

# Managing high-risk fresh cows

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## Abstract

Although fresh cows are often managed as homogeneous groups, tools are becoming available to identify cows at high risk for specific disease conditions, as well as information which describes cows that are most likely to respond to disease interventions. This approach is particularly applicable to hypocalcemia, because it occurs in a short time window around calving and because it has clear risk factors. New data show that early lactation hypocalcemia clearly reduces milk yield and increases risk for displaced abomasum and early lactation culling. Oral calcium supplementation can be targeted to individual cows. The response to oral calcium bolus supplementation around calving is greatest for cows with higher milk production in the previous lactation and for lame cows.

**Key words:** dairy cattle, hypocalcemia, calcium, lactation

## Résumé

Bien que les vaches fraîches vèlées font souvent l'objet d'une gestion en tant que groupe homogène, il existe de plus en plus d'outils pour identifier les vaches présentant des risques élevés de maladies spécifiques, ainsi que de l'information décrivant les vaches qui répondront le plus vraisemblablement aux interventions en cas de maladie. Cette démarche est particulièrement applicable à l'hypocalcémie, parce qu'elle survient au cours d'une courte période proche du vêlage, et parce qu'elle présente des facteurs de risque évidents. De nouvelles données indiquent que l'hypocalcémie lors de la lactation réduit nettement la production de lait et augmente le risque de déplacement de la caillette et de réforme au début de la lactation. Un supplément de calcium administré par voie orale peut être utilisé pour certaines vaches. La réaction au supplément de calcium administré par voie orale autour de la période de vêlage est plus importante chez les vaches ayant eu une plus grande production de lait au cours de la lactation précédente ainsi que chez les vaches qui boitent.

## Overview - Identifying High Risk Fresh Cows and Intervention Strategies

Limited information is available to assist veterinarians and dairy producers to identify high-risk fresh

cows. Many of the risk factors for early lactation herd removal (live culling or death) have been characterized. Using a very large Dairy Herd Improvement Association (DHIA) data set, workers from Florida reported that the oldest cows (parity  $\geq 4$ ) are at highest risk for death in early lactation, followed (in order) by parity 1, parity 3, and parity 2 cows.<sup>26</sup> Higher milk yield has been associated with lower risk for herd removal.<sup>13,26</sup> This finding is not necessarily intuitive, and suggests that cows with relatively lower milk yield in the previous lactation could be included as high-risk cows. Additional measures identified from the large DHIA data set as risk factors for death or herd removal included long days open and longer dry periods.<sup>25</sup>

Studies evaluating the effect of early lactation lameness on the risk for herd removal have been contradictory. Determining the cause of the lameness appeared to resolve the issue; Ontario workers reported that cows lame because of white line lesions, ulcers, or hemorrhage were at higher risk for herd removal, but that infectious causes of lameness were not associated with culling risk.<sup>4</sup> No studies have specifically evaluated pre-calving lameness as a risk factor for postpartum performance.

Cows giving birth to stillborn calves<sup>1,15</sup> or experiencing dystocia<sup>15</sup> are at higher risk for postpartum problems; cows giving birth to twins may not be at higher risk.<sup>15</sup> Australian workers<sup>7</sup> reported that increased length of time on the prepartum diet reduced the risk for culling but increased the hazard of clinical mastitis. Gestation length is likely related to length of time on the prepartum diet.

Measuring blood metabolites in fresh cows can help predict risk for early lactation removal from the herd.<sup>27,29</sup> However, there are practical limitations (laboratory costs, labor costs, and possible delays in knowing the laboratory result) in using blood metabolites on a routine basis to identify high-risk fresh cows. A slightly different approach, using intensive early detection of ketosis by frequent blood testing of early lactation cows with a cow-side beta-hydroxybutyric acid (BHBA) test followed by early treatment with oral propylene glycol, gave excellent results.<sup>18,19</sup> Unfortunately, low-cost cow-side tests are not available for all fresh cow disease conditions.

Identification of high-risk groups for fresh cow problems can allow for targeting of certain cows for more intensive diagnostic testing or for targeting prophylactic treatments. However, knowing the high-risk groups

does not necessarily equate to increased effectiveness of management strategies or prophylactic treatments directed at preventing these problems. Additional research data are necessary to precisely establish which subpopulations of cows respond well to specific interventions and to quantify the effect of each intervention.

