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Mineral Disorders and Nutrition for the Fresh Cow

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I. Milk Fever and Subclinical Hypocalcemia

Hypocalcemia (low blood calcium) is an important determinant of fresh cow health and milk production. Five key principles shape our understanding of this common metabolic disease and how to manage it.

- Most second and greater lactation cows have a transient hypocalcemia around calving (Kimura et al., 2006).
- Hypocalcemia is linked to other fresh cow problems (Goff, 2008, Oetzel, 2011)
- Supplementation with oral calcium is the preferred approach for supporting cows that are exhibiting early signs of milk fever but are still standing (Oetzel, 2011).
- Subclinical hypocalcemia has greater associated costs to your dairy than do clinical cases of milk fever (Oetzel, 2011).
- Even herds with successful anionic salts programs and minimal cases of clinical milk fever will benefit from strategic use of oral calcium supplements (Oetzel, unpublished data, 2012).

The start of each new lactation challenges a dairy cow's ability to maintain normal blood calcium concentrations. Milk (including colostrum) is very rich in calcium, and cows must quickly shift their priorities to adjust for this sudden calcium outflow. 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) (Goff, 2008, Kimura et al., 2006).

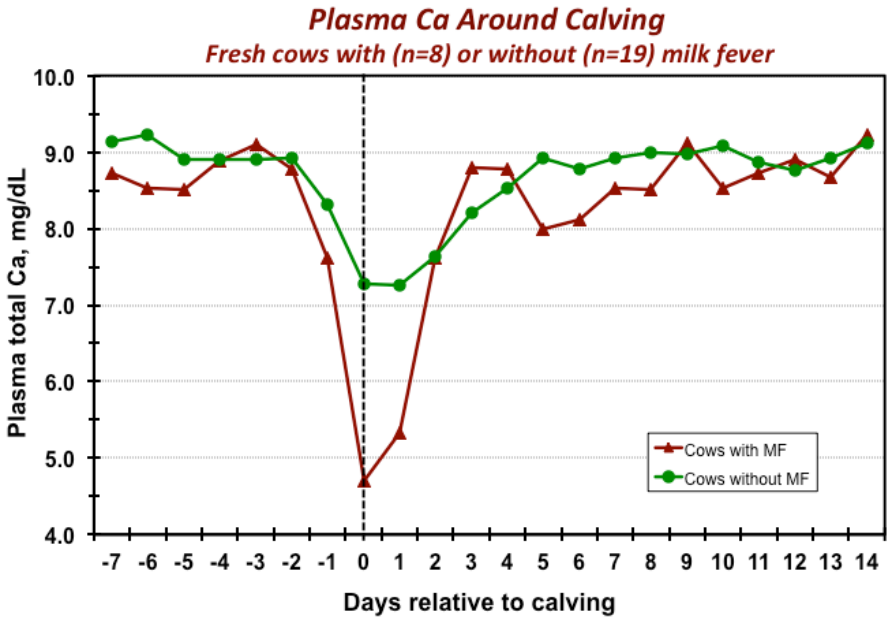

Figure 1. Plasma concentrations of total calcium before and after calving in mature Jersey cows with or without clinical milk fever (Kimura et al., 2006).

Subclinical Hypocalcemia Overview. 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 (Goff, 2008, Oetzel, 2011). This happens because blood calcium is essential for muscle and nerve function -

particularly functions that support skeletal muscle strength and gastro-intestinal 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 (Goff, 2008). This is illustrated in Figure 2.

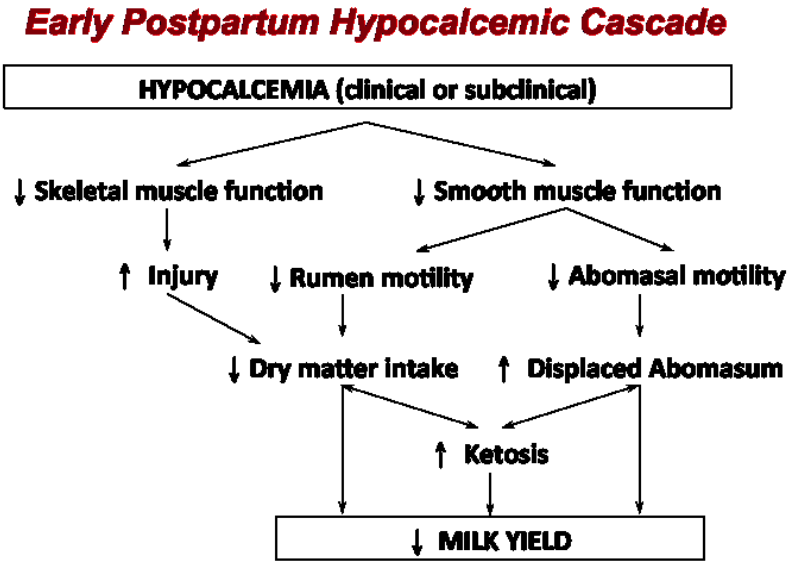

Figure 2. Proposed mechanisms for reduction in milk yield in early lactation cows due to hypocalcemia.

