Student Clinical Paper

A Review of Methods Used in the Prevention of Milk Fever in Dairy Cows

Michael Coe, *B.S.*
Class of 1993, Kansas State University
College of Veterinary Medicine
Manhattan, KS

Introduction

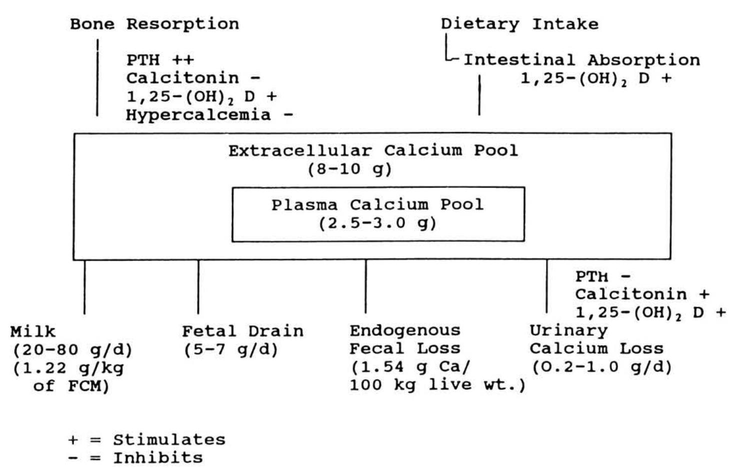
Hypocalcemic periparturient paresis (milk fever) is a significant economic problem in dairy and beef cows[1]. There are many hypotheses for the development of milk fever which include inadequate hormone production, lost ability to respond to calcium regulatory hormones (i.e., decline in intestinal hormone receptors),[2] and dietary factors such as calcium level and balance of the diet. Clinical or subclinical hypocalcemia increases the risk of secondary disorders such as decreased milk production, retained placenta, mastitis, metritis, left displaced abomasum and uterine prolapse. [3,4] For these reasons prevention is very important. Several methods of milk fever prevention are available each having specific advantages and disadvantages with no one method being effective or appropriate in all situations. The goal of this paper is to briefly review calcium homeostasis, to present four methods of prevention of milk fever and to discuss advantages, disadvantages and mode of action of each method.

Calcium Homeostasis and Lactational Demands for Calcium.

Bovine plasma calcium concentrations are normally maintained at 9-10 mg/dl. Paresis or clinical milk fever will occur if plasma calcium levels fall to ≥5-6 mg/dl.[2] Subclinical hypocalcemia is defined as any plasma calcium level below 9 mg/dl at which clinical signs are not seen. However, subclinical hypocalcemia will predispose the cow to the same secondary disorders as the cow clinically ill with milk fever.

In order to maintain a plasma calcium (Ca) level at 9-10 mg/dl the cow requires 25-30 g of absorbed Ca each day.[2] This daily maintenance requirement includes endogenous fecal loss which is approximately 1.54 g Ca/100 kg live weight, fetal calcium drain which ranges from 5-7 g Ca/day, and calcium drain of lactation which is approximately 1.22 g/kg of 4% fat-corrected milk. Holstein milk normally contains approximately .13% calcium. On the day of parturition, however, a dairy cow will produce 10 liters or more of colostrum containing ≥ .23% Ca. This is two fold higher than normal milk and nine times as much as the entire plasma calcium pool [5]. This explosively sudden change can overwhelm calcium homeostatic mechanisms. As a result most cases of milk fever occur within 24 hours after parturition.[5] Complicating this scenario is the low efficiency of absorption of dietary calcium. Only 38% of the dietary calcium available is actually absorbed and this efficiency decreases as cows age.[2] To meet their high calcium demand of lactation and overcome the relatively low efficiency of calcium absorption, bone must be mobilized. As much as 13% of bone mass is lost by the time cows reach peak lactation.[2]

