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Multiple episodes of 1080 (sodium monofluoroacetate) intoxication in a California calf-raising operation

John M. Adaska,[1] Guillermo Rimoldi, Patricia C. Blanchard, John Champagne, Robert H. Poppenga, Michelle Mostrom

Abstract. Over a 1-y period, a California calf-raising operation experienced 4 separate episodes of sudden death in 4–6-mo-old steers. Each episode occurred in 1–3 contiguous pens on 1 of 3 properties owned by the operation, but eventually all 3 properties were involved. In each episode, animals appeared normal at the evening feeding but at the subsequent morning feeding were found dead or dying. Remaining live calves had a stiff gait and were often dribbling urine, but did not show respiratory signs until they were down and agonal. At postmortem examination, calves consistently had moderate-to-large numbers of ecchymotic and suffusive hemorrhages on the epicardial surface and moderate-to-large amounts of fluid in the pericardial sac. Pulmonary edema and/or moderate amounts of watery fluid in the thoracic and abdominal cavities were present in a smaller percentage. On histologic examination, the myocardium had variable myofiber degeneration characterized by hypereosinophilia and fragmentation with mild interstitial infiltrates. Testing of heart and liver samples for monensin found levels lower than in previous cases of monensin toxicity. Rumen content was negative for oleandrin and grayanotoxins. Sodium monofluoroacetate (trade name: 1080) was consistently detected at ⩾10 ppb in kidney and liver, and was concluded to be the cause of the intoxication.

Key words: Bovine; myocardial necrosis; sodium monofluoroacetate

Over a 1-y period, a large California calf-raising operation with 3 separate ranches experienced multiple episodes of sudden death of numerous calves 4–6 mo of age, with a total loss of >275 animals. The first episode occurred on ranch A. Animals were normal the previous evening at 1730. The next morning, at 0530, ~50 dead or dying calves out of 90 total were found in 1 pen. Clinical signs were seen in 10–15% of the animals that were still alive, and included stiff gait and passive dribbling of urine progressing to animals being down and paddling. An adjacent pen also contained 90 animals and 2–5% had clinical signs and eventually died. There were no sick animals or death losses in similar aged animals on ranches B and C. Most of the feed (a total mixed ration [TMR]) from the previous evening's feeding had been consumed, but what remained was removed immediately. The rate of new cases decreased rapidly, with 10 deaths the next day and no new cases after 48 h. Six calves were submitted to the Tulare branch of the California Animal Health and Food Safety Laboratory (CAHFS).

Episode 2 occurred ~5 mo after the initial cases, and >200 animals died in 3 adjacent pens on ranch C. Sixteen calves were submitted to CAHFS for testing. Episode 3 occurred ~7 mo after the initial case, with 12 animals dying in a single pen on ranch B. Six calves were submitted for testing. Episode 4 occurred on ranch B ~11 mo after the initial episode. Initially, 12 calves died in a single pen, with 6 submitted the first day and 1 calf submitted to CAHFS the following day. One week later, an unknown number of calves died in 2 different pens on the same ranch (ranch B) and 6 were submitted to CAHFS.

On postmortem examination, the most consistent finding was moderate-to-large amounts of pale yellow fluid in the pericardial sac (Fig. 1a), often with thin strands of coagulated protein, and moderate-to-severe ecchymotic and suffusive hemorrhages on the epicardial surface of the heart (Fig. 1b). A small percentage of the calves also had increased thin watery fluid in the abdominal and thoracic cavities (Table 1). Almost half of the calves had small areas (usually <10%) of the cranioventral pulmonary parenchyma that were dark red, meaty, consolidated, and sank when placed in formalin. On histologic examination, heart sections had acute myocardial degeneration and necrosis, with mild suppurative interstitial

California Animal Health and Food Safety Laboratory System (Adaska, Blanchard, Poppenga) and Veterinary Medicine Teaching and Research Center (Champagne), School of Veterinary Medicine, University of California, Davis, CA; Clemson Veterinary Diagnostic Center, Columbia, SC (Rimoldi); Veterinary Diagnostic Laboratory, North Dakota State University, Fargo, ND (Mostrom).

