

## **COMMON SYNDROMES AFFECTING TRANSITION COWS**

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### **INTRODUCTION**

Efficient milk production continues to require the dairy cow to experience gestation and parturition each yr. 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 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.

The bovine feto-placental mass and its demand for energy, protein, and minerals increases dramatically with increasing gestational age. By the end of gestation, daily development of the fetus requires about 0.82 of Mcal NeL, 117 g of protein, 10.3 g of calcium, 5.4 g of phosphorus, and 0.2 g of magnesium (NRC, 2001). However, the metabolic demands imposed on the cow by the formation of colostrum far exceed the demands of the fetus. The production of just 10 kg of colostrum the d of calving will require that 11 Mcal NeL, 140 g of protein, 23 g of calcium, 9 g of phosphorus, and 1 g magnesium be supplied from the diet or brought in to the mammary gland from body stores. The high demand for nutrients imposed on the body by the increased activity of the mammary gland cannot always be met, resulting in development of such metabolic diseases as milk fever and the ketosis-fatty liver complex.

The act of parturition and the onset of lactation impose tremendous physiologic challenges to the homeostatic mechanisms of the cow. This review will attempt to describe what is known and, maybe more importantly, what is unknown about the physiologic changes occurring in the periparturient dairy cow and their relationship to development of disease.

### **MEETING THE ENERGY DEMANDS OF LACTATION**

Ketosis is diagnosed whenever there are elevated levels of ketones in the blood, urine, or milk of a cow. The disease is always characterized by a decline in blood glucose as well. In 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, especially in early lactation when dry matter intake is still low. As a result, the cow must utilize body fat as a source of energy. Every good cow will utilize body reserves in early lactation to help her make milk. However, there is a limit to the amount of fatty acid that can be handled and used for energy by the liver (and to some extent the other tissues of the body). When this limit is reached, the fats are no longer burned for energy but begin to accumulate within the liver cells as triglyceride. Some of the fatty acids are converted to ketones. The appearance of these ketones in the blood, milk, and urine is diagnostic of ketosis. As fat accumulates in the liver it reduces liver function - and a major function of the liver in the dairy cow is to produce glucose.

Recent work (Grummer, 1993) demonstrates the importance of feed intake at calving on the etiology of the fatty liver-ketosis syndrome. On average, dry matter intake decreases by 20-30% 1 or 2 days before calving, and does not recover until 1 to 2 days after calving (Bertics et al., 1992, Marquardt et al., 1977). Interestingly, liver biopsies showed that liver triglycerides were increased 3-fold by the d of calving. Triglyceride buildup in the liver is a much earlier phenomena than previously assumed. Even more interesting; when cows were fitted with rumen fistulas and dry matter intake was not allowed to drop around the time of calving by forcing feed into the rumen, liver lipids and triglycerides increased only a small amount. Similar results were also achieved by daily drenching of cows with propylene glycol (1 L/d) during the week before and after calving (Studer, et al., 1993).

The conclusion is that energy intake must not be compromised during the days around calving. Any factor restricting feed intake around calving (such as milk fever or retained placenta) increases fat accumulation in the liver, affecting the energy deficit of the cow and increasing the risk of fatty liver-ketosis.

### **STRATEGIES FOR PREVENTION OF NEGATIVE ENERGY BALANCE AND KETOSIS** **CONTROL BODY CONDITION OF COWS.**

Cows should calve with a body condition score (BCS) of 3.25 - 3.75. Cows with BCS of 3.25 will eat better than cows with BCS of 3.75. However a 3.75 BCS cow that is well managed could potentially produce more milk.

### **WHAT CAN YOU DO WITH THOSE FAT HEIFERS OR DRY COWS THAT ARE OVERWEIGHT?**

With very careful management it is possible to place these animals on a poorly digestible diet (straw plus trace minerals and a little soymeal to get  $N_e$  between 0.9 and 1.1 Mcal / kg and about 11% crude protein) at dry off to drop

body condition scores, then place cows on the herd close-up ration for the 2-3 wks before calving. The idea is to create a hungry cow that will go ahead and eat well once she calves. This strategy requires accurate breeding dates! Trying to reduce weight in the last 3 weeks of pregnancy will mobilize body fat and nearly guarantee fatty liver development!

### **ADAPTING THE RUMEN TO HANDLE HIGH ENERGY DIETS**

Two factors protect the mid-lactation cow from rumen acidosis. The microbes in her rumen are acclimated to high starch diets allowing bacterial species that breakdown lactic acid to grow. It appears to take about 3 weeks to build up a rumen population of bugs capable of handling starches – hence a common recommendation to bring cows onto a close-up ration 3 weeks before calving.

The rumen wall of the mid-lactation cow has long wide papillae projecting into the rumen fluid. This increases the surface area of the rumen wall and allows for more rapid transfer of the volatile fatty acids produced during fermentation of feedstuffs into the blood for transport to the liver and other tissues. One study suggested that as much as 50% of the absorptive area may be lost during the first 7 wk of the dry period (Dirksen et al., 1985). And in this study it took nearly 5 weeks of exposure to high grain diets to restore rumen papillae length.

Recommendation: Our own observations suggest that American cows do not suffer such a large decline in rumen papillae length – probably because our far off dry cow rations tend to incorporate at least some starch (corn silage) so rumen papillae length does not decline as much so 3 weeks in the close-up pen should be adequate for cows. However, heifers do seem to benefit (socially and from a nutritional standpoint) from a longer period of time (5 wks) on the close-up ration. Cows carrying twins should also enter the close-up pen 5 weeks before expected calving date. They need the extra calories and they usually calve 2 weeks early! Remember too that the standard deviation for calving date is + or - 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 should be started on pre-fresh rations 23 days before their due date.