### Hypocalcemia Overview

Hypocalcemia is particularly amenable to strategies tailored to individual cows or targeted groups of cows. First, a substantial proportion of cows are affected by hypocalcemia. Average blood calcium concentrations noticeably decline in second or greater lactation cows around calving, with the lowest concentrations occurring about 12 to 24 hours after calving (Figure 1).<sup>12,17</sup>

A cow does not necessarily have to become recumbent (down) to be negatively affected by hypocalcemia. With or without obvious clinical signs, hypocalcemia has been linked to a variety of secondary problems in post-fresh cows.<sup>12,22</sup> This happens because blood calcium is essential for muscle and nerve function – particularly functions that support skeletal muscle strength and gastrointestinal motility. Problems in either of these areas can trigger a cascade of negative events that ultimately reduce dry matter intake, increase metabolic diseases, and decrease milk yield.<sup>12</sup> This is illustrated in Figure 2.

Subclinical hypocalcemia can be defined as low blood calcium concentrations without clinical signs of milk fever. Subclinical hypocalcemia affects about 50% of second and greater lactation dairy cattle fed typical pre-fresh diets. If anions are supplemented to reduce

the risk for milk fever, the percentage of hypocalcemic cows is reduced to about 15 to 25%.<sup>21</sup>

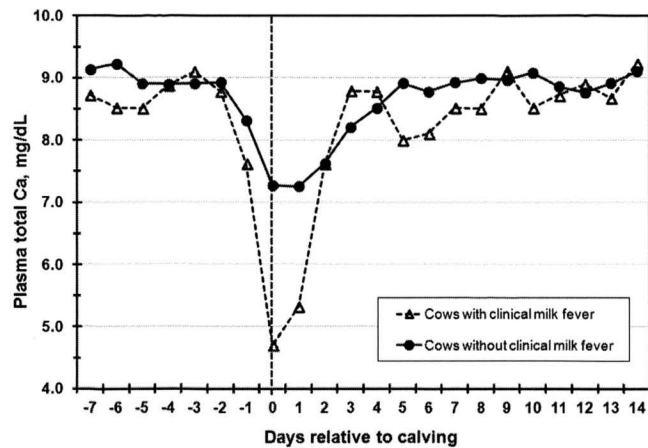
Subclinical hypocalcemia is more costly than clinical milk fever because it affects a much higher percentage of cows in the herd.<sup>22</sup> For example, if a 2000-cow herd has a 2% annual incidence of clinical milk fever and each case of clinical milk fever costs \$300,<sup>14</sup> the loss to the dairy from clinical cases is about \$12,000 per year. If the same herd has a 30% annual incidence of subclinical hypocalcemia in second and greater lactation cows (assume 65% of cows in the herd) and each case costs \$125 (an estimate that accounts for milk yield reduction and direct costs due to increased ketosis and displaced abomasum), then the total herd loss from subclinical hypocalcemia is about \$48,750 per year. This is about four times greater than the cost of the clinical cases.

A recently published, large multi-site study shows that hypocalcemia around calving is most strongly associated with reduced milk yield<sup>3</sup> and increased risk for displaced abomasum.<sup>2</sup> These studies also demonstrated that the cutpoint for serum total calcium is higher (about 8.5 mg/dl) than was previously assumed (Figures 3 and 4).

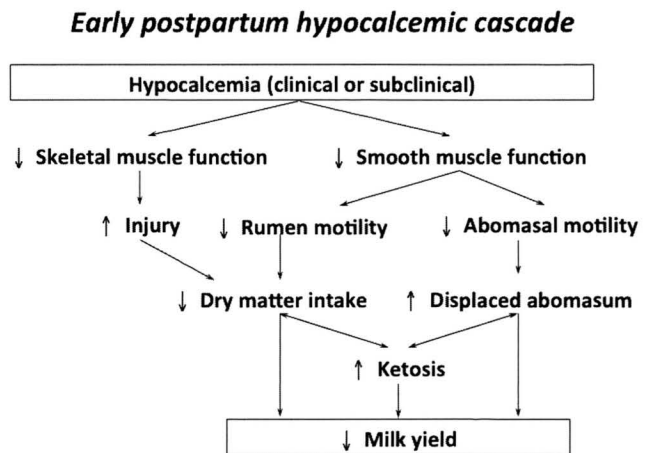
### Treatments for Subclinical Hypocalcemia and Clinical Milk Fever

