# Dicumarol Toxicity in a Herd of Ayrshire Cattle Fed Moldy Sweet Clover

**Willem DeHoogh**
*Fourth Year Student*
*College of Veterinary Medicine*
*University of Illinois, Urbana, IL 61801*



### Introduction

Sweet clover (dicumarol) poisoning is an important livestock problem especially affecting cattle raised in the Northern and Central United States.[5] The production of dicumarol occurs in damaged or moldy sweet clover hay or silage, and once ingested results in a depletion of vitamin K-dependent clotting factors. A hemorrhagic syndrome develops with clinical signs ranging from mild anemia to massive hemorrhage, hypovolemia, and death. The severity of signs depends on the amount of dicumarol ingested. The following case report illustrates the common history and clinical signs of a herd affected with sweet clover poisoning, and the diagnostic work-up and treatment pursued.

### History

On February 21, 1989, the University of Illinois Veterinary Medical Teaching Hospital was contracted to assist a private practitioner with an outbreak of lameness and acute death in an Ayrshire herd. The owner of the herd had discovered a dead yearling heifer two mornings ago, without any prior signs of illness. The following morning he discovered another dead yearling, again without any signs. On the morning of the 21st, one more yearling was dead, five were stiff or lame – primarily in one limb – and one had subcutaneous swelling over the neck and shoulder area.

The owner was milking 40 cows, and had 5 dry cows, 12 yearling heifers, and 2 bred heifers. The yearling heifers were the only group showing clinical signs. The owner was feeding 3-4# haylage/head/day, free-choice alfalfa hay, and a grain mixture (corn, protein supplement) to his lactating cows. The yearling heifers were being fed free-choice haylage, some dry hay, and 2# of grain/head/ day. It was undetermined what he was feeding his dry cows and bred heifers. Further questioning revealed that the haylage consisted of mature chopped sweet clover and alfalfa. The owner recalled switching from grass haylage to this haylage one to two weeks before the outbrerak, and had noticed some moisture on the sides of his stave silo and some mold growth on the haylage. From the history, sweet clover poisoning was suspected. The owner transported his remaining nine yearlings to the Teaching Hospital for examination and treatment. He also submitted two haylage samples and a bulk tank milk sample for dicumarol toxicologic testing.

### Physical Examination and Diagnostic Tests

Nine one-year-old Ayrshire heifers, ranging in weight from 238# to 495# were presented to the Teaching Hospital for confirmation of the diagnosis and for treatment. Physical examination revealed lameness (3), epistaxis (3), subcutaneous hematomas (2), shivering (3), and depression (2) (see Table 1). The lame animals were stiff and often favored one limb, but the joints were not palpably swollen or warm. Blood was drawn to evaluate clotting times, severity of anemia, and hydration status (Table 1).

TABLE 1.*

| Heifer No. | PCV | TP | PT | Clinical Signs |
|---|---|---|---|---|
| 1 | 15 | 4.2 | >30 | hematoma RR-leg, lame LR, hematoma-neck, epistaxis, shivering, depressed |
| 2 | 29 | 6.1 | >30 | none |
| 3 | 36 | 6.4 | >30 | epistaxis-left nostril |
| 4 | 17 | 7.8 | >30 | hematoma-shoulder area, epistaxis, depressed |
| 5 | 29 | 6.4 | >30 | none |
| 6 | 37 | 6.5 | >30 | stiff, shivering |
| 7 | 28 | 6.2 | >30 | LR leg stiff |
| 8 | 27 | 5.3 | >30 | shivering, muscular twitching, muffled heart sounds |
| 9 | 28 | 6.5 | >30 | none |

* TP = total protein; PT = prothrombin time (seconds); PTT = partial thromboplastin time (seconds).

### Treatment and Follow-up Tests

Since Prothrombin Times (PT) were elevated (>30 seconds), all nine heifers were treated with a single IV injection of vit. $K_1$ at a dose of 0.5 mg/# (1.1 mg/kg). Heifers #1 and #4 were severely anemic (PCV=15 and 17% respectively). These two heifers were given 10 ml/kg whole blood IV in addition to the vit. $K_1$ treatment. All animals were put in stalls for quiet confinement, and given good quality alfalfa hay.

