CASE REPORT

Clinical Signs and Pathology of Accidental Monensin Poisoning in Sheep

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Summary
The clinical signs and postmortem findings in sheep from two flocks accidentally poisoned with monensin are described. Clinical signs began within 24 hours of exposure to monensin. In the acute stages they consisted of lethargy, stiffness, muscular weakness, a stiff gait and recumbency. Feed refusal was seen in one flock but not in the second. Subacute to chronic clinical signs were decreased muscle volume of the rump and thigh. When forced to run, chronically affected sheep had a stiff, stiff legged, rocking horse gait.

Gross postmortem changes were not always visible. Where visible, they affected skeletal muscles and consisted of pale streaking, with atrophy in the chronic stages. Lesions were most severe in muscles of the rump and hind limbs. Microscopically myofiber swelling and hyalinization were seen with interstitial mononuclear cell reaction and extensive sarcoplasmic mineralization in some cases. Chronic lesions consisted of fibrosis and myofiber atrophy. In lambs less than one month old, diffuse gastrointestinal hemorrhage was the only finding.

Résumé
Les signes cliniques et la pathologie de l’empoisonnement accidentel de moutons par le monensin

Cet article décrit les signes cliniques et les lésions macroscopiques que les auteurs notèrent chez des moutons de deux troupeaux, victimes d’une intoxication accidentelle par le monensin. Les signes cliniques apparaissent dans les 24 heures qui suivent l’ingestion de monensin. La phase aiguë de l’intoxication se caractérisait par la léthargie, de la raideur des membres, de la faiblesse musculaire, une démarche emphatique et du décubitus. Les moutons d’un des deux troupeaux refusaient aussi de manger. L’évolution vers la phase chronique de l’intoxication comportait une atrophie des muscles de la croupe et des membres pélviens. Lorsqu’on faisait courir les moutons rendus à la phase chronique de l’intoxication, ils affichaient une démarche emphatique, semblable au trottement du cheval.

Lorsque des lésions macroscopiques accompagnaient la condition, elles se traduisaient par des stries blanchâtres dans les muscles squelettiques; dans les cas chroniques, elles allaient jusqu’à l’atrophie musculaire. Les muscles les plus touchés étaient ceux de la croupe et des membres pélviens. Les lésions microscopiques incluaient un gonflement et une dégénérescence hyaline des fibres musculaires, ainsi qu’une infiltration du tissu conjonctif interstitiel par des mononucléaires; dans certains cas, plusieurs fibres dégénérées arboreraient aussi de la calcification. Les lésions chroniques se traduisaient par de la fibrose et de l’atrophie des fibres musculaires. Les agneaux âgés de moins d’un mois ne présentaient que des hémorragies gastro-intestinales diffuses.

Introduction
Monensin is an antibiotic demonstrated to have coccidiostatic (3,9) and growth promotant properties (6). It promotes growth in ruminants by favoring ruminal production of propionic acid (11). Its chemical properties and biochemical actions have been adequately described by several authors (2,11,13). Accidental poisoning of domestic animals with monensin has been reported in cattle (2), horses (1,10,13), dogs (14) and poultry (7,12). The LD₅₀ of monensin varies considerably from species to species and is reported to be 2-3 mg/kg body weight for horses (1), 21.9 mg/kg for cattle (2) and 200 mg/kg for chickens (2). Accidental poisoning of sheep with monensin has not been previously reported.

This paper describes the clinical findings and postmortem lesions observed in two sheep flocks following accidental inclusion of high levels of monensin in the ration.

Case 1
History and Clinical Findings
A flock of 160 Suffolk ewes raised in semiconfinement in west central Alberta experienced serious illness in February of 1980. Several ewes and growing lambs began exhibiting muscle stiffness the day after arrival of new loads of both grower and ewe rations. Over the next week several month old lambs became depressed and exhibited abdominal pain and scouring. One ewe was found off feed and weak in the hind limbs. Her milk production stopped, but there were no signs of mastitis.

Over a two week period three ewes, three one month old lambs and two yearling rams died. Posterior paresis, stiffness, abdominal pain and diarrhea were observed in many of these animals prior to death.

A number of yearling animals, ewes, and yearling lambs lost condition and exhibited intermittent stiffness and reluctance to move. Despite the replacement of the feed, the loss of condition of the yearling ewes and rams continued. Particularly noticeable was a reduced muscle mass in the hind quarters. Residual stiffness lasted
for as long as three months in about half of the flock. Many would appear normal when standing still but when forced to run moved with an irregular loping gait. All of the growing animals were unthrifty. They were consuming a large amount of feed but their gains in weight and condition were poor. The yearling rams lost so much condition that it was very difficult to prepare them for spring sale.