Clinical signs of milk fever in dairy cattle around calving may, for convenience, be divided into three stages. Stage I milk fever is early signs without recumbency. It may go unnoticed because its signs are subtle and transient. Affected cattle may appear excitable, nervous, or weak. Some may shift their weight frequently and shuffle their hind feet.<sup>22</sup>

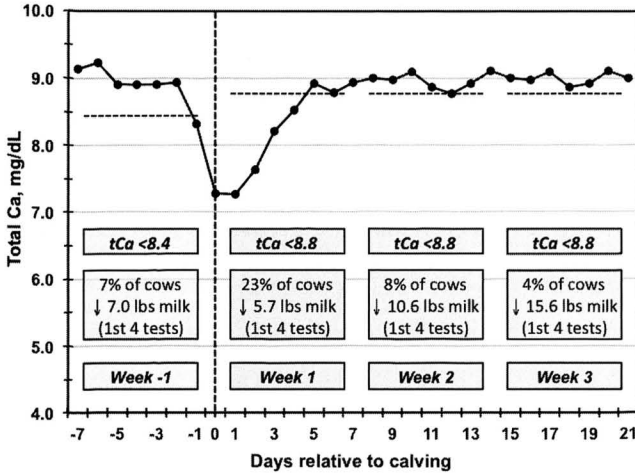
Some cows become hypocalcemic at times other than calving and exhibit clinical signs similar to those



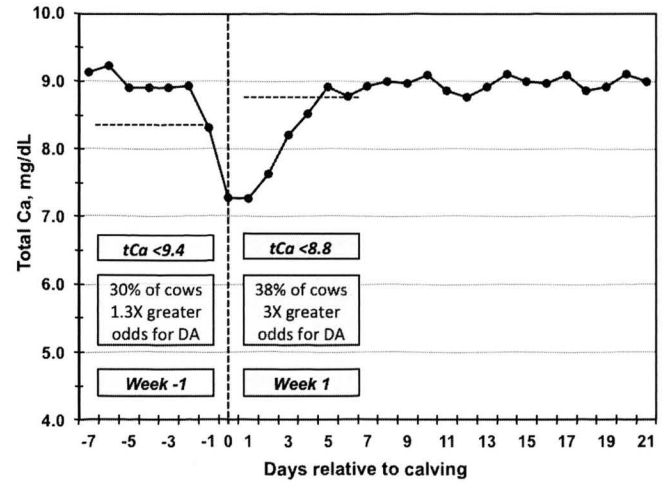
**Figure 1.** Plasma concentrations of total calcium before and after calving in mature Jersey cows with (n=8) or without (n=19) clinical milk fever. Data adapted from Kimura K, Reinhardt TA, Goff JP. Parturition and hypocalcemia blunts calcium signals in immune cells of dairy cattle. *J Dairy Sci* 2006;89:2588-2595.



**Figure 2.** Proposed mechanisms for reduction in milk yield in early lactation cows due to hypocalcemia.



**Figure 3.** Effect of serum total calcium on milk yield for the first four DHI tests after calving. Different cutpoints were derived for serum samples collected on weeks -1, 1, 2, and 3 after calving. Data are from 2,365 cows in 55 Holstein herds in Canada and the US and are adapted from Chapinal N, Carson ME, LeBlanc SJ, Leslie KE, Godden S, Capel M, Santos JE, Overton MW, Duffield TF. The association of serum metabolites in the transition period with milk production and early-lactation reproductive performance. *J Dairy Sci* 2012;95:1301-1309. Reference line for total calcium is from Kimura K, Reinhardt TA, Goff JP. Parturition and hypocalcemia blunts calcium signals in immune cells of dairy cattle. *J Dairy Sci* 2006;89:2588-2595.



