Managing and Monitoring Energy Metabolism of the Transition Cow

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Management to support the metabolic adaptations related to energy metabolism that a dairy cow undergoes during the transition period and early lactation is a critical factor in transition period success. Energy balance is tightly linked with reproductive performance (Butler and Smith, 1989), aspects of health and immunity (LeBlanc, 2010), and markers of excessive negative energy balance are generally negatively associated with milk yield (Ospina et al., 2010). Although a common notion is that milk yield is the major driver of negative energy balance, several data summaries (Santos et al., 2009; reviewed by Grummer et al., 2010) suggest that the relationship of negative energy balance is actually greater with dry matter intake (DMI) than with milk yield. Therefore, the major determinant of successful management of energy metabolism in transition cows may be the degree and rate to which energy intake increases during the early postpartum period.

Clearly, nutritional and environmental management of dairy cattle during the dry and transition period have important carryover ramifications both for DMI and overall lactational and reproductive performance along with health in early lactation. The purpose of this paper is to briefly overview intake regulation in dairy cattle, describe key metabolic changes in transition cows as they integrate with intake regulation and then to review key nutritional factors during both the prepartum and postpartum period that impact peripartal DMI and energy metabolism so that we can optimize subsequent performance and health outcomes. Finally, I will describe

INTAKE REGULATION IN DAIRY CATTLE

The first key concept to understand is that intake regulation in dairy cattle is complex. The various metabolic factors that influence DMI in dairy cattle were well-reviewed by Ingvartsen and Andersen (2000) and includes a variety of direct and indirect signals related to the environment, immune system, adipose tissue, signals from the gut and pancreas, and energy sensing of the liver relative to overall energy demand (Figure 1). It is likely that changes in these signals (and cow-to-cow variation in response to various environmental and metabolic stimuli) are responsible both for changes in overall average pen DMI but also variation in cow to cow DMI that likely is more associated with transition management challenges than average pen DMI per se.

More recently, Allen and coworkers (Allen et al., 2005; Allen et al., 2009) proposed that a major regulator of DMI in ruminants, and particularly dairy cattle, was hepatic energy status. This is largely driven by oxidation of fuels such as propionate derived from ruminal fermentation of rapidly fermentable carbohydrates and nonesterified fatty acids (NEFA), which are increased in the bloodstream during periods of negative energy balance and body fat mobilization (Figure 2).

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In periods when oxidative fuel metabolism by the liver exceeds liver energy requirements, the brain is signaled to decrease DMI. As will be discussed more in detail below, this theory is particularly attractive in explaining metabolic influences on DMI during the prepartum period. As will be described below, modulation of these pathways, particularly by propionate is less likely during the immediate postpartum period because of the large increases in liver energy demands along with other reasons that will be discussed below.

METABOLIC ADAPTATIONS IN THE TRANSITION COW

It is well-recognized that the dairy cows undergo important metabolic adaptations during late pregnancy to support fetal demands and at the onset of lactation to support milk production. These homeorhetic adaptations involved in the regulation of nutrient and energy partitioning during late pregnancy and early lactation occur in a variety of target tissues, and typically involve changes in responses of tissues such as adipose tissue and muscle to homeostatic signals such as insulin and epinephrine (Bauman and Currie, 1980; Bell, 1995). As described above, one major adaptation includes a large increase in glucose demand by the mammary gland that is supported by dramatically increased glucose output by the liver (Reynolds et al., 2003). In addition, peripheral tissues (primarily skeletal muscle) decrease their use of glucose for fuel (Bauman and Elliot, 1983; Petterson et al., 1993), thereby sparing glucose for use by the gravid uterus and lactating mammary gland. Furthermore, increased mobilization of body fat stores facilitated by changes in adipose tissue metabolism contributes to meeting increased whole-body needs for energy at the onset of lactation (Petterson et al., 1994). The net result of these adaptations is coordinated support of fetal needs and subsequent high milk production in the face of decreasing and eventually insufficient DMI during late pregnancy and early lactation.

These changes in tissue metabolism that occur in dairy cows during the transition period are mediated largely by changes in responses to hormonal signals such as insulin. Decreased responses of these tissues to insulin are referred to in general terms as insulin resistance. As referenced above, some aspects of insulin resistance (such as those related to skeletal muscle) are very favorable for support of pregnancy and lactation because of glucose sparing for the fetus and lactating mammary gland (Bell, 1995). At the same time, we believe that insulin resistance in adipose tissue may contribute to the increasing circulating concentrations of NEFA and decreasing DMI as cows approach calving. Allen et al. (2005) suggested that the increased circulating concentrations of NEFA during late pregnancy and subsequent oxidation of these NEFA by the liver is the cause of the decreased DMI as cows approach calving. Increased resistance of adipose tissue to insulin would predispose to the cow to mobilize NEFA, hence potentially creating a vicious cycle of NEFA mobilization and DMI reduction during the late prepartum period. This would also help to explain metabolically why high body condition score (BCS) cows have lower DMI and more rapid decreases in DMI during the prepartum period than cows of moderate or low BCS (Grummer et al., 2004).

Several years ago, we became interested in further understanding the nature and timing of insulin resistance, with specific focus on determining whether the relationships of NEFA and DMI could be modulated during the transition period. Initial research conducted in our lab (Smith, 2004) suggested that adipose tissue in periparturient dairy cows actually may be more refractory to insulin during the prepartum period than during the postpartum period. Subsequent work also generally supported the concept that insulin resistance may be greater during the prepartum period than the postpartum period (Smith et al., 2006).