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% (Oetzel, 2004).

Subclinical hypocalcemia is more costly than clinical milk fever because it affects a much higher percentage of cows in the herd (Oetzel, 2011). 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 (Guard, 1996), 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 4 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 (Chapinal et al., 2012) and increased risk for displaced abomasum (Chapinal et al., 2011). These studies also demonstrated that the cutpoint for serum total calcium is higher (about 8.5 mg/dl) than was previously assumed (see 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 (Oetzel, 2011).

Some cows become hypocalcemic at times other than calving and exhibit clinical signs similar to those described above for Stage I milk fever. Such non-parturient hypocalcemias are often triggered by periods of unusual stress or decreased dry matter intake. This condition is most commonly seen in

cows in the first 2 to 10 days of lactation, cows that are in heat, cows with severe digestive upsets, or cows suffering from severe (toxic) mastitis (Oetzel, 2011).

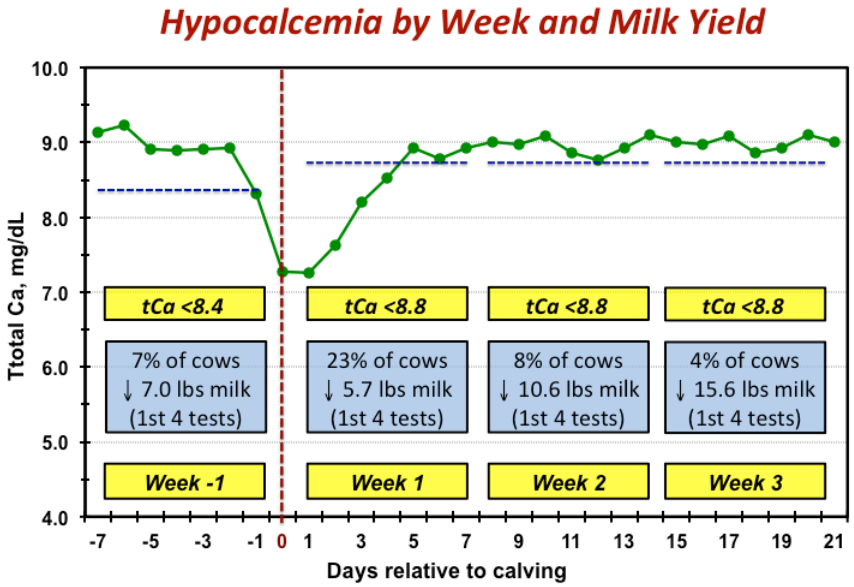

Figure 3. Effect of serum total calcium on milk yield for the first 4 DHI tests after calving. Different cutpoints were derived for serum samples collected on weeks -1, 1, 2, and 3 after calving. Data are from 2,365 cows in 55 Holstein herds in Canada and the US (Chapinal et al., 2012) .

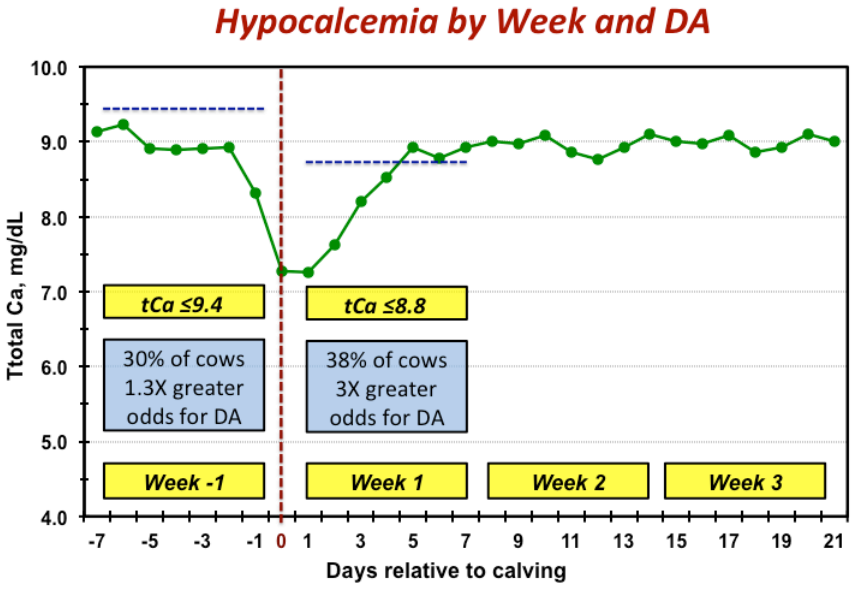

Figure 4. Effect of serum total calcium on the odds for displaced abomasum after calving. Different cutpoints were derived for serum samples collected on weeks -1, 1, 2, and 3 after calving. Data are from 2,365 cows in 55 Holstein herds in Canada and the US (Chapinal et al., 2011).