Calcium homeostasis is regulated by parathyroid hormone (PTH), vitamin D_3, and calcitonin (Figure 1). PTH and vitamin D_3 both increase plasma calcium concentrations. PTH stimulates renal calcium resorption and causes bone resorption by increasing the number of osteoclasts as well as increasing osteoclastic activity. Vitamin D increases bone resorption by work-



Adapted from J. Dairy Sci. 74:4023 Fig. 1 (2)

Figure 1. Calcium Homeostasis

ing with PTH to stimulate osteoclastic activity. Vitamin D also stimulates increased calcium absorption from the intestine. Thus, plasma concentrations of 1,25-dihydroxyvitamin D are inversely correlated with plasma calcium concentration but directly related to plasma PTH concentration in all cows. Cows which suffer from recurring hypocalcemia and paresis after calving fail to produce as much 1,25-dihydroxyvitamin D as other milk fever cows.[5] On the other side of regulation, calcitonin is released from the thyroid gland to stimulate bone formation and to promote renal excretion of calcium. Thus calcitonin will decrease plasma calcium levels.

Prevention of Milk Fever.

Four different approaches have been used to prevent milk fever: (1) restriction of calcium prepartum, (2) peroral calcium supplements, (3) injection of 1-α-hydroxyvitamin D_3 plus 25-hydroxyvitamin D_3 and (4) manipulation of the dietary cation-anion electrolyte balance during late pregnancy.

(1) *Calcium restricted prepartum diet.* This is the traditional method of milk fever prevention and consists providing a diet very restricted in calcium to cows in late gestation. Dietary calcium level must be at or below 30 grams/day to be effective. The rationale to this approach is that feeding a low calcium diet prepartum will stimulate PTH secretion and 1,25-dihydroxyvitamin D production prior to parturition. These in turn will activate calcium transport mechanisms in bone and the intestine which are needed to adapt to the lactational calcium demand. This method of prevention is well accepted by dairy producers. However, it is difficult to achieve[6] and does not always work in situations where the choice of feedstuffs are limited and a high quality, low calcium diet cannot be formulated. Fortunately we have options to feeding calcium restricted diets to our close up dry cows which may well provide a more complete prevention program.

(2) *Oral calcium supplements.* In this approach, milk fever is prevented by oral administration of Ca-salts. This method is dependent on providing high levels of calcium to the cow at the time of peak demand. These calcium supplements usually contain calcium chloride ($CaCl_2 \bullet 2H_2O$) which can have an irritative effect on the mucosa of the oral pharynx, esophagus and rumen. Three such calcium supplements are available for use. They are: Ca-oil (200 g $CaCl_2 \bullet 2H_2O$ emulsified in 380 g soybean oil and 200 g water plus 20 g aroma-mixture), Ca-capsule (126 g $CaCl_2 \bullet 2H_2O$, 45 g $CaSO_4$, 7 g $MgCl_2$ and 2 g calcium stearate, covered with 10 g animal fat) and Ca-gel (200 g $CaCl_2 \bullet 2H_2O$ in a hydroxyethylcellulose-gel).[7]

The efficacy of oral administration of calcium supplements was demonstrated in a study by Pehrson and Jonsson.[8] Their treatments included a preparation of CaCl2-hydroxycellulose formulated with 54 g Ca per dose, a Ca-capsule that contained 46 g calcium as $CaCl_2$ and $CaSO_4$, and a placebo capsule containing sand. The prophylactic effect on milk fever by repeated (daily) oral administration of these calcium salts preparations just prior to and soon after parturition was similar for both products showing a 50% reduction of milk fever in those cows effected during their previous lactation.[8] Pehrson and Jonsson suggested that of these treatments the Ca-capsule held an advantage since the risk of aspiration was eliminated and the sharp taste of the calcium salts was masked.[8] A disadvantage of the Ca-gel treatment is that the unpleasant taste and irritative effect of the salt can elicit struggling efforts from the cow at administration. Any complications from laryngeal trauma would be aggravated by the presence of $CaCl_2$ in the lesion. Thus, extreme care must be taken when administering this type of product.