### **STRATEGIES TO INCREASE TOTAL CALORIE INTAKE IN THE FRESH COW**

High starch rations in the close-up pen. The majority of studies that have compared the effects of low starch close-up rations (high forage) with high starch close-up rations have concluded that the number of calories consumed both pre-fresh and post-fresh is increased, largely because dry matter intake is increased. The amount of body fat mobilized (as assessed by monitoring blood NEFA and liver fat accumulation) is also generally decreased, a reflection of the improved energy status of the cow. Starches are converted to propionate in the rumen of

the cow. Propionate is the major precursor for making glucose in the liver. Most of the structural carbohydrates in forages are going to be converted to acetate – good for milk fat support but the cow cannot use acetate to make glucose.

How high can we push the NFC (roughly equivalent to increasing the starch content in most cases) in the pre-calving and post-calving diet? Most nutrition guidelines would suggest that NFC for close-up rations be kept between 33 and 38% of the ration. A recent study by Minor et al., 1998 utilized close-up rations that were 43.8% NFC as compared to a close-up ration of just 23.5% NFC. Dry matter intake pre-calving was elevated from 10.2 kg /d to 13 kg /d by increasing the starch content of the ration. The cows fed the high NFC rations pre- and post-calving had about a 5 lb increase in milk production / day as well. Because the animals were adapted to the higher starch pre-calving the cows could be safely moved to a post-calving ration that was 46.5% NFC without suffering rumen acidosis and laminitis. In contrast changing from a pre-fresh ration that was 23.5% NFC to a post-calving ration that was 41.7% NFC resulted in greater laminitis. This points out that the changes in energy content must not be drastic. Cows can handle high starch rations but it takes time to step them up to the hotter rations.

Increasing starch concentration of the pre-calving ration is not likely to cause rumen acidosis in the pre-calving cow because of the overall low intakes of the dry cow. However, putting more starch in generally means you have reduced the fiber (NDF) content of the ration and this is where the problem lies as it can increase the susceptibility of the herd to displacement of the abomasum. The key is to feed a forage that supplies adequate effective fiber (i.e. particles that are greater than 1.5 inches long that help form a raft on top of the rumen fluids), and is not so long or so unpalatable that it is sorted out by the cows. This often means chopping the forages going into the TMR and adjusting moisture content (a good target is 55-60% dry matter) so sorting is less likely. In some cases the addition of good clean straw can supply good effective fiber while allowing room in the ration for the added starch in both the pre-calving and post-calving rations. Alfalfa haylages, by and large very palatable, may not supply enough effective fiber to form a good rumen mat and it is this mat that is critical to prevention of left displaced abomasum. Corn silage chopped with less than 1/2 inch theoretical length of cut also does not contribute greatly to formation of the rumen raft.

**Safe and Standard Recommendation:** Close-up rations should contain from 35-38% NFC. The total NDF should be a minimum of 33% and preferably at least 26% forage NDF.

The immediate post-calving ration can then safely be increased to 40-42% NFC. Keep NDF of the fresh cow diet above 27% and forage NDF at least 21% of the ration.

“Cutting edge” or “Crazy” Recommendation: Close-up rations should contain from 38-42% NFC. The total NDF should be a minimum of 30% and preferably maintain at least 26% forage NDF. The immediate post-calving ration can then be increased to 44% NFC. Again, keep NDF of the fresh cow diet above 27% and forage NDF at least 21% of the ration.

It is absolutely essential that forages be eaten and not sorted from this type of diet strategy in both the close-up and fresh cow pens!! It may be necessary to add chopped straw or grass hay to these rations to ensure adequate effective fiber. In general this type of approach is too dangerous to be recommended.

NEW IDEA - The latest thoughts are that the key to preventing liver fat build-up is to prevent a drastic decline in feed intake (even if dropping from a high intake to a reasonable intake) as the delta change in feed intake seems to drive adipose fat mobilization. Limit feeding of a higher energy ration seems to work as well as ad lib feeding of such a ration (Holcomb et al., 2001). However limit feeding cows is not practical on the farm, as one cow always gets more feed than her weaker herd mates. One way to “limit” feed intake of the close-up cow is to feed a higher forage ration. The idea is that the cow will eat to her energy needs and to get this energy she will consume fairly large amounts of the forage diet and will remain “hungry” as she approaches calving and starts lactating. Daily dry matter intake pre-calving is reduced when compared to dry matter intake of cows fed the higher starch rations. However, proponents of this approach believe the depression in dry matter intake during the days immediately before and after calving is less severe in the high forage diets. These diets do seem to be able to reduce the incidence of early lactation displaced abomasums. One concern is that the shift from a lower energy pre-calving diet to a high energy lactating ration will be too great a change and cause rumen acidosis. However, these diets do not seem to have a higher incidence of rumen acidosis.

Research trials suggest that the high forage approach may reduce milk production over cows fed the high starch diets. I think that the high starch cow is similar to a race car – it will go faster and produce more milk – providing it does not crash. The higher forage diets may not win every race but fewer cows will crash and burn on these diets. Very good managers can make both diets work very well. It is likely that more attention should be paid to the comfort and environment of the cow than to the starch content of her diet.

#### **STRATEGY – ADD FAT TO PRE-FRESH AND POST-FRESH RATIONS TO “SPARE THE BODY’S GLUCOSE”**

The idea behind this strategy is that muscle and other body tissues can burn diet fat for energy instead of blood glucose. Unfortunately, most studies find no benefit and perhaps some increase in Non-esterified fatty acid content of blood when fat (both rumen protected or unprotected have been examined) is added to the close-up diet (Skaar et al., 1989). Studies done with cows in early

lactation also are not encouraging as the added fat generally has the effect of reducing feed intake in early lactation (Salfer et al. 1995). Once animals are eating well, adding limited amounts of fat to the ration generally increases milk production and improves body condition.