Heifer #1 was found dead on the morning of February 22nd and was submitted for necropsy. Gross lesions consisted of markedly pale mucous membranes, a 30 by 7 cm diameter subcutaneous (SQ) mass dorsal to the right scapula containing a large quantity of unclotted sanguineous fluid (hemorrhage), diffuse SQ hemorrhage over the right foreleg extending into flexor and extensor muscle groups, and multifocal petechial hemorrhages beneath the thymic capsule, subepicardially, and subendocardially. Other lesions included occasional ecchymotic hemorrhages along the spinal column, reddened kidney and mesenteric lymph nodes, small quantities of reddened synovial fluid in all joints, and occasional reddened synovia. Microscopic lesions were consistent with hemorrhage. Also noted was moderate, acute, diffuse, periacinar hepatocellular degeneration, presumably due to cellular hypoxia.

Heifer #4 remained stable with very little improvement over five days of observation (Table 2). On the second day of hospitalization, the right carpal joint was slightly enlarged and the right shoulder region was swollen. On day six, the PT was again >30 seconds and the animal was treated with another 0.5 mg/# of vit. $K_1$ IV. The heifer clinically improved and was released several days later.

TABLE 2.* Heifer #4

| Day | PCV | TP | PT | PTT |
|---|---|---|---|---|
| 1 | 17 | 7.8 | >30 | - |
| 2 | 17 | 7.8 | >30 | - |
| 3 | 16 | 7.0 | 26.8 | - |
| 4 | 15 | 7.0 | - | >100 |
| 5 | 17 | 7.0 | - | - |
| 6 | 19 | 7.4 | 39.9 | 59 |
| 7 | 19 | 7.3 | - | - |

*TP = total protein; PT=prothrombin time (seconds); PTT = partial thromboplastin time (seconds)

Of the other seven heifers, five had PT <30 seconds on day two and were released on day three. Two heifers had PT >30 seconds and low PCV values on day two and were retained for further monitoring. One improved without treatment and the other required one more dose of vit. $K_1$ on day five. The owner reported no recurrences in this group of yearling heifers.

Five days following admission of the yearlings, the owner brought in two heifers that had been bred but had delayed returns to estrus, and one dry cow that had aborted her calf. The two heifers were found to have elevated PT's but were not anemic, and were treated with vit. $K_1$ as above. The cow had a slightly elevated PT, but therapy did not seem warranted as all animals had been removed from the suspect haylage for five days.

No further clinical signs of dicumarol toxicity were seen in this herd. The owner did report that his cats had been in the haylage after the above incident and had subsequently lost their litters.

A toxicologic screen performed on the haylage revealed levels from 20–27.7 ppm dicumarol. The bulk tank milk sample was negative. Liver samples were submitted from the necropsied heifer, and yielded levels of 1.1 ppm dicumarol, which is considered diagnostic for sweet clover poisoning.

### Discussion

Sweet clover poisoning is an important problem affecting many herds annually, especially in the Northern and Central Plains of the United States.[5] Sweet clover is often used as hay or haylage due to its comparable quality, utility, and cost to alfalfa.[2] The anticoagulant toxicity that is associated with sweet clover feeding occurs when sweet clover is naturally spoiled or damaged and made into hay or haylage. The toxic principle is dicumarol which is produced by fungal action on sweet clover substrates (namely coumarin). This action is a dimerization and oxidation process that converts the relatively non-toxic coumarin to the toxic dicumarol.[5] The process occurs under high moisture conditions as the clover is cut and baled or made into haylage. Sweet clover pasture is not affected.[1]

The action of dicumarol is to compete directly with vit. K for the enzyme vit. K epoxide reductase. This enzyme is responsible for recycling vit. K from its inactive to its active form. With the enzyme tied up, active vit. K is depleted and the production of the vit. K -dependent clotting factors is inhibited.[5] Thus, unless vit. K is replenished, the dependent clotting factors are soon depleted and hemorrhage ensues. These clotting factors include factors VII, IX, X, and II (prothrombin), which participate in the intrinsic, extrinsic and common clotting pathways. Since factor VII has the shortest half-life (6.2 hrs.), the extrinsic pathway is shut down first, usually with no clinical signs. Diagnosis can be made at this point by measuring

the Prothrombin Time (PT). Times greater than 30 seconds in the cow are abnormal. With further depletion of clotting factors, the intrinsic pathway shuts down and clinical signs of diffuse hemorrhage are seen. Laboratory evaluation at this time will reveal an elevated partial thromboplastin time (PTT or APTT) as well as an elevated PT.[5]