An example of the irritative effect of calcium chloride on the mucosa of the oral pharynx and esophagus was demonstrated by a case presented to Kansas State University Veterinary Medical Teaching Hospital in January, 1992. The case involved two fresh cows with a history of respiratory distress, coliform mastitis, scours after calving and successful treatment of clinical hypocalcemia. An oral calcium gel product had been used by the owner to treat both cows. One cow also suffered from epistaxis, an intermandibular swelling and black feces. Both were euthanized and necropsied. Necropsy revealed retropharyngeal abscesses in both animals that had eroded into an artery in one cow. Both cows had peritoneal adhesions in the right paralumbar fossa apparently caused by intraperitoneal administration of calcium. Some residual calcium gel also was observed in the retropharyngeal space in one cow. It was concluded that the calcium gel product had been improperly administered by the owners. The cows' struggling upon administration and the salts' irritating effect on the injured areas negated the otherwise effective use of the calcium gel product to treat clinical hypocalcemia. Thus, client education on proper administration of these products is very important.

Even when properly delivered into the rumen, peroral calcium supplementation is not without its drawbacks. The most common is reduced feed intake after administration. Investigators have attempted to determine the cause for the reduced intake. In one experiment two Ca-supplements were compared. Both showed an irritative and ulcerogenic effect on the rumen wall and all cows suffered reduced feed intake after treatment.[7] After the trial, these investigators suggested several mechanisms for the observed reduction in feed intake which included increased osmotic pressure, the effect of unsaturated fatty acids (oil from the preparation) on rumen function and etching of the rumen wall.[7] Normal osmotic pressure of the rumen in a fasted animal is 240-280 mOsmol/l. This value increases to 350-420 mOsmol/l 2-3 hours post-feeding then gradually returns to normal 5-9 hours later.[7] Above 350 mOsmol/l there is an increasingly negative effect on feed intake.[9] If the rumen has a nominal volume of 80 liters the increase after a single dose of Ca-gel or Ca-oil will be about 50 mOsmol/l. One Ca-capsule will increase ruminal osmotic pressure by only 36 mOsmol/l because of its lower content of $CaCl_2$.[7] None of these preparations however, will increase ruminal osmotic pressure above its normal range. When unsaturated fatty acids (oils) are added to the rumen there may be a reduction in cellulolytic activity which may decrease fiber degradation and increase ruminal retention time.[7] These effects would be temporary however, and the rumen population would rapidly recover. Etching of the rumen wall by the calcium salt could occur if the epithelium had been previously damaged. Taken together, all these possible reasons for reduced feed intake attributed to administration of calcium-supplements may cause a temporary reduction (1 day) in feed intake on the order of 10-15% .[7] Overall this probably would not be significant.

(3) *Use of 1-α-hydroxyvitamin D_3 and 25-hydroxyvitamin D_3*. Hodnett *et al.* [10] demonstrated that IM injection of a combination of 1-α-hydroxyvitamin D_3 and 25-hydroxyvitamin D_3 reduced parturient paresis in aged Holstein dairy cows fed a diet high in calcium. Before this many workers had confirmed that vitamin D_3 as the natural vitamin[11] or its synthetic analogs [12,13,14] are effective for the prevention of parturient paresis. For effective prevention these injected compounds must be converted to 1,25-dihydroxyvitamin D which stimulates intestinal calcium absorption and thus helps maintain plasma calcium levels.