Recommendation - do not use supplemental fats until after 2-3 weeks into lactation.

#### **STRATEGY: INCREASING DIETARY PROTEIN IN TRANSITION AND FRESH COW RATIONS.**

The fresh cow loses significant amounts (60 –80 lbs) of muscle in the first weeks of lactation. She is primarily using the amino acids in her muscle to produce glucose. This strategy suggests that by feeding a high protein ration before calving we can build-up muscle reserves that the cow can draw on in early lactation to help her make glucose. Several studies were done suggesting less ketosis and less loss of body condition when dietary protein of the close-up ration was increased to 16-17% crude protein with 38--44% of the protein being rumen bypass protein (Van Saun, et al., 1993, Holtenius et al, 1993, Vandehaar et al., 1999). Some of these studies were complicated by changes in energy along with protein in the “high protein diet” treatments. Unfortunately a review of the recent literature does not support increasing diet protein (either as rumen bypass or even when adding essential amino acids) in pre-fresh rations as a means of improving health or milk production. Most studies suggest there is no gain made by increasing diet crude protein or rumen undegradable protein in close-up rations and a few studies suggest that high protein diets are even detrimental to the cows (Putnam et al., 1999, Greenfield et al., 2000).

#### **SO HOW MUCH PROTEIN DO WE FEED THE CLOSE-UP COWS?**

Santos and colleagues (2000) did a nice study to try to answer this question. They fed 2 levels of dietary protein, 12.7 or 14.7%, to heifers and cows for the three weeks prior to calving. These diets were 36 and 40% rumen undegradable protein respectively. Increasing protein in the close-up diet had no effect on milk production, blood glucose, post-partum body condition score, colostrum immunoglobulin content, or days to first corpus luteum formation in the cows. However, heifers responded to the higher dietary protein in the close-up pen with greater milk production (6.6 lbs/d on average). However blood glucose, post-partum body condition score, colostrum immunoglobulin content, and days to first corpus luteum formation were not improved by the high protein diet.

Recommendation: Cows need a certain amount of metabolizable protein to meet their maintenance needs and those of the calf. This is about 900 g protein /day in late gestation (NRC, 2001). If we add in another 150 – 200 g / day to account for development of the mammary gland we can predict the cow needs about 1100 g metabolizable protein / day. It seems that in most cases this is supplied when cows are fed 12-13% protein close-up rations. Heifers need 15% crude protein close-up rations – they are still trying to grow and in general

eat less on a body wt basis than do cows so the diet must be more protein dense. What if there is a mix of heifers and cows in the close-up pen? I recommend feeding 15% crude protein. Most diets fed pre-partum will have plenty of rumen undegradable protein to allow rumen bacteria to produce enough metabolizable protein to meet the needs of the close-up cows and heifers so feeding rumen “bypass protein” is not a major concern. In fact, animal sources of bypass protein (blood or fish meal) may reduce feed intake of the dry cow.

#### **HOW MUCH PROTEIN SHOULD BE IN “FRESH COW RATIONS”.**

When only one ration is fed to lactating cows that ration is generally formulated based on the higher intakes of cows at mid-lactation and well balanced rations containing around 16.5-17% protein will meet the protein requirements for milk production. However, studies demonstrate time and again that the low dry matter intake of the fresh cow will dictate that the amount of protein leaving the body as milk will exceed the amount she will obtain from a 17% protein diet. So, in addition to using body muscle to meet energy needs in early lactation she must also use body muscle to meet the protein needs of milk production.

If you are willing to formulate a special diet for fresh cows (first 2 wks of lactation), should the protein content of that ration be increased? Some early studies that attempted to improve protein balance in the fresh cow by increasing diet protein utilizing soymeal and alfalfa as sources of protein failed to improve protein balance. Unfortunately the protein in these feedstuffs is mostly rumen degradable. The rumen bugs have only a limited capacity to utilize the ammonia freed up during rumen digestion. Once that is exceeded the rest of the rumen degradable protein is wasted and useless to the cow. A few recent studies have suggested that adding rumen undegradable protein or adding certain essential rumen bypass amino acids to the fresh cow ration could benefit the cow and result in higher milk production (Blauwiekel et al., 1997, Khorasani et al., 1996, Armentano et al., 1993, Volden H. 1999, Iwanska et al., 1999, Garcia-Bojalil et al., 1998, McCormick et al., 1999).

However not all studies show a response. In a well done study by Palmquist and Weiss, (1994) blood meal was added to provide a good source of rumen bypass protein to fresh cows with no benefit. However, in this study adding blood meal reduced feed intake. It is therefore critical that the rumen bypass or amino acid supplements not reduce feed intake.

Safe Recommendation – Fresh cow pen rations should have 17-18% crude protein with 10.5 –11% of the ration being rumen degradable protein and the rest bypass protein.

Cutting edge recommendation– Increase diet protein in the fresh cow pen to 18-19 %. Limit rumen degradable protein to 10.5% of the ration. The rest

should be rumen undegradable protein (i.e. trying to formulate a 40-45% bypass protein ration!) Try to utilize a palatable source of rumen bypass protein such as expellers soybean meal. Animal protein may be utilized, but the amount must be limited because of poor palatability. Lysine should be about 7.2% and methionine should be 2.4% of the metabolizable protein reaching the small intestine of the cow (NRC, 2001). This can be difficult to achieve but the ratio of lysine:methionine should be kept as close to 3:1 as possible. If available, this may be an opportune time to utilize bypass amino acids in the ration. Generally, in corn based rations, lysine is the amino acid limiting milk production while methionine is more of a problem in barley based rations.