As a result of this work and other circumstantial evidence that accentuated insulin resistance during the prepartum period contributes to lower peripartal DMI, elevated NEFA concentrations, and increased body condition score (BCS) loss during early lactation, we wanted to determine whether specific modulation of insulin resistance in adipose tissue during the prepartum period would decrease NEFA mobilization and change the patterns of DMI and NEFA during the transition period. Using an experimental approach, we administered compounds (thiazolidinediones; TZD) analogous to those used to treat Type II diabetes in humans to dairy cows during the prepartum period. In the first study, TZD administration tended to decrease circulating concentrations of NEFA and tended to increase DMI during the period from 7 days before calving until 7 days after calving (Smith et al., 2007). Importantly, TZD administration did not appear to interfere with the glucose sparing by peripheral tissues that is important for support of pregnancy and lactation.

In a second study (Smith et al., 2009) conducted using larger numbers of cows, we replicated the results of the first experiment in that TZD administration during the prepartum period decreased circulating NEFA concentrations and increased DMI during the immediate pre- and postpartum periods. In addition, TZD administration improved postpartum energy balance, decreased BCS loss, and decreased days to first ovulation in treated cows. These results suggested that specific modulation of insulin resistance in adipose tissue could have very positive effects on metabolic changes during the transition period and have substantial carryover effects on the dynamics of metabolism and performance during early lactation. It should be noted that this work was conducted as proof of concept relative to the mechanisms of metabolic regulation; TZD currently is not available in a form that can be used practically in the dairy industry and would require regulatory approval before such use.

PREPARTUM NUTRITIONAL MANAGEMENT AND RELATIONSHIPS WITH PERIPARTAL DRY MATTER INTAKE

Although modulation of insulin resistance using pharmaceutical approaches is intriguing, it causes us to ask questions regarding which aspects of nutritional management may influence insulin resistance. During the past few years, energy nutrition of cows during the dry period has received substantial renewed attention (Drackley and Janovick-Guretzky, 2007) and an increasing body of information suggests that energy nutrition may interact with insulin resistance during the late prepartum period.

For many years, the emphasis of researchers and industry professionals was to maximize DMI in order to ensure that cows consumed enough energy during the dry period. This strategy was supported in part by research that demonstrated that cows with lower NEFA concentrations during the last two weeks before calving on commercial dairy farms had decreased incidence of most postcalving metabolic disorders (displaced abomasum, ketosis, retained placenta, mastitis; Dyk, 1995). Given that higher DMI typically results in lower circulating NEFA, the association between higher DMI and improved health and performance was implied. Our experience would suggest that many farms indeed had improved health and performance when management changes were implemented that increased DMI of cows, particularly during the close-up period.

On the other hand, evidence suggests that plane of nutrition, in particular energy intake during the prepartum period, modulates the degree of insulin resistance and hence the relationships between NEFA and DMI during the immediate peripartal period. Mashek and Grummer (2003) reported that cows that had larger decreases in DMI during the prepartum period, generally because of higher DMI during weeks 3 and 4 before calving, had higher concentrations of plasma NEFA and liver triglycerides during the postpartum period. More direct experimental evidence was provided by Douglas et al. (2006), who reported that cows fed at 80% of calculated energy requirements for the entire dry period had lower NEFA concentrations during the postpartum period, lower concentrations of both circulating glucose and insulin during the prepartum period, and higher DMI during the postpartum period than cows consuming 160% of predicted energy requirements throughout the dry period. Similarly, Holcomb et al. (2001) reported that cows subjected to feed restriction during the late prepartum period had blunted NEFA curves during the periparturient period. In addition, Holtenius et al. (2003) determined that cows that were dramatically overfed (178% of calculated energy requirements) for the last 8 weeks before calving had higher concentrations of insulin and glucose during the prepartum period, greater insulin responses to glucose challenge during the prepartum period, and higher concentrations of circulating NEFA during the postpartum period than cows fed for 75 or 110% of calculated energy requirements. Furthermore, Agenas et al. (2003) reported that the same cows fed for 178% of calculated energy requirements prepartum had lower DMI and prolonged negative energy balance during the postpartum period compared with cows assigned to the other two prepartum treatments. Dann et al. (2006) demonstrated that overfeeding (150% of calculated energy requirements) during the far-off period may have exacerbated insulin resistance as cows approached calving, resulting in higher NEFA and BHBA and lower DMI and energy balance during the first 10 days postcalving.

Recently, we compared responses to insulin through glucose tolerance tests conducted on dry cows fed a high energy, corn silage-based (~ 0.69 Mcal/lb of NEL; 170% of predicted energy requirements) ration versus a high straw, bulky diet (~ 0.61 Mcal/lb of NEL; 119% of predicted energy requirements; Schoenberg and Overton, 2012). Responses of NEFA to the glucose tolerance test were more refractory in the cows fed the high energy diet, suggesting that feeding the high energy diet to dry cows accentuated the insulin resistance expressed in adipose tissue. Collectively, these results support that overfeeding energy to dry cows results in changes in metabolism that in turn likely predispose cows to decreased DMI and higher NEFA during the immediate peripartal period.