[1]Corresponding author: John M. Adaska, California Animal Health and Food Safety Laboratory System, School of Veterinary Medicine, University of California, Davis, 18760 Road 112, Tulare, CA 93274. jmadaska@ucdavis.edu

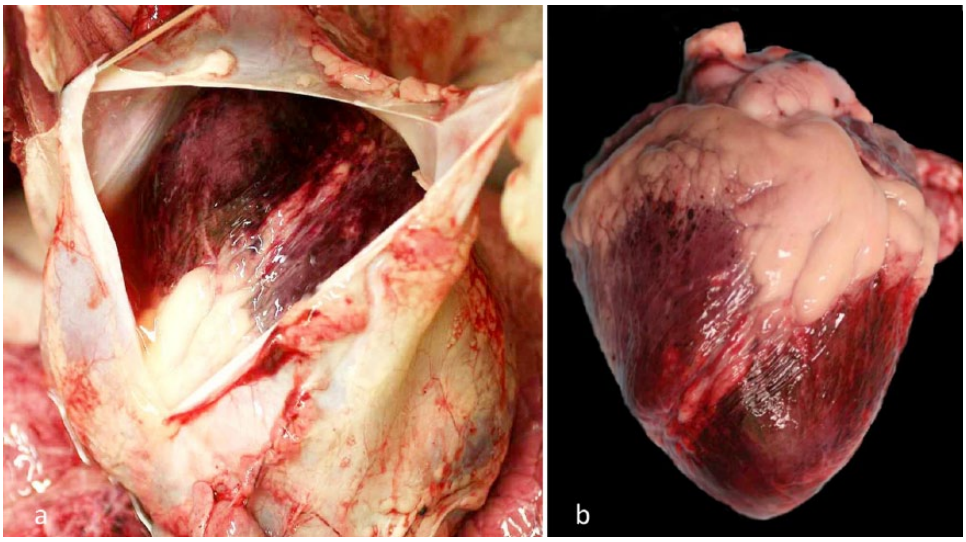

Figure 1. Myocardial hemorrhage following sodium monofluoroacetate (trade name: 1080) toxicosis in a calf. **a.** Epicardial hemorrhage and hydropericardium. **b.** Petechial and ecchymotic epicardial hemorrhages.

Table 1. Postmortem and histologic lesions detected in calves during multiple episodes of sodium monofluoroacetate (trade name: 1080) intoxication in a California calf-raising operation.

	Episode			
	1	2	3	4
Postmortem				
Epicardial hemorrhage	5/6	13/16	6/6	10/13
Hydropericardium	5/6	11/16	6/6	9/13
Hydrothorax	3/6	1/16	1/6	0/13
Ascites	3/6	0/16	0/6	0/13
Histology				
Myocardial degeneration and necrosis	6/6	16/16	6/6	11/13
Myocardial hemorrhage	5/6	9/16	3/6	6/13
Myocarditis	6/6	16/16	6/6	11/13
Pulmonary edema	3/6	3/16	2/6	2/13
Pulmonary congestion	3/6	2/16	2/6	4/14

Data presented as number of cattle with lesions/number submitted.

myocarditis in some areas. Lesions were characterized by mild perivascular interstitial edema and mild mixed inflammatory infiltrates of neutrophils and macrophages (Fig. 2a). Rare-to-small numbers of individual myofibers as well as small clusters of myofibers were fragmented, with contraction bands and/or mild vacuolation (Fig. 2b–2d). In addition, there was marked epicardial hemorrhage. Lung sections often had variable degrees of congestion as well as protein-rich fluid filling alveolar spaces (Table 1).

The consistent location of the lesions in the myocardium and the histologic changes were not typical of an infectious cause, and therefore differential diagnosis of myocardial degeneration and necrosis focused on myocardial toxins. These included ionophore feed additives, alkaloid compounds (including *Taxus* spp.), oleander glycoside, grayanotoxins, and moniliformin. In similar cases identified at CAHFS-Tulare, monensin and oleander glycosides have been the most commonly detected agents. Nontoxic causes of cardiac lesions under consideration included selenium and vitamin E deficiency.

