

Physiological Adaptations in Transition Dairy Cows

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Introduction

Dairy cows undergo tremendous changes during the transition from late gestation to early lactation. The importance of this period in determining health, productivity, and profitability has been underscored by the intense interest in nutrition and management of dairy cows during the transition period over the last several years. The fundamental driver of the physiological changes is to ensure provision of adequate nutrients for the calf, both prenatally and postnatally. Dairy production has capitalized on this metabolic drive by selecting for higher and higher milk production. After parturition, nutrient demand is not able to be met through feed intake alone because the rate of dry matter intake (DMI) increase is slower than the rate of milk energy output. As a result, the magnitude of metabolic challenge faced by modern dairy cows is almost staggering. As demonstrated in Table 1, requirements for net energy of lactation (NE_L) essentially double “overnight” as cows calve and commence lactation.

Table 1. Calculated net energy of lactation (NE_L) requirements (Mcal/d) for dairy cows and heifers 2 days before vs. 2 days after parturition.

Function	725-kg cow		570-kg heifer	
	Pre-fresh	Fresh	Pre-fresh	Fresh
Maintenance	11.2	10.1	9.3	8.5
Pregnancy	3.3	---	2.8	---
Growth	---	---	1.9	1.7
Milk production	---	18.7	---	14.9
Total	14.5	28.8	14.0	25.1

Calculated from NRC (2001). Assumes precalving body weight with average decrease for calf and fluid loss at calving, milk production of 25 kg/d for cow and 20 kg/d for heifer, each containing 4% fat.

The fact that many cows are able to meet this challenge without difficulty speaks to the fact that the metabolic adaptations necessary to support milk production are a component of the factors being genetically selected. The nutrient and energy deficits after parturition are met by

mobilization of body reserves and by decreasing nonessential use of glucose in non-mammary tissues. Metabolic adaptations are mediated by an exquisite pattern of hormonal shifts and changes in tissue responsiveness to those hormones. For example, growth hormone (GH) is increased around parturition and in early lactation (Grum et al., 1996), which increases responsiveness of adipose tissue to lipolytic signals such as norepinephrine. The resulting increase of nonesterified fatty acids (NEFA) from adipose tissue are used as alternate fuels for much of the rest of the body, and are also converted by the liver to ketone bodies. The ketones serve as alternate water-soluble fuels that can replace glucose in many tissues, thus conserving glucose for milk synthesis.

While a majority of cows are able to weather the metabolic challenges associated with initiation of milk synthesis, the fact that, on average, roughly 1 in 2 cows succumbs to some health problem during the transition period (Ferguson, 2001) underscores the fragility of the system.

Given the central importance of management during the transition period in determining profitability and cow well-being, the purpose of this presentation is to review some of the metabolic adaptations that occur. Newer information from our research program and others on control of these adaptations and how they impact our recommendations for nutrition and management schemes for transition cows is emphasized. Several comprehensive reviews on various aspects of transition cow biology and management are available for more information (Bell, 1995; Grummer, 1995; Goff and Horst, 1997; Drackley, 1999; Bell et al., 2000; Drackley et al., 2001).

Metabolic Changes During the Transition Period

As calving approaches, concentrations of progesterone in blood decrease and those of estrogen remain high or increase (Grummer, 1995). The high circulating estrogen is believed to be one important factor that contributes to decreased dry matter intake (DMI) around calving (Grummer, 1993). During the last 3 wk of pregnancy, nutrient demands by the fetal calf and placenta are at their greatest (Bell, 1995), yet DMI may be decreased by 10 to 30% compared with intake during the early dry period. This in itself may not be cause for alarm, as decreased food or feed intake around parturition is a common finding in many mammalian species (Friggens, 2003).

After calving, the initiation of milk synthesis and rapidly increasing milk production greatly increases demands for glucose for milk lactose synthesis, at a time when feed intake has not reached its maximum. Because much of the dietary carbohydrate is fermented in the rumen, little glucose is absorbed directly from the digestive tract. Consequently, dairy cows rely almost exclusively on gluconeogenesis (synthesis of glucose) from propionate in the liver to meet their glucose requirements. Limited feed intake during the early postpartal period means that supply of propionate for glucose synthesis also is limited. Amino acids from the diet or from skeletal muscle breakdown as well as glycerol from mobilized body fat contribute to glucose synthesis. Glucose supply to the mammary gland also is enhanced by the decreased oxidative use of glucose that accompanies the initiation of lactation (Drackley et al., 2001). In turn, glucose is directed to the mammary gland by the low circulating insulin concentration because mammary

uptake of glucose is independent of insulin, in contrast to adipose and skeletal muscle.