This knowledge has supported the evolution in recommendations for energy nutrition of dairy cows during both the far-off and close-up periods during the past several years, with the goal of meeting, but not dramatically exceeding, energy requirements. My target range for both the far-off and close-up periods is between 110 and 120% of energy requirements. In practice, this can be achieved by formulating diets during the far-off period to contain no more than 0.59 to 0.63 Mcal/lb of NEL in order to achieve the target NEL intake of approximately 15 to 17 Mcal for Holsteins during this timeframe. During the close-up period, conventional recommendations as described above have been to maximize DMI, and hence energy intake. Although this still applies in many herd situations, we believe that some well-managed herds in which close-up cows consume large amounts of feed (> 31 to 32 lbs/day of dry matter in comingled cow/springing heifer groups) have increased rates of metabolic disorders because of excessive energy intake during the close-up period. Accordingly, some of these herds have had success in moderating energy intake during the close-up period in group-feeding situations by incorporating straw or other low potassium, low energy forage to lower overall dietary energy concentration. Our recommendations would be to formulate the close-up diet at approximately 0.64 to 0.66 Mcal/lb of NEL if the group is a commingled cow/heifer group and approximately 0.61 to 0.63 Mcal/lb of NEL if the group is composed of mature animals and DMI is high. This lower energy diet also can be an acceptable one-group dry cow approach if overall herd management dictates such an approach. Diets formulated in these ranges will help to ensure adequate, but not excessive energy intake within the dynamics of group-feeding and competition among animals.

Diets formulated using a combination of corn silage and straw to form the forage component of the diet typically can have between 5 to 10 lbs of chopped straw, making feeding management a critical component of implementation of bulky, low energy dry cow diets. As described by Drackley (2007), the three key components of this implementation are 1) prevention of sorting, 2) ensuring continuous and non-crowded access to the TMR, and 3) careful monitoring of dry matter content and attention to detail. Most of these diets will contain added water in order to aid with prevention of sorting. A final point relative to these types of diets is that it is important to account for the metabolizable protein requirements of the cow during late pregnancy. These diets typically contain lower amounts of ruminally fermentable carbohydrate than those that have been typically fed for the last ten to fifteen years, and therefore will supply less metabolizable protein from ruminal bacteria. Inclusion of rumen-undegradable protein sources to result in total metabolizable protein supply of at least 1,100 to 1,200 g/d for typical Holstein cows is critical for early lactation performance and overall success. Furthermore, in anecdotal cases where these diets have been linked with lower milk yield during early lactation, I speculate that energy intake may have been pushed too low or RUP supplementation may be inadequate to meet metabolizable protein needs, especially during the close-up period.

POSTPARTUM NUTRITIONAL MANAGEMENT AND RELATIONSHIPS WITH DRY MATTER INTAKE AND METABOLISM IN EARLY LACTATION

The amount of research specifically conducted to explore the relationships of postpartum nutritional management and the dynamics of DMI and BCS during early lactation has been very limited. Allen et al. (2009) would suggest that feeding highly fermentable diets to cows during early lactation would decrease DMI and overall energy status. I contend that modulation of DMI by propionate during very early lactation is less likely than at other phases of lactation for several reasons. First, NEFA likely are the predominant oxidative fuel for liver during this period and so any hypophagic effect of propionate would depend upon NEFA supply to the liver. Second, we demonstrated that there is a positive correlation between liver capacity to convert propionate to glucose and fat free NEL intake (proxy for carbohydrate intake) in cows at d 1 and 21 postcalving that does not exist either before calving or at peak lactation (Drackley et al., 2001). This suggests that the liver has the capacity to direct additional propionate toward glucose. Third, hepatic energy requirements increase dramatically at the onset of lactation (Reynolds et al., 2003). The first point is supported by recent work (Stocks and Allen, 2012), in which they determined that the hypophagic effects of propionate increased when hepatic acetyl CoA concentrations are higher, as they would be if cows were mobilizing large amounts of adipose tissue with the corresponding proportionate uptake of NEFA by the liver.

The limited work in fresh cows (with the exception of the results from Dann and Nelson, 2011) suggests that feeding more fermentable diets during early lactation does not decrease DMI or negatively impact other aspects of performance and metabolic health. Andersen et al. (2002; 2003) fed cows either a low (25% concentrate) or high (75% concentrate) diet with whole crop barley silage as the forage base from calving through 8 wk postcalving. Feeding the high energy diet did not affect DMI, increased net energy intake and milk yield, and did not affect BCS change in early lactation. Cows fed the high energy diet had greater liver capacity to convert fatty acids to CO_2, lower capacity to convert fatty acids to triglycerides in liver, and lower blood ketones (Andersen et al., 2002).

Rabelo et al. (2003; 2005) fed cows and first calf heifers either low or high energy diets prepartum followed by either low or high energy diets postpartum until d 20 postcalving, then all cows were fed the high energy diet through d 70 postcalving. The postcalving diets were based upon alfalfa silage and corn silage – the “low” energy diet contained 29.9% NDF and 41.4% NFC; the “high” energy diet contained 24.9% NDF and 47.2% NFC. Cows fed the high energy diet postpartum tended to have higher DMI and had higher energy intake from d 1 to 30; overall effects of treatment from d 1 to 70 postcalving were not significant. Rates of increase of milk production were greater for cows fed high energy diets postcalving, and plasma concentrations of BHBA were substantially lower for cows fed the high energy diet on d 7 and 21 postcalving.