### **WHAT IS THE PROBLEM WITH FEEDING EXCESS PROTEIN?**

There are certainly environmental issues associated with feeding excess nitrogen to the cow. But it can also be detrimental to the cow in that excess nitrogen absorbed from the diet must be excreted from the body by coupling 2 nitrogen atoms to a carbon atom to form urea. Unfortunately that carbon comes from a carbohydrate source, i.e. the cow is burning up glucose to get rid of nitrogen. While not a huge energy cost overall it should be avoided when possible. For example a dry cow getting 17% crude protein when she only needs 12% crude protein will have to consume approximately 3/4 lb extra feed to supply the energy needed to get rid of that extra nitrogen.

### **ABOMASAL PHYSIOLOGY**

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 one third at 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 (Habel, 1981). After calving, the uterus retracts back 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<sub>2</sub> 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% (Daniel, 1983). 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 (Goff et al., 1996).

Volatile fatty acids within the abomasum have been demonstrated to reduce abomasal contractility (Breukink, 1991). A high grain, reduced forage diet can promote the appearance of VFA in the abomasum by reducing the depth of the rumen raft or raft (made up primarily of the long fibers of forages). The rumen raft captures grain particles so that they are fermented at the top of the rumen lyeur. The VFAs produced at the top of the rumen lyeur are generally absorbed across the rumen wall with little VFA entering the abomasum. In cows with an inadequate rumen raft, 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 good rumen raft is also necessary to stimulate rumen contraction in the cow. And since abomasum contraction is closely linked to rumen contraction through the vagal nerve reflex, if the rumen has inadequate raft to stimulate contraction then the abomasum also will not contract. A thick rumen raft is generally present during the dry period when cows are fed a high forage diet, but the depth of the rumen raft is rapidly reduced in early lactation as the amount of grain in the ration is increased. The rumen raft also rapidly disappears if the cow experiences a pronounced decline in dry matter intake in early lactation. This is another reason why cows with retained placenta, milk fever, or ketosis are at increased risk of displaced abomasums. Since the rumen raft 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.

So how do we maintain a good rumen raft in the cow while increasing the grain in her ration to get more milk? The fast answer is to get adequate fiber into the cow to maintain a healthy rumen. But what does this truly require? I prefer the definition that fiber useful to the cow, in terms of rumen health, must stimulate

chewing and saliva secretion in the cow. When a cow first eats from a bunk or from a pasture she spends very little time chewing her feed before swallowing. Later she finds a quiet place to lie down and she regurgitates those longer particles so she can chew them into particles fine enough to be digested and pass out of the rumen. As nutritionists we use neutral detergent fiber (NDF) as a measure of the fiber in ruminant rations. And in general terms as NDF increases the amount of time spent chewing increases. However, it must be remembered that NDF is a chemical measurement made on a feed sample. The laboratory value for NDF is exactly the same in long stemmed hay as it is in that same hay ground fine. But the cow will spend much more time chewing the long stem hay. Similarly, NDF coming from many non-forage fiber sources such as soybean hulls is too small in particle size and too rapidly digested to cause very much chewing in a cow (Mertens, 1997). Even within forages, a kg of NDF coming from wheat straw will cause much greater chewing in the cow than will a kg of NDF coming from good quality, readily digested alfalfa. Meeting the chewing requirements of the cow is a major problem contributing to displacement of the abomasums and also rumen acidosis. As a nutritionist the reliance on NDF target values alone can get us into trouble. Combining NDF determinations with some determination of physical size will greatly increase success. A convenient means of assessing particle size of the ration is the Penn State particle separator box. Full details on the use of this apparatus is given at the following website. <http://www.das.psu.edu/dcn/CATFORG/PARTICLE/index.html>

## **MINERAL METABOLISM PROBLEMS**

### **HYPOCALCEMIA AND MILK FEVER**

Hypocalcemia, especially if it is severe enough to cause milk fever, will begin a cascade of secondary problems in the fresh cow. Hypocalcemia (low blood calcium, not just milk fever) impairs abomasal contractions increasing the chance for displacement of the abomasums. It can also prevent the teat sphincter from closing after milking allowing bacteria access to the mammary gland resulting in more mastitis. The stress of hypocalcemia causes secretion of cortisol, which further impairs the immune system of the fresh cow. Milk fever and low blood calcium reduce feed intake, increasing the risk of ketosis in the cow as well.

We now believe that hypocalcemia occurs because the dairy cow is in an alkaline blood condition, largely because of the high potassium content of the forages utilized in close-up cow rations. A second major cause of hypocalcemia is inadequate magnesium absorption from the close-up and fresh cow rations leading to low blood magnesium concentration. We believe that when blood magnesium is marginally low it interferes with the body's ability to regulate blood calcium concentration.

### **1. DIETARY CATION-ANION DIFFERENCE AND ACID-BASE STATUS**

The difference between the total number of non-metabolizable cations and anions in the blood is referred to as the Strong Ion Difference. Strong ions enter the blood from the digestive tract making the cation-anion difference of the diet the ultimate determinant of blood Strong Ion Difference. Once absorbed the concentration of Strong Ions in the blood is regulated by the kidneys. Adjustment of the Strong Ion Difference of the blood is slower than respiratory control of blood pH but is capable of inducing much greater changes in blood pH.