Ancillary laboratory testing (Table 2) initially focused on the possibility of ionophore toxicity given that the ration was known to include monensin. Because most of the feed had been consumed in episode 1 (ranch A), there was some uncertainty if the feed sampled for toxicology was representative of what had been provided to the calves during the first episode. Monensin was undetectable in most serum and tissue samples, and when it was detected, the levels were well below values associated with toxicity.[7] In cases of monensin toxicity, death losses typically build slowly to a peak at 7–10 d post-exposure, followed by a steeper decrease in death losses. Thus, the pattern of death losses in episode 1 was not typical of those seen in cases of monensin toxicity. Liver vitamin E levels were found to be below the normal range in 6 of 8 calves in which it was evaluated during episode 2, which occurred on ranch C (Table 2). Beginning with episode 2, and because of the cardiac degeneration and necrosis, which had been described previously in sheep, the possibility of exposure to sodium monofluoroacetate (trade name: 1080) was pursued.[3]

Frozen kidney, liver, and rumen contents from animals submitted during episodes 2–4 were submitted to the North Dakota State University Veterinary Diagnostic Laboratory (NDSU-VDL; Fargo, ND) for determination of sodium fluoroacetate.[1] Kidney and liver samples were homogenized, extracted with tungstic acid, partitioned into ethyl acetate and evaporated, derivatized with pentafluorobenzylbromide, and

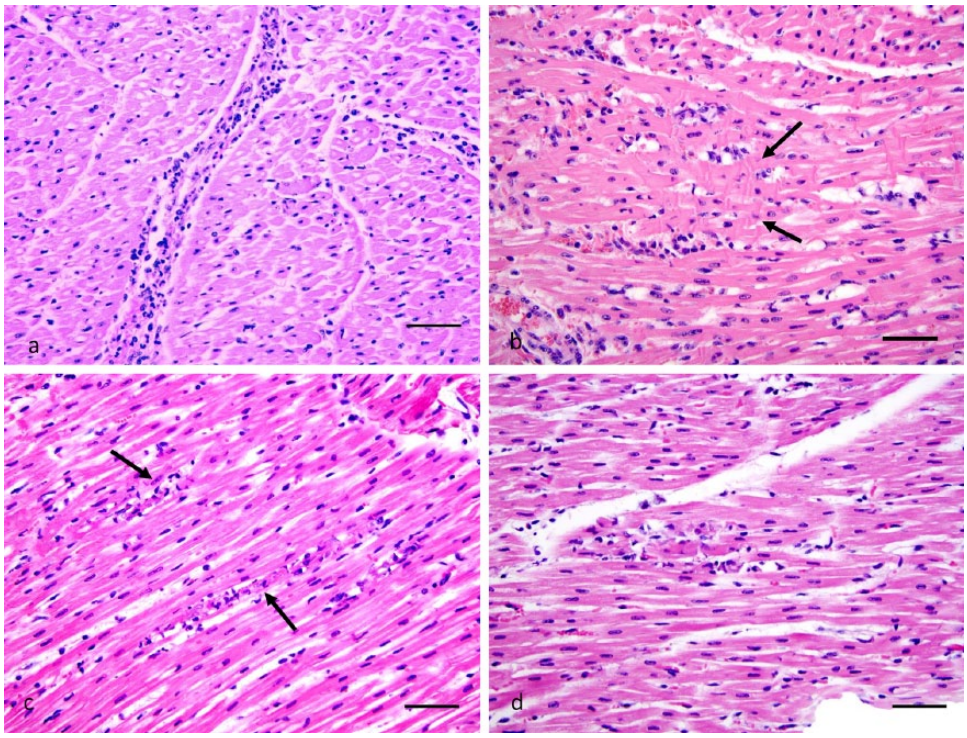

Figure 2. Myocardial necrosis in a calf with sodium monofluoroacetate (trade name: 1080) toxicosis. H&E. Bars = 50 µm. **a.** Interstitial inflammation with mixed leukocytes including small numbers of neutrophils. **b.** Contraction bands (arrows). **c.** Necrosis of individual myofibers (arrows). **d.** Necrosis of a small cluster of myofibers.

analyzed by gas chromatography–mass spectrometry (6890 GC/5973 MS, Agilent, Wilmington, DE) using specific ion monitoring. Recovery of fluoroacetate during the procedure was monitored using a ^{14}C-fluoroacetate spike. The limit of quantitation in tissue is 10 µg/kg (ppb) fluoroacetate.