Two basic rations were fed to this flock. One was a grower ration fed to growing lambs and show stock consisting of soybean meal, steam rolled barley, molasses, limestone, dicalcium phosphate, vitamins, urea and selenium. The second ration was fed to the ewes and used as creep feed for their lambs. This was essentially the same as the grower ration, but contained a greater amount of soybean meal. Monensin was added to both rations by request of the owner at the feed mill. The level requested was 60 ppm in the final ration. The grower ration was fed at 0.75 kg per head per day with hay provided ad libitum.

The two rations had been fed essentially unchanged for the previous two years. On February 6, new loads of both grower and creep feed were delivered. The yearling animals refused to eat the new grower feed and their owner attempted to entice them to eat it by mixing the new feed with some of the old feed. Despite this, there was still a feed refusal problem and the yearlings did not consume as much as expected. They continued to eat a normal or slightly increased amount of hay. The grower feed was in front of the sheep until February 18 when it was removed and replaced with a new batch.

The feed for the ewes and their lambs was also fed beginning February 6 but a palatability problem was not encountered. This feed was provided until February 19 when new feed was introduced.

**Postmortem and Laboratory Findings**

**Month Old Lambs**

The three one month old lambs which died were brought to the Provincial Regional Animal Health Laboratory for postmortem examination. Similar lesions were found in each lamb. Diffuse hemorrhage was present throughout the mucosa of the gastrointestinal tract. In one lamb this hemorrhage was most severe in the abomasal fundus while in two others it did not begin until the midjejunum and extended from there throughout the ileum, colon and cecum. Intestinal contents were blood stained. The rumen and abomasum of each lamb contained hay, creep feed and very little milk. Internal organs of all lambs were pale as the result of blood loss into the gastrointestinal tract. As an incidental finding, one lamb had a mild locally extensive bronchopneumonia.

Sections of internal organs were fixed in 10% neutral buffered formalin, processed routinely, sectioned at 6 μ and stained with hematoxylin and eosin. Microscopic examination of the abomasum of the lamb that grossly exhibited abomasal hemorrhage revealed severe vascular congestion of the mucosa with areas of hemorrhage into the lamina propria. There was a minimal inflammatory response present with small numbers of eosinophils and degenerating neutrophils in the lamina propria.

Intestinal sections from all three lambs revealed severe vascular congestion with many areas of hemorrhage into the lumen. The mucosal lamina propria was edematous and the lymphatics of villi dilated. A diffuse infiltrate of eosinophils and mononuclear cells was present throughout the lamina propria but was most intense in the villi. In some sections of intestine there was severe hemorrhage but no inflammation. All other organs were microscopically normal.

Aerobic and anaerobic cultures of intestine and abomasum of the month old lambs yielded only *Escherichia coli*. Selenium analysis of the liver of one lamb yielded a level of 0.51 ppm which was considered normal. Heavy metal screening of the intestinal contents revealed insignificant traces of lead, arsenic and mercury (less than 0.1 ppm of each). Results of monensin analysis of feed are presented in Table 1.

**Ewes**

Complete carcasses of the other sheep which died were not made available for postmortem examination. The owner had opened one of the ram lambs and reported white streaks in the musculature, some of which he described as looking like rice grains. Portions of organs and various muscles from one of the dead ewes were frozen and presented by the owner for examination at a later date. Autolytic changes were advanced in the tissues of this ewe, but fine white longitudinal streaks were observed in the skeletal muscles.

On April 18, one live ewe lamb typical of those which showed atrophy of the hind limbs and unthriftiness was made available for postmortem examination. When at rest this ewe had a hunched stance and when forced to move exhibited a stiff rocking horse gait. She was euthanized with intravenous barbiturates and a postmortem examination performed. There were no gross lesions other than atrophy of hind limb muscles.

In both ewes, the most significant microscopic findings were present in the skeletal muscles which revealed multiple calcified fibers and generalized interstitial fibrosis. Muscle fibers stained poorly, had granular sarcoplasm and showed loss of cross striations.