In theory all the cations and anions in the diet are capable of exerting an influence on the Strong Ion Difference of the blood. The major cations present in feeds and the charge they carry are sodium (+1), potassium (+1), Ca (+2), and Mg (+2). The major anions and their charges found in feeds are chloride (-1), sulfate (-2), and phosphate (assumed to be -3). Cations or anions present in the diet will only alter the Strong Ion Difference of the blood if they are absorbed into the blood. The trace elements present are absorbed in such small amounts that they are of negligible consequence to acid-base status. Organic acids such as the volatile fatty acids are generally absorbed in the undissociated form so that they carry both a positive and negative charge into the blood. They also are rapidly metabolized within the liver so they have only a small effect on blood pH under most circumstances. However in the case of lactic acidosis the lactate anion can build-up in the blood of the affected animal and cause severe metabolic acidosis.

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:

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

This equation is useful, although it must be kept in mind that Ca, Mg, and P absorbed from the diet will also influence blood pH. 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:

$$(0.2 \text{ Ca}^{++} + 0.16 \text{ Mg}^{++} + \text{Na}^+ + \text{K}^+) - (\text{Cl}^- + 0.6 \text{ S}^{--} + 0.64 \text{ P}^{--})$$

This equation suggests that the major dietary factors determining blood and urine pH are Na, K and Cl. It also suggests that sulfate is less acidifying than chloride, in general agreement with the findings of Oetzel et al. (49). Tucker et al (64) felt that sulfate was about 60% as acidifying as chloride. The particular coefficient is less important than the concept that chloride may be the better choice of acidifying agent. A complete equation should probably also include ammonium as this cation seems to contribute to the cation content of the blood as well, especially when certain high nitrogen grass silages are included in the diet of the cow (11).

Most nutritionists using the equation  $((\text{Na}^+ + \text{K}^+) - (\text{Cl}^- + \text{S}^{2-}))$  have a target DCAD for milk fever prevention of about -50 mEq/kg. Using the more physiologically relevant equation,  $(0.2 \text{ Ca}^{++} + 0.16 \text{ Mg}^{++} + \text{Na}^+ + \text{K}^+) - (\text{Cl}^- + 0.60 \text{ S}^{2-} + 0.64 \text{ P}^{3-})$ , the target DCAD should still be about -50 mEq/kg. The true usefulness of the equation is that it helps you predict how certain minerals will affect the acid-base balance. For example if sodium chloride (NaCl) is fed to the cow both the sodium cation and the chloride anion are nearly 100% absorbed from the diet into the blood. The blood gains salt but since the number of positively and negatively charged particles entering the blood is the same there is no net change in electrical charge of the blood and the pH is not altered. However if calcium chloride ( $\text{CaCl}_2$ ) is fed, approximately 15% of the calcium cation equivalents (remember calcium carries a charge of +2) will enter the blood while nearly 100% of the negatively charged chloride will enter the blood. There are more negatively charged particles entering the blood than positively charged particles and the  $\text{H}^+$  of the blood must increase to offset the electrical imbalance. When  $\text{H}^+$  increases, the pH decreases, meaning the blood has been acidified.

Several of the variables in the above DCAD equations are fixed reducing the usefulness of the equations when formulating rations. A strategy this author uses is to set dietary Ca at 0.8-1.0%. Then I set dietary P and Mg at 0.35-0.4%. I keep dietary sulfur above 0.25% (to ensure adequate substrate for rumen microbial amino acid synthesis) but below 0.4% (to avoid possible neurological problems associated with sulfur toxicity (27)). The key to clinical milk fever prevention is to keep sodium and potassium as close to the requirement of the cow as you can (0.10-0.15% for Na and 1.0% for potassium). The key to reduction of subclinical hypocalcemia is to then add chloride to the ration to counteract the effects of even low levels of potassium on blood alkalinity. In practice we find that the level of chloride needed will be about 0.5% less than the level of potassium. So if the lowest ration potassium that can be achieved is 1.4% K then the amount of chloride needed to acidify the cow properly will be approximately 0.9%. There is a limit to the amount of chloride a cow will ingest so it is important to reduce diet potassium and important to choose a palatable source of chloride when manipulating DCAD. Traditionally this was done by adding anionic salts such as ammonium chloride, calcium chloride, or magnesium sulfate to the ration. Unfortunately these salts often reduced feed intake in cows causing more problems than it was curing. We believe that chloride is a more effective acidifier than sulfate anions. We also have demonstrated that hydrochloric acid is a more effective acidifying agent than the traditional anionic salts and also appears to be more palatable. Several commercial firms are now producing anion supplements that are based on hydrochloric acid that has been dried down onto a suitable carrier to make a safe supplement. Beware that liquid hydrochloric acid creates fumes that are toxic and corrosive, making it very unsafe to use on dairies.

These are simply guidelines and are based on the setting of certain parameters at constant values as outlined above. Urine pH of the cows is a better gauge of the appropriate diet DCAD than any formula (37). Urine pH on high cation diets is generally above 8.2. Limiting dietary cations (primarily potassium) will reduce urine pH only a small amount (down to 7.8). For optimal control of subclinical hypocalcemia and milk

fever the average pH of the urine of Holstein cows should be between 6.2 and 6.8, which essentially requires addition of anions to the ration. In Jersey cows the average urine pH of the close-up cows has to be reduced to between 5.8 and 6.3 for effective control of hypocalcemia. If the average urine pH of any group of cows is between 5.0 and 5.5, excessive anions have induced an uncompensated metabolic acidosis and the cows will suffer a decline in dry matter intake. Urine pH can be accurately checked 48 or more hrs after a ration change. Urine samples should be free of feces and made on midstream collections to avoid alkalinity from vaginal secretions. In cows offered feed twice / day the timing of the urine collection does not seem critical. In cows fed fresh feed just once / day the diurnal variation in urine pH can be a full pH unit. The best estimate of acid-base status in cows fed one time /day appears to be from samples obtained 6-9 hrs after fresh feed was offered.

