀ of bromethalin is 2.38 to 5.6 mg/kg in bait¹ for dogs and 0.4 to 0.71 mg/kg in bait¹ for cats. Severe intoxication does occur at oral dosages below the LD₅₀.

ASYMPTOMATIC PATIENTS

Calculating a Dose

To determine whether a dog or cat has ingested a toxic amount, it is use-

ful to calculate the dose of the anticoagulant involved:

Step 1 — Assume the worst-case scenario. What is the most that the animal could have consumed?

Step 2 — Multiply the percentage of active ingredient by 10 to get the milligrams of active ingredient per gram of rodenticide.

Step 3 — Multiply milligrams per grams by the amount of rodenticide ingested in grams.

Step 4 — Divide by kilograms of body weight to determine the dose ingested.

For example, a 20-lb dog ingests part of a box of brodifacoum rat bait weighing 0.75 oz. The concentration of the bait is 0.01%. The owner cannot say how much of the bait was left because she threw the box away, but she does not think the dog could have ingested more than 1 to 2 tsp.

Clients should be advised never to leave bromethalin out in the open where pets might have access to it.



Step 1 — The worst-case scenario is 0.75 oz (1 oz = 28.4 g; therefore, 0.75 oz = 21.3 g of bait).

Step 2 — $0.01\% \times 10 = 0.1$ mg active ingredient per gram of bait

Step 3 — 0.1 mg/g \times 21.3 g of bait = 2.13 mg active ingredient in 0.75 oz of bait

Step 4 — 2.13 mg/9.1 kg of body weight = 0.23 mg/kg

Decontamination and Laboratory Testing

For bromethalin, decontamination should be performed when a suspected dose of 0.1 mg/kg or higher is ingested by dogs and 0.05 mg/kg or higher is ingested by cats.² Dogs ingesting doses less than 0.1 mg/kg and cats ingesting doses less than 0.05 mg/kg are not expected to develop signs of toxicity.² If there are no contraindications (e.g., seizure disorder, lethargy, megacolon) and the exposure occurred within 2 to 4 hours, emesis should be induced using apomorphine or 3% hydrogen peroxide.

If emesis is not productive, one dose of activated charcoal should be given to bind to the poison and help prevent it from being absorbed into the system as it moves through the intestinal tract. If the exposure occurred hours

or days ago, it may still be beneficial to give activated charcoal. If the amount or time of ingestion is unknown, repeated doses of activated charcoal should be given. The recommended dose of activated charcoal is 1 to 2 g/kg. For dogs that have ingested 0.5 to 0.75 mg/kg of bromethalin or cats that have ingested 0.1 to 0.3 mg/kg, continuing decontamination with a total of three doses of activated charcoal given every 8 hours is recommended.² For dogs and cats that have ingested larger amounts, further decontamination with a total of six doses of activated charcoal given every 8 hours is recommended.² Unless the animal develops diarrhea, it is recommended that a cathartic be added to every third dose of activated charcoal to enhance excretion.

SYMPTOMATIC PATIENTS

Clinical Signs of Toxicosis

Healthy animals can become symptomatic as early as several hours after ingesting a large amount of bromethalin or as late as 7 days after ingesting a small amount. Common signs include the following:

Dogs – Tremors, ataxia, depression, tachypnea, hyperreflexia, loss of vocalization, recumbency, anorexia, vomiting, death³

Cats – Ataxia, focal motor seizures, vocalization, rigidity, decreased proprioception, abdominal distension, recumbency, depression, death⁴

Other signs – Generalized seizures, head pressing, hyperesthesia, coma, hyperexcitability, nystagmus, hyperthermia, cyanosis, miosis, drooling

Bromethalin toxicosis may imitate other toxicoses (e.g., those of ethylene glycol, chlorpyrifos [in cats], metaldehyde, zinc phosphide, tremorgenic mycotoxins) or disease processes (e.g., cerebral or spinal trauma, tick paralysis, rabies, distemper).

Treatment

Because signs are so difficult to control once they begin, early and aggressive decontamination is the key to success when dealing with bromethalin. Once clinical signs have developed, mannitol, dexamethasone, and furosemide have been used to reduce cerebral edema and cerebrospinal fluid pressure; in experimentally dosed dogs, however, these drugs were of little benefit in slowing the development or reducing the severity of signs.⁵

Ginkgo biloba has reduced mortality in rats but only if given at the time of exposure to bromethalin.⁶ The efficacy of ginkgo in preventing or treating signs of bromethalin toxicosis has not been demonstrated in dogs or cats.

Diazepam and barbiturates are recommended for controlling seizures.⁵ Seizures that are unmanageable with diazepam and barbiturates may respond to gas anesthesia or propofol.

Supportive care should include supplemental feeding if the animal is anorectic and thermoregulation to prevent

hyperthermia. Animals showing mild to moderate signs of bromethalin toxicosis (e.g., depression, ataxia, weakness) can recover, but recovery may be slow, taking days to weeks. Not all animals make a full recovery, especially in instances of severe toxicosis; some may have permanent neurologic effects.

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