**Case 2**

**History and Clinical Findings**

A commercial flock of 424 feeder lambs ranging in age from two to four

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<tr>
<th>Case 1</th>
<th>Ewe ration received February 6</th>
<th>160 ppm monensin</th>
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<td>Grower ration received February 6</td>
<td>550 ppm monensin</td>
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<th>Case 2</th>
<th>Samples take from three feeders</th>
<th>152 ppm monensin</th>
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<td>Feed delivered August 1</td>
<td>164 ppm monensin</td>
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<tr>
<td></td>
<td>Feeder 1</td>
<td>158 ppm monensin</td>
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<tr>
<td></td>
<td>Feeder 2</td>
<td>11 g/tonne feed</td>
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In Canada, monensin can be provided to sheep by veterinary prescription only.
months in the south central region of Alberta reported an acute onset of illness on the morning of August 2, 1980. This followed receipt of a shipment of commercial 16% market lamb grower on August 1. On August 2, six growing lambs exhibited incoordination and muscle weakness. By the morning of August 3, 24 lambs were down or having difficulty standing. That afternoon the feeders were boarded up and a new load of feed obtained and provided to the feeder lambs. By the late afternoon of August 3, 30 lambs were down and considerably more were depressed and/or walking stiffly. Most lambs were eating considerably less feed than normal by this time and it took them several days after the new load of feed was provided for them to consume the same amount of feed daily as they had prior to the onset of illness.

On August 4, one lamb died (Lamb A). This lamb and three clinically ill lambs were submitted for postmortem examination. The three live lambs were kept for observation. One lamb was euthanized on August 5 (Lamb B) and a second died August 9 (Lamb C). The third was euthanized August 13 (Lamb D). Postmortem examinations were performed immediately after the death of each lamb. During the period of observation all lambs remained down. Initially they would not eat, but lambs C and D did start to eat small amounts of hay over a two or three day period.

The lambs remaining on the farm had recovered by August 7 to the point that most were not showing clinical signs. However, 20 to 30 younger lighter lambs were seriously set back. These had sunken sides, protruding spines and hips, and wasted musculature. Three of these lambs were presented on August 19 for euthanasia and postmortem examination (Lambs E, F and G).

Postmortem and Laboratory Findings

Lamb A was found to be in good bodily condition. There was marked pulmonary edema and congestion. The abomasal mucosa was markedly hyperemic. Skeletal muscles were grossly normal. Microscopic examination revealed significant lesions restricted to the musculoskeletal system. Changes were multifocal in their distribution and consisted of swelling of individual myofibers with increased cytoplasmic eosinophilia and granular degeneration. A mononuclear cell infiltrate was present between muscle and fibers.

Lamb B was in good condition. The muscles of the pelvis and hind limbs were pale and dry. There were no other significant gross findings. Microscopic changes were similar to those of lamb A.

Lambs C and D had lost body condition but still retained fat reserves. Significant gross lesions were confined to skeletal muscles which exhibited diffuse pallor, white linear longitudinal streaks, lack of lustre and a dry texture. The muscles of the hind limbs were most severely affected although those of forelimbs, trunk and loins were also affected. Microscopic lesions in these lambs were similar to those in the two previously described. In addition there were areas of sarcoplasmic mineralization and interstitial fibroblast proliferation.

Analysis of blood and liver for selenium was performed in lambs B, C and D. Selenium levels were normal, blood concentrations varying from 0.35 to 0.61 ppm and liver concentrations from 0.15 to 0.29 ppm. Serum calcium and magnesium values were all within normal limits in these three lambs.

Postmortem examination of lambs E, F and G revealed them to be thin with diffuse pallor of the muscles of the hind limbs and, to a lesser degree, other skeletal muscles. The heart of one lamb was more pale than normal. Microscopic examination revealed eosinophilia of individual muscle fibers with interstitial infiltration of some mononuclear cells. Liver selenium level of each of these animals was normal.

Analysis of feed samples taken from four separate self feeders on August 4 revealed insignificant levels of nitrate nitrogen, \( \text{KNO}_3 \), lead and arsenic. Heavy metals other than lead and arsenic were not detected. Three samples of the feed delivered August 1 and fed to the lambs August 1-3 were collected and analyzed for monensin by the Plant Products Division of Agriculture Canada. Results of analysis are presented in Table 1.

Discussion

Once it was established that striated muscles were the target of the disease process in each case, the differentials considered were monensin toxicity, vitamin E/selenium responsive disease (white muscle disease) and sarcosporidiosis. Initially, heavy metal poisoning, nitrate poisoning, vitamin D toxicity, selenium poisoning, clostridial enterotoxemia and lactic acidosis had been considered but these latter diseases were ruled out on the basis of gross and microscopic postmortem lesions and toxicological analyses.

In both outbreaks vitamin E/selenium responsive disease can be ruled out based upon feed and tissue levels of selenium. Vitamin E was added to the feeds in both cases. This was assumed to rule out vitamin E deficiency as vitamin E assays are not readily available.