Ultimately, 41 calves were submitted for autopsy from >275 that were known to have died during the 4 episodes on the 3 ranches. Thirty-nine of the calves had a fairly regular and consistent pattern of postmortem and histologic lesions involving the heart. Two animals did not have heart lesions: one died from *Salmonella* Dublin septicemia, and the other died from severe, widespread chronic pneumonia with obliterative bronchiolitis that was negative for both viral and bacterial pathogens. Neither animal had detectable levels of 1080 in the kidney. Of the animals submitted for postmortem examination and that had histologic heart lesions, 18 were tested for the presence of 1080 in 1 or more tissues, and the compound was detected in 17 animals, with kidney being the most consistently positive tissue. The detected levels in kidney ranged from 10.0 to 84.1 ppb; liver levels ranged from 10.8 to 21.5 ppb. According to NDSU-VDL, any detection of 1080 above the threshold of detection is significant and an indication of exposure to toxic doses. Attempts were made to extract fluoroacetate from feed (3 samples, episode 4, ranch B) and rumen contents (2 samples, episode 2, ranch C); however, the recovery was not reliable, and 1080 was only detected in 1 rumen sample (55.1 ppb). Because the feed bunks are generally emptied by the calves between the evening and morning feedings, the negative feed testing results may be explained by the uncertainty that the feeds available for testing were representative of those containing the toxicant. Negative test results in rumen content might be explained by the rapid absorption and metabolism of 1080.

Sodium monofluoroacetate was originally introduced as a rodenticide in the United States in 1946. The compound has significant toxicity in non-target species, and as a result, its use has been markedly limited and regulated since the 1990s.[6] To date, sodium monofluoroacetate is a restricted-use pesticide in the United States that may be used only by trained, certified applicators and which is only registered for use in livestock protection collars (https://archive.epa.gov/pesticides/reregistration/web/pdf/3073fact.pdf). Livestock protection collars are fitted around the neck of small ruminants and when a predator, such as a coyote, bites the animal on the neck, the rubber bladder in the collar is punctured and delivers a lethal dose of the compound to the predator. In 1998, the voters of California approved a ballot resolution that banned the use of 1080 as well as sodium cyanide (http://www.lao.ca.gov/ballot/1998/4_11_1998.htm). In other countries, 1080 is widely used in baiting programs to protect agriculture and for the control of non-native species.[4] Sodium monofluoroacetate has a high degree of toxicity when administered orally (https://archive.epa.gov/pesticides/reregistration/web/pdf/3073fact.pdf). Toxicity of 1080 is a result of its

Table 2. Toxicology testing performed during multiple episodes of sodium monofluoroacetate (trade name: 1080) intoxication in a California calf-raising operation.

		Episode			
Test	Organ/sample	1	2	3	4
Sodium monofluoroacetate (1080)	Kidney		3/3	5/5	9/12*
	Liver				5/6
	Rumen content		1/2		
	Feed				0/3
Ionophore screen	Rumen content	2/2			
	Serum	5/7†‡			
	Heart	1/3†	0/3		
	Feed	2/3§	7/8§	5/5¦	3/3¦
	Liver		0/6		
Heavy metal screen	Liver	0/6	0/6		
Cholinesterase	Brain	0/3			
Alkaloid screen#	Rumen content	0/2	0/3		
Nitrate screen (dipstick)	Aqueous humor	0/2			
Oleander glycosides	Rumen content	0/2			
	Urine		0/3		
Selenium	Liver	0/6	0/8		0/12
Zn/Al phosphide	Rumen content	0/2			
Grayanotoxins I & II	Rumen content		0/3		
Macrolide antibiotics	Liver		0/3		
Moniliformin	Feed		0/7		
Trace element screen	Serum		7/7¶		
Vitamin E	Liver		6/8**		