Although these studies (Andersen et al., 2002; Rabelo et al., 2003) suggest that higher energy diets are preferable during the postcalving period, the diets fed by Andersen represent the extremes and those fed by Rabelo are both higher energy diets by industry standards. Recently, we (McCarthy et al. 2013a) examined effects of starch level (21.5 vs. 26.2%) and monensin inclusion (0 vs. 450 mg/d) in the ration fed for the first 21 d postcalving. Cows fed the higher starch diet had increased DMI and faster increases in milk yield during the first 3 wk postcalving than cows fed the lower starch diet; cows fed monensin had higher DMI and increased milk yield (4.8 lbs/d) during the first 9 wk postcalving. This improved performance, particularly for cows fed monensin, was underpinned by changes in liver capacity for propionate utilization such that liver from cows fed monensin converted more propionate to glucose relative to CO_2 (McCarthy et al., 2013b).

USE OF ANALYTES RELATED TO ENERGY METABOLISM IN HERD-LEVEL DIAGNOSTICS – NEFA & BHBA

Oetzel (2004) characterized well the typical use of blood analytes related to energy metabolism in transition management diagnostics – NEFA during the prepartum period to assess precalving energy status and BHBA during the postpartum period to assess incidence of subclinical (and clinical) ketosis. This approach was supported in part by work conducted in Michigan (Cameron et al., 1998) that associated increased prepartum concentrations of NEFA, reflective of negative energy balance, with a greater incidence of displaced abomasum. Duffield et al. (1998) defined and characterized subclinical ketosis in herds in Ontario during the postpartum period and demonstrated that administration of monensin in a controlled-release capsule would decrease the incidence of subclinical ketosis in dairy cows during early lactation.

Recently, our group conducted a large-scale evaluation of the associations of prepartum NEFA and postpartum NEFA and BHBA with postpartum health, milk production, and reproductive performance in dairy herds in the northeastern US (Ospina et al., 2010a, 2010b, 2010c). In order to have been included in the study a herd must have: 1) had greater than 250 milking cows, 2) housed cows in free-stalls, 3) fed a total mixed ration (TMR), and 4) participated in DHIA and/or use Dairy Comp 305 (Valley Ag. Software, Tulare CA). Farms were visited once and during the farm visit two cohorts of animals were selected: those 14 to 2 days prepartum and those 3 to 14 days postpartum. Within each cohort, convenience samples of 15 apparently healthy animals were evaluated. Briefly, 10 mL of blood was collected from the coccygeal vein or artery into a red-top tube. The sera from the prepartum cohort were analyzed for NEFA and the sera from animals sampled after calving were analyzed for NEFA, BHBA. For all animals sampled, the incidence of the diseases of interest [displaced abomasum (DA), clinical ketosis (CK), and metritis (MET) and/or retained placenta (RP)] within 30 days in milk, time to pregnancy within 70 days post voluntary waiting period and Mature Equivalent 305 (ME 305) milk at 120 days in milk were recorded. The final dataset included 100 herds with an average herd size of 840 cows. A total of 2758 cows were sampled within these herds (1440 animals sampled prepartum and 1318 sampled postpartum) with an approximate distribution of 35% primiparous (entering first lactation) and 65% multiparous (entering second or greater lactation) cows.

Critical threshold values for prepartum NEFA and postpartum NEFA and BHBA and the associated risk ratios for disease are presented in Table 1. If animals had prepartum serum NEFA concentrations greater than about 0.30 mEq/L, they were twice as likely to develop one or more of the diseases of interest. Animals with postpartum serum NEFA and BHBA concentrations greater than about 0.60 mEq/L and 10 mg/dL, respectively, were four times as likely to develop one of more of the diseases of interest than animals with lower concentrations of these metabolites. The risk ratio for individual disorders varied widely within these groups. These results are consistent with prior work and support the importance of maintaining adequate energy intake prepartum and controlling body condition score loss and overall energy status during the postpartum period with respect to disease.

The relationships of prepartum NEFA and postpartum NEFA and BHBA with reproductive performance for the first 70 days after voluntary waiting period are described in Table 2. Animals with prepartum NEFA greater than about 0.3 mEq/L were nearly 20% less likely to become pregnant than animals with lower concentrations. Animals with greater than about 0.70 mEq/L of NEFA (while controlling for BHBA) and/or greater than 10 mg/dL of BHBA were 13 to 16% less likely to become pregnant than animals with lower concentrations. In all models, multiparous cows were less likely than primiparous cows to become pregnant in the first 70 days following the voluntary waiting period.

Associations of analytes related to energy metabolism with subsequent milk production (assessed as mature-equivalent 305-day lactational milk, predicted at approximately 120 DIM) are depicted in Table 3. Regardless of parity, animals with greater than about 0.3 mEq/L of NEFA during the prepartum period had nearly 700 kg less ME305 projected milk than animals with lower concentrations. During the postpartum period, there were interesting differences in associations of energy-related analytes with milk production depending upon parity. In primiparous cows (heifers), postpartum NEFA concentrations greater than about 0.6 mEq/L and BHBA concentrations over about 9 mg/dL were associated with increased milk yield. In multiparous cows, postpartum NEFA concentrations greater than about 0.7 mEq/L and BHBA concentrations greater than about 10 mg/dL were associated with lower predicted milk yield.

Among animals sampled during the prepartum period (2 to 14 days before calving), 45% of primiparous animals and 26% of multiparous cows had NEFA concentrations at or above 0.3 mEq/L. Among animals sampled during the postpartum period (3 to 14 days after calving), 25% of primiparous animals and 33% of multiparous cows had NEFA concentrations at or above 0.7 mEq/L. Furthermore, 15% of primiparous animals and 27% of multiparous cows had BHBA concentrations at or above 10 mg/dL. In the vast majority of participating farms, primiparous and multiparous animals would have been commingled during the period before calving– these results suggest that heifers in particular may be compromised from the standpoint of energy intake relative to requirements in these systems. Furthermore, these energy-related analytes appear more likely to be elevated in multiparous cows than primiparous cows during the period after calving.