Sarcosporidiosis was deleted from the list of differentials because mature sarcocysts were the only form of this organism seen microscopically. These were present in the cardiac muscle when seen, yet the most severe damage in each case was in the skeletal muscles. Schizonts were not encountered in any animal.

Monensin toxicity was considered to be the cause of the disease process in each case based upon the selective destruction of skeletal muscle, the very high levels of monensin in the feed, and the close association between onset of clinical signs and the introduction of feed containing excessive monensin. This latter association was very close in case 2 where exposure only occurred for a two day period.

The clinical signs seen in both of the outbreaks described here began within 24 hours of initial exposure to monensin containing feed and in the acute stage consisted of lethargy, stiffness, muscular weakness, a stilted gait and recumbency. Feed refusal was noted in case 1 but not in case 2. This might be related to the higher feed levels of monensin found in case 1.

Subacute to chronic clinical signs associated with excessive dietary monensin on these two farms were decreased feed conversion efficiency, continued stiffness in more seriously affected animals and decreased muscle volume of the rump and thigh region. Seriously affected sheep exhibited a stiff-legged rocking horse gain when running.

Gross postmortem changes, where
visible, affected skeletal muscles and were most common and severe in the muscles of the rump and hind limbs. They ranged from pallor and dryness of muscle in the acute stages to shrinking of muscle masses and pale streaking of muscle in the subacute to chronic stages. In only one lamb was pallor of the myocardium observed. In very young lambs (<1 month) the only postmortem finding was diffuse, severe gastrointestinal hemorrhage.

Microscopic lesions were present in striated muscles and were more severe and numerous in the muscles that grossly were most severely affected, as would be expected. In the acute stages these consisted of myofiber swelling and hyalinization with loss of cross striations and fragmentation of the sarcoplasm accompanied by an intercellular mononuclear cell infiltration. In some animals there was extensive calcification of the sarcoplasm. Chronic changes were those of fibrosis of the damaged muscle tissue with secondary degenerative changes in surviving myofibers due to the fibrosis.

Descriptions of monensin poisoning in sheep are uncommon in the veterinary literature. One report refers indirectly to monensin poisoning in sheep and mentions that doses of 2 and 4 mg of monensin per kg body weight daily for four days caused listlessness and feed refusal. A dose of 8 mg/kg for two days was associated with the death of one of two test lambs while the other was listless and anorexic for three days and lost 1 kg of body weight. Postmortem lesions related to monensin were not found in the lamb that died after being fed 8 mg/kg monensin nor in one of the lambs given 4 mg/kg that was killed and necropsied (4).

In a report of a study performed to determine the effects of various levels of dietary monensin on growth and feed efficiency in lambs, lethargy, reduced feed consumption, diarrhea, stiffness and reluctance to move were reported in the first five days after monensin feeding began. These effects were most severe and widespread in two groups of lambs receiving 20 ppm and 30 ppm monensin in the feed, but were also reported in 5% of the control animals which were not receiving monensin. The condition was tentatively diagnosed as acidosis (8).

Cattle poisoned with monensin rapidly become anorexic and within two days are reluctant to move. Clinical signs of chronic passive congestion develop and deaths will occur up to a month or more following exposure. Postmortem lesions are those of myocardial degeneration and microscopically vacuolation of myocardial fibers occurs (2).

Of the domestic animals, horses are the most sensitive to monensin, the LD50 for adults being 2-3 mg/kg body weight (1). The salient clinical features of monensin toxicosis in horses as described by a number of authors are those of weakness, especially in the hind limbs, progressive ataxia, tachycardia, abdominal pain and respiratory distress (1,10,13). Serum glutamic oxalate transaminase (SGOT) is reported to rise 2-10 x in the first 24 hours, while lactic dehydrogenase (LDH) rises 2-6 x over 24-36 hours with primarily cardiac and erythrocyte isoenzyme patterns being raised (1). Postmortem examinations have revealed acute cardiovascular collapse and myocardial degeneration (10).

Clinical signs associated with high levels of monensin in the feed in dogs are those of extreme weakness, elevated LDH and SGOT, myoglobinuria and greatly elevated creatine phosphokinase (14). Postmortem lesions in dogs poisoned with monensin are those of a degenerative myopathy (5).

The clinical signs seen in sheep are similar to those of horses and dogs in that they are referable to skeletal muscle damage. In the feed refusal, stiffness, reluctance to move and recumbency, they are similar to the clinical signs in cattle but cattle differ in that the main damage is to the striated musculature of the heart and signs of chronic passive congestion develop. Chronic passive congestion was not seen in any of the sheep examined in this study. In sheep the muscular damage is major to the hind limbs and minor to the myocardium.

The diagnosis of monensin poison-