The total intake of energy by cows after calving usually is less than energy requirements, even in healthy cows (Bell, 1995). The high ratio of growth hormone to insulin in blood of cows allows mobilization of long-chain fatty acids from adipose tissue (body fat) to attempt to make up the deficit between intake and requirements (i.e., negative energy balance). Fatty acids released from adipose tissue circulate as NEFA, which are a major source of energy to the cow during this period. The concentration of NEFA in blood reflects the degree of adipose tissue mobilization (Pullen et al., 1989); therefore, as negative energy balance increases, more NEFA are released from body fat and the concentration of NEFA in blood increases.

Adipose tissue depots in the cow are oriented toward mobilization of NEFA at this time, rather than lipid deposition (McNamara, 1991). Lipogenesis (fat synthesis) is essentially shut down, and the sensitivity to lipolytic signals (epinephrine and norepinephrine) is greatly enhanced. In recently completed research, we demonstrated that the increase of NEFA in blood in response to an intravenous epinephrine challenge was greatly increased at 7 d after calving relative to 10 d before calving, and was greater at 7 d than at 14 d postpartum (Underwood et al., 2003, unpublished). Consequently, stressors and poor nutritional management that cause decreases in voluntary DMI will result in large increases in NEFA immediately after calving. Moreover, factors secreted in response to infection, stress, or trauma result in increased NEFA concentration and increased fat in liver (Herd et al., 1983). The mediators responsible for such responses most likely are the cytokines (tumor necrosis factor " ", interleukin-1, and interleukin-6, among others).

As the concentration of NEFA in blood increases around calving or in early lactation, more NEFA are taken up by the liver (Emery et al., 1992). Once taken up by the liver, NEFA can be 1) completely oxidized to carbon dioxide to provide energy for the liver, 2) partially oxidized to produce ketone bodies that are released into the blood and serve as fuels for other tissues, or 3) reconverted to storage fat (triglycerides). Ruminants have an inherently low capacity for synthesis and secretion of very-low density lipoproteins (VLDL) to export triglyceride from the liver (Kleppe et al., 1988; Pullen et al., 1989), but a similar capacity to reconvert NEFA back to triglyceride (Kleppe et al., 1988; Graulet et al., 1998). Moreover, the rate of production of triglycerides in the liver is increased at the time of calving (Grum et al 1996; Litherland et al., 2003, unpublished). Consequently, cows fed typical diets during the dry period and transition period have an increased concentration of triglyceride in the liver 1 day after calving (Skaar et al., 1989; Grum et al., 1996). If NEFA uptake by the liver becomes excessive, fatty liver may develop. Negative energy balance and carbohydrate insufficiency in the liver after calving leads to increased production of ketone bodies, which can result in ketosis. Our recent research suggests that ad libitum feeding of high-energy diets during the dry period can increase esterification capacity and decrease oxidation capacity in liver at 1 d post-calving, which would favor deposition of triglyceride in liver (Litherland et al., unpublished).

Factors that regulate the disposition of NEFA between oxidation and esterification in the liver of dairy cows still are not well understood. The primary site of control in many non-ruminant species seems to be at the entry of NEFA into the mitochondria where they can be oxidized to

carbon dioxide or to the ketone bodies. Entry into the mitochondria is controlled by the enzyme carnitine palmitoyltransferase (CPT-1). We have recently demonstrated that activity of CPT-1 and its sensitivity to the key inhibitor molecule malonyl-CoA is changed little during the transition, even during an induced (feed restriction) ketosis model (Dann et al., 2001).

We have also studied the activity of an auxiliary pathway of fatty acid oxidation that occurs in the peroxisomes. This pathway may be a component of the adaptations of fatty acid metabolism in liver during the periparturient period. Increases in peroxisomal fatty acid oxidation capacity in the liver may help the liver to cope with the large influx of NEFA from body fat mobilization (Grum et al., 1996, 2002) and help to prevent large accumulation of fat in the liver.

Maintaining optimal liver function is central to the ability of cows to make a smooth transition into heavy milk production. As the degree of fatty infiltration increases, normal functions of the liver are affected adversely. In particular, fat infiltration impairs the ability of the liver to detoxify ammonia to urea (Strang et al., 1998). Blood ammonia concentrations were positively correlated with the degree of fat accumulation in the liver of cows shortly after calving (Zhu et al., 2000). Ammonia decreases the ability of the liver to convert propionate to glucose (Overton et al., 1999), thus linking fat accumulation to impaired gluconeogenesis in liver (Drackley et al., 2001).

Fatty liver also impairs the ability of the liver to detoxify endotoxin, and thereby renders the cow extremely sensitive to endotoxic shock and death (Andersen et al., 1996). In severe fatty liver, normal functions of the liver are severely depressed, which results in the condition of "fatty liver syndrome" or "clinical fatty liver" (Morrow, 1976). Feed intake and carbohydrate status of the cow are important in determining the extent of body fat mobilization, fatty liver, and ketone body production in the liver. Fat infiltration per se evidently does not lead to liver failure (Rehage, 1996) but may be a contributing factor at least in some circumstances.

