

Optimizing Intake in Dry and Prefresh Cows

Thomas R. Overton, Ph.D.
Department of Animal Science
Cornell University
Ithaca NY 14853
o: 607.255.2878; f: 607.255.1335
email: tro2@cornell.edu

Introduction

Achieving high dry matter intake (DMI) during early lactation is a major determinant of transition cow management success, as energy balance is tightly linked with reproductive performance (Butler and Smith, 1989) and aspects of health and immunity (LeBlanc, 2010). Although a common notion is that milk yield is the major driver of negative energy balance, several data summaries (reviewed by Grummer et al., 2010) suggest that the relationship of negative energy balance is actually greater with DMI than with milk yield.

Clearly, nutritional and environmental management of dairy cattle during the dry and transition period have important carryover ramifications both for DMI during early lactation 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 and environmental management factors that impact DMI so that we can optimize energy and nutrient intake and subsequent outcomes.

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 Ingvarsten 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 based

upon the 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). 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. My opinion is that the actual modulation DMI by these pathways during the immediate postpartum period is much less likely, in part because of the large increase in demand for oxidative fuel by liver to support the dramatic increases in hepatic gluconeogenesis that occur postpartum (Reynolds et al., 2003) along with the increased capacity of liver to utilize propionate during the postpartum period (Drackley et al., 2001).

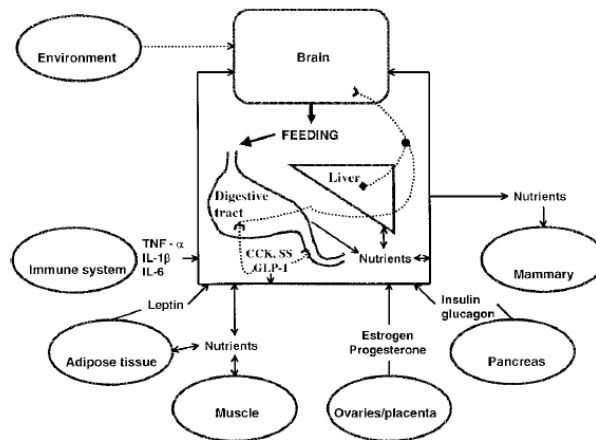


Figure 1. “Simplified” diagram on intake regulation in dairy cattle. From Ingvarnsen and Andersen, 2000.

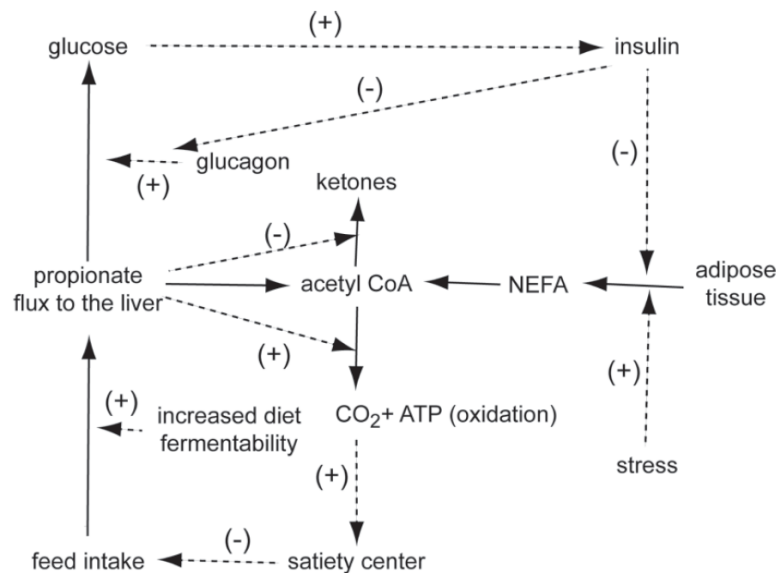


Figure 2. Mechanisms of intake regulation according to the hepatic oxidation theory. From Allen et al., 2009.

Metabolic Adaptations in the Transition Cow

It is well-recognized that 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 dry matter intake (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. As indicated above, 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 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.

Nutritional Management and Its Relationship to Insulin Resistance and Metabolic Health

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, increasing 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 periparturient 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. Recently, 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.

This knowledge has led to an 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 comingled 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 in the range of 1,100 to 1,200 g/d 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, especially during the close-up period.

Environmental Factors and Role in Intake Regulation

In addition to factors related to nutritional management and diet formulation, there are clearly effects of facilities and other environmental factors on DMI, and likely cow to cow variation in DMI in particular. Cook and Nordlund (2004 and updated proceedings papers since) clearly outlined considerations for managing stocking density, pen moves, and other facility considerations for transition cow housing and management. In addition, heat stress abatement and comingling of cows and heifers are other key facility and management factors that affect DMI and transition period outcomes.

Cook and Nordlund (2004 and subsequent) base much of their key recommendations (e.g., 30” of feed bunk space per animal, favoring very short stays in maternity pens, all-in all-out management of prefresh pens) on effects on DMI. Some of these effects may be direct as a result of feed access and others may be mediated by aspects of stress physiology and how they influence the metabolism described in the first part of this paper.

Recently, we (Huzzey and Overton, 2010) described a study in which we evaluated the effects of overstocking (200% vs 100% stocking of feedbunk and stalls) on feeding behavior, aspects of stress physiology, and metabolism of dry cows. Despite marked changes in feeding pattern, average feeding time per animal was nearly identical between the two groups and average pen DMI was actually increased in the overstocked group (~ 33 lbs of DMI vs. 31 lbs DMI). Consistent with other research evaluating stocking density effects on feeding behavior, rates of feed intake were higher in the overstocked group. Despite higher DMI, the overstocked group of cows had higher NEFA and tended to have elevated concentrations of cortisol breakdown metabolites in feces, indicative of a role of stress physiology in cow responses to treatment. In addition to the overall effects on the group, the heifers that were commingled with the older cows clearly were impacted to a greater extent by the increased stocking density. This notion would be consistent with that of Cook and