Factors to Concentrate on to Prevent Periparturient Disease in the Dairy Cow With Special Emphasis on Milk Fever

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Efficient milk production continues to require the dairy cow to experience gestation and parturition each year. The transition from pregnant, non-lactating to non-pregnant, lactating is too often a disastrous experience for the cow. Most of the metabolic diseases of dairy cows - milk fever, ketosis, retained placenta, and displacement of the abomasum - occur within the first 2 weeks (wk) of lactation. The etiology of many of those metabolic diseases that are not clinically apparent during the first 2 wk of lactation, such as laminitis, can be traced back to insults that occurred in early lactation. In addition to metabolic disease, the overwhelming majority of infectious diseases, especially mastitis, but also diseases such as Johne's disease and Salmonellosis, become clinically apparent during the first 2 wk of lactation. The well-being of the cow and her profitability could be greatly enhanced by understanding those factors that account for the high disease incidence in periparturient cows.

Three basic physiologic functions must be maintained during the periparturient period if disease is to be avoided. These are: 1. adaptation of the rumen to high energy density lactation diets to reduce the degree of negative energy balance experienced by the cow; 2. maintenance of normocalcemia; and 3. reducing the degree of immunosuppression that occurs around parturition. Both metabolic disease and infectious disease incidence are greatly increased whenever one or more of these physiological functions is impaired. The etiological role of each of these three physiological factors on the development of each of the common diseases encountered during the periparturient period is discussed more fully in reference.[17] A brief discussion of the etiology of several important periparturient diseases is presented below.

Mastitis

A high proportion of new intramammary infections occur during the first wk of the dry period when milk flow ceases to flush bacterial invaders from the teat canal and before the gland is fully involuted.[51] However, these infections often do not result in clinical mastitis. While many of these infections are eliminated by the immune cells during the dry period, some are simply held in check until lactation begins. Clinical mastitis is most likely to occur during the first month of lactation, especially coliform mastitis,[15, 52] and is often the result of infection established during the dry period or during early lactation. This raises two important questions. Why do subclinical mammary infections obtained early in the dry period become clinical mastitis infections in early lactation, and why is the fresh cow's udder so susceptible to infection? At least part of the answer is that the activity of the immune system of the cow is depressed during the wk before and after calving. Neutrophils obtained from cows during the first wk of lactation exhibit impaired ability to ingest and kill bacteria. [39, 45] The ability of lymphocytes to respond to mitogens and to produce antibody is also impaired around parturition.[33,37,38,40,66] The serum concentration of other components of the immune system such as immunoglobulin, complement, and conglutinin are also decreased at parturition in dairy cows.[40,55] Intramammary infections held in check during the dry period can overcome the weakened immune system to become clinical mastitis cases at parturition. Coupled with the recrudescence of existing infections, the gland is also at increased risk of new infection around the time of parturition. As the mammary secretions change over to colostrum, the level of lactoferrin declines which increases the amount of

iron available for bacterial growth.[62] The keratin plug sealing the teat breaks down about 7 to 10 days (d) before parturition,[52] permitting bacteria easier access to the gland. At parturition, most dairy cattle become hypocalcemic (some to the point of developing milk fever) which is suspected to impair smooth muscle contraction vital to closure of the teat sphincter after milking. Why the immune system is depressed at parturition is currently unknown, although in another section of this review the possible effects of various endocrine and nutritional factors will be discussed.

Retained Placenta

The fetal membrane villi should separate from the maternal caruncles within a few hours (hr) of calving. Numerous factors are thought to be important in determining whether the placenta is successfully expelled. Gross *et al.* [23] reported that injection of PGF2 within 1 h of calving dramatically reduced the incidence of retained placenta in dexamethasone-induced calvings, suggesting that PGF2_ production is deficient in cows developing retained fetal membranes. However, other researchers have not found prostaglandin treatment to be effective in the prevention or treatment of retained fetal membranes.[6, 57]

Numerous studies have been conducted to try to demonstrate a hormone deficiency or excess that is responsible for the retained fetal membrane syndrome, but no clear conclusions are evident.[8] A great deal of epidemiological evidence exists that links milk fever with an increased incidence of retained fetal membranes.[9] Presumably the hypocalcemia prevents uterine contractions necessary for expulsion of the placenta. While uterine contraction may be a factor in expulsion of the placenta in those cases in which the placenta is free of the caruncles, in most cases uterine contraction is actually stronger and more protracted in cows with retained placenta than in cows that expel the placenta normally.[6]