The rapidity of the increase in glucose demand for milk production at calving places a strain on the ability of the cow to provide that glucose. Feed intake, and therefore propionate supply, increases less rapidly than milk production. During the first week after calving, it can be estimated that the supply of glucose from fermentation of dietary carbohydrates consumed may fall short of glucose demands by as much as 500 g/d (Drackley et al., 2001). Glucogenic amino acids and glycerol from body fat mobilization likely contribute to making up this shortfall. In support of this idea, we have measured by indirect methods a three-fold increase in rates of muscle protein mobilization during the first week after calving compared with prepartum values (Overton et al., 1998). Likewise, the capacity of liver tissue to convert alanine, an important glucogenic amino acid, into glucose was 198% of prepartum (21 d before calving) values on d 1 after calving, whereas capacity for conversion of propionate to glucose was increased by only 119% (Overton et al., 1998). Expression of mRNA for the key regulatory enzymes involved (pyruvate carboxylase and phosphoenolpyruvate carboxykinase) changed in a similar manner in the liver (Greenfield et al., 2000). These responses seem to be in response to a glucose deficit per se, because we could reproduce them in male sheep by injection of phlorizin, a compound that causes excretion of glucose in the urine (Overton et al., 1999).

In practical terms, this emphasizes the importance of dietary provision of metabolizable protein. Lack of response in milk production to increased rumen-undegradable protein supplementation, except in first-calf heifers (Van Saun et al., 1993; Santos et al., 2001), has been common in the literature (see Bell et al., 2000) and in our own experience (Underwood et al., 2001).

Nevertheless, the importance of maintenance of maternal stores of protein on long-term health, productivity, and reproduction is backed by strong indirect evidence (Bell et al., 2000).

Function of the immune system is depressed during the transition period (Mallard et al., 1998). Decreased ability of the immune system to respond to infectious challenges likely is responsible for the high incidence of environmental mastitis around calving, as well as the high incidence of metritis. Reasons for the decreased immune function are not well understood. Vitamins A and E as well as a number of the trace minerals (selenium, copper, zinc) play a role in enhancing immune function. Recent evidence suggests that negative energy balance or protein balance may be a major contributing factor (Goff, 1999). This finding relates well to the common observation that cows which seem to be the most stressed by nutrition and environmental factors, as judged by excessive loss of body condition, are the most likely to become ill. In particular, an inadequate supply of metabolizable protein has been related to impaired function of the immune system (Houdijk et al., 2001). Recent evidence linking retained placenta to a malfunction of the immune system (Kimura et al., 2002) suggests that protein nutrition also might impact the incidence of retained placenta.

The sudden onset of milk synthesis in the udder results in a tremendous demand for calcium. As a result, blood calcium concentrations can drop precipitously at calving, leading to milk fever. Smaller decreases in blood calcium, called subclinical hypocalcemia, are believed to be contributing factors in disorders such as displaced abomasum and ketosis by decreasing smooth muscle function, which is critical for normal function of the digestive tract (Goff and Horst, 1997). Hypocalcemia also leads to increased secretion of cortisol, which is believed to be a factor in increased incidence of retained placenta (Goff, 1999). Until the ability of the digestive tract to absorb calcium can increase, calcium must be obtained by breaking down bone. Metabolic acidosis caused by a negative dietary cation-anion difference (DCAD) favors mobilization of calcium from bone, whereas high dietary potassium concentrations and positive DCAD suppress this process (Horst et al., 1997).

The underlying basis for most of the metabolic adaptations is alterations of expression of key genes in response to hormonal and developmental cues. Progress in understanding these changes likely will accelerate in the next few years with the advent of expression profiling or microarray tools. In these techniques, the abundance of mRNA for thousands of genes can be quantified simultaneously on a glass slide about the size of a microscope slide. Our initial efforts in this area (Lor et al., 2003, 2004, unpublished), using a bovine cDNA microarray developed at the University of Illinois, has demonstrated that expression of hundreds of genes changes in the mammary gland and liver of cows as they move from late pregnancy into early lactation.

Relation of Nutritional Management during the Transition to Physiological Changes

In view of the dynamic nature of physiological changes during the transition period discussed

above, goals of nutritional and environmental management during this period can be summed up as follows:

- 1) Maximize the appetite of the cow at and after calving.
- 2) Provide a palatable, well-balanced, and highly digestible diet to allow the cow to attempt to meet her nutritional requirements.
- 3) Maintain (or enhance) immune function.
- 4) Minimize the extent of body fat mobilization around calving to that which is “normal” for the cow.
- 5) Provide adequate metabolizable protein to meet amino acid requirements for maintenance, fetal or milk requirements, and immune function.
- 6) Maintain blood calcium and magnesium at and after calving.

While it is not the focus of this paper to review various nutritional management strategies for transition cows, a few comments on various aspects of this topic in relation to the periparturient physiological changes are warranted.