## **B. MG STATUS**

As already discussed the integrity of the interaction between PTH and its receptor is vital to Ca homeostasis. Hypomagnesemia (blood magnesium below 1.8 mg/100 ml plasma) is also capable of interfering with the ability of PTH to act on its target tissues. When PTH binds to its receptor this normally initiates activation of adenylate cyclase, resulting in production of the second messenger cyclic AMP, or phospholipase C, resulting in production of the second messengers diacylglycerol and inositol 1,4,5-triphosphate. Both adenylate cyclase and phospholipase C require Mg for full activity. In man, it is well recognized that hypomagnesemia can cause hypocalcemia and that Mg therapy alone restores the serum Ca concentration to normal; Ca and/or vitamin D therapy are ineffective (55).

Ordinarily, PTH will cause increased renal tubular reabsorption of Mg, so the kidneys are excreting less of the excess dietary Mg absorbed. This causes blood Mg to be elevated in the typical milk fever cow (25). However if dietary Mg is insufficient or if rumen absorption of Mg is impaired, there is no excess Mg to conserve and the plasma Mg concentration will fall below 1.85 mg/dl as a result of the lactational drain of Mg. Sampling the blood of several cows within 12 hrs after calving is an effective index of the Mg status of the periparturient cows. If serum Mg concentration is not at least 2.0 mg/dl it suggests inadequate dietary Mg absorption and that hypomagnesemia may be contributing to hypocalcemia in the herd. Mg content of the close-up dry cow ration should be at least 0.35 - 0.4% to ensure adequate Mg absorption during this critical period.

Heifers do not need anionic salts. They may perform more poorly as a result of reduced feed intake. Again this is more of a problem when the unpalatable anionic salts are used. Ideally heifers would be fed separately from older cows – they perform better on higher protein diets, without anions, and, when housed separately, do not have to compete with cows for bunkspace. Heifers do respond to the lower potassium diets with less udder edema. When chloride is utilized as an anion source it has a diuretic effect, which may decrease udder edema in some herds. However this may not be true when ammonium chloride salts are used.

## **FREQUENTLY ASKED QUESTIONS ON DCAD**

### *Are some anions better than no anions?*

In my opinion – yes. But the full benefit of anion supplementation is only seen when urine pH (and blood pH) are adequately acidified. Many nutritionists are reluctant to add anions, as they do not feel the urine pH will be monitored properly. They prefer to control potassium in the diet and maybe use a small amount of calcium chloride and magnesium sulfate to get adequate levels of calcium and magnesium into the ration. This is probably better than no anion program but will not give total control of subclinical hypocalcemia.

### *What level of calcium do I feed if I am not going to add anions to the diet?*

A. If potassium can be controlled (get total ration K < 1.6% at least) then the diet calcium content does not seem critical. I like to get calcium to at least 0.8% and I will use a bit of calcium sulfate or calcium chloride to increase calcium if needed. I will not add calcium carbonate (limestone) just to reach the 0.8% Ca concentration. I would rather add no calcium than add calcium carbonate.

B. If you have no control over potassium in the diet (grazing systems are particularly hard to control) then I might consider trying to control hypocalcemia by instituting a “very low calcium” diet. For this to work the diet cannot supply more than 25 g calcium / day!! This only works when the forages are low in calcium (certain grass species that may be less than 0.35-0.4% Ca) and total feed intake is limited (grazing dry cows eat 6-8 kg / day, which is much less than confined dry cows consuming TMR, which eat 10-14 kg / day). Consuming 7 kg /d of a 0.35 % Ca grass will supply 24.5 g calcium / day. As can be seen this strategy can be difficult to implement.

## **LOW POTASSIUM FORAGES**

The major culprit causing low blood calcium is high potassium coming into the ration from forages. Sodium is also very bad but generally is not very high in forages unless they are grown in soils that have been irrigated for a long time. **FIND or GROW LOW POTASSIUM FORAGES FOR YOUR CLOSE-UP DRY COWS.** Limit potash and manure applications. Rely on corn silage as a major feedstuff for close-up cows. It is palatable, and usually low in potassium. Some low potassium byproduct feeds should also be considered. I like to use beet pulp without molasses, brewers grains, and corn gluten feed. **DO NOT TRUST POTASSIUM VALUES DETERMINED BY NEAR INFRARED ANALYSIS.** Potassium and most minerals need to be determined by wet chemistry analyses.

It is also possible to grow forages with increased levels of chloride in them. Therefore it is possible to find low potassium, high chloride forages that are ideal for use in the dry cow ration. Beware that chloride analysis are not done well by every laboratory. (NOTE: IN LACTATION HIGH DCAD FORAGES ACTUALLY INCREASE MILK PRODUCTION!)

## **ACUTE HYPOPHOSPHATEMIA**

Beef cows fed a diet marginal in P will have a chronic hypophosphatemia of 0.6 - 1.1 mmol/L or 2-3.5 mg/dl. In late gestation plasma P can decline precipitously as the growth of the fetus accelerates and removes substantial amounts of P from the maternal circulation. These animals often become recumbent and are unable to rise, though they appear fairly alert and will eat feed placed in front of them. Cows carrying twins are most often affected. Plasma P concentration in these recumbent animals is often less than 0.3 mmol/L or 1 mg/dl. The disease is usually complicated by concurrent hypocalcemia, hypomagnesemia, and in some cases hypoglycemia.