The efficacy of intramuscular administration of vitamin D analogs was examined in a trail in which the prepartum diet of alfalfa silage and hay was supplemented with a grain mixture supplying 100 g of Ca/day from ground limestone (location#1). Total calcium intake was 270 g per day.[10] It was found that an intramuscular dose of .5 mg 1-α-hydroxyvitamin D_3 plus 4 mg 25-hydroxyvitamin D_3 increased plasma 1,25-dihydroxyvitamin D concentration through parturition.[10] This treatment raised prepartum plasma calcium approximately 2 mg/dl and plasma phosphorus was raised 4-5 mg/dl higher than untreated controls. The incidence of parturient paresis in location #1 was reduced from 33 to 8%.[10] Yet, at a different location (#2) with the same treatments, the incidence was not reduced. Hodnett *et al.*[10] suggested that a dramatically lower level of calcium in the prepartum diet at location #2, a typical dry cow diet as opposed to 270 g/day level at location #1 may have accounted for the difference in effectiveness of the treatment. A key point to understand is that an elevated level of absorbable calcium is needed to allow maximal 1,25-dihydroxyvitamin D-stimulated intestinal calcium absorption and hence, help maintain plasma calcium following parturition.[10]

One pitfall with the use of intramuscular injection of 25-hydroxyvitamin D_3 is that milk fever can still occur in treated cows if they calve within 3 days of the infection or after 10 days following infection. In other words, for full effectiveness parturition must occur within a 7-day window.[10] This requires good record-keeping by the producer. Complicating this is the fact that gestational lengths vary. For example, the gestation interval for bovine twins is 5 days shorter than for single calves.[15] The use of 1-α-hydroxyvitamin D_3, a synthetic analog of vitamin D_3 which is hydroxylated to 1,25-dihydroxyvitamin D in the liver, can overcome part of this dilemma. This compound is effective in preventing milk fever from about 24 h to 4 d following administration.[10] Thus, a combination of the natural vitamin D and a synthetic analog provides a wider window and allows more flexibility to this form of prevention. Disadvantages are that two or more intramuscular infections can be involved and that vitamin D_3 can be toxic at $15x10^6$ IU (375 mg).[16] Toxicity is therefore not likely, however clinical manifestations of vitamin D toxicity include[16] severe anorexia, pasty discharge about the eyes and flaccid udders. When near death affected animals exhibit polypenia, rapid pounding pulse and ketosis. The cows also are weak, recumbent and often show a febrile response.

(4) *Dietary cation-anion electrolyte balance.* Dietary cation-anion difference (DCAD) or dietary electrolyte balance is an approach now being used in dairy cattle nutrition.[17,18] The goal is to alter the metabolic environment in the prepartum cow to allow increased bone calcium mobilization and increased absorption of dietary calcium. Dietary electrolytes are balanced according to the changes they contain. The minerals considered in the electrolyte balancing are usually sodium, potassium, chlorine and sulfur.[17] The most commonly used expressions to calculate DCAD are meq [(Na+K)-Cl] /100 g or meq (Na+K)-(Cl+S).[3,5,19,20] Common sources of anionic (negatively charged) salts are ammonium chloride (NH_4Cl), ammonium sulfate [$(NH_4)_2SO_4$], calcium sulfate ($CaSO_4 \bullet 2H_2O$), calcium chloride ($CaCl_2$), and magnesium sulfate (epsom salts; $MgSO_4 \bullet 7H_2O$). Oetzel *et al.*[20] found that of six anionic salts tested (five of those listed above), all exhibited a similar potential to affect the animal's systemic acid-base balance. Further, all the salts had similar effects on urinary excretion of calcium and all were equally palatable.[20] When selecting these salts, however, keep in mind that sulfur should not exceed .35% of dietary dry matter.[21] A recommended level of feeding of these compounds is about 200 grams of a combination with about 40-50% as ammonium

chloride.[17] Although it is theoretically possible to feed anionic salts containing ammonium at a level that is potentially toxic, it is not likely because of their poor palatability.[22]

Field studies have indicated no difficulties in feeding 150 to 200 g Ca/cow/day if anionic (acidogenic) agents are supplemented properly .[19] Oetzel *et al.*[22] suggested that cows be started on the diet slowly, increasing the amount of anionic salts over a period of 6 days beginning three weeks prior to expected calving. If palatability reduces intake, adding the salts to a total mixed ration effectively hides their unpleasant taste. Other means of increasing palatability of these salts is to include them in distillers grains, molasses, flavoring agents and/or by pelleting them with carriers. Farmland Industries currently has two anionic dry-period formulations: "Farmland Dry Opti-Tech Anion Pack" and "Farmland Dry Opti-Tech 20 Anion Complete". The Anion Pack is intended to be fed at 1 lb/day added to a total mixed ration or added to at least 10 lb of grain mix, whereas the Anion Complete is formulated to be fed at 8 lb/day and can be topdressed. Both formulations should be fed the last 2 to 3 weeks of the dry-period (Farmland Industries, Inc., Kansas City, MO 64116).