Close-up groups and diets

The close-up diet approach is today’s version of the “steam-up diet”, a concept that has been in existence since at least 1928 (Boutflour 1928). It seems logical that use of separate close-up and fresh cow diets, especially when fed as a total mixed ration (TMR), should help cows come onto feed faster and more smoothly after calving, with a lower incidence of postpartum health disorders. The general concept of ration changes during the transition is that nutrient density is increased gradually from that fed to far-off dry cows to the higher nutrient density required for fresh cows. Because DMI of closeup cows declines by 10 to 30% during the last 7 to 14 days before calving, increased nutrient density may allow maintenance of the same intake *amounts* (pounds or grams per cow per day) of key nutrients such as protein despite lower total feed intake. The typical decrease in DMI before calving results in the need to increase contents of crude protein and NE_L by about 2 percentage units and 0.20 Mcal/kg of DM, respectively, in the close-up diet.

Current interest and support for the close-up diet of higher nutrient density (i.e., more cereal grains and less forage) stems from an elegant experiment by Bertics et al., (1992). In that experiment, researchers prevented the normal drop in DMI by force-feeding the refusals into one group of cows fitted with ruminal cannulas. The diet was a 50:50 mixture (DM basis) of corn silage and alfalfa silage, supplemented with vitamins and minerals. Force-fed cows had greater plasma glucose concentrations 2 d before calving and less liver triglyceride accumulation at 1 d after calving and tended ($P < 0.11$) to produce more 3.5% fat-corrected milk (46.1 vs. 41.7 kg/d) during the first 28 d of lactation. Of interest, however, is that by d 14 after calving, force-fed cows had greater plasma NEFA concentrations and by d 28 had similar liver triglyceride concentrations.

While implementation of close-up diets has been adopted enthusiastically by the industry in the

US, surprisingly few data are available to support their actual effectiveness in decreasing the incidence of health problems or increasing milk yield. VandeHaar et al., (1999) fed close-up diets with energy densities of 1.30, 1.49, and 1.61 Mcal/kg to cows during the last 28 d before calving. While prepartum DMI tended ($P < 0.11$) to be increased by about 1.5 kg/d for cows fed the highest energy diet compared with cows fed the lowest energy density, there was no difference in postpartum DMI, milk production, energy balance, or loss in body condition. Although numbers of cows were too small to make reliable inferences about health data, the number of health problems actually was numerically greater for the high density diet (11) than for the lowest density diet (5). Other studies have shown no differences in postpartum responses to widely differing nutrient intakes during the close-up period (Dewhurst et al., 2000; Holcomb et al., 2001).

Despite the relative lack of data supporting their efficacy, close-up rations have been widely adopted and in many cases seem to have proven beneficial in the field. In many cases, the aspects associated with the management of a group of close-up cows have become more important than the particular diet that is fed. Regardless, producers should be cautioned not to extend feeding of the close-up diet too long. Overfeeding high-starch rations (high in corn silage and grains) during the entire dry period is detrimental to cow performance. Our own research (Douglas et al., 1998; Dann et al., 2003, unpublished) indicates that this appears to be true even if cows are not overconditioned, which is well known to be detrimental (Fronk et al., 1980; Van Den Top et al., 1995). While a limited period (e.g., 3 weeks) of close-up feeding may be warranted, producers should not extend this more aggressive feeding program to the entire dry period.

Non-nutritional components of a good close-up program may be as important, or more important, than the nutritional strategy. The importance of low-stress and comfortable environments for transition cows has been discussed at this conference previously (Drackley, 2001). The questionable nutritional importance of the close-up group has been underscored again by a recent experiment from our laboratory, in which cows ($n = 36$ per group) had essentially equal DMI and milk production after calving when fed the same close-up diet at either ad libitum intake or in restricted amounts sufficient for only 80% of calculated precalving NE_L requirements (Dann et al., 2003, unpublished).

Dry matter intake

Regulation of DMI during the periparturient period is complex and largely not understood (Ingvarsen and Andersen, 2000). Based on high correlations between DMI 1 d before calving and DMI at 21 d after calving (Grummer, 1995), a major focus on maximizing prepartum DMI has existed in the field. Given the lack of significant differences, or in fact even improvements in postpartum DMI for cows restricted (Douglas et al., 1998) or limit-fed (Holcomb et al., 2001) during the dry period, this relationship may have been overemphasized or misinterpreted. Recently, we analyzed (Drackley, 2003, unpublished) the relationships between prepartum and postpartum DMI and the accumulation of lipid in the liver after calving from a previous data set (Douglas et al., 1998). Our hypothesis was that the change in DMI before calving was more

highly related to postpartum DMI and fat accumulation in the liver than the absolute DMI.