At the onset of lactation the production of colostrum and milk draws large amounts of P out of the extracellular P pools. This alone will often cause an acute decline in plasma P levels. In addition if the animal is also developing hypocalcemia, PTH will be secreted in large amounts that increases urinary and salivary loss of P. In dairy cows, plasma P concentrations routinely fall below the normal range at parturition and in cows with milk fever plasma P concentrations are often between 0.3 and 0.6 mmol/L or 1 and 2 mg/dl. Plasma P concentrations usually increase rapidly following treatment of the hypocalcemic cow with intravenous Ca solutions. This rapid recovery is due to a reduction in PTH secretion, reducing urinary and salivary loss of P. The calcium injection also stimulates resumption of gastrointestinal motility allowing absorption of dietary P and reabsorption of salivary P secretions (17).

Some animals developing acute hypophosphatemia do not recover normal plasma P concentration. This is sometimes the case in cows that are classified as "downer cows". This syndrome often begins as milk fever but unlike the typical milk fever cow, plasma P remains low (below 1 mg/dl) in some of these cows despite successful treatment of the hypocalcemia. Protracted hypophosphatemia in these cows appears to be an important factor in the inability of these animals to rise to their feet, but why plasma P remains low is unclear. In some cases the inability to absorb the salivary phosphate is secondary to poor rumen motility, but not in all cases. Excessive cortisol secretion could also be driving blood P concentration down (32). How this occurs is unknown. Treatment of cows with phosphate containing solutions (orally or intravenously) can effect a recovery in some animals (10) (18). The syndrome does not appear to be caused by low P diets as affected cows are often receiving diets containing 0.4% dietary P.

## **“PUMPING” OR “DRENCHING” COWS**

Abraham Lincoln said it was better to sit silently and let people think you were a fool than to open your mouth and prove it. At the risk of proving to be a fool I will give my 2 cents on drenching cows.

Because of the problems and cost and poor results associated with feeding energy precursors to cows that typically **go off feed the day of calving anyway** we got going on drenching cows. Ric Grummer's group had done some nice work showing that drenching cows for several days before and after calving (1 Liter propylene glycol/ day) greatly decreased NEFA and liver fat deposition. We have tried propylene glycol, calcium propionate (a source of calcium and a glucose precursor) and glycerol (used years ago but too high priced - until biodiesel industry caused price drops recently) and the blood profiles we could produce in the animals here in our NADC lab herd looked good - reduce NEFA for at least several hrs immediately after drenching and for calcium propionate also get a boost in calcium. Sandy Stokes and I set out to see if there was anything to this in a commercial setting. First we looked at calcium propionate (1.5 lb / drench) vs. propylene glycol (300 mls/drench) in 2.5 gal water vs. water alone giving it just at calving and at 24 hrs after calving. Cows getting propylene glycol averaged 3.1 kg more milk / day than water treated cows in early lactation ( $p < .05$ ). Cows getting the calcium propionate also made more milk (1.4 kg / day) but this was not statistically significant. Cows (removing the heifers from the data set) made 1.8 kg / day more but it still was not significant. One thing to keep in mind is that it is difficult to show a milk effect of less than 3-4 kg / day unless you have a large number of cows – sire effects alone make variation in milk production difficult to deal with. By the way this herd was a very well managed herd and the herd was averaging 40 kg milk / day (Stokes and Goff, 2001).

We have also tried using glycerol on farms. One less than ideally managed herd responded with 2.6 kg more milk / day in glycerol treated cows. Not statistically significant – only 50 cows per treatment. Blood profiles showed reduced NEFA etc. On another dairy (much better managed than the first) the same treatment had no effect and the cows actually lost nearly a kg of milk – again not statistically significant. That herd we did no blood work.

Several other studies have been done now (Pickett et al., 2003) and most show an acute drop in NEFA after drenching. None can show a significant milk benefit – usually because too few cows are used in the study. We are trying to see if electrolytes are needed or helpful. Is the water alone a key component to the drenches? How about magnesium, yeast, aspirin? We don't have enough cows or money to give you a full report on each yet. Then what about the combinations??

So is drenching worth it?? I don't have a good answer. I can say that it is not just a band-aid for poor nutrition as the first herd we worked with – where we did enough cows to get statistical significance -was an excellent herd where pre-

fresh intakes were around 16 kg / day. If you can get 1 kg more milk / day the cost is certainly paid back many fold.

Now if you are brave enough or foolish enough to try this I suggest you try to keep some kind of records on it – drenching is too laborious to do if there is no measurable benefit.

### **WHAT GOES INTO A DRENCH?**

Energy precursors - choices are propylene glycol (about \$\$2.50/ kg), calcium propionate (\$1.80 / kg) or sodium propionate (\$2.10 / kg), or glycerol (\$0.80/ kg). All can be toxic in high doses so you cannot just give a large dose. In the case of propylene glycol and glycerol it appears to cause osmotic changes in the brain and short term (and sometimes permanent) neuro problems. Ca propionate seems to be relatively safe until you get blood calcium too high. I haven't drenched sodium propionate very much so I don't have much on toxicity.

### **SO HOW MUCH?**

#### **ENERGY SOURCES**

**Propylene glycol** - I limit to 300 mls / drench. I don't think the rumen smells very good at higher doses and I think (anecdotal evidence based on just a few cows) that 1 liter doses decrease rumen motility.

**Calcium propionate** - 1 lb / cow in smaller cows and Jerseys. 1.5 lbs for bigger cows. 3 lbs will kill most cows from hypercalcemia.

**Glycerol** - 500 - 750 mls seems to work well. We look at glucose profiles following drenching and I don't think we see much benefit with the larger doses we used in some earlier field trials.

I am beginning to think there is a limit to the amount of glucose precursor that can be sent thru the gluconeogenic pathway at one time. So combinations of these substances, each at its recommended dose, are more likely to hurt than help the cows.