Ospina et al. (2010c) also used this dataset to compare herds with greater than 15% of animals over the critical thresholds for the analytes during the prepartum and postpartum periods with those with less than 15% of animals over the thresholds during each period and results from this analysis are presented in Table 4. It should be noted that the numbers in this table reflect the associations among all animals in the herd, not just sampled animals in the study. As suggested by the results in the table, those herds with more than 15% of animals with prepartum NEFA and/or postpartum NEFA and BHBA over the critical thresholds had slightly greater disease incidence, poorer reproductive performance, and lower ME305 projected milk yield in both primiparous and multiparous cows. In the U.S. system, the associations of these analytes at the herd-level with decreased milk yield and poorer reproductive performance would be much more economically meaningful than those with disease incidence.

In terms of practical application of this information, we believe that measurement of energy-related analytes is a useful tool for monitoring herds, evaluation of potential opportunities for improved transition cow management, or diagnostics. In terms of the target windows, we recommend sampling 15 to 20 cows per group within the windows of interest described above – prepartum samples should be analyzed for NEFA and postpartum samples can be analyzed for NEFA and/or BHBA. The cowside blood or milk tests for BHBA described above are very accurate and represent an excellent first step or front line analysis because of convenience and cost. Furthermore, milk BHBA testing is now available in some parts of North America (e.g. Valacta in Quebec) and we believe that midinfrared BHBA analyses will become more commonly available through routine herd testing. We see this as having great potential to help herds have information regarding their success with transition cow programs at regular intervals.

Because the incidence of herds with high postpartum NEFA in our dataset was much greater than that with high postpartum BHBA, we would encourage practitioners and consultants to take the extra step and consider analysis for postpartum NEFA in situations where they believe that early lactation milk production and reproductive performance are compromised yet the BHBA data are unrevealing. Finally, prepartum NEFA continue to be useful in helping to identify situations in which larger than desired proportions of prepartum cows have compromised energy status.

Table 5 describes three possible outcomes and potential interpretations for a herd to consider after NEFA and/or BHBA evaluation in prepartum and postpartum groups. If NEFA is elevated in prepartum cows, it is generally a good signal that either energy intake as a whole is inadequate or facility/management issues exist and are causing significant cow to cow variation in DMI and hence NEFA concentration. Independent of postpartum analyte values, we associate elevated prepartum NEFA with negative disease, reproductive, and production outcomes at the herd level (Table 5). The most likely analyte pattern for a herd that is overfeeding energy either far-off or close-up is low NEFA values prepartum but high NEFA and/or BHBA values postpartum. Herds and consultants should remember, however, that a number of factors specific to either nutritional management or facility/grouping management also can elevate postpartum concentrations of NEFA and/or BHBA independent of prepartum values. Typically, when herds are overfed either far-off or close-up, we see a subsequent rapid and marked loss of BCS among fresh cows – NEFA testing of the fresh cows can help to confirm this.

SUMMARY AND CONCLUSIONS

Success in management of energy metabolism during the transition period depends upon excellent management in a number of different areas to manage the dynamics of DMI and body condition mobilization along with optimize performance. Our understanding of the metabolic regulation underpinning the changes that occur in energy metabolism of cows during the transition period is increasing, and with this understanding has come new potential opportunities for enhancing transition cow health and performance. Controlling energy intake of cows during the prepartum period (both far-off and close-up) is an important factor that predisposes cows to smoother adaptations to lactation. Furthermore, available information suggests that feeding higher starch diets and monensin during the early postpartum period promotes higher energy intake and milk yield along with better metabolic status during the postpartum period. Finally, herd-side tools (e.g., Precision Xtra BHBA meter) allow frontline monitoring of energy metabolism in transition cows with solid associations of these results with downstream outcomes. Testing NEFA also can be useful and provide additional insight for troubleshooting or further evaluation of metabolic health of transition cows at the herd-level.

REFERENCES

Agenas, S., E. Burstedt, and K. Holtenius. 2003. Effects of feeding intensity during the dry period. 1. Feed intake, body weight, and milk production. J. Dairy Sci. 86:870-882.

Allen, M. S., B. J. Bradford, and K. J. Harvatine. 2005. The cow as a model to study food intake regulation. Ann. Rev. Nutr. 25:523-547.

Allen, M. S., B. J. Bradford, and M. Oba. 2009. The hepatic oxidation theory of the control of feed intake and its application to ruminants. J. Anim. Sci. 87:3317-3334.

Andersen, J. B., N. C. Friggens, K. Sejrsen, M. T. Sorensen, L. Munksgaard, and K. L. Ingvartsen. 2003. Livest. Prod. Sci. 81:119-128.

Andersen, J. B., T. Larsen, M. O. Nielsen, and K. L. Ingvartsen. 2002. Effect of energy density in the diet and milking frequency on hepatic long chain fatty acid oxidation in early lactating dairy cows. J. Vet. Med. A 49:177-183

Bauman, D. E., and W. B. Currie. 1980. Partitioning of nutrients during pregnancy and lactation: a review of mechanisms involving homeostasis and homeorhesis. J. Dairy Sci. 63:1514-1529.