In that analysis (Drackley, 2003, unpublished), DMI for wk 3 postpartum was not correlated with DMI prepartum, but DMI for wk 1 postpartum was correlated with DMI for wk -1 ($r = 0.44$, $P < 0.01$). In contrast, DMI for wk 3 postpartum was correlated ($P < 0.01$) with percent changes in DMI during the last 3 wk ($r = 0.43$) or last 2 wk ($r = 0.41$) prepartum. The DMI for wk 1 postpartum was correlated ($P < 0.01$) with percent changes in DMI during the last 3 wk ($r = 0.34$), last 2 wk ($r = 0.49$), or last week ($r = 0.39$) prepartum. Contents of total lipid and TG in liver at d 1 postpartum were negatively related to decreases in DMI during the last 3 wk ($r = -0.63$ and -0.63), last 2 wk ($r = -0.67$ and -0.65), and last 1 wk ($r = -0.42$ and -0.38) prepartum. Thus, it appears that changes in DMI prepartum, and not the absolute DMI *per se*, are more highly related to poor intakes and fatty livers after calving. This emphasizes the importance of good management that maintains cows healthy and comfortable before calving. In this way, high DMI may be more of an indicator of the overall comfort and well-being of the close-up cows rather than a cause for its success.

Carbohydrates

Adequate fiber of sufficient particle size is needed to maintain good rumen function, prevent displaced abomasum, and achieve high DMI. On the other hand, excessive NDF content may limit intake. Cows during the last 3 wk before calving seem to consume no more than about 0.9% of their body weight as NDF (unpublished observations from available research data). Sufficient nonfiber carbohydrates (sugars and starch provided by grains) must be present to provide adequate energy in the form of propionic acid for glucose synthesis and to help suppress synthesis of ketone bodies.

Considerable emphasis has been placed in recent years on increasing the starch content of close-up or pre-fresh groups (Grummer, 1995; Minor et al., 1998; VandeHaar et al., 1999). Starches promote relatively greater ruminal production of propionate, which triggers insulin release and helps restrain body fat mobilization. Increasing starch also tends to improve total DMI, diet digestibility, and ruminal fermentation over forages alone (Grummer, 1995). Another proposed benefit of additional grains in the prepartum diet is to adapt the ruminal tissues and the rumen microbial population to the type of diet that will be fed after calving (Goff and Horst, 1997). Grain feeding increases length of the rumen papillae in comparison to feeding only poorly digestible roughages (Dirksen et al., 1985). It has been proposed that rumen papillae elongate in the presence of increased concentrations of the volatile fatty acids, thereby increasing the absorptive surface in the rumen and helping to prevent acidosis after calving. However, recent research has indicated that this likely is not a large factor in transition success of cows fed more typical close-up diets (Andersen et al., 1999).

Other methods exist to increase energy intake by pre-fresh cows. Simply using higher quality forages can have a major impact on ration energy density. High-fiber by-product feeds such as soy hulls, beet pulp, corn gluten feed, and wheat midds that are highly digestible also can improve total energy intake. While fermentation of fibrous feeds typically is thought to result in more

acetate than propionate production in the rumen, greater fermentability still increases total energy supply and supply of propionate for glucose production. Relative effects of cereal grains and corn silage versus highly digestible fibrous concentrates and higher quality grass or legume forages is a topic of current research. For example, precalving diets based on either high starch or high fibrous byproducts showed few differences in postpartum performance (Smith et al., 2002).

Body Condition

Dairy cows, like other mammals, undergo a normal cycle of body energy storage and mobilization, with increased body fat storage during mid-gestation and increased body fat mobilization during early lactation. Over the long term, dairy cows appear to “strive” to maintain some normal degree of body fatness (Friggins, 2002). Evidence for this phenomenon include the classic study by Garnsworthy and Topps (1982) and our own recent data (Douglas and Drackley, 1999, unpublished), showing that cows that are forced away from their desired body condition (either fatter or thinner) before calving eventually converge to a similar body condition score by 4 to 8 wk after calving. Management systems must recognize this basic phenomenon, and not try to circumvent the genetically programmed metabolic patterns during the lactation cycle. However, management or environmental circumstances that force cows away from the optimal body condition (i.e., too thin, too fat) may result in increased risk for health problems.

It is well known that overconditioned cows (>4.0 on a 5-point scale) are at greater risk for development of metabolic problems (Morrow, 1976; Fronk et al., 1980; Van Den Top et al., 1995). Overconditioned cows have poorer DMI after calving (Bines and Morant, 1983; Fronk et al., 1980) and readily break down their excessive stores of body fat. Obesity leads to increased susceptibility to the complex of metabolic disorders and infectious diseases known as the "fat cow syndrome" (Morrow, 1976). Assuming that fresh cow management is good, a thinner cow should have a better appetite after calving than a heavier cow.

In the recent experiment from our laboratory mentioned earlier (Douglas et al., 1998), we fed two diets during the dry period either at ad libitum intake or at restricted intake. Cows were housed individually in tie-stalls during the dry period. Diets contained the same calculated energy density (NE_L of 1.43 Mcal/kg) and were either high fat (4% of DM) or control. Cows fed ad libitum consumed about 157% of NRC (1989) NE_L requirements for dry cows and restricted cows were offered only enough feed to meet 80% of NRC recommendations. Body condition score at dry-off averaged about 3.0 (5-point scale). Cows fed either ration ad libitum gained about 0.2 body condition score units during the dry period, whereas restricted cows lost about 0.5 body condition units from dry-off to calving. Cows fed either ration in restricted amounts had less triglyceride in liver on day 1 after calving, and had faster rates of DMI increase after calving. Cows fed for ad libitum intake during the dry period produced about 2 kg/d less than restricted-fed cows (not significant). Of interest is that cows in both ad libitum and restricted groups reached the same body condition by about 5 wk after calving.