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 (Oetzel, 2011). Cows absorb an effective amount of calcium into her bloodstream within about 30 minutes of supplementation. Blood calcium concentrations are supported for only about four to six hours afterwards (Goff and Horst, 1993, 1994) for most forms of oral calcium supplementation.

Intravenous (IV) calcium is not recommended for treating cows that are still standing (Oetzel, 2011). Treatment with IV calcium rapidly increases blood calcium concentrations to extremely high and potentially dangerous levels (Goff, 1999). 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 (Oetzel, 2011). Cows treated with IV calcium often suffer a hypocalcemic relapse 12 to 18 hours later (Curtis et al., 1978, Thilsing-Hansen et al., 2002). The problems with IV calcium treatment are illustrated in Figure 5.

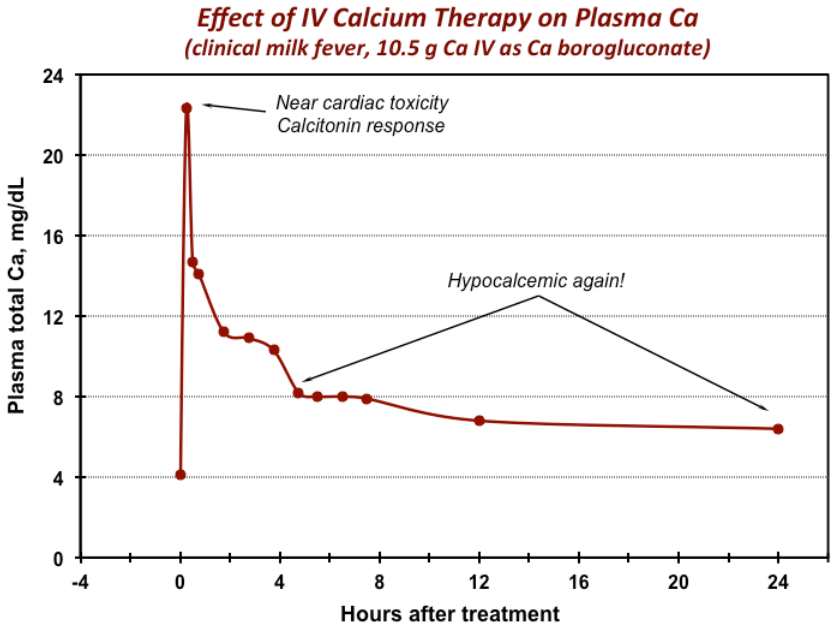

Figure 5. Effect of IV calcium treatment with 10.8 g of elemental calcium on serum total calcium concentrations in a mature Jersey cow with clinical milk fever (Goff, 1999).

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 (Oetzel, 2011).

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 (Doze et al., 2008). 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 to swallow, followed by a second oral supplement about 12 hours later (Oetzel, 2011, Thilsing-Hansen et al., 2002).

Transient hypocalcemia can occur in cows whenever they go off feed or have periods of decreased intestinal motility (DeGaris and Lean, 2008). 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, Huber et al. (1981) noted that 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 (Oetzel, unpublished data, 2012). 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 (Oetzel, unpublished data, 2012). These cows gave 6.8 lbs 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 (Goff and Horst, 1993, 1994). 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.