**Figure 4.** Effect of serum total calcium on the odds for displaced abomasum after calving. Different cutpoints were derived for serum samples collected on weeks -1, 1, 2, and 3 after calving. Data are from 2,365 cows in 55 Holstein herds in Canada and the US and are adapted from Chapinal N, Carson M, Duffield TF, Capel M, Godden S, Overton M, Santos JE, LeBlanc SJ. The association of serum metabolites with clinical disease during the transition period. *J Dairy Sci* 2011;94:4897-4903. Reference line for total calcium is from Kimura K, Reinhardt TA, Goff JP. Parturition and hypocalcemia blunts calcium signals in immune cells of dairy cattle. *J Dairy Sci* 2006;89:2588-2595.

described above for Stage I milk fever. Such non-parturient hypocalcemia are often triggered by periods of unusual stress or decreased dry matter intake. This condition is most commonly seen in cows in the first two to 10 days of lactation, cows that are in heat, cows with severe digestive upsets, or cows suffering from severe (toxic) mastitis.<sup>22</sup>

Oral calcium supplementation is the best approach for hypocalcemic cows that are still standing, such as cows in Stage 1 hypocalcemia or who have undetected subclinical hypocalcemia.<sup>22</sup> A cow absorbs an effective amount of calcium into her bloodstream within about 30 minutes of supplementation.<sup>9</sup> Blood calcium concentrations are supported for only about four to six hours afterwards<sup>9,10</sup> for most forms of oral calcium supplementation.

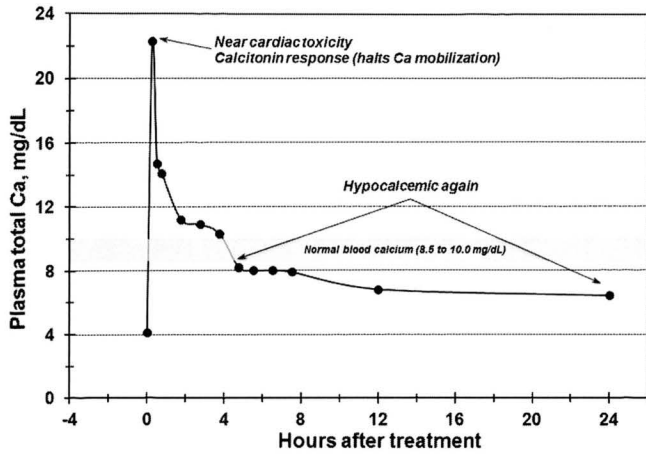
Intravenous (IV) calcium is not recommended for treating cows that are still standing.<sup>22</sup> Treatment with IV calcium rapidly increases blood calcium concentrations to extremely high and potentially dangerous levels.<sup>11</sup> Extremely high blood calcium concentrations may cause fatal cardiac complications and (perhaps most importantly) shut down the cow's own ability to mobilize the calcium she needs at this critical time.<sup>22</sup> Cows

treated with IV calcium often suffer a hypocalcemic relapse 12 to 18 hours later.<sup>5,30</sup> The problems with IV calcium treatment are illustrated in Figure 5.

Cows in Stage II milk fever are down but not flat out on their side. They exhibit moderate to severe depression, partial paralysis, and typically lie with their head turned into their flank. Stage III hypocalcemic cows are flat out on their side, completely paralyzed, typically bloated, and are severely depressed (to the point of coma). They will die within a few hours without treatment.<sup>22</sup>

Stage II and Stage III cases of milk fever should be treated immediately with slow IV administration of 500 ml of a 23% calcium gluconate solution. This provides 10.8 grams of elemental calcium, which is more than sufficient to correct the cow's entire deficit of calcium (about 4 to 6 grams). Giving larger doses of calcium in the IV treatment has no benefit.<sup>8</sup> Treatment with IV calcium should be given as soon as possible, as recumbency can quickly cause severe musculoskeletal damage.

To reduce the risk for relapse, recumbent cows that respond favorably to IV treatment need additional oral calcium supplementation once they are alert and able



**Figure 5.** Effect of IV calcium treatment with 10.5 g of elemental calcium on serum total calcium concentrations in a mature Jersey cow with clinical milk fever. Data adapted from Goff JP. Treatment of calcium, phosphorus, and magnesium balance disorders. *Vet Clin North Am Food Anim Pract* 1999;15:619-639.

to swallow, followed by a second oral supplement about 12 hours later.<sup>22,30</sup>

Transient hypocalcemia can occur in cows whenever they go off feed or have periods of decreased intestinal motility.<sup>6</sup> It can be difficult to tell which comes first – the hypocalcemia or the gastrointestinal stasis. Whatever the case, the two problems can positively reinforce each other. During the experimental induction of hypocalcemia,<sup>16</sup> ruminal contractions ceased well before the onset of clinical signs of milk fever. Off-feed cows, particularly in early lactation, are very likely to benefit from prompt oral calcium supplementation.