Bauman, D. E. and J. M. Elliot. 1983. Control of nutrient partitioning in lactating ruminants. In Biochemistry of Lactation. T. B. Mepham (ed.). Elsevier Science Publishers, Amsterdam, NL, pp. 437-468.

Bell, A. W. 1995. Regulation of organic nutrient metabolism during transition from late pregnancy to early lactation. J. Anim Sci. 73:2804-2819.

Butler, W. R., and R. D. Smith. 1989. Interrelationships between energy balance and postpartum reproductive function in dairy cattle. J. Dairy Sci. 72:767-783.

Cameron, R. E., P. B. Dyk, T. H. Herdt, J. B. Kaneene, R. Miller, H. F. Bucholtz, J. S. Liesman, M. J. VandeHaar, and R. S. Emery. 1998. Dry cow diet, management, and energy balance as risk factors for displaced abomasums in high producing dairy herds. J. Dairy Sci. 81:132-139.

Dann, H. M., N. B. Litherland, J. P. Underwood, M. Bionaz, A. D'Angelo, J. W. McFadden, and J. K. Drackley. 2006. Diets during far-off and close-up dry periods affect periparturient metabolism and lactation in multiparous cows. J. Dairy Sci. 89:3563-3577.

Dann, H. M., and B. H. Nelson. 2011. Early lactation diets for dairy cattle – focus on starch. Proceedings, Cornell Nutrition Conference for Feed Manufacturers. Syracuse, NY.

Douglas, G. N., T. R. Overton, H. G. Bateman II, H. M. Dann, and J. K. Drackley. 2006. Prepartal plane of nutrition, regardless of dietary energy source, affects periparturient metabolism and dry matter intake in Holstein cows. J. Dairy Sci. 89:2141-2157.

Drackley, J. K. 2007. Energy for dry and transition cows revisited. Proceedings, 8th Fall Dairy Conference. PRO-DAIRY and College of Veterinary Medicine, Cornell University, Ithaca, NY. pp. 69-78.

Drackley, J. K., and N. A. Janovick-Guretzky. 2007. Controlled energy diets for dry cows. Proceedings, 8th Western Dairy Management Conference, Reno, NV. Oregon State Univ., Corvallis, pp. 7-16.

Drackley, J. K., T. R. Overton, and G. N. Douglas. 2001. Adaptations of glucose and long-chain fatty acid metabolism in liver of dairy cows during the periparturient period. J. Dairy Sci. 84:E100-E112.

Dyk, P. B. 1995. The association of prepartum non-esterified fatty acids and body condition with peripartum health problems on 95 Michigan dairy farms. M. S. Thesis, Michigan State University, East Lansing.

Grummer, R. R., D. G. Mashek, and A. Hayirli. 2004. Dry matter intake and energy balance in the transition period. Vet. Clin. Food Anim. 20:447-470.

Grummer, R. R., M. C. Wiltbank, P. M. Fricke, R. D. Watters, and N. Silvia-Del-Rio. 2010. Management of dry and transition cows to improve energy balance and reproduction. J. Reprod. Dev. 56:S22-S28.

Holcomb, C. S., H. H. Van Horn, H. H. Head, M. B. Hall, and C. J. Wilcox. 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., S. Agenas, C. Delavaud, and Y. Chilliard. 2003. Effects of feeding intensity during the dry period. 2. Metabolic and hormonal responses. J. Dairy Sci. 86:883-891.

Huzzey, J. M., and T. R. Overton. 2010. Measuring the effect of stress during the transition period on subsequent health and performance of dairy cattle. Proceedings, Cornell Nutrition Conference for Feed Manufacturers. Syracuse, NY. pp. 76-86.

Ingvartsen, K. L., and J. B. Andersen. 2000. Integration of metabolism and intake regulation: A review focusing on periparturient animals. J. Dairy Sci. 83:1573-1597.

LeBlanc, S. 2010. Monitoring metabolic health of dairy cattle in the transition period. J. Reprod. Dev. 56:S29-S35.

Mashek, D. G., and R. R. Grummer. 2003. The ups and downs of feed intake in prefresh cows. Proc. Four-State Nutr. Conf. LaCrosse, WI. MidWest Plan Service publication MWPS-4SD16. pp. 153-158.

McCarthy, M. M., T. Yasui, C. M. Ryan, G. D. Mechor, and T. R. Overton. 2013a. Performance of dairy cows as affected by dietary starch level and supplementation with monensin during early lactation. 96(Suppl. 1):400.

McCarthy, M. M., T. Yasui, S. H. Pelton, C. M. Ryan, G. D. Mechor, and T. R. Overton. 2013b. Hepatic gluconeogenesis in dairy cows as affected by dietary starch level and supplementation with monensin during early lactation. J. Dairy Sci. 96(Suppl. 1):48.

Oetzel, G. R. 2004. Monitoring and testing dairy herds for metabolic disease. Vet. Clin. North Am. Food Anim. Pract. 20:651-674.

Ospina, P. A., D. V. Nydam, T. Stokol, and T. R. Overton. 2010a. Associations of elevated nonesterified fatty acids and beta-hydroxybutyrate concentrations with early lactation reproductive performance and milk production in transition dairy cattle in the northeastern United States. J. Dairy Sci. 93:1596-1603.

Ospina, P. A., D. V. Nydam, T. Stokol, and T. R. Overton. 2010b. Evaluation of nonesterified fatty acids and beta-hydroxybutyrate in transition dairy cattle in the northeastern United States: Critical thresholds for prediction of clinical diseases. J. Dairy Sci. 93:546-54.