Results of this experiment indicated that under our controlled conditions, there was no advantage to feeding higher-energy diets during the dry period to try to add body condition to cows in moderately thin body condition going into the dry period. Earlier research also supports this concept (Kunz et al., 1985).

Nutrition During the Far-Off Dry Period

Because of the frustrating lack of repeatable success with close-up period nutritional manipulation in decreasing incidence of health problems and increasing subsequent production, we have begun to explore whether events during the far-off dry period may impact transition success. In a recently completed experiment (Dann et al., 2003a,b), we fed a moderate-energy diet ($NE_L \sim 1.60$ Mcal/kg) either for ad libitum access or in restricted amounts to supply only 80% of calculated requirements during the early dry period. We also fed a high-forage, low-energy diet ($NE_L \sim 1.30$ Mcal/kg; close to NRC requirements) that contained about 26% of the DM as chopped wheat straw. At 21 d before expected calving half of each group was switched to a typical close-up type diet fed for ad libitum intake, while the other half was fed the close-up diet at restricted intake (80% of energy requirements). Results from this experiment showed that far-off diet affected post-calving DMI and tended to affect milk production; cows that had ad libitum access to the higher nutrient diet had poorer performance than cows fed the bulky low energy diet or the restricted diet. In contrast, the close-up diets (ad libitum or restricted) had virtually no effect on transition outcome.

Our current working hypothesis to explain these results is development of insulin resistance in the overfed cows. All cows were in moderate to low body condition, but the metabolic profiles of these cows resembles that seen in overconditioned cows. Our cows overfed for the first five weeks of the dry period had similar blood glucose but greatly elevated insulin (indirectly indicating insulin resistance) and during the close-up period had greater concentrations of NEFA and BHBA than cows fed restricted amount of the same diet or the bulky low energy diet. Our hypothesis is that suppression of adipose lipolysis was decreased by impairment of insulin's antilipolytic signals, thereby leading to increased NEFA and decreased appetite. Others have provided evidence of insulin resistance due to overconsumption of energy during the dry period (Holtenius et al., 2003). We are currently following up on several aspects related to these phenomena.

Conclusions

Dairy cows undergo a tremendous set of metabolic adaptations as they go from late pregnancy to early lactation. These changes normally are exquisitely coordinated by hormonal changes to support the new physiological state of lactation, the concept known as homeorhesis. However, these adaptive processes fail or are overcome by environmental influences in too many cows, resulting in periparturient illness. Research to continue to increase our understanding of the adaptive processes and how they are affected by precalving nutrition and environmental influences will undoubtedly improve our management capabilities for cows during the transition

period. We are currently studying the impact of nutritional management during the long-ignored far-off dry period as a key in these adaptations.

References

- Andersen JB, Sehested J, Ingvarsen KL (1999) Effect of dry cow feeding strategy on rumen pH, concentration of volatile fatty acids and rumen epithelium development. *Acta Agric Scand Sect A Anim Sci* 49:149-155.
- Andersen PH, Jarlov N, Hesselholt M, Baek L (1996) Studies on in vivo endotoxin plasma disappearance times in cattle. *Zentralbl Veterinarmed A* 43:93-101.
- Bauman DE, Currie WB (1980) Partitioning of nutrients during pregnancy and lactation: a review of mechanisms involving homeostasis and homeorhesis. *J Dairy Sci* 63:1514-1529
- Bell AW (1995) Regulation of organic nutrient metabolism during transition from late pregnancy to early lactation. *J Anim Sci* 73:2804-2819.
- Bell AW, Burhans, WS, Overton, TR (2000) Protein nutrition in late pregnancy, maternal protein reserves and lactation performance in dairy cows. *Proc Nutr Soc* 59:119-136.
- Bertics SJ, Grummer RR, Cadorniga-Valino C, Stoddard EE (1992) Effect of prepartum dry matter intake on liver triglyceride concentration and early lactation. *J Dairy Sci* 75:1914-1922.
- Bines JA, Morant SV (1983) The effect of body condition on metabolic changes associated with intake of food by the cow. *Br J Nutr* 50:81-89.
- Boutflour RB (1928) Limiting factors in the feeding and management of milk cows. In: *Rep World's Dairy Congr* pages 15-20.
- Dann HM, Drackley JK, Morin DE (2001) Effects of prepartum intake, postpartum induction of primary ketosis, and periparturient disorders on carnitine palmitoyltransferase I activity in dairy cows. *J Dairy Sci* 84(Suppl. 1):352. (Abstr.).
- Dewhurst RJ, Moorby JM, Dhanoa MS, Evans RT, Fisher WJ (2000) Effects of altering energy and protein supply to dairy cows during the dry period. 1. Intake, body condition, and milk production. *J Dairy Sci* 83:1782-1794.
- Dirksen GU, Liebich HG, Mayer E (1985) Adaptive changes of the ruminal mucosa and their functional and clinical significance. *Bov Pract* 20:116-121.
- Douglas GN, Drackley JK, Overton TR, Bateman HG (1998) Lipid metabolism and production by Holstein cows fed control or high fat diets at restricted or ad libitum intakes during the dry period. *J Dairy Sci* 81(Suppl 1):295 (Abstr).
- Drackley JK (1999) Biology of dairy cows during the transition period: the final frontier? *J Dairy Sci* 82:2259-2273.
- Drackley, J. K. 2001. Nutrition and management of transition dairy cows: An integration of nutrition and stress physiology. Pages 113-134 *in* Proc. California Anim. Nutr. Conf., Fresno, CA. California Grain and Feed Assoc., Sacramento, CA.
- Drackley JK, Overton TR, Douglas GN (2001) Adaptations of glucose and long-chain fatty acid metabolism in liver of dairy cows during the periparturient period. *J Dairy Sci* 84(E Suppl):E100-E112.
- Emery RS, Liesman JS, Herdt TH (1992) Metabolism of long chain fatty acids by ruminant liver. *J Nutr* 122:832-837
- Ferguson JD (2001) Nutrition and reproduction in dairy herds. In: *Proc. 2001 Intermountain*