Even herds with successful anionic salts programs and minimal clinical cases of milk fever will benefit from strategic use of oral calcium supplements.<sup>23</sup> Start by supplementing all standing cows who have clinical signs of hypocalcemia and all down cows following successful IV treatment. For herds with a high incidence of hypocalcemia, it may also be economically beneficial to strategically supplement all fresh cows with oral calcium. Finally, cows with high milk yield in the previous lactation (>105% of herd average ME milk production) and lame cows have the best response to oral calcium supplementation.<sup>23</sup> These cows gave 6.8 lb (3.1 kg) more milk at first DHI test compared to unsupplemented cows.

### Types of Oral Calcium Supplementation

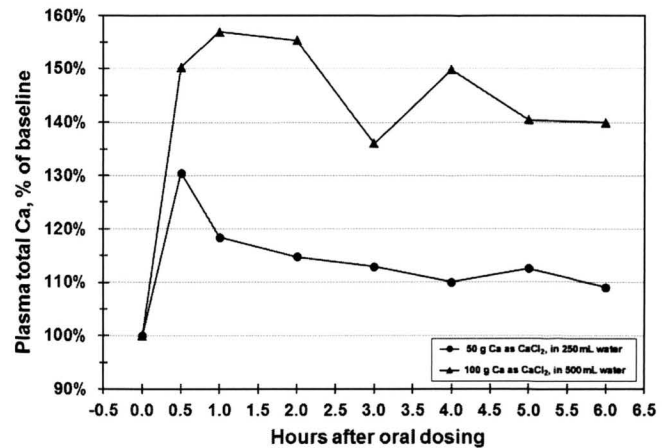
The source of calcium in an oral supplement and its physical form greatly influence calcium absorption and blood calcium responses. A series of experiments has

shown that calcium chloride has the greatest ability to support blood calcium concentrations.<sup>9,10</sup> This can be explained by its high calcium bioavailability and its ability to invoke an acidic response in the cow, which causes her to mobilize more of her own calcium stores. Providing a typical amount of elemental calcium chloride (e.g., 50 grams of elemental calcium) in a small oral dose (e.g., 250 mL water) provided the best absorption (Figure 6). Administering 100 grams of elemental calcium from calcium chloride in water resulted in an excessive increase in blood calcium concentrations - perhaps enough to shut down the cow's own calcium homeostatic mechanisms and to invoke a calcitonin response to protect her from hypercalcemia.

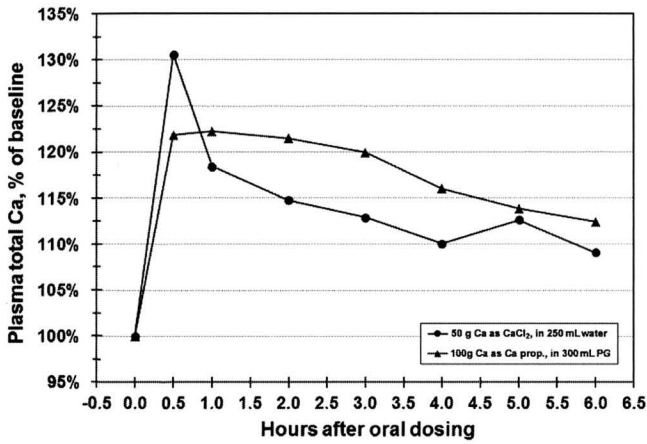
The risk of aspiration is great when thin liquids are given orally, and calcium chloride is very caustic to upper respiratory tissues. Calcium propionate is more slowly absorbed (presumably because it is not acidogenic) and must be given at higher doses of elemental calcium (usually 75 to 125 grams – Figure 7). Calcium propionate has the property of being glucogenic as well as providing supplemental calcium.

Calcium carbonate in water did not increase blood calcium concentrations at all (Figure 8).<sup>9</sup> This may be explained by its poorer bioavailability and by the alkalogenic response it can invoke.