Workers from the Netherlands are conducting studies which suggest that the immune system plays a role in retained placenta. In a series of interesting experiments, Gunnink[26,27] demonstrated that leukocytes (primarily lymphocytes) of cows that would expel the placenta normally had a strong chemotactic response to cotyledon material suspended in a Boyden chamber. In striking contrast, cows that failed to expel the placenta normally had peripheral blood leukocytes that exhibited little to no chemoattraction to the cotyledon suspension. This inability to attack cotyledon material was evident several d before parturition in those cows that would develop a retained placenta. Gunnink proposes that placental tissue becomes a dead foreign body at the time of parturition, which the body must recognize and "reject" in order to complete separation of the fetal membranes. Perhaps immunosuppression at calving has implications for fetal membrane expulsion in addition to infectious disease susceptibility. In partial support of this theory, a loss in neutrophil chemoattraction for fetal membrane tissue after parturition, but not before, has also been observed[7] in cows with retained fetal membranes. These workers also reported that neutrophil superoxide production was impaired before calving in those cows that would develop metritis after calving. One Dutch study[36] suggests that retained placenta is more likely to occur in those pregnancies where the fetus has the same major histocompatibility complex antigens (MHC class I) as the cow. Since MHC class I antigens are important in recognition of "self" antigens these studies suggest that failure to recognize the placenta as foreign can increase the incidence of retained placenta. Could inbreeding, common in dairy cattle, be a factor contributing to retained placenta?

When parturition is induced with glucocorticoids it is often accompanied by retained placenta. Milk fever cows have several fold higher plasma cortisol concentrations at calving than do non-milk fever cows. Could the imunosuppressive effects of the glucocorticoids be the reason for the higher incidence of retained placenta in these two situations?

Displaced Abomasum

In the non-pregnant cow, the abomasum occupies the ventral portion of the abdomen, very nearly on the midline, with the pylorus extending to the right side of the cow caudal to the omasum. As pregnancy progresses, the growing uterus occupies an increasing amount of the abdominal cavity. The uterus begins to slide under the caudal aspects of the rumen, reducing rumen volume by about one third at the end of gestation. (Perhaps this contributes to the decline in dry matter intake observed near the end of gestation). This also forces the abomasum forward and slightly to the left side of the cow, although the pylorus continues to extend across the abdomen to the right side of the cow.[28] After calving, the uterus retracts toward the pelvic inlet which, under normal conditions, allows the abomasum to return to its original position. During left displacement of the abomasum, the pyloric end of the abomasum slides completely under the rumen to the left side of the cow. Three factors are believed to be responsible for allowing the abomasum to move to the left side of the cow. First, the rumen must fail to take up the void left by the retracting uterus. If the rumen moved into its normal position on the left ventral floor of the abdomen, the abomasum would not be able to slide under it. Second, the omentum attached to the abomasum must have been

stretched to permit movement of the abomasum to the left side. These two factors constitute opportunity for displacement. A third factor necessary to cause abomasal displacement is abomasal atony. Normally, gases produced in the abomasum (from fermentation of feedstuffs or CO_2 released when bicarbonate from the rumen meets the HCl of the abomasum) are expelled back into the rumen as a result of abomasal contractions. It is felt that these contractions are impaired in cows developing left displacement of the abomasum. The cause of abomasal atony is less clear.

A decline in plasma calcium concentration around parturition linearly decreases abomasal contractility, which is suspected to lead to atony and distension of the abomasum. At plasma calcium concentration of 5 mg%, abomasal motility is reduced by 70% and strength of contractions by 50%.[11] At a plasma calcium concentration of 7.5 mg/dl, the motility and strength of abomasal contractions were reduced by 30% and 25%, respectively. Clinical signs of milk fever (down cows) often are not seen until calcium is about 4 mg%. In a recent study of plasma calcium concentrations in periparturient Holstein cows, we found that 10 to 50% of cows remained subclinically hypocalcemic (plasma calcium <7.5 mg/dl) up to 10 d after calving, depending on herd efforts to combat milk fever.[19]

Volatile fatty acids within the abomasum have been demonstrated to reduce abomasal contractility.[5] A high grain, reduced forage diet can promote the appearance of VFA in the abomasum by reducing the depth of the rumen matte or raft (made up primarily of the long fibers of forages). The rumen matte captures grain particles so that they are fermented at the top of the rumen liqueur. This also slows fermentation of grains which can prevent sudden drops in rumen pH. The VFAs produced at the top of the rumen liqueur are generally absorbed by the rumen with little VFA entering the abomasum. In cows with an inadequate rumen matte, grain particles fall to the ventral portion of the rumen and reticulum where they are fermented or pass on to the abomasum (where they can then be fermented to some extent). The VFA produced in the ventral rumen can pass through the rumenoreticular orifice to enter the abomasum before the rumen can absorb them. A thick rumen matte is generally present during the dry period when cows are fed a high forage diet, but the depth of the rumen matte is often reduced in early lactation; especially if the cow experiences a pronounced decline in dry matter intake. Since the rumen matte also stimulates regurgitation of the cud and mastication, the release of saliva, which promotes rumen buffering, is decreased when cows are placed on a higher grain ration. Also, early in lactation, the underdeveloped ruminal papillae allow more of the VFA produced in the ventral rumen to escape the rumen than would a highly absorptive ruminal mucosa typical of later lactation.