The clinical signs seen with sweet clover poisoning vary with the degree of exposure, namely the amount of dicumarol in the feed and the amount of feed ingested.[1] Classically, anemia is detected by pale mucous membranes, a strong, rapid heartbeat, and a weak pulse. Weakness is often seen, as well as SQ and IM hematomas. Uncontrollable bleeding can occur during surgery, parturition, estrus, or following trauma. Lameness is also often noticed as a result of hemarthrosis. Pregnant animals have been known to abort or give birth to weak or listless calves that may also uncontrollably bleed.[4]

The amount of dicumarol in the feed has been shown to correlate with the amount of time required for clinical signs to develop.[3] H.H. Casper et al. determined that hay containing 10-20 ppm dicumarol resulted in no clinical signs after 100 days of feeding. Thirty ppm dicumarol resulted in clinical signs at 132-139 days. At 60-70 ppm dicumarol, clinical signs were seen at 17-23 days. They determined levels of 50-70 ppm dicumarol to be toxic.[3] In this herd, the two haylage samples submitted contained 20 and 27.7 ppm dicumarol. These levels would not appear to be harmful after only 1-2 weeks of feeding. However, random sampling may yield variable results due to an unevenness of spoiling, and thus not reflect the actual dicumarol ingested over time. The 1.1 ppm dicumarol level detected in the dead heifer confirmed that toxic levels had been ingested.

This case illustrates the importance of the amount of feed ingested as well as the dicumarol content. The lactating cows never showed any clinical signs despite eating the same haylage as the heifers. The difference was that the heifers ate the haylage free-choice and the cows only received 3-4#/day.

The diagnosis of sweet clover poisoning requires a careful analysis of the feeds used and the conditions of processing and storage. Any use of sweet clover hay or haylage, especially under high moisture conditions should alert one to the possibility of dicumarol poisoning. Analysis of feed samples, estimation of clotting parameters and other appropriate clinical signs can lead one to a sufficient diagnosis to institute treatment.

Treatment consists of removing all animals from the source and replenishing vit. K.[2] This can usually be adequately achieved by replacing the contaminated source with good quality alfalfa hay. (Alfalfa is high in available vit. K.) For severe cases, parenteral injection of vit. $K_1$ is recommended as well as whole blood transfusions (10 ml/kg) if the animal is extremely anemic. Vit. $K_1$ has been shown effective at a dose of 0.5 mg/# (1.1 mg/kg), given either IV or IM. Care must be taken to not cause further hematomas (use of a small gauge needle is recommended). Vit. $K_3$ has been shown to be ineffective for treatment in ruminants.[2] Most cases improve within five days of removal of the toxic feed source.

## Summary

Dicumarol toxicity is an important problem associated with the feeding of damaged sweet clover. The toxic principle is formed from the conversion of coumarin (normally present in sweet clover) to dicumarol by the action of various fungi. Dicumarol competitively inhibits vit. K epoxide reductase, an enzyme necessary for the recycling of vit. K. Clotting factors VII, IX, X, and II are vit. K -dependent and thus are soon depleted resulting in an hemorrhagic syndrome. Clinical signs include anemia, weakness, hematoma formation, uncontrollable bleeding, lameness, and abortion. Treatment consists of removing animals from the source and replenishing vit. K. This case report illustrates a herd outbreak involving yearling heifers, bred heifers, and a dry pregnant cow. Four animals died, two possible early embryonic deaths occurred, and one cow aborted. The rest responded to treatment without further recurrence or complications.

*Faculty Adviser: Dr. Dawn Morin*

## References

1. Knight, M.W., *Moldy Sweet Clover Disease*. Unpublished. 1986. 2. Alstad, A.D., Casper, H.H., Johnson, L.J., Vitamin K Treatment of Sweet Clover Poisoning in Calves. *JAVMA* 187(7):729-731. 1985. 3. Casper, H.H., Alstad, A.D., Monson, S.B., Johnson, L.J., Dicumarol Levels in Sweet Clover Toxic to Cattle. *Amer. Vet. Lab. Diag. Ann. Proc.* 41-48:6-11. 1982. 4. Casper, H.H., Sweet Clover Poisoning in Pregnant Cows and Calves. *Vet. News.* 5(2):15. 1982. 5. Damaged or Moldy Sweet Clover Hay. *Toxicology Lecture Notes*, University of Illinois, College of Vet. Med., Vet. Biosciences 320, pp. 763-766. 1988.