New Rodenticide on the Block: Diagnosing Bromethalin Intoxication in Wildlife

Stella McMillin
California Department of Fish and Wildlife, Rancho Cordova, California
Melanie S. Piazza
WildCare, San Rafael, California
Leslie W. Woods and **Robert H. Poppenga**
California Animal Health and Food Safety Laboratory, Davis, California

ABSTRACT: Bromethalin is being used more widely for commensal rodent control because of increased regulation on second-generation anticoagulant rodenticides. Wildlife losses in California are tracked by the California Department of Fish and Wildlife. Bromethalin is a neurotoxicant which is not thought to cause secondary poisoning. From August 2014 to January 2016, 24 cases of bromethalin intoxication were investigated in California. These include 11 raccoons, 11 striped skunks, one gray fox, and one fox squirrel. Most of these occurred in Marin County, where active surveillance of wildlife for rodenticide exposure is occurring. Bromethalin exposure should be evaluated when a wild animal that may have accessed bait is showing neurological signs. Trauma and distemper should be ruled out. Histological changes may be found in the central nervous system but are not always present. The tissue of choice for toxicological analysis is adipose. It is likely that bromethalin intoxication is under-reported in the rest of the state and may be mistaken for distemper infection or trauma. Primary exposure of wildlife to bromethalin could be prevented by placing baits in tamper- resistant bait stations.

KEY WORDS: bromethalin, neurotoxicant, nontarget poisoning, raccoon, rodenticides, skunk

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INTRODUCTION

The California Department of Fish and Wildlife (CDFW) Wildlife Investigations Laboratory (WIL) has statewide responsibility for monitoring health issues in California's wildlife. In addition to ongoing surveillance of population health, wildlife mortality events are investigated to determine the role of disease and contaminant exposure, in addition to other factors. Pesticide-related losses are of particular concern because of CDFW's shared responsibility with the California Department of Pesticide Regulation for protecting fish and wildlife from adverse effects of pesticides. In the case of pesticide uses that cause documented harm to wildlife, remedial measures may be recommended.

In July 2014, second-generation anticoagulant rodenticides became restricted materials in California. At that time, they were largely replaced by first-generation anticoagulant rodenticide and by bromethalin products in retail outlets. The first documented wildlife loss in California from bromethalin intoxication occurred in 2012 (Bautista et al. 2013). Since then, WIL has been tracking bromethalin intoxication cases in California to determine the frequency of exposure, the species affected, circumstances of exposure, and components of successful diagnosis. WildCare of Marin County has also been monitoring rodenticide exposure in wildlife and their observations are also reported.

The first bromethalin products were registered in California in 1990. There are 56 bromethalin products currently registered in California in a variety of forms, including loose bait blocks, place packs, mole worms, pellets, and blocks enclosed in tamper-resistant bait stations (CDPR Product/Label Database, http://apps.cdpr.ca.gov/ereglib/main.cfm). Bromethalin baits are sold to the public for commensal rodent and mole control.

Bromethalin is a neurotoxicant that, when ingested, is metabolized in the liver to the toxic metabolite desmethylbromethalin. Desmethylbromethalin's toxicity is caused by uncoupling of oxidative phosphorylation, which results in decreased cellular production of adenosine triphosphate production, a failure of sodium-potassium pumps, and the disruption of osmotic control, causing fluid accumulation in the myelin sheaths, resulting in cerebral and spinal cord edema and increased cerebrospinal fluid pressures (van Lier and Cherry 1988). Neurological dysfunction signs differ depending on ingested dose and exposed species. Sublethal doses may result in a paralytic syndrome which includes seizures and rear leg paralysis. This syndrome may have a delayed onset and may result in death due to respiratory failure, or eventual recovery. For lethal doses, the onset is more rapid and signs include muscle tremors and hyperexcitability before death from respiratory failure (Dorman 2004). There is no known antidote for bromethalin intoxication.

Cats are more sensitive to bromethalin (with lethal doses as low as 0.4 mg/kg) than dogs (2.38 - 5.6 mg/kg), other tested mammals (rats, mice), and birds (Dorman 2004). Dogs fed rats poisoned with bromethalin for two weeks showed no signs of intoxication, indicating that bromethalin did not cause secondary toxicosis (Jackson et al. 1982). No toxicity values are available for raccoons and skunks. If they have similar sensitivity to dogs, several 0.5-oz bait blocks would be required to administer a toxic dose; if they are more similar in sensitivity to cats, a little more than one bait block could result in intoxication.

BROMETHALIN CASES IN CALIFORNIA

From August 2014 to January 2016, six cases of bromethalin intoxication in wildlife were investigated by CDFW. These cases were submitted either by wildlife rehabilitators or USDA Wildlife Services personnel throughout California. During this same time period, 18 cases were reported by WildCare Rehabilitation Center in Marin County as a part of WildCare's Rodenticide Diagnostic and Advocacy Program, and surveillance study. Of these 24 cases, 11 were raccoons (*Procyon lotor*), 11 were striped skunks (*Mephitis mephitis*), one was a gray fox (*Urocyon cinereoargenteus*), and one was a fox squirrel (*Sciurus niger*). Affected animals were generally found near residences. However, animals dying in more remote locations would be unlikely to be observed and submitted for analysis.