Ketosis-Fatty Liver Complex

In early lactation, the amount of energy required for maintenance of body tissues and milk production exceeds the amount of energy the cow can obtain from her diet. As a result, the cow must utilize body fat as a source of energy. However, there is a limit to the amount of fatty acid that can be oxidized to completion by the tricarboxylic acid (TCA) cycle of the liver or exported from the liver as very low density lipoprotein. When this limit is reached, triglycerides accumulate within the hepatocytes impairing their function and acetyl-CoA that is not incorporated into the TCA cycle is converted to acetoacetate and ß-hydroxybutyrate. The appearance of these ketone bodies in the blood, milk, and urine is diagnostic of ketosis, and usually becomes clinically evident from 10 d to 3 wk after calving. Gluconeogenesis becomes impaired, resulting in hypoglycemia. The cow becomes further depressed, reducing feed intake further and reducing milk production. The liver of the overconditioned cow is, for some reason, more limited in ability to oxidize fatty acids than the liver of a thinner cow. Of special interest is the observation that the rise in estrogens at parturition can have deleterious effects on energy balance in the cow. Estrogen can enhance triglyceride deposition within the liver when plasma non-esterified fatty acids are elevated.[25] Numerous salient reviews[24,43,50,69] offer hypotheses to explain why the liver has a limited capacity for the oxidation of fatty acids, including a lack of oxaloacetate to maintain a functioning TCA cycle, lack of carnitine necessary for mitochondrial transport and oxidation of acetyl-CoA, lack of niacin, and a host of endocrine factors. However, identification of the biochemical defect that limits efficient oxidation of fatty acids remains elusive.

Recent results of work done at Iowa State University[14] and the University of Wisconsin[3] demonstrate the importance of feed intake at calving on the etiology of the fatty liver-ketosis syndrome. In the average cow, dry matter intake decreases precipitously by 20-30% on d 1 or 2 before calving, and does not recover until 1 to 2 d after calving.[3,44] Interestingly, liver biopsies taken several wk before calving, at calving, and 4 wk into lactation showed that liver triglycerides were increased 3-fold by the d of calving. By 4 wk into lactation, the liver triglycerides were 4-fold higher than before calving. Triglyceride buildup in the liver is a much earlier phenomena than previously assumed. Even more interestingly, if cows are fitted with rumen fistulas and dry matter intake is not allowed to drop around the time of calving by forcing feed into the rumen through the fistula, liver lipids and triglycerides increase only a small amount. Similar results were also achieved by daily

drenching of cows with propylene glycol (1 L/d) during the periparturient period.[59]

The conclusion is that energy intake must not be compromised during the d before calving. Any factor that exacerbates the reduction in feed intake experienced at calving increases the energy deficit of the cow and the risk of fatty liver-ketosis. This would seem to explain why cows that have had milk fever are at much greater risk of going on to develop ketosis.

Endogenous opioid peptides circulate at only very low levels in early gestation. However, during the last month of gestation, ß-endorphin concentrations in blood are increased and decline to baseline levels about 48 h after calving. Met-enkephalin concentrations rise rapidly at calving.[13] It is thought that the rise in opioid peptides as parturition approaches reduces the perception of pain experienced by the cow during parturition. The endorphins and enkephalins are potent opioid receptor agonists. Opiates are often used in the treatment of diarrheal diseases because of their ability to decrease motility of the gastrointestinal tract.[34] Can the rise in endogenous opioids at parturition slow gastrointestinal motility and play a role in the depression in feed intake observed at calving, or the development of a displaced abomasum?

Hypocalcemia and Milk Fever

The onset of lactation places such a large demand on the calcium homeostatic mechanisms of the body that most cows develop some degree of hypocalcemia at calving.[20,30] In some cases, plasma calcium concentrations become too low to support nerve and muscle function, resulting in parturient paresis or milk fever. The factors, such as dietary cation-anion balance and blood alkalinity, that determine the degree of hypocalcemia a cow will experience at calving will be discussed later. However, it now seems clear that hypocalcemia has some widespread effects on the cow that predispose the cow to other periparturient diseases.[9]

Cows developing milk fever have higher plasma cortisol concentrations than non-milk fever cows,[21,31,42] which may exacerbate immunosuppression ordinarily present at calving. Hypocalcemia also results in the loss of muscle tone in the uterus and teat sphincter, which, combined with the immunosuppressive effects of the excess cortisol, may account for the increased incidence of retained placenta and mastitis observed in cows with milk fever. Loss of uterine muscle tone is a major cause of uterine prolapse, and this disease process is almost always due to hypocalcemia.[49]

Milk fever cows also exhibit a greater decline in feed intake after calving than non-milk fever cows,[18,44] exacerbating the negative energy balance commonly observed in early lactation. In addition, hypocalcemia prevents secretion of insulin,[42] preventing tissue uptake of glucose which would exacerbate lipid mobilization at calving, increasing the risk of ketosis. The decline in feed intake associated with milk fever would reduce rumen fill (so rumen sits above floor of abdomen) and the depth of the rumen matte allowing more VFA into the abomasum. It also would reduce abomasal contractility. All these effects of hypocalcemia predispose the cow to displacement of the abomasum.