The mechanism of action by which dietary cation-anion difference or dietary electrolyte balance prevents milk fever appears to be through an effect on systemic acid-base status. As presently understood, cows fed diets formulated with a negative DCAD value (i.e., high in anionic salts) in late pregnancy develop a mild metabolic acidosis[19,23] which causes mobilization of calcium from bone.[19,23] This was shown by Moore who examined the effects of pH on ionized calcium (iCa) concentration in human blood in vitro over a pH range of 6.8 to 7.8. He found instantaneous and completely reversible changes in iCa concentrations.[23] Blood concentrations of iCa increased in a linear or slightly sigmoidal fashion with decreasing pH, which may be due to competition between calcium and H^+ for binding sites on plasma proteins.[9] Supplementation of ammonium salts resulted in an increased input of iCa into the blood calcium pool.[23] However, in addition to the simple dissociation of protein-bound calcium, total input of iCa into blood calcium depended mainly on calcium absorbed from the intestine and calcium mobilized from bone.[23]

In another study, Beede and Wang[23] conducted a study in which eight nonpregnant, nonlactating Jersey cows were used to determine the effects of ammonium chloride and sulfate on acid-base status and calcium metabolism. Calcium homeostasis was challenged by infusing the cows with Na_2-EDTA to induce hypocalcemia. They found that cows fed the treatment diet (98 g NH_4Cl and 98 g $(NH_4)_2SO_4$/cow/day) had lower blood pH, higher ionized calcium in blood, and more urinary excretion of calcium, titratable acid, and ammonium than cows fed the control diet. Cows fed the treatment diet had greater quantities of ionized calcium in the blood and also recovered faster after receiving an equal amount of Na_2-EDTA (an ion chelator) than did the control cows. The authors concluded that supplementation with NH_4Cl and $(NH_4)_2SO_4$ induced a subclinical metabolic acidosis which improved the cow's ability to maintain blood iCa and plasma total calcium concentrations close to normal when the demand for calcium was increased suddenly by Na_2-EDTA infusion.[23]

Beede *et al.*[19] reported the results from a large field experiment in which the effects of feeding an anionic diet (-25 meq/100 g DM) were compared to feeding a slightly cationic diet (+5 meq/100 g DM) diet during the late prepartum period. The anionic diet contained 108 g NH_4Cl, 53 g $(NH_4)_2SO_4$ and 34 g $MgSO_4 \bullet 7H_2O$ per cow per day. The cationic diet which contained the same basal ingredients except it had slightly less Ca and Cl and more sulfur. Both diets were balanced according to NRC requirements for dry cows.[4] Results showed that plasma concentrations of iCa (4.31 versus 3.80 mg/dl) and total plasma calcium (7.94 versus 7.10 mg/dl) were higher for cows fed the anionic diet than the cationic diet. Milk yield was 3.16% percent greater for cows fed the anionic diet compared with cows fed the cationic one. They also found reproductive performance improved in cows fed the anionic diet. This was determined by quantifying pregnancy rates at 100, 150, 200, and 250 days postpartum, services per conception, average days to first service and average days open for pregnant cows.[23]