Data presented as number of samples positive or abnormal/number tested. Blank cells indicate testing not performed.
* Two animals did not have heart lesions, and 1080 was not detected.
† Monensin detected at levels lower than expected with toxicity.
‡ Two samples were from live animals and were positive.
§ Monensin detected at recommended levels.
¦ Lasalocid detected at recommended levels and monensin at trace levels.
Alkaloid screen included anabasine, atropine, coniine, deltaline, nicotine, scopolamine, spateine, and taxine.
¶ Copper levels 0.51–0.79 ppm; normal range 0.8–1.5 ppm. Normal levels in all livers on heavy metal screen.
** Values: 1.2, 1.3, 2.1, 2.4, 2.7, and 2.7 ppm; normal range >3.3 ppm.

structural similarity to acetate, which has an important role in cellular metabolism. Fluoroacetate is not itself toxic but is metabolized to fluorocitrate that then inhibits the Krebs cycle to cause cellular energy depletion, accumulation of citric and lactic acid, and interference with cellular respiration.[9] Organs comprised of cells with a high metabolic rate, such as the heart, are most susceptible. In addition, citrate accumulates in the blood and binds to serum calcium, potentially causing cardiac arrhythmias.[4] The median lethal dose (LD_{50}) and 95% confidence intervals for compound 1080 were calculated as 0.393 (0.247–0.625) mg/kg in adult cows and 0.221 (0.149–0.327) mg/kg in calves.[8] For a 110-kg calf, the LD_{50} is 25 mg, with a total of 2.5 g potentially causing the death of 50 of 100 calves. Sublethal amounts of 1080, when administered orally, were rapidly eliminated from the plasma of sheep and goats with most occurring in the urine during the first 48 h post-exposure.[2] Terminal signs in experimentally dosed cattle have been reported to last ⩽20 min and have been described as urination, staggering, falling down, "slight spasms," "in-place running," and death.[8]

Monofluoroacetate occurs naturally in a wide variety of plants that are found primarily in Africa, South America, and Australia. Most of these plants are in the genus *Gastrolobium*, but others are members of the following genera: *Acacia, Palicourea, Tanaecium, Amorimia, Dichapetalum*, and *Tapura*.[5] These plants do not occur naturally in California, but some may be intentionally cultivated as ornamental plants.

The clinical signs and postmortem and histologic lesions in this series of episodes are consistent with 1080 (sodium monofluoroacetate) toxicosis. Marked epicardial hemorrhages with moderate-to-large amounts of pericardial fluid (~100–200 mL) were the most consistent postmortem findings in affected calves, with the most consistent histologic finding being acute myocardial necrosis. Similar histologic findings were reported in a case of 1080 toxicity in sheep.[3] Kidney was the most consistently positive tissue for 1080 when samples from dead calves were tested. Previous work suggests that urine might be a useful sample in live calves for up to 12–24 h post-exposure.[2] During episode 2 (ranch C), liver vitamin E levels were found to be low in 6 of 8 calves

tested, and this may have promoted the development of heart lesions because of the resulting diminished antioxidant capacity. Primary vitamin E deficiency was ruled out as the cause of the acute death losses in each episode because the pattern of death losses was not consistent with this entity.

Ultimately, the source for the 1080 involved in the episodes reported herein was not determined. Local law enforcement investigated beginning with episode 2, and included interviews with current employees of all 3 ranches. No suspect was identified, but the consensus opinion was that this was a malicious introduction of the toxicant into the feed provided to a small number of pens. The feeding practices on all 3 premises included mixing large batches of a TMR on ranch B. Individual batches were then fed to 15–20 pens on 1 or more of the ranches depending on factors such as the animal population and number of pens populated with calves at the time. The fact that the death losses usually occurred in only 1 or 2 pens suggests that the 1080 was delivered by top dressing the feed in the bunks. Because access to 1080 is tightly controlled, the only manufacturer in the United States was asked about sales in California but none had occurred since 1998 when the use of 1080 was banned in California. It was noted by the manufacturer that 1080 is very stable, and it is possible that the toxicant had been stored after its purchase prior to 1998. Interestingly, the CAHFS system had a case of 1080 toxicosis of undetermined source in pastured sheep in a geographically distant location 4 y before the episodes reported herein.[3]

Declaration of conflicting interests

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