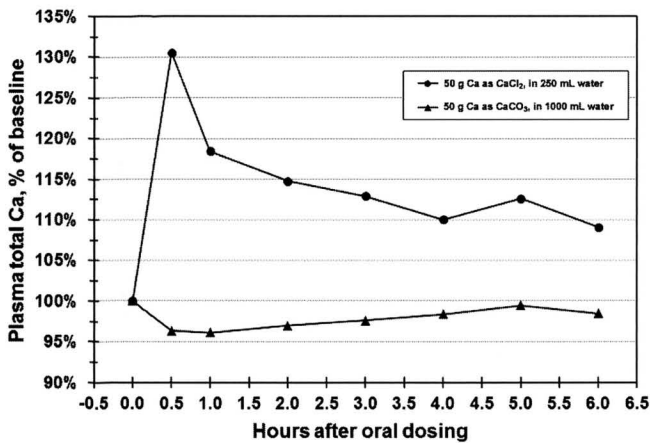
A combination of calcium chloride and calcium sulfate delivered in a fat-coated bolus<sup>a</sup> resulted in more sustained improvements in blood calcium concentrations (Figure 9) than were observed in previous studies with oral calcium chloride or calcium propionate in water.<sup>28</sup>



**Figure 6.** Effect of two different doses of oral calcium chloride on plasma total calcium concentrations, expressed as percent of baseline values. Data adapted from Goff JP, Horst RL. Oral administration of calcium salts for treatment of hypocalcemia in cattle. *J Dairy Sci* 1993;76:101-108.

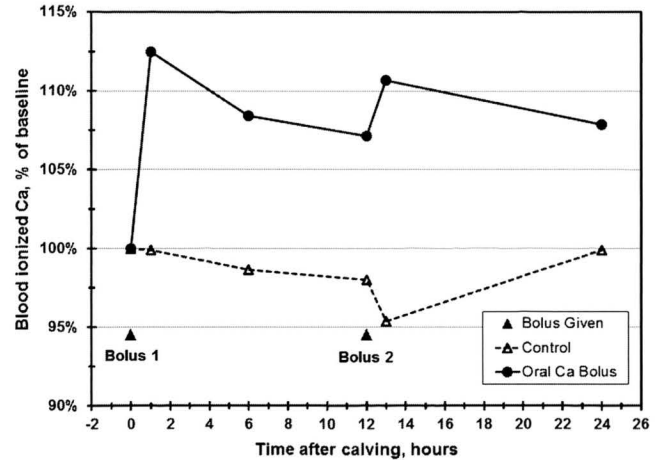


**Figure 7.** Effect of oral calcium chloride and oral calcium propionate on plasma total calcium concentrations, expressed as percent of baseline values. Data adapted from Goff JP, Horst RL. Oral administration of calcium salts for treatment of hypocalcemia in cattle. *J Dairy Sci* 1993;76:101-108 and from Goff JP, Horst RL. Calcium salts for treating hypocalcemia: carrier effects, acid-base balance, and oral versus rectal administration. *J Dairy Sci* 1994;77:1451-1456.



**Figure 8.** Effect of oral calcium chloride and oral calcium carbonate on plasma total calcium concentrations, expressed as percent of baseline values. Data adapted from Goff JP, Horst RL. Oral administration of calcium salts for treatment of hypocalcemia in cattle. *J Dairy Sci* 1993;76:101-108.

This encapsulated version of calcium salts had the advantages of not having an unpleasant taste to the cow, having little to no waste of the oral formulation, no risk for aspiration pneumonia, and a more prolonged release of the oral calcium.<sup>26</sup> These workers reported



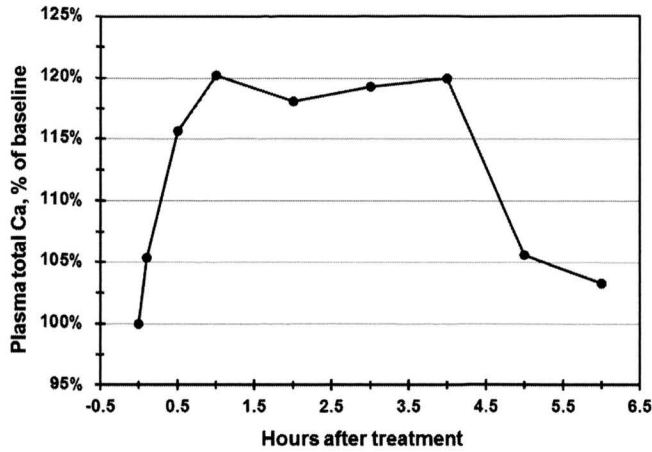
**Figure 9.** Effect of administration of two fat-coated oral calcium boluses<sup>a</sup> on blood ionized calcium concentrations (expressed as percent of baseline) at calving and 12 hours later. Experimental animals were Holstein cows (n=20) with hypocalcemia at calving. Data adapted from Sampson JD, Spain JN, Jones C, Carstensen L. Effects of calcium chloride and calcium sulfate in an oral bolus given as a supplement to postpartum dairy cows. *Vet Ther* 2009;10:131-139.