Dietary Effects on Acid-Based Metabolism and Clinical Implications of these Effects on Milk Fever Risk in Dairy Cattle.

In order to prevent blood calcium from decreasing, the cow must replace calcium lost to milk by withdrawing calcium from bone or by increasing the efficient absorption of dietary calcium. Bone calcium mobilization is regulated by parathyroid hormone (PTH) produced by the parathyroid glands located in the neck. Whenever there is a drop in blood calcium, blood PTH levels increase dramatically. A second hormone, 1,25-dihydroxyvitamin D, is required to stimulate the intestine to efficiently absorb dietary calcium. This hormone is made within the kidney from vitamin D in response to an increase in blood PTH. Put simply, MF occurs when cattle do not remove enough Ca from their bones and the diet to replace Ca lost to milk. This occurs because a key hormone involved in Ca metabolism, parathyroid hormone, acts only poorly on bone or kidney tissues when the blood pH is high.[18] Blood pH of cattle is often alkaline because forage K is often excessively high.

Since Stewart[58] proposed the strong-ion difference theory our understanding of the factors that determine the pH of blood has greatly increased. Put simply, the basic tenet of this theory is that the electrical charge of a solution, whether it be a glass of water or extracellular fluids, must always be neutral. When cations (positively charged ions) exceed anions (negatively charged ions) in a solution the pH is increased. When anions exceed cations the pH decreases.

Blood pH is ultimately determined by the number of positive and negative charges entering the blood from the diet. The major cations present in feeds and the charge they carry are sodium (+1), potassium (+1), calcium (+2), and magnesium (+2). The major anions and their charges found in feeds are chloride (-1), sulfate (-2), and phosphate (-3). The difference between the number of cation and anion particles absorbed from the diet determines the pH of the blood. The cation-anion difference of a diet is commonly described in terms of mEq/kg of just sodium, potassium, chloride, and sulfate as follows:

$$\text{Dietary Cation-Anion Difference (DCAD)} = (Na^+ + K^+)-(Cl^- + S^{--}).$$

This equation is useful, although it must be kept in mind that calcium, magnesium, and phosphorus absorbed from the diet will also influence blood pH. Any positively or negatively charged ion that enters the blood will change the blood pH. In recent months we have evaluated the relative acidifying activity of various anionic salts by feeding them to dry cows and evaluating their ability to reduce urine pH (which reflects the changes in blood pH). These data lead us to believe the DCAD of a diet and its acidifying activity is more accurately described by the following equation: $(0.15\ Ca^{++} + 0.15\ Mg^{++} + Na^{+} + K^{+}) - (Cl^{-} + 0.25\ S^{--} + 0.5\ P^{---})$.

This equation suggests that the major dietary factors determining blood and urine pH are Na, K and Cl. This equation offers a more rational approach to use of DCAD in milk fever prevention.

Milk Fever

The onset of lactation incurs a sudden and large demand for calcium from the blood of the dairy cow. To avoid MF the blood pH needs to be decreased. The best way to do this is to reduce the K content (and in some areas of the country, the Na content) of the diet fed to the prepartum cow. Removing potassium from the ration can present a problem. All plants must have access to a certain amount of K to obtain maximal growth. However alfalfa, other legumes, and at least some grasses accumulate K within their tissues to concentrations that are well above that required for optimal growth of the plant if soil potassium is high. Optimal growth of alfalfa occurs when the plant K concentration is 1.7-2.0%. Alfalfa often contains much higher levels. Lanyon reported[41] that the K concentration of alfalfa samples submitted by Pennsylvania producers averaged 3.1% K, ranging from 1.42 to 4.05%. Many producers fertilize alfalfa heavily with potassium to increase the plant's resistance to winter kill. However it is unlikely that any benefit is seen by increasing plant potassium beyond 2.5%. It appears that current agronomic practices encourage overfertilization with K, resulting in luxury consumption of K by plants which can be detrimental to the health of the periparturient dairy cow. What practices can be instituted by the producer so that a low K forage crop can be obtained for the transition cow ration?

Low potassium forages

Grasses - Corn is actually a warm season grass. Corn silage tends to be 1.1-1.5% potassium. It is difficult to find any other forage this low in potassium. Some other warm season grasses, such as switchgrass, big bluestem, and indiangrass tend to be low in potassium also but they are low in protein and digestibility.