Ospina, P. A., D. V. Nydam, T. Stokol, and T. R. Overton. 2010c. Association between the proportion of sampled transition cows with increased nonesterified fatty acids and β-hydroxybutyrate and disease incidence, pregnancy rate, and milk production at the herd level. J. Dairy Sci. 93:3595-3601.

Petterson, J. A., F. R. Dunshea, R. A. Ehrhardt, and A. W. Bell. 1993. Pregnancy and undernutrition alter glucose metabolic responses to insulin in sheep. J. Nutr. 123:1286-1295.

Petterson, J. A., R. Slepetis, R. A. Ehrhardt, F. R. Dunshea, and A. W. Bell. 1994. Pregnancy but not moderate undernutrition attenuates insulin suppression of fat mobilization in sheep. J. Nutr. 124:2431-2436.

Rabelo, E., R. L. Rezende, S. J. Bertics, and R. R. Grummer. 2005. Effects of pre- and postfresh transition diets varying in dietary energy density on metabolic status of periparturient dairy cows. J. Dairy Sci. 88:4375–4383.

Rabelo, E., R. L. Rezende, S. J. Bertics, and R. R. Grummer. 2003. Effects of transition diets varying in dietary energy density on lactation performance and ruminal parameters of dairy cows. J. Dairy Sci. 86:916–925.

Reynolds, C. K., P. C. Aikman, B. Lupoli, D. J. Humphries, and D. E. Beever. 2003. Splanchnic metabolism of dairy cows during the transition from late gestation through early lactation. J. Dairy Sci. 86:1201-1217.

Santos, J.E.P., H. M. Rutigliano, and M. F. S'a Filho. 2009. Risk factors for resumption of postpartum estrous cycles and embryonic survival in lactating dairy cows. Anim. Reprod. Sci. 110:207–221.

Schoenberg, K. M., and T. R. Overton. 2012. Effects of plane of nutrition and 2,4-thiazolidinedione on insulin responses and adipose tissue gene expression in dairy cattle during late gestation. J. Dairy Sci. 95:670-682.

Smith, K. L. 2004. Effects of prepartum carbohydrate source and chromium supplementation in dairy cows during the periparturient period. M. S. Thesis. Cornell Univ., Ithaca, NY.

Smith, K. L., W. R. Butler, and T. R. Overton. 2009. Effects of prepartum 2,4-thiazolidinedione on metabolism and performance in transition dairy cows. J. Dairy Sci. 92:3623-33.

Smith, K. L., A. K. Rauf, B. C. Benefield, A. W. Bell and T. R. Overton. 2006. Responses of tissues to insulin as affected by homeorhetic state in dairy cattle. J. Dairy Sci. 89(Suppl. 1):352. (Abstr.).

Smith, K. L., S. E. Stebulis, M. R. Waldron, and T. R. Overton. 2007. Prepartum 2,4-thiazolidinedione alters metabolic dynamics and dry matter intake of dairy cows. J. Dairy Sci. 90:3660-3670.

Stocks, S. E., and M. S. Allen. 2012. Hypophagic effects of propionate increase with elevated hepatic acetyl coenzyme A concentration for cows in the early postpartum period. J. Dairy Sci. 95: 3259-3268.

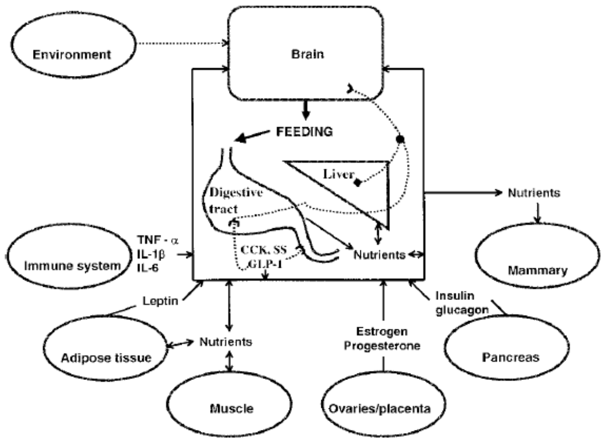

Figure 1. "Simplified" diagram on intake regulation in dairy cattle. From Ingvartsen and Andersen, 2000.

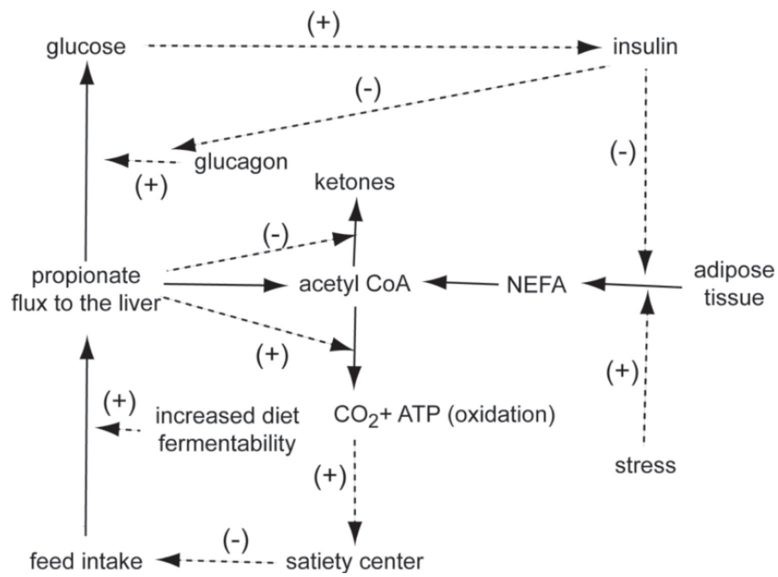

Figure 2. Mechanisms of intake regulation according to the hepatic oxidation theory. From Allen et al., 2009.