a four-fold reduction in the odds for developing clinical milk fever in cows that were supplemented with four boluses around calving.<sup>24</sup>

### Subcutaneous Calcium Treatment

Subcutaneous calcium can be used to support blood calcium concentrations around calving, but has substantial limitations.<sup>11</sup> Absorption of calcium from subcutaneous administration requires adequate peripheral perfusion. It may be ineffective in cows that are severely hypocalcemic or dehydrated. Subcutaneous calcium injections are irritating and can cause tissue necrosis; administration should be limited to no more than 75 mL of a 23% calcium gluconate solution (about 1.5 g elemental calcium) per site. Calcium solutions that also contain glucose should not be given subcutaneously. Glucose is very poorly absorbed when given by this route. Abscessation and tissue sloughing may result when glucose is given subcutaneously.

The kinetics of subcutaneously administered calcium indicate that it is well-absorbed initially, but that blood concentrations fall back to baseline values in about six hours (Figure 10).<sup>11</sup> Thus, repeat doses would be necessary to equal the sustained blood calcium support that is possible with oral calcium boluses.



**Figure 10.** Effect of subcutaneous administration of 500 mL of 23% calcium gluconate on plasma total calcium, expressed as percent of baseline. The 500 ml solution was divided into 10 different sites. Data adapted from Goff JP. Treatment of calcium, phosphorus, and magnesium balance disorders. *Vet Clin North Am Food Anim Pract* 1999;15:619-639.

### Timing of Oral Calcium Supplementation Relative to Calving

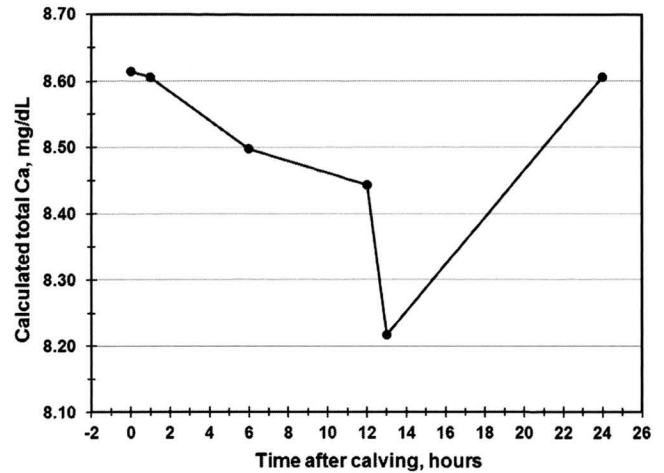
Strategies for giving oral calcium supplements around calving should include at least two doses - one at calving and a second dose the next day. The expected nadir in blood calcium concentrations occurs between 12 and 24 hours after calving (Figure 11).<sup>11,28</sup> Giving only one oral calcium supplement around calving time leaves the cow without support when her blood calcium concentrations are naturally the lowest. It is interesting to note that the original protocols for oral calcium supplementation called for four doses - one about 12 hours before calving, one at calving, one 12 hours post-calving, and one 24 hours post-calving. It was very difficult to predict when a cow was in fact about 12 hours from expected calving, and many cows calved without receiving this dose.<sup>20</sup> The dose at calving is not practically challenging to administer, and providing a dose sometime the day after calving will provide critical support around the time of nadir and can still be practical in large dairies where the post-fresh pen is locked up just once daily.

### Endnote

<sup>a</sup>Bovicalc<sup>®</sup>, Boehringer Ingelheim Vetmedica, St. Joseph, MO

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**Figure 11.** Blood total calcium concentrations (extrapolated from ionized calcium results) from 10 control cows. Experimental animals were Holstein cows (n=10) with hypocalcemia at calving. The nadir in calcium concentrations occurs sometime between 12 and 24 hours after calving. Data adapted from Sampson JD, Spain JN, Jones C, Carstensen L. Effects of calcium chloride and calcium sulfate in an oral bolus given as a supplement to postpartum dairy cows. *Vet Ther* 2009;10:131-139.

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