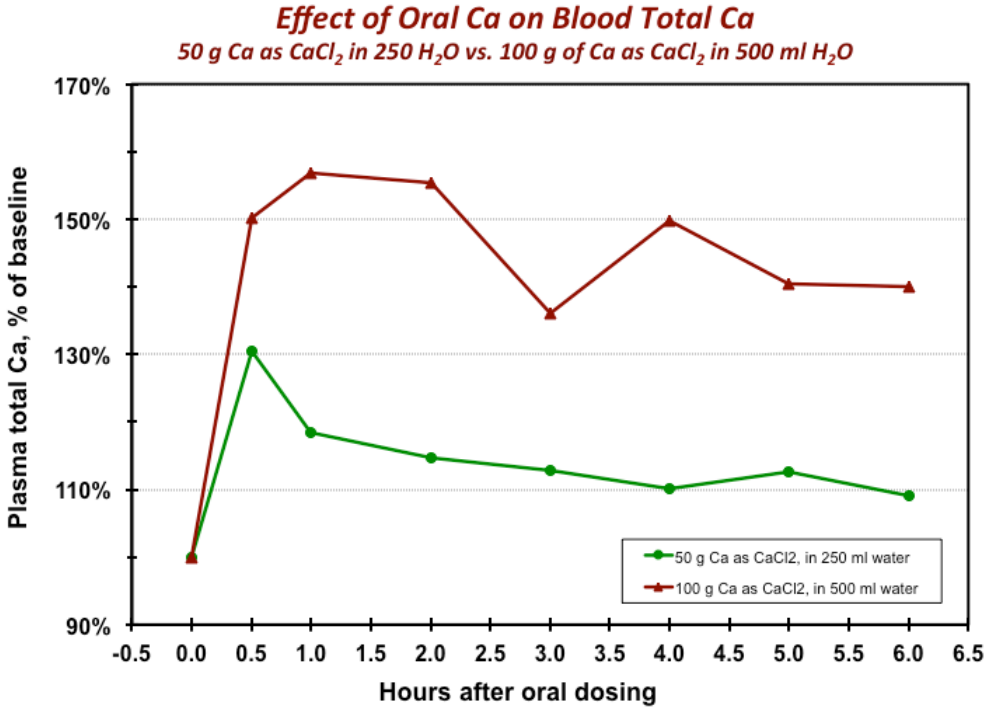

Figure 6. Effect of two different doses of oral calcium chloride on plasma total calcium concentrations, expressed as percent of baseline values (Goff and Horst, 1993).

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 - see Figure 7). Calcium propionate has the property of being glucogenic as well as providing supplemental calcium.

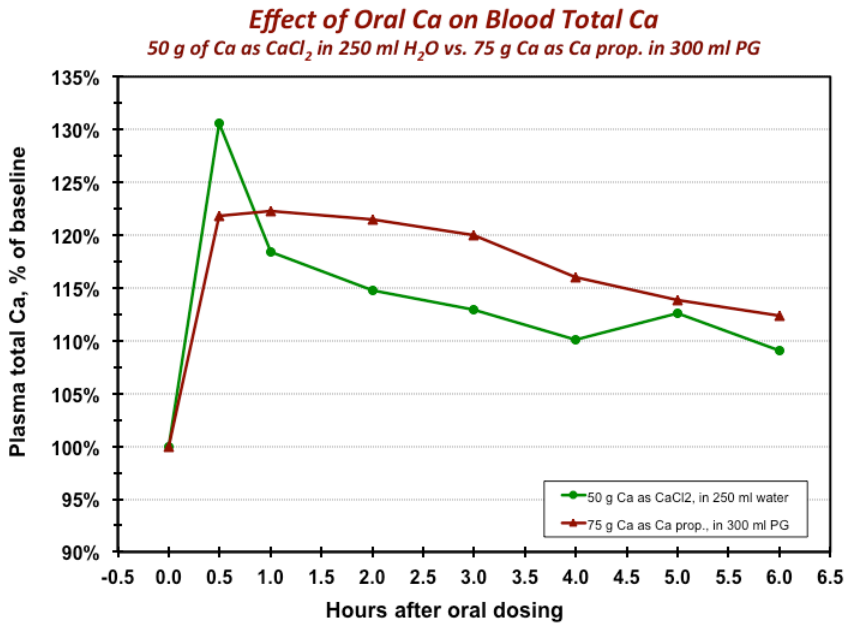

Figure 7. Effect of oral calcium chloride and oral calcium propionate on plasma total calcium concentrations, expressed as percent of baseline values (Goff and Horst, 1993, 1994).

Calcium carbonate in water did not increase blood calcium concentrations at all (see Figure 8) (Goff and Horst, 1993). This may be explained by its poorer bioavailability and by the alkalogenic response it can invoke.