Cool season grasses such as bluegrass, orchardgrass, and brome tested lower in potassium than alfalfa did 20 years ago. At that time these hayfields were unlikely to receive fertilizer. The tremendous increase in the number of cows on each farm has not been accompanied by an increase in the amount of land available for spreading manure. As a result hayfields that were not fertilized in the past are now being used extensively as a place to get rid of animal wastes. Cool season grasses have a fibrous root system which makes them very efficient utilizers of soil potassium. They will actually out compete alfalfa for potassium - this is why your alfalfa stand eventually becomes grassy. Research at the Miner Institute[60] indicates that timothy accumulates potassium to a lesser extent than other grasses and the second cutting of grass hays generally contain less potassium than the first cuttings.

Legumes - In the past alfalfa and other legumes were left out of dry cow rations because they were high in calcium. However we now know that dietary calcium has little effect on the alkalinity of the cow's blood under practical conditions so it does not induce milk fever. By restricting potassium application to the soil it is possible to grow alfalfa that is as low in potassium as many of the grass hays. However, this eventually allows grasses to take over the stand and increases winterkill. One option may be to withold potassium fertilization from a field that is in its last year of production and harvest that field specifically for the dry cows. However it can take several years to deplete soil potassium reserves if plant potassium values have been high. Some other rules of thumb - alfalfa potassium content is highest in alfalfa harvested in the early vegetative stage. Full bloom alfalfa may be more suitable for the dry cow. Potassium is released from wet soil more readily than from dry soil. Most years the first cutting of alfalfa will have a higher potassium content than later cuttings.

The key to milk fever prevention is to find a low potassium hay source and combine it with corn silage to form the basis for your dry cow ration. Try to formulate a total ration with less than 2% potassium. Limit access to pasture and watch to see if cows are eating bedding. Oat straw bedding is particularly high in potassium.

Anionic salts

Adding anions to the diet of the cow can counteract the effects that dietary potassium and sodium have on blood pH. Commonly used anion sources are calcium chloride, ammonium chloride, magnesium sulfate, ammonium sulfate, and calcium sulfate. All anionic salts are unpalatable as they give a strong salty taste to the diet. Sulfate salts may be slightly more palatable than chloride salts - but since they are much less effec-

tive acidifiers of the blood their use is not highly recommended. If used inappropriately they will cause inappetance and actually exacerbate fresh cow problems. Therefore they should be used sparingly. The pH of the urine of the close-up dry cow can tell you if the blood of the cow remains too alkaline or if you have added too many anionic salts. In herds experiencing a milk fever problem the urine of close-up dry cows will be very alkaline with a pH above 8.0. For successful control of milk fever the average pH of the urine of the cows (Holstein) should be between 6.0 and 6.5. In Jersey cows the average urine pH of the close-up cows has to be reduced to between 5.8 and 6.2 for effective control of milk fever. If the average urine pH is between 5.0 and 5.5 you have probably added too many anions to the diet and the cows will suffer a decline in dry matter intake. Various formulas exist to tell you how much of an anionic salt to add to the diet. Most nutritionists using the equation (Na^{+} + K^{+}) - (Cl^{-}+S^{--}) have a target DCAD for milk fever prevention of about -50 mEq/kg. Using the more physiologically relevant equation, (0.15 Ca^{++} + 0.15 Mg^{++} + Na^{+} + K^{+})- (Cl^{-} + 0.2 S^{--} + 0.3 P^{---}), the target DCAD should be around +200 and+300 mEq/kg. These are simply guidelines and are based on the setting of certain parameters at constant values as outlined below.

Urine pH of the cows will be the better gauge of the appropriate diet DCAD than any formula. Some of the variables in the above formulas are somewhat fixed. Dietary magnesium should be set at 0.4% (higher than NRC reccommendations). We like to use magnesium sulfate in our close-up rations to supply magnesium in a readily soluble form, not because it is an effective source of anions to prevent milk fever. Magnesium chloride, where available, would be another good method of raising diet magnesium to 0.4% and would give a stronger acidifying effect. The diet should supply between 35 and 50 g phosphorus daily so diet phosphorus will be set at about 0.4 %. More than 80 g Phosphorus / day will inhibit renal synthesis of 1,25-dihydroxyvitamin D which can induce milk fever. Dietary S should not exceed 0.4%. Some studies have reported a polioencephalomalacia-like syndrome (non-responsive to thiamine) when dietary sulfate is raised above 0.4%. In addition our results suggest that adding more sulfate is a poor choice because it is a fairly ineffective acidifying agent. Dietary Cl can nearly always be raised to 0.5% with little effect on dry matter intake. Most diets will require closer to 0.6% Cl for effective prevention of hypocalcemia. Getting ration Cl above 0.8% will often risk inappetance in the animals. Dietary Ca remains somewhat difficult to set. In a controlled trial there has been no advantage in keeping dietary calcium low (less than 40 g /day).[18] Anecdotal evidence and at least two published trials suggest that high dietary calcium concentrations (<0.5 % Ca) are desirable when coupled with anionic salts and helps prevent hypocalcemia.[1,46] Good results have been achieved by feeding as high as 180 g calcium /day. However when limestone is used to achieve these high dietary calcium levels the alkalinizing effect of the added calcium carbonate can be a factor. More importantly the limestone is taking up room in the ration that might better be used for energy sources. We currently set dietary calcium between 1 and 1.2% which is fairly easily achieved, especially if calcium chloride is used as one of the anionic salts. More work needs to be done on availability of the different calcium sources and the role of dietary calcium during the periparturient period. Anionic salts generally add between $5 and $9 to feed costs for a close-up dry cow. We are currently investigating the use of hydrochloric acid preparations as a source of anions for the dry cow. These have proved more palatable, in our hands, than traditional anionic salts as they impart an acidic taste rather than a salty taste to the ration and should be less expensive as well.