Nutr. Conf., Salt Lake City, UT. Utah State Univ., Logan. pages 65-82.

- Friggens NC (2003) Body lipid reserves and the reproductive cycle: towards a better understanding. *Livest Prod Sci* (in press).
- Fronk TJ, Schultz LH, Hardie AR (1980) Effect of dry period overconditioning on subsequent metabolic disorders and performance of dairy cows. *J Dairy Sci* 63:1080-1090.
- Garnsworthy PC, Topps JH (1982) The effect of body condition of dairy cows at calving on their food intake and performance when given complete diets. *Anim Prod* 35:113-119.
- Goff JP (1999) Mastitis and retained placenta - relationship to bovine immunology and nutrition. In: Kennelly J (ed.) *Adv. Dairy Technol.* 11:185-192.
- Goff JP, Horst RL (1997) Physiological changes at parturition and their relationship to metabolic disorders. *J Dairy Sci* 80:1260-1268.
- Graulet B, Gruffat D, Durand D, Bauchart D (1998) Fatty acid metabolism and very low density lipoprotein secretion in liver slices from rats and preruminant calves. *J Biochem* 124:1212-1219.
- Greenfield RB, Cecava MJ, Donkin SS (2000) Changes in mRNA expression for gluconeogenic enzymes in liver of dairy cattle during the transition to lactation. *J Dairy Sci* 83:1228-1236.
- Grum DE, Drackley JK, Clark JH (2002) Fatty acid metabolism in liver of dairy cows fed supplemental fat and nicotinic acid during an entire lactation. *J Dairy Sci* 85:3026-3034.
- Grum DE, Drackley JK, Younker RS, LaCount DW, Veenhuizen JJ (1996) Nutrition during the dry period and hepatic lipid metabolism of periparturient dairy cows. *J Dairy Sci* 79:1850-1864.
- Grummer RR (1993) Etiology of lipid-related metabolic disorders in periparturient dairy cows. *J Dairy Sci* 76:3882-3896.
- Grummer RR (1995) Impact of changes in organic nutrient metabolism on feeding the transition dairy cow. *J Anim Sci* 73:2820-2833.
- Herdt TH, Liesman JS, Gerloff BJ, Emery RS (1983) Reduction of serum triacylglycerol-rich lipoprotein concentrations in cows with hepatic lipodosis. *Am J Vet Res* 44:293-296.
- Holcomb CS, Van Horn HH, Head HH, Hall MB, Wilcox CJ (2001) Effects of prepartum dry matter intake and forage percentage on postpartum performance of lactating dairy cows. *J Dairy Sci* 84:2051-2058.
- Holtenius K, Agenäs S, Delavaud C, Chilliard Y (2003) Effects of feeding intensity during the dry period. 2. Metabolic and hormonal responses. *J Dairy Sci* 86:883-891.
- Horst RL, Goff JP, Reinhardt TA, Buxton DR (1997) Strategies for preventing milk fever in dairy cattle. *J Dairy Sci* 80:1269-1280.
- Houdijk JGH, Jessop NS, Kyriazakis I (2001) Nutrient partitioning between reproductive and immune functions in animals. *Proc Nutr Soc* 60:515-525.
- Ingvartsen KL, Andersen JB (2000) Integration of metabolism and intake regulation: a review focusing on periparturient animals. *J Dairy Sci* 83:1573-1597.
- Kleppe BB, Aiello RJ, Grummer RR, Armentano LE (1988) Triglyceride accumulation and very low density lipoprotein secretion by rat and goat hepatocytes in vitro. *J Dairy Sci* 71:1813-1822.