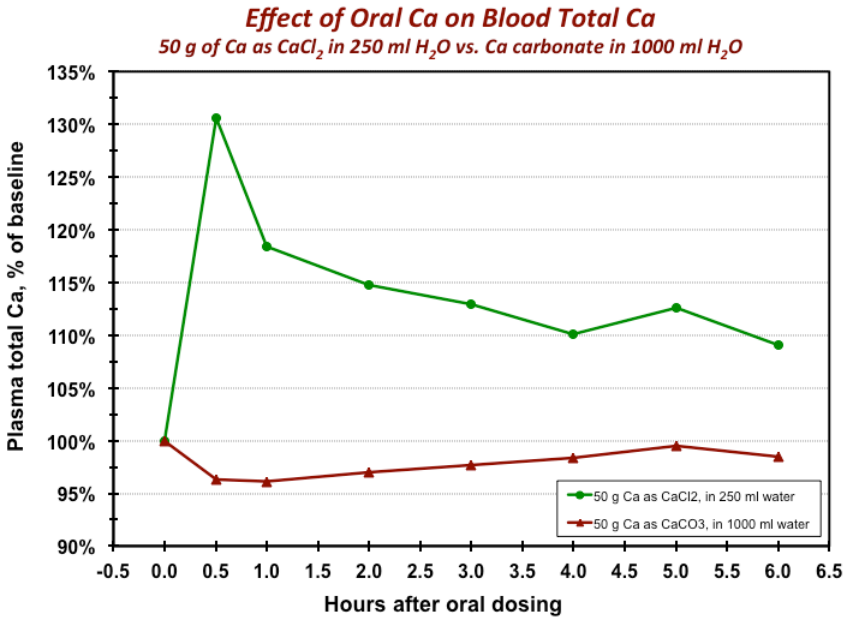

Figure 8. Effect of oral calcium chloride and oral calcium carbonate on plasma total calcium concentrations, expressed as percent of baseline values (Goff and Horst, 1993).

A combination of calcium chloride and calcium sulfate delivered in a fat-coated bolus (Bovikalc®, Boehringer Ingelheim Vetmedica, St. Joseph, MO) resulted in more sustained improvements in blood calcium concentrations (see Figure 9) than were observed in previous studies with oral calcium chloride or calcium propionate in water (Sampson et al., 2009). According to Pehrson and Jonsson (1991), 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. These workers reported a 4-fold reduction in the odds for developing clinical milk fever in cows that were supplemented with 4 boluses around calving (Pehrson and Jonsson, 1991).

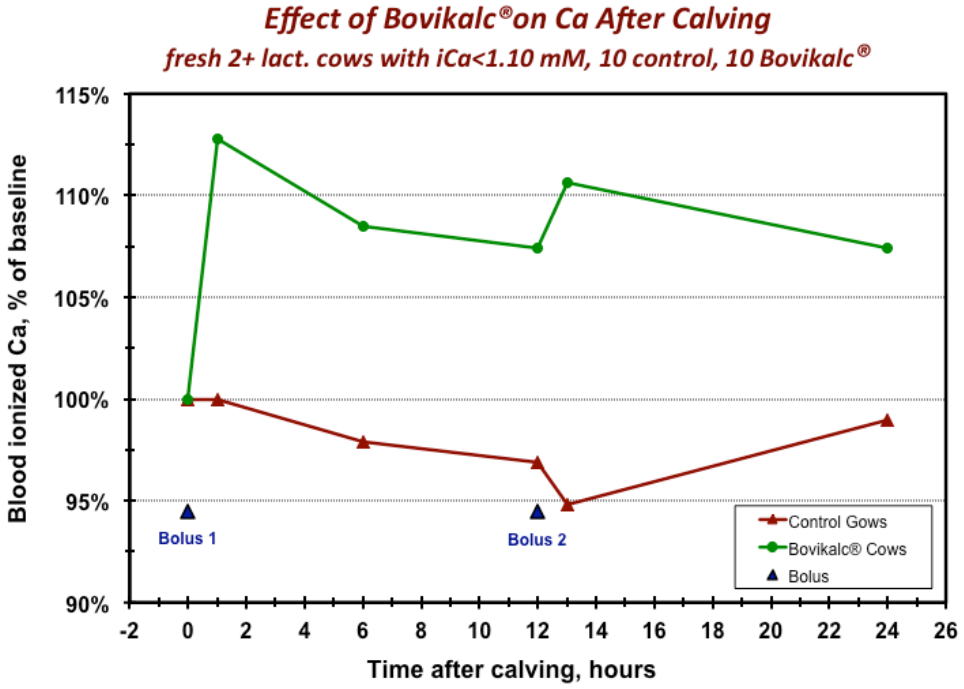

Figure 9. Effect of administration of two Bovikalc® boluses on blood ionized calcium concentrations (expressed as percent of baseline) t calving and 12 hours later. Experimental animals were Holstein cows (n=20) with hypocalcemia at calving (Sampson et al., 2009).

Subcutaneous Calcium Treatment. Subcutaneous calcium can be used to support blood calcium concentrations around calving, but has substantial limitations (Goff, 1999). 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 6 hours (see Figures 10 and 11) (Goff, 1999). Thus, repeat doses would be necessary to equal the sustained blood calcium support that is possible with oral calcium boluses.

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 calving and a second dose the next day. The expected nadir in blood calcium concentrations occurs between 12 and 24 hours after calving (see Figure 12) (Goff, 2008, Sampson et al., 2009). 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 4 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 at cow was in fact about 12 hours from expected calving, and many cows calved without receiving this dose (Oetzel,

1996). 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.