Anionic diets prepartum may enhance milk production and health in the subsequent lactation, simply because hypocalcemia is decreased and the animal does not have the secondary problems associated with milk fever[2,4,47] It is difficult to assess the economic impact of subclinical hypocalcemia. It seems likely that if milk fever is associated with loss of muscle tone (i.e., abomasum, teat sphincters) and ruminal stasis, subclinical hypocalcemia will be associated with these same problems to a lesser degree. The impact of subclinical hypocalcemia on herd health may be nearly as great as milk fever because it is much more common than milk fever.

Rumen Physiology as a Factor Limiting Energy Intake

It is not unusual for a high producing Holstein cow 3 months into lactation to consume 20 kg DM / day with 50% of that DM as grain. Yet that same 20 kg DM fed to the fresh cow would likely result in rumen acidosis- if you could get the cow to consume that much. **Why do the fresh cow and mid-lactation cow have different responses to the same feed?**

Upon dry-off, the cow is fed a high forage ration that is less energy dense and higher in neutral detergent fiber than the lactation ration. This affects rumen function in two ways. The bacterial population shifts away from the lactate producers (bacteria possessing amylase, such as *Streptococcus bovis*, and lactobacilli) as a result of the decrease in readily fermentable starches in the diet.[68] Therefore, the population of those bacteria (primarily *Megasphaera elsdenii* and *Selenomonas ruminatium*) capable of converting lactate to acetate, propionate, or longer chain fatty acids useful to the cow declines. The higher forage diet increases

the population of cellulytic bacteria, but also increases populations of methane-producing bacteria, which is generally regarded as an inefficient use of dietary energy.[35] Another effect of the lower energy diet of the early dry period is a reduction in the papillae length and volatile fatty acid (VFA) absorptive capacity of the ruminal mucosa. As much as 50% of the absorptive area may be lost during the first 7 wk of the dry period.[12] If the fresh cow is now abruptly switched to a high energy lactation diet, she is at risk of developing rumen acidosis because the lactate producers will respond rapidly to the higher starch diets and produce high amounts of lactate. The lactate converting bacterial population responds only slowly to a change in diet, requiring 3 to 4 wk to reach levels that will effectively prevent lactate from building up in the rumen. Lactate is a 10 X stronger acid (pKa = 3.86) than propionate (pKa = 4.87), acetate (pKa = 4.76), or butyrate (pKa = 4.82), so that its presence has a somewhat greater effect on rumen pH than the VFA. Also, lactate and the VFA are absorbed by rumen epithelium when in the free acid state only. As the pH of the rumen decreases more of the VFA exists in the free acid state. Because the pKa of lactate is lower than the VFA, it is absorbed more slowly than acetate, propionate, or butyrate from the rumen. Perhaps more importantly, the poorly developed rumen epithelia of the unadapted cow is not able to absorb the VFA quickly enough to prevent a build up of organic acids within the rumen, which can cause rumen pH to fall to the point where the protozoa and many of the bacteria within the rumen are killed or inactive. The lactic acid, and the endotoxins and histamine released as the rumen flora die, are absorbed systemically, and affect the microvasculature of the growing hoof wall, which can then result in clinical laminitis.[48] Metabolic acidosis will follow rumen acidosis if the amount of organic acid absorbed into the blood exceeds the ability of the liver and other tissues to metabolize these anions. Again, because of the lower pKa of lactate, it will have a greater effect on blood pH than the VFA.