- Kunz PL, Blum JW, Hart IC, Bickel H, Landis J (1985) Effects of different energy intakes before and after calving on food intake, performance and blood hormones and metabolites in dairy cows. *Anim Prod* 40:219-231.
- Mallard BA, Dekkers JC, Ireland MJ, Leslie KE, Sharif S, Lacey Vankampen C, Wagter L, Wilkie BN (1998) Alteration in immune responsiveness during the peripartum period and its ramification on dairy cow and calf health. *J Dairy Sci* 81:585-595.
- McNamara JP (1991) Regulation of adipose tissue metabolism in support of lactation. *J Dairy Sci* 74:706-719.
- Minor DJ, Trower SL, Strang BD, Shaver RD, Grummer RR (1998) Effects of nonfiber carbohydrate and niacin on periparturient metabolic status and lactation of dairy cows. *J Dairy Sci* 81:189-200.
- Morrow DA (1976) Fat cow syndrome. *J Dairy Sci* 59:1625-1629.
- National Research Council (1989) *Nutrient Requirements of Dairy Cattle*. 6th rev. ed. Natl. Acad. Press, Washington, DC.
- National Research Council (2001) *Nutrient Requirements of Dairy Cattle*. 7th rev. ed. Natl. Acad. Press, Washington, DC.
- Overton TR, Drackley JK, Douglas GN, Emmert LS, Clark JH (1998) Hepatic gluconeogenesis and whole-body protein metabolism of periparturient dairy cows as affected by source of energy and intake of the prepartum diet. *J Dairy Sci* 81(Suppl 1):295 (Abstr).
- Overton TR, Drackley JK, Ottemann-Abbamonte CJ, Beaulieu AD, Emmert LS, Clark, JH (1999) Substrate utilization for hepatic gluconeogenesis is altered by increased glucose demand in ruminants. *J Anim Sci* 77:1940-1951.
- Pullen DL, Palmquist DL, Emery RS (1989) Effect on days of lactation and methionine hydroxy analog on incorporation of plasma fatty acids into plasma triglycerides. *J Dairy Sci* 72:49-58.
- Rehage J (1996) Investigations about the risk of liver failure in dairy cows with fatty liver in the model of cows with left abomasal displacement. *Habil-Thesis, Hannover School of Veterinary Medicine, Hannover, Germany.*
- Santos JEP, DePeters EJ, Jardon PW, Huber JT (2001) Effect of prepartum dietary protein level on performance of primigravid and multiparous Holstein dairy cows. *J Dairy Sci* 84:213-224.
- Skaar TC, Grummer RR, Dentine MR, Stauffacher RH (1989) Seasonal effects of prepartum and postpartum fat and niacin feeding on lactation performance and lipid metabolism. *J Dairy Sci* 72:2028-2038.
- Smith KL, Waldron MR, Overton TR, Drackley JK, Socha MT (2002) Performance of dairy cows as affected by prepartum dietary carbohydrate source and supplementation with chromium throughout the periparturient period. *J Dairy Sci* 85(Suppl. 1):23. (Abstr.).
- Strang BD, Bertics SJ, Grummer RR, Armentano LE (1998) Effect of long-chain fatty acids on triglyceride accumulation, gluconeogenesis, and ureagenesis in bovine hepatocytes. *J Dairy Sci* 81:728-739.
- Underwood JP, Drackley JK, Clark JH (2001) Intake and production by Holstein cows fed different amounts and sources of supplemental protein prepartum and postpartum. *J Dairy Sci* 84(Suppl 1):364 (Abstr).

- Van Den Top AM, Wensing T, Geelen MJH, Wentink GH, Van=t Klooster AT, Beynen AC (1995) Time trends of plasma lipids and enzymes synthesizing hepatic triacylglycerol during postpartum development of fatty liver in dairy cows. *J Dairy Sci* 78:2208-2220.
- Van Saun RJ, Idleman SC, Sniffen CJ (1993) Effect of undegradable protein amount fed prepartum on postpartum production in first lactation Holstein cows. *J Dairy Sci* 76:236-244.
- VandeHaar MJ, Yousif G, Sharma BK, Herdt TH, Emery RS, Allen MS, Liesman JS (1999) Effect of energy and protein density of prepartum diets on fat and protein metabolism of dairy cattle in the periparturient period. *J Dairy Sci* 82:1282-1295.
- Zhu LH, Armentano LE, Bremmer DR, Grummer RR, Bertics SJ (2000) Plasma concentration of urea, ammonia, glutamine around calving, and the relation of hepatic triglyceride, to plasma ammonia removal and blood acid-base balance. *J Dairy Sci* 83:734-740.