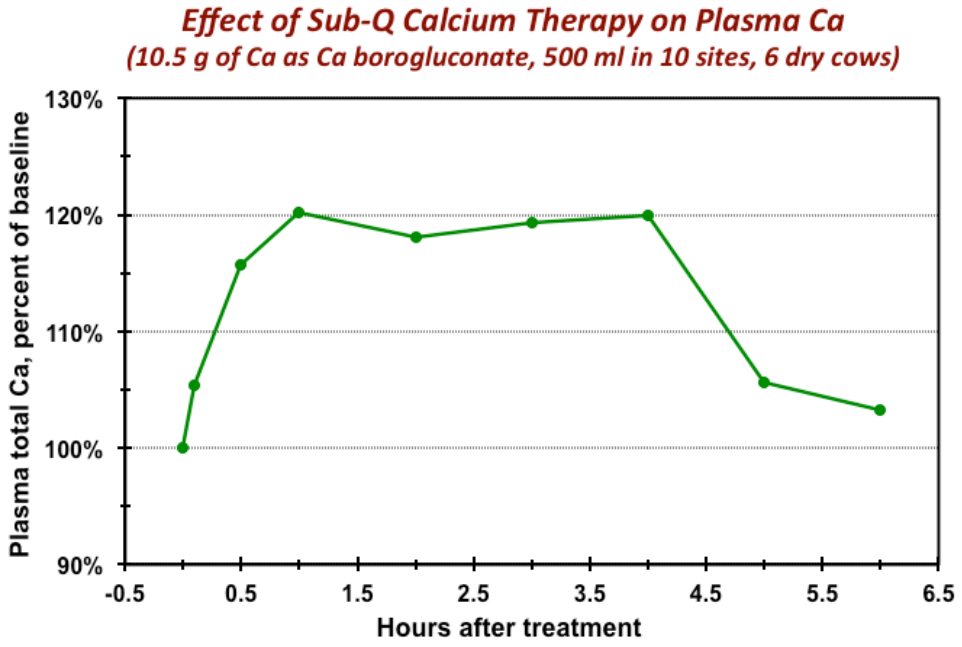

Figure 10. Effect of subcutaneous administration of 500 ml of 23% calcium gluconate on plasma total calcium, expressed as percent of baseline. The 500 ml solution was divided into 10 different sites (Goff, 1999).

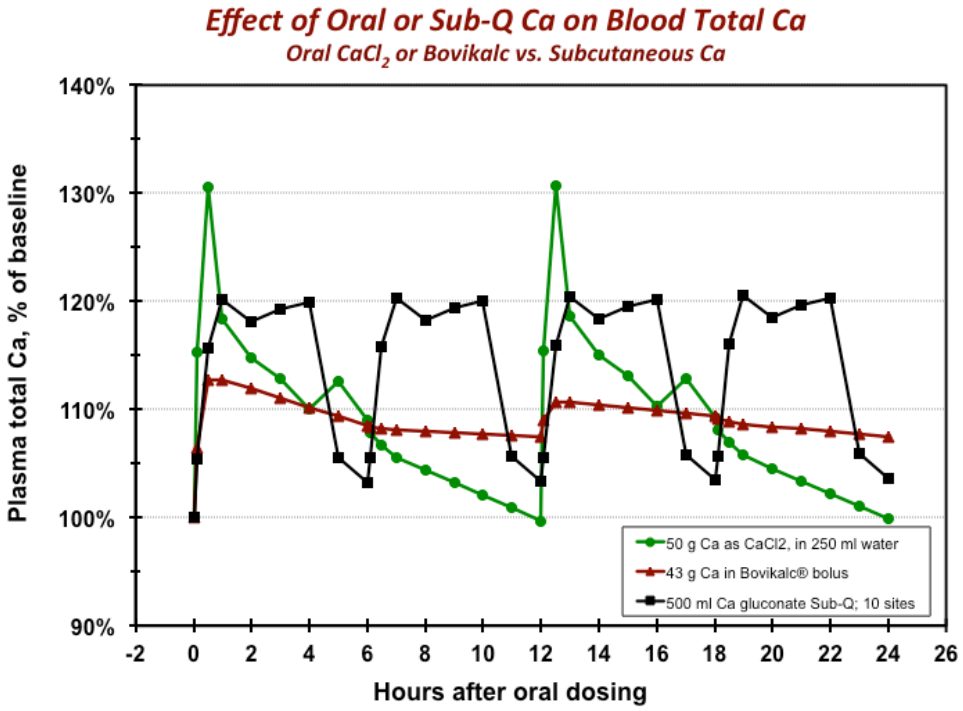

Figure 11. Effect of subcutaneous administration of 500 ml of 23% calcium gluconate 4 times vs. oral administration of 50 g of elemental calcium from calcium chloride 2 times vs. oral administration of a Bovikalc® 2 times on calcium concentrations, expressed as percent of baseline. Data are from (Goff, 1999, Goff and Horst, 1993, Sampson et al., 2009).