Prevention of lactate build-up within the rumen can be reduced by adapting the rumen flora to a high starch diet to induce high populations of those bacteria capable of converting lactate to acetate, propionate, or long chain fatty acids. Fully adapting the rumen flora to a high starch diet requires about 3 to 4 wk.[34] Increasing ruminal papillae length and width increases rumen absorption of lactate and other VFAs, which also helps prevent the decline in rumen pH (arguably, it may exacerbate systemic metabolic acidosis). Full development of ruminal papillae requires about 5 wk of concentrate feeding, with the greatest increase in papillae length and ruminal absorption capability occurring the final 2 wk of adaptation.[12] In the US, it is common to begin concentrate feeding to cows 2 to 3 wk before calving, presumably to adapt the cow to the high grain diet she will receive in lactation. Perhaps the grain feeding should be initiated 5 wk before calving? Remember too that the standard deviation for calving date is + 9 days - thus, to ensure that 95% of cows in a herd will be on a pre-fresh ration for at least 2 wks before freshening means that cows in the herd would be started on pre-fresh rations 23 days before their due date.

Endocrine and Nutritional Influences on Periparturient Immunosuppression

Estrogens, which increase dramatically at the end of gestation, have been found in some experiments to stimulate the humoral immune response,[63] but most workers agree they have a strong suppressive effect on cell-mediated immunity.[67] Glucocorticoids have long been used as powerful immunosuppressive agents. Plasma cortisol concentrations (primarily of maternal adrenal origin) of the cow increase from 4 to 8 ng/ml 3 d before calving to 15 to 30 ng/ml at parturition and the d after calving. The cortisol secretion response is even more pronounced in those cows that develop milk fever.[21] Thus, the immunosuppressive effects of the plasma estrogen and cortisol increases observed in the periparturient period would be likely suspects as causative agents of the immunosuppression observed at calving.

Chronic deficiencies of energy, protein, minerals, or vitamins have repeatedly been associated with increased disease susceptibility as a result of depressed immune function. Parturition and the onset of lactation impose a large metabolic stress on the cow, which can cause relatively acute, lasting from 1 d to several wk, deficiencies of nutritional factors necessary for maintenance of the immune system. Partly because of the poor development of the digestive tract, it is impossible for the high producing dairy cow to ingest enough feed to meet the lactational demands for energy and protein. Therefore, the dairy cow is in negative energy and protein balance in early lactation, which impairs immune function. Severe energy deficiency in early lactation can also cause ketoacids to accumulate in the blood, which can further impair lymphocyte function.[16] Plasma concentrations of vitamin A (retinol) and vitamin E (tocopherol) were found to decrease 38% and 47%, respectively, in dairy cows at parturition,[22] which caused plasma levels of these vitamins to fall to levels that would be diagnostic of chronic deficiency. While a portion of the serum loss of these vitamins may be due to sequestration within colostrum, it also appears that they are being consumed at a higher rate at calving as a result of increased immunologic and metabolic stress. Vitamin A and vitamin E supplementation in the periparturient cow can improve immune responses,[10,29,53,56,61] and is often associated with a decrease

in the incidence of mastitis in dairy cows.[53,54] A point to be made here is that the vitamin and mineral requirements of the cow have generally not been determined for the periparturient cows, and that these requirements appear to be considerably higher than would be predicted from data obtained in cows outside this time frame. It would seem logical to conclude that any nutritional insults to the immune system would add to the immunosuppression caused by the hormonal changes associated with parturition.

Conclusions and Guidelines

I. Prepare the rumen so that high energy feeds can be fed early in lactation to meet the energy needs of the cow.

- stimulating the growth of "lactate metabolizing" bacterial species in the rumen.
- stimulating gowth of the rumen wall so absorption of nutrients is maximized.

How do we do this?

- need to introduce grain into the ration of the cow for at least 3 weeks before due date. Heifers especially may need to be on this diet for 5 weeks.
  - in total mixed ration herds this means feeding a ration that has from .71 - .73 Mcal / lb feed for last three weeks of pregnancy, last 5 weeks for heifers
  - in herds fed hay and a concentrate mix separately, grain should be introduced 4 weeks before calving and increased slowly over a period of two weeks so that during the last 2 weeks before calving the cows are eating .75 - 1% of their body weight as concentrate (8-12 lbs / day). If corn silage comprises a majority of the forage this number can be reduced. FEED HAY BEFORE GRAIN TO FORM A MATTE IN RUMEN TO SLOW GRAIN FERMENTATION!
- Protein content of pre-partal ration for older cows is more difficult. Protein requirements of fetus and for cow maintenance are probably met with diets as low as 12% crude protein. Yet in some studies (64, 65) cows responded best when dietary protein was increased to 16%. THIS AUTHOR STAYS WITH 16% PROTEIN - THOUGH NOT FOR ANY WELL-DOCUMEMTED SCIENTIFIC REASON.

Protein content of the transition ration should be 16% for heifers to accommodate growth of the heifer.

To maximize feed intake cows need to be dried off at body condition scores of 3.5. Above 3.75 is too fat and feed intake at calving will be depressed leading to fatty liver and ketosis.