It has been observed that addition of chloride to a prepartum diet high in cations increases the 1,25-dihydroxyvitamin D response to hypocalcemia.[5] From this angle, Goff *et al.*[5] looked at the effects of both a highly cationic diet (+978 meq/kg of DM) and a highly anionic diet (-228 meq/kg of DM) on 1,25-dihydroxyvitamin D, parathyroid hormone, and plasma hydroxyproline concentration. Hydroxyproline is an amino acid unique to collagen released during bone resorption thus a good index of bone resorption activity. They found that cows fed the cationic diet had significantly lower plasma calcium concentrations on the day of and 2 days after calving compared with those fed the anionic diet prepartum.[5] Since renal 1-α-hydroxylation of 25-hydroxyvitamin D should have been stimulated to the same degree in both groups, they expected secretion of PTH in response to hypocalcemia in cows fed the cationic diet to be similar to that in cows fed the anionic diet.[5] They found that this was not the case however, and suggested that the kidneys were temporarily refractory to PTH stimulation. In addition, the study showed that plasma hydroxyproline concentration was greater in cows fed the anionic diet and that its concentration tended to increase during the week prior to parturition indicating increased bone resorption. In cows fed the cationic diet plasma hydroxyproline concentrations tended to decrease just prior to parturition indicating decreased bone resorption.[5] This evidence suggested that cows fed highly cationic diets are less responsive to PTH than those fed highly anionic diets where the stimulatory effects of PTH are enhanced during a subsequent metabolic acidosis. It was concluded that cationic diets decrease the ability of both bone and renal tissues to respond to PTH stimulation.[5]

Other work by Vagg and Payne[24] showed that a small calcium pool exists in solution in fluids surrounding bone cells which is readily exchangeable with the blood calcium pool. They estimated this pool in an adult cow to contain 6-10 g of calcium. In addition, this readily exchangeable bone fluid calcium pool can be increased 5-6 g by feeding ammonium chloride to induce metabolic acidosis, which would assist in prevention of milk fever.[24]

Maintaining proper cation-anion balance throughout the lactation and dry periods is important to maximize the cow's productivity. To prevent milk fever in periparturient cows, an anionic diet is fed. To increase milk production during lactation a slightly cationic diet is fed. In other words, dry cows respond to a negatively-balanced DCAD ration, whereas lactating cows seem to respond more to a positively-balanced DCAD ration. Thus it is necessary to balance electrolytes according to the cows' needs. Related research[25,26] indicates that lactating cows fed a ration containing approximately +20 meq per 100 g DM produced 1.5 to 2.9 kg/d more milk than cows receiving a cation-anion balanced ration of about -13 meq per 100 g of DM.

One method by which to monitor if adequate levels of anionic salts are being provided is to check urine pH. Normal ruminant urine pH is alkaline, averaging 8.2. Once a slight metabolic acidosis has been initiated, urine pH will decrease about one unit. In one study, during the week prior to parturition urine pH averaged 7.2 in cows fed an anionic diet and 8.3 in those fed a cationic diet.[5]

Current information indicates that addition of anions to reduce the excess cation balance of prepartum diets can increase tissue response to parathyroid hormone and enable the cow to better adapt to the calcium demands of lactation. In practice the first attempt to reduce the alkalinity of the prepartum diet should be accomplished by removing sources of defined cations.[17] One such example are buffers used in the lactating cow ration which are cations. In addition, anionic diets may enhance absorption of calcium from the gut but only when calcium intake is high.[23] Thus, when using anionic salts to lower the alkalinity of the prepartum diet as a means of milk fever prevention it is important to remember to provide an adequate level of dietary calcium. It has been indicated that 150-200 g/Ca/cow/day can be supplemented if anionic salts are also supplemented properly.[19]

Since milk yield can be improved by more than 3% and that reproductive performance also can be improved in cows fed an anionic diet the late prepartum period over that in cows fed a more traditional, calcium restricted diet, I feel that there is merit in determining the feasibility of using anionic salts in dairies where clinical milk fever is not a problem, but where subclinical hypocalcemia may be. Published studies to date have reported a wide range of negative anionic balance values. Specific guidelines and recommendations are not yet available, but some nutritionist are recommending a slightly negative cation-anion balanced ration in herds where milk fever is a problem. Studies are needed to determine the value needed to accomplish efficacy when using anionic salts to cause a metabolic acidosis.