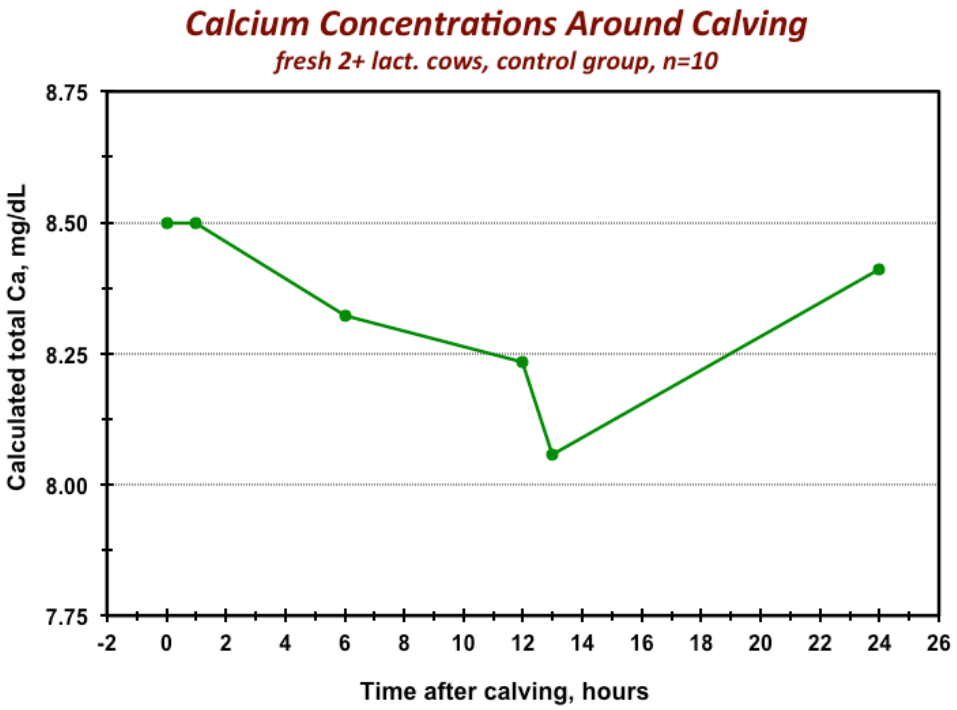

Figure 12. Blood total calcium concentrations (extrapolated from ionized calcium results) from 10 control cows. Experimental animals were Holstein cows (n=10) with hypocalcemia at calving. The nadir in calcium concentrations occurs sometime between 121 and 24 hours after calving (Sampson et al., 2009).

Milk Fever Prevention - Dietary Calcium Restriction. The traditional method of preventing milk fever has been to restrict calcium intake during the dry period. If extremely low calcium diets (< 20 grams of daily calcium) are fed before parturition and high-calcium diets are fed after parturition, the incidence of milk fever can be drastically reduced (Green et al., 1981). Low calcium diets prior to calving apparently prevent the cow's active intestinal calcium absorption and bone calcium resorption mechanisms from becoming quiescent and unable to respond to the sudden calcium outflow that occurs at parturition. Calcium intake during the dry period is usually restricted by replacing some or all of the alfalfa in a dry cow diet with a grass hay and using additional corn silage and concentrates. This approach can work in some dairy herds. If milk fever (clinical and subclinical) is not a problem in a herd and this feeding program is being used, then it probably should not be changed.

Milk Fever Prevention - Dietary Acidification. Dietary acidity or alkalinity is more important in controlling milk fever than calcium intake. The use of diets low in dietary cation-anion difference (DCAD) to prevent milk fever has been extensively studied and reviewed (DeGaris and Lean, 2008). In short, a large meta-analysis (Charbonneau et al., 2006) demonstrated that reducing pre-fresh DCAD by 300 meq/kg of diet dry matter (a typical approach) reduced the odds for clinical milk fever 5.1-fold, reduced urinary pH from 8.1 to 7.0, and reduced dry matter intake by 11.3%. It is important to implement a low DCAD strategy only in herds that already have good intakes in the pre-fresh group and can withstand an 11% intake reduction.

Despite the expected decrease in pre-fresh dry matter intake, post-fresh intakes are generally improved when low DCAD diets are fed (Eppard et al., 1996, Joyce et al., 1997). Beede et al. (1992) reported increased milk yield (3.6% more ME milk) when low DCAD diets are fed.