Payoff - less ketosis, fewer displaced abomasums, less rumen acidosis and less lameness due to laminitis in early lactation.

II. Prevent major decrease in blood calcium concentration at calving.

Because a tremendous amount of calcium is being put into colostrum and milk the cow's blood can become deficient in calcium. Severe cases result in milk fever. Less severe cases result in feed intake depression and poor muscle tone which in turn causes retained placenta, displaced abomasum, and environmental mastitis (especially because the teat end won't close properly after milking).

How do we do this?

Dietary measures

1. Control cation-anion balance
   - milk fever is usually caused by the presence of high potassium (and in some cases sodium in heavily irrigated parts of N. America) cations in the diet. To some extent potassium can be counteracted by adding anionic salts to the diet, such as calcium chloride, ammonium chloride, or magnesium sulfate.
2. Provide adequate magnesium
   - a lack of magnesium will prevent the hormones that defend against a drop in blood calcium from working properly. **We recommend dietary magnesium levels that are much higher than current NRC recommendations**.

A good mineral profile for a transition cow (last 3-4 weeks of gestation) diet

calcium	1-1.2%
phosphorus	0.4 - 0.5 %
magnesium	0.4 %
sodium	as close to 0.1% as possible
potassium	as close to 0.7% as possible

This is a problem - most diets will be workable if you can get down to 1.5-1.8% potassium

- sulfur 0.3- 0.4%
- chloride high enough to bring AVERAGE urine pH between 6 and 6.8**
  (target for Jerseys is between 5.8 and 6.5)

Our current philosophy is to formulate the ration using forages with the lowest potassium content that we can find that are still reasonably well digestible. Corn silage is excellent. Beet pulp without molasses, some distillers grains or brewers grains, and corn gluten feed can often be used as well in the diet. First cutting of hays or alfalfa are generally higher in potassium than late cuttings grown under dry conditions. DO NOT TRUST POTASSIUM VALUES DETERMINED BY NEAR INFRARED ANALYSIS.

Next add magnesium sulfate or magnesium chloride to the diet to bring magnesium content to 0.4%. Then , if needed, add dicalcium phosphate to bring phosphorus to .45%. Then I add calcium chloride to bring chloride to 0.55%. Add calcium carbonate to bring cal-

cium to 1%. In some cases a small amount of calcium propionate (0.25 lbs/day) can also be used to help increase dietary calcium and at the same time supply propionate which the cow will convert to glucose (problem = cost).

This is where I start. If urine pH is not low enough I will add more calcium chloride to the ration. Add as little as possible to get the job done - too much risks knocking the cows off feed as anionic salts are generally unpalatable.

FUTURE - Hydrochloric acid may be available as a cheap and more palatable source of anions to prevent milk fever. I would then use it in place of calcium chloride and would likely add some calcium carbonate to diets to get to 1% calcium though some calcium could come from calcium propionate .

3. Oral calcium supplements the day of calving

- boost blood calcium for 6-10 hrs at time the cow needs them most.

Calcium chloride based supplements	*Calcium propionate based*
advantages	advantages
- cheaper	-not as irritating
- less volume to give	-rapidly absorbed
- rapidly absorbed	-supplies energy and calcium
disadvantages	disadvantages
- caustic!!	- requires more volume
	- slightly more expensive

Drenches are more effective than gels or pastes but have greater chance of causing aspiration pneumonia if they go into the windpipe instead of the stomach when administered incorrectly!!

III. Maintaining a strong immune system

At calving all cows' white blood cells show a decreased ability to fight off infections which increases the susceptibility to mastitis and uterine infections. In part the immune suppression is thought to be due to changes in hormones at calving. However, better nutrition can also strengthen the immune system at this time.

How do we do this?

1. Prevent milk fever
   - milk fever causes tremendous release of cortisol which inactivates the immune cells
2. Feed adequate selenium
   - 0.3 ppm is legal limit in USA. In some situations this is not enough!
   - injectable selenium may be an option.
3. Feed vitamin E to animals without access to pasture.
   - Recent work (Ohio State University) suggesting that adequate vitamin E requires 2000 IU / day for the 2 weeks before and after calving. Much higher than NRC suggests!!! Expensive, but worth it if it prevents just one case of mastitis / 100 cows.
   - injectable vitamin E is an option also. 5 g intramuscularly 30 days before calving and again within a week of calving. Occasional abscess at injection site!
4. Prevent energy and protein deficiency (See 1 above)
5. Supply trace minerals at 20 - 50% above NRC recommendations to account for decline in dry matter intake that accompanies calving.
   - copper and zinc deficiency seem to be the problems we see most in Midwest - often caused by too much iron in the ration and the water!!

Payoff

Less mastitis, retained placenta (enhancement of neutrophil attack on fetal tissues!) and uterine infection.

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