Carcasses submitted to WIL and to WildCare were necropsied either at WIL or at the California Animal Health and Food Safety Laboratory (CAHFS) at Davis. All associated diagnostic tests, including toxicology, histology, immunohistochemistry, and virology were performed at CAHFS.

DIAGNOSIS OF BROMETHALIN INTOXICATION

The decision to test a wild animal for bromethalin exposure is typically based on the presence of neurological signs before death in a species likely to ingest bait. Individuals of these species found dead without signs of trauma may also be tested. Since the limited data available indicate that secondary toxicity from bromethalin is unlikely, the animals most likely exposed are generalist omnivores in residential settings such as skunks, raccoons, and foxes. However, as the secondary exposure data is very limited, predatory species with unexplained neurological signs should also be tested.

The most common behavioral signs that were observed in intoxicated animals included severe lack of coordination, falling to the side and inability to right themselves, peddling in the air, staggering, and dragging rear limbs as if there was pelvic or spinal trauma. Other signs included repetitive yawning, tremors, shivering, and hypersalivating. The animal may also have bulging eyes and labored breathing. As it is unknown when the exposure occurred, it is not possible to determine the timing of the onset of symptoms; however, previous reports of wildlife and pet exposure indicate that symptoms start within ten hours of exposure and generally cause death within two to four days (Doorman 2004). Nonlethal cases may take several weeks to resolve (Dorman 2004). While most individuals died or were euthanized within two days of submission, one symptomatic raccoon submitted to WildCare showed signs for 17 days before being euthanized. Prolonged signs have been described as part of a paralytic syndrome caused by a sublethal dose of bromethalin (Dorman 2004). No symptomatic individuals recovered.

Unfortunately, bromethalin intoxication does not typically cause gross changes that are apparent at necropsy. Occasionally, the bait may be present in the digestive tract; however, its color and texture is common to other baits (typically blue or green). In the majority of carcasses examined, no digestive contents were present. While unlikely to yield definitive results, necropsy is helpful in ruling out other diagnoses, such as trauma and canine distemper virus (CDV). In particular, when antemortem signs such as staggering or dragging rear limbs are reported, it is important to check for cranial or spinal damage during necropsy. The absence of damage may indicate a toxic cause. Rabies and CDV infection in raccoons, skunks, and foxes may cause neurological signs such as convulsions, tremors, chewing fits, and lack of fear of humans (Williams 2001).

Histological analysis is often more helpful than gross necropsy in diagnosing bromethalin intoxication. Spongy degeneration and edema of the white matter of the brain, spinal cord, and optic nerve have been reported in individuals of several species that had died from bromethalin intoxication (Dorman 2004, Bautista et al. 2013). However, these changes may not be present in cases of intoxication or, if present, are nonspecific and can be attributed to autolysis of the carcass prior to necropsy (Bautista et al. 2013). Of the 22 cases reviewed for this paper for which histological analysis was performed, histological changes in the white matter of the central nervous system were reported in five.

Exposure to bromethalin is confirmed by detection of the metabolite desmethylbromethalin in appropriate tissue, typically either adipose or brain tissue, but also occasionally digestive contents. Extracts from those tissues are analyzed using HPLC-MS/MS. The limit of detection is typically 0.050 µg/g (50 ppb). In one case, desmethylbromethalin was detected in adipose tissue but not brain tissue, a finding also confirmed by Bautista et al. (2013). Brain tissue should be used for analysis only when sufficient adipose tissue is not available.

Most of these submissions were also submitted for immunohistochemistry to rule on CDV and rabies. No submissions tested positive for either virus.

DISCUSSION

The large number of cases reported in Marin County where active surveillance is occurring indicates that many cases throughout the rest of the state are likely going unreported. Neurological behaviors indicating bromethalin intoxication may be mistaken for signs of distemper. In one case in Santa Cruz County, two raccoons from the same area were submitted together with signs attributed to distemper. One of these raccoons did have distemper, but the death of the other raccoon was attributed to bromethalin intoxication. In addition, apparent paralysis of rear legs associated with bromethalin intoxication may appear to indicate trauma, such as vehicular impact. For several individuals, trauma was given as the reason for intake but upon examination had no signs of trauma and tested positive for bromethalin. To address the issue of under-reporting, CDFW is actively performing outreach to wildlife rehabilitation centers and wildlife professionals to encourage submittal for toxicological analysis of any wildlife showing neurological signs.

The presumptive route of exposure was direct ingestion of rodenticide bait. While these baits may have been intended as rodent control, both raccoons and skunks are sometimes considered pest animals, and the non-target exposure may have been intentional. In addition to the

skunks and raccoons, a fox squirrel and a gray fox were also confirmed to have died from bromethalin intoxication. While it is very likely that the squirrel ingested the bait directly, the route of exposure of the gray fox is unknown. Baits, formulated to be palatable to rodents, may also be attractive to foxes. Although there have been no confirmed cases of secondary poisoning from bromethalin, there is very little data to exclude this possibility (Jackson et al. 1982). Continued monitoring of carnivores will be helpful in determining the occurrence of secondary exposure. Primary exposure could be prevented by ensuring that any bromethalin baits placed outside are secured in a tamper-resistant bait station.

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Investigation of wildlife losses would not be possible without the efforts of wildlife rehabilitators throughout the state.

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