Table 1. Receiver operator characteristic (ROC) curve determination of critical NEFA (mEq/L) and BHBA (mg/dL) thresholds as predictors of disease and risk ratios of disease based upon these critical thresholds (Ospina et al., 2010b).

	Prepartum cohort (2 to 14 days prepartum)			
Disease	**Critical prepartum NEFA[1]**	**Risk Ratio**	**95 % CI[2]**	**P-value**
DA	0.27	2.0	1.1 – 3.7	0.03
CK	0.26	1.8	1.2 – 2.5	0.001
Met and/or RP	0.37	2.2	1.6 – 3.0	< 0.0001
Any of the three	0.29	1.8	1.4 – 2.2	< 0.0001
	Postpartum cohort (3 to 14 days postcalving)			
Disease	**Critical postpartum NEFA[1]**	**Risk Ratio**	**95 % CI[2]**	**P-value**
DA	0.72	9.7	4.2 – 22	<0.0001
CK	0.57	5.0	2.3 – 11	<0.0001
Met	0.36	17	2.0 – 134	0.008
Any of the three	0.57	4.4	2.6 – 7.3	< 0.0001
Disease	**Critical BHBA[1]**	**Risk Ratio**	**95 % CI[2]**	**P-value**
DA	10	6.9	3.7 – 12.9	<0.0001
CK	10	4.9	3.2 – 7.3	<0.0001
Met	7	2.3	1.1 – 5.1	0.037
Any of the three	10	4.4	3.1 – 6.3	<0.0001

[1] Highest combination of specificity and sensitivity based upon ROC analysis
[2] Risk ratio confidence interval

Table 2. Cox proportional hazard model of the effect of NEFA (mEq/L) and/or BHBA (mg/dL), covariates, and animals clustered within herds on days to conception after voluntary waiting period (Ospina et al., 2010a).

Sampled population	**Variable**	**Hazard**	**P-value**
Prepartum cohort	NEFA ≥ 0.27	0.81	0.01
	Parity	0.73	0.001
Postpartum cohort	NEFA ≥ 0.72	0.84	0.05
	BHBA ≥ 10	0.93	0.4
	Parity	0.81	0.01
Postpartum cohort	BHBA ≥ 10	0.87	0.1
	Parity	0.80	0.01

Table 3. Mixed models for the effect of NEFA (mEq/L) and/or BHBA (mg/dL), covariates, and herd as a random effect on milk production assessed as ME305 milk at 120 days in milk (Ospina et al., 2010a).

Sampled Population	Variable	Difference in ME milk yield (kg)	P-value
Prepartum	NEFA ≥ 0.33	-683	0.001
	Parity	-556	0.01
Postpartum -- heifers	NEFA ≥ 0.57	+488	0.02
	BHBA ≥ 10	-143	0.5
Postpartum -- heifers	BHBA ≥ 9	+ 403	0.04
Postpartum -- cows	NEFA ≥ 0.72	-647	0.001
	BHBA ≥ 10	-165	0.4
Post-partum -- cows	BHBA ≥ 10	-393	0.04

Table 4. Herd-level impacts of elevated prepartum and postpartum nonesterified fatty acids (NEFA) and postpartum beta-hydroxybutyrate (BHBA) in commercial dairy farms (Ospina et al., 2010c)

Metabolite level	Herd alarm	Herd-level impact
Prepartum NEFA (14 to 2 d prepartum) > 0.3 mEq/L	> 15%	- 1.2% 21-d pregnancy rate + 3.6% disease incidence - 282 kg ME305 milk
Postpartum NEFA (3 to 14 d postpartum) > 0.6 (heifers) – 0.7 (cows) mEq/L	> 15%	- 0.9% 21-d pregnancy rate + 1.7% disease incidence Heifers: - 288 kg ME305 milk Cows: -593 kg ME 305 milk
Postpartum BHBA (3 to 14 d postpartum) > 10 (cows) – 12 (heifers) mg/dL	> 15% > 20%*	- 0.8% 21-d pregnancy rate + 1.8% disease incidence *Heifers: -534 kg ME305 milk Cows: -358 kg ME 305 milk

15% of 15 animals sampled = 2 to 3 animals over threshold; 90% confidence interval that it sample represents herd prevalence

Table 5. Interpretation of energy-related metabolites [nonesterified fatty acids (NEFA) and beta-hydroxybutyrate (BHBA)] to assess herd-level opportunities.

Scenario	Likely cause and possibilities
High prepartum NEFA High postpartum NEFA and/or BHBA	Likely starting with low DMI in close-up cows Too low energy in prefresh diet, facility and/or management issues (grouping, stocking density, heat stress?)
High prepartum NEFA Low postpartum NEFA and/or BHBA	Low DMI in close-up cows Sampling the survivors in the fresh pen? Is herd outmanaging or putting band-aids on fresh cow issues?
Low prepartum NEFA High postpartum NEFA and/or BHBA	Is herd overfeeding energy either far-off or close-up? Diet or facility/management issues specific to maternity/fresh group