#### **CALCIUM SOURCES**

Calcium propionate discussed above.

Calcium chloride is another possibility. Very caustic and I don't like it especially in cows that were on anionic salts pre-calving. Too acidifying. But if

you want to use it the proper dose would be around 120 g anhydrous calcium chloride / drench. (=50 g Calcium)

Do you need a calcium source in a drench? We thought it would be good – as studies we did in California (Goff et al., 1996) showed some benefits on reduction of hypocalcemia. But if cows are fed anionic salts properly before calving there seems to be little benefit to an additional calcium drench as a fairly large study in Florida shows (Melendez et al., 2002).

## **MAGNESIUM**

Whenever you give a calcium supplement you should also give a magnesium source as the calcium shuts off PTH secretion and blood magnesium falls precipitously. I like to give 220 g magnesium sulfate.7H<sub>2</sub>O (epsom salts) with these calcium drenches to help maintain normal blood magnesium. Other magnesium sources are not soluble enough.

## **ELECTROLYTES**

Potassium chloride - I used to think this was only good in cows off feed but I am thinking now (again minimal data) that this might also be useful in these drenches. I give 110 g / drench. DON'T GO MUCH HIGHER THAN THIS- too much risk of heart blockage!!

## **OTHER**

Yeast - I give 120 g / drench - no data - just seems like a good idea.

**Aspirin** - 2-3 boluses ground up. I use the 240 grain tablets and I give 3 of them so that comes out to about 45 g of aspirin / cow. Does it do any good? I don't know. May not even be legal to use aspirin in this way. But I figure we see many low grade fevers in fresh cows. I suspect there is also a certain amount of pain associated with the passage of a 100 lb object thru the pelvis that might inhibit appetite. I like to think the aspirin might get her feeling well enough to go up to the bunk and eat.

**Water** - I usually use 3-5 gallons / drench. We are now looking at the blood work from cows given 5 vs. 10 gallons in a drench. I can't really see much difference yet. I do think the greater volume increases work and problems from aspiration. Does it weigh down the rumen and prevent LDA???? I have No data.

Alfalfa meal or expellers soymeal or even cornmeal - 1-1.5 kg fine ground so I can pump it through the tube into the rumen. Often more of a pain in the neck due to plugged pumps than it is worth. If I could easily get rumen fluid into each cow I would do that, certainly I do it for sick cows - I have found that nearly every sick cow benefits from a rumen transfaunation with about 1-2 gal rumen juice.

You can pick and choose which of the above you want to use - sorry - no great data to back them up.

### **HOW TO GET IT INTO THE COW?**

Our studies were all done with the Magrath esophageal tube and pump. One man can operate it quite simply. However you can expect to drown 1 in 250 cows. I think the problem is mostly from impatience during pumping. The Cow should be chewing on the tube when you pump. Pump too fast and you get reflux back up esophagus and into throat. **HOOK THIS SYSTEM UP TO A MOTORIZED PUMP AND KISS THE COW GOOD-BYE.** You will exceed their ability to get it into the rumen and drown cows.

Because of the drowning issue I have switched over to the FLUX tube being sold by Thomas Geishauser up in Guelph. It is a longer tube that goes all the way into the rumen. I then use the magrath pump hooked up to the FLUX tube. If I was looking at a lot of cows I would probably mechanize the pumping with a sump pump since it would now be safe since it extends all the way into the rumen. Even with the flux tube – **CHECK PLACEMENT OF TUBE BEFORE PUMPING** - usually I can feel two hard objects in throat rather than one and I know I have succeeded in placing the tube into the esophagus. Feeling just one hard object means your tube is inside the trachea.

I don't drench more than once per 24 hrs. The doses of the ingredients listed above were done with that in mind. Giving every 12 hrs would likely prove toxic.

I hope this helps. Drenching remains poorly researched, but I suspect many of you may be thinking of giving it a try. At least I hope you don't repeat my mistakes. Just maybe you will get some of the responses we have gotten.

### **MASTITIS AND RETAINED PLACENTA**

There has been some association between the development of retained placenta and the incidence of mastitis. We have recently confirmed studies begun by Gunnink (1984) that suggest the two are likely linked because both are due to immune suppression in affected cows. Gunnink's theory suggested the fetal placenta must be recognized as "foreign" tissue and rejected by the immune system after parturition to cause expulsion of the placenta. We hypothesized that impaired neutrophil function causes retained placenta. We examined the ability of neutrophils to recognize fetal cotyledon tissue as assessed by a chemotaxis assay that utilized a placental homogenate obtained from a

spontaneously expelled placenta as the chemoattractant. Neutrophil killing ability was also estimated by determining myeloperoxidase activity in isolated neutrophils. Blood samples were obtained from 142 periparturient dairy cattle in 2 herds. Twenty cattle developed RP (14.1 %). Neutrophils isolated from blood of cows with RP had significantly lower neutrophil function in both assays prior to calving and this impaired function lasted for 1-2 wk after parturition. Addition of antibody directed against interleukin-8 (IL-8) to the cotyledon preparation used as a chemoattractant inhibited chemotaxis by 41% suggesting one of the chemoattractants present in the cotyledon at parturition is IL-8. At calving plasma IL-8 concentration was lower in RP cows ( $51 \pm 12$  pg/ml) than in cows expelling the placenta normally ( $134 \pm 11$  pg/ml) (Kimura et al., 2002). These data suggest neutrophil function determines whether or not the cow will develop RP. These data also suggest that depressed production of IL-8 may be a factor affecting neutrophil function in cows developing RP. This suppressed immune system could also explain why the same cows are more susceptible to mastitis. Retained placenta probably does not cause mastitis but is symptomatic of a depressed immune system.

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