I have summarized several experimental trials and field studies in Table 1 that illustrate the decrease incidence of milk fever when DCAD is considered and anionic salts are added to the dry cow ration. At locations A, B, C, and D there was a dramatic decrease in the percent incidence of milk fever. Even though location E did not have a large numerical decrease in percent incidence the incidence was still reduced by 50%.

Table 1: Incidence of milk fever and DCAD of each diet.[a]

Diet	Location (reference #)				
	A(25)	B (22)	C (3)	D (5)	E (19)
Control[b]	80 (+400)	75 (+258)	47 (+33)	26 (+978)	9 (+ 50)
Treatment[c]	33 (- 50)	10 (-103)	0 (- 13)	4 (-228)	4 (-250)

[a] Values in table are the percentage of cows with clinical milk fever. The value in parentheses is the DCAD is expressed as meq/kg/DM using the equation [(Na+K)-(S+Cl)]

[b] Control diets all had a positive anion-cation balance.

[c] Treatment diets all had added anionic salts and a calculated anion-cation balance close to or below zero.

The data in Table 1 indicate that the use of anionic salts in dry cow rations will be effective in most herds. However the degree of prevention will be highly variable depending on the current incidence of milk fever and management practices on the dairy. The greatest decrease in clinical milk fever will be seen in those herds with the most severe problems.

Conclusions

A major objective in prepartum cows is to reduce stress of parturition and the onset of lactation by preventing clinical and subclinical milk fever. Now we have options to feeding calcium restricted diets to our close up dry cows. The 3 options are oral calcium, vitamin D injections and the use of anionic salts. The method of administering oral calcium is dependent on providing high levels of calcium to the cow at the time of peak demand. However the need for repeated treatment requires that the cow be manipulated multiple times during an already stressful period. Intramuscular injection of vitamin D_3 reduces the incidence parturient paresis in dairy cows if fed a diet high in calcium. For full effectiveness, however, parturition must occur within a 7-day window of administration. Even with good record keeping it is likely that two or more injections will be required. The use of an anionic prepartum diet prevents milk fever by increasing intestinal absorption of calcium as well as increasing bone calcium resorption without the need for manipulation of the cow or repeated intramuscular injections. By using a cationic-anionic balance strategy the dairy cow's endocrine system has an opportunity to prepare the animal for the tremendous calcium drain of lactation. In that anionic salts are delivered in the feed, prevention of milk fever is accomplished in a non-invasive manner. Regardless of the method chosen for prevention of milk fever the benefits of reduction in milk fever related diseases as well as increase in milk production is economically significant to the dairy producer.

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Reference

1. Naylor, J.M., S.L. Ralston. (1991) Large Animal Clinical Nutrition. St. Louis, *Mosby-Yearbook*. p 24. 2. Goff, J.P., T. A. Reinhardt and R.L. Horst. 1991. Enzymes and factors controlling vitamin D metabolism and action in normal and milk fever cows. *J Dairy Sci.* 74:4022-4032. 3. Block, E. 1984. Manipulating dietary anions and cations for prepartum dairy cows to reduce incidence of milk fever. *J Dairy Sci.* 67:2939-2948. 4. Curtis, C.R., H. N. Erb, and G. J. Sniffen. 1983. Association of parturient hypocalcemia with periparturient disorders in Holstein cows. *J Am Vet Med Assoc.* 183:559. 5. Goff, J.P., R.L. Horst, G.A.Kiess, H.H. Dowlen, F.J. Mueller, and J.K.Miller. 1991. Addition of chloride to a prepartal diet high in cations increases 1, 25-Dihydroxyvitamin D Response to Hypocalcemia. *J Dairy Sci.* 74:3863-3871. 6. Kendall, K.A., K.E. Harshbarger, R.L. Hays, and E.E. Ormiston. 1970. Responses of dairy cows to diets containing varied levels of calcium and phosphorus. *J Dairy Sci.* 53:681. 7. Aaes, O. 1991. Reduced feed intake in cows after peroral calcium supplements. *The Bovine Practitioner* No. 26:30. 8. Pehrson, B. and M. Jonsson. 1991. Prevention of milk fever by oral administration of encapsulated Ca-salts. *The Bovine Practitioner* No. 26:36. 9. Anderson, S.B. 1984. Thesis. Royal Veterinary and Agriculture University, Copenhagen. 10. Hodnett, D., W. Neal, A. Jorgensen, and H.F. Deluca. 1992. 1α-Hydroxyvitamin D_3 plus 25-Hydroxyvitamin D_3 reduces parturient paresis in dairy cows fed high dietary calcium. *J Dairy Sci.* 75:485-491. 11. Hibbs, J.W. and W.D. Pounden.1955. Studies on milk fever in dairy cows. IV. Prevention by short-term, prepartum feeding of masive doses of vitamin D. *J Dairy Sci.* 38:65. 12. Bar, A., M. Sachs, and S. Hurwitz. 1980. Observations of the use of 1α-hydroxycholecalciferol in the prevention of bovine parturient paresis. *Vet Rec.* 106:529. 13. Gast, D.R., J.P. Marquardt, N.A. Jorgensen and H.F. DeLuca. 1977. Efficacy and safety of 1α- Hydroxyvitamin D_3 for prevention of parturient paresis. *J Dairy Sci.* 60:1910. 14. Goff, J.P., R.L. Horst. 1990. Effect of subcutaneously released 24F-1, 25-Hydroxyvitamin D_3 on incidence of parturient paresis in dairy cows. *J Dairy Sci.* 73:406. 15. Roberts, S.J. 1986. *Veterinary Obstetrics and Genital Diseases Theriogenology.* Third Edition. p. 100. 16. Littledike, E.T. and R.L. Horst. 1982. Vitamin D_3 toxicity in dairy cows. *J Dairy Sci.* 65:749. 17. Harris, B. 1992. Maintaining proper cation-anion balance in dry cow rations. *Nutrinews* Vol. 4, No. 1, p. 5. 18. Oetzel, G.R. 1991. The role of anion-cation balance in nutrition. Bovine Practitioners Nutrition and Physiology in Animal Health, *2nd Annual Conference Proceedings.* 19. Beede, D.K., C. Wang, G.A. Donoval, L.F. Archbald and W. K. Sanchez. 1991. Dietary cation-anion difference (electrolyte balance) in late pregnancy. *The Bovine Proceedings* 24:51-55. 20. Oetzel, G.R., M.J. Fettman, D.W. Hamar, and J.D. Olson. 1991. Screening of anionic salts for palatability, effects on acid-base status, and urinary calcium excretion in dairy cows. *J Dairy Sci.* 74:965-971. 21. National Research Council. 1989. Nutrient requirement of dairy cattle. No. 6. Nutrient requirements of domestic animals. Natl Acad Sci, Washington, DC 22. Oetzel, G. and K. Nordlund. 1991. Prevention of parturient paresis in a Jersey herd by feeding anionic salts during the prepartum period. *The Bovine Practitioner* No. 26:33. 23. Beede, D.K. and C. Wang. 1992. Effects of ammonium chloride and sulfate on acid-base status and calcium metabolism of dry Jersey cows. 1992. *J Dairy Sci.* 75:820. 24. Vagg, M.J. and J.M. Payne. 1970. The effects of ammonium chloride induced acidosis on calcium metabolism in ruminants. *British Vet J* 126.531. 25. Tucker, W.B., G.A. Harrrison, and R. W. Hemken. 1988. Influence of dietary cation-anion balance on milk, blood, urine, and rumen fluids in lactating dairy cattle. *J Dairy Sci.* 71: 346. 26. West, J.W., B.G. Mullinix, and T.G. Sandifer. 1991. Changing dietary electrolyte balance for dairy cows in cool and hot environments. *J Dairy Sci.* 74:1662. 27. KSU-VMTH. Clinical case report. January 1992.