Milk Fever Prevention - Dietary Magnesium. **M**agnesium also plays an important role in maintaining calcium homeostasis around calving (DeGaris and Lean, 2008). A large meta-analysis

(Lean et al., 2006) found that increasing dietary magnesium greatly reduced the odds for clinical milk fever. Magnesium is known to participate in calcium homeostasis via release of parathyroid hormone and the synthesis of the active form of vitamin D (1,25 dihydroxycholecalciferol). Total intakes of about 40 to 50 grams of dietary Mg (about 0.30 to 0.45% of diet dry matter, depending on total dry matter intake) have been suggested (DeGaris and Lean, 2008), although this is complicated because of the interactions between other dietary factors such as DCAD, dietary calcium, and dietary phosphorus.

Milk Fever Prevention - Controlling Body Condition Score. Over-conditioned cows (body condition score >3.5, using a 1 to 5 scale) had 3.3X greater odds of clinical milk fever compared to cows that were not over-conditioned (Heuer et al., 1999).

II. Magnesium Disorders - Grass Tetany and Subclinical Hypomagnesemia

Acute Hypomagnesemia (Grass Tetany). Grass tetany is a relatively rare disorder in dairy cattle. It is most likely to occur in lactating cows consuming lush, succulent grass pastures. These pastures contain less magnesium than found in more mature grass pastures. The incidence of grass tetany may rise as more herds adopt rotational grazing strategies. Prevention of grass tetany is usually not challenging, as it requires only adequate supplementation of magnesium in the diet. If grazing herds consume some concentrates, it is not difficult to supplement those concentrates with adequate magnesium. It is difficult to deliver supplemental magnesium to cattle on pasture that are not receiving supplemental concentrates.

Hypomagnesemia may also be related to excessively high dietary potassium relative to magnesium, because high potassium inhibits ruminal absorption of magnesium (Martens and Schweigel, 2000). Ideal K:Mg ratio for pre-fresh dry cows is less than 4:1. Some areas (e.g., north central Wisconsin) have soil types that tend to lead to high potassium / low magnesium forages. In these situations, it may be necessary to increase dietary magnesium concentrations to .40% or higher by adding extra magnesium oxide to the diet.

Hypomagnesemia is often accompanied by hypocalcemia and hypophosphatemia, which can make treatment complicated. Intravenous treatment should provide about 2 to 3 grams of elemental magnesium and is given in conjunction with intravenous calcium. Subcutaneous administration of 200 to 400 ml of a 25% magnesium sulfate solution is often more practical in cows that are convulsive.

Subclinical hypomagnesemia. Subclinical hypomagnesemia is poorly understood but may be fairly common in dairy cattle. Subclinical hypomagnesemia may be an important trigger for non-parturient hypocalcemia in lactating dairy cows. Oral supplementation with 200 to 400 ml of a 50% magnesium sulfate solution (100 to 200 grams of magnesium sulfate) can be used when subclinical hypomagnesemia is suspected. Fresh cow drench formulations often provide about 200 grams of magnesium sulfate per dose and are pumped with about 5 gallons of water.

III. Phosphorus Disorders - Hypophosphatemia

Most cases of clinical milk fever have some degree of hypophosphatemia with the hypocalcemia. This hypophosphatemia occurs because elevations in PTH cause phosphorus loss via saliva and urine. Normal blood phosphorus concentrations are usually restored when the hypocalcemia is corrected with supplemental calcium alone – supplemental phosphorus is not typically required. Restoring normocalcemia halts the PTH secretion and phosphorus loss and increases gastro-intestinal motility, which allows for absorption of the phosphorus lost via the saliva (Goff, 1999, 2006).

Some cows are unable to restore normal blood phosphorus concentrations, even after blood calcium has been corrected and stabilized. Reasons for this are unknown. Whether or not

hypophosphatemia causes clinical signs in peripartum cows is unclear and controversial. Treating the hypophosphatemia is prudent, as long as it is not done at the exclusion of other treatments or with a high expectation of success. Treatment could be intravenous administration of an available source of phosphorus (e.g., 23 g of sodium monophosphate dissolved in 1 liter of saline) or by oral phosphorus supplementation such as 200 grams of sodium monophosphate in about 2 gallons of warm water (Goff, 1999, 2006). Hypophosphite sources of phosphorus are unavailable to the cow and are of no value in treating hypophosphatemia (Goff, 1999).

There is no specific nutritional prevention for hypophosphatemia. The best actions are to prevent hypocalcemia and to make sure that there is adequate phosphorus in the pre- and post-fresh diets (although this is an extremely rare situation). Increasing phosphorus in the pre-calving diets increases the risk for milk fever and ultimately for hypophosphatemia (Lean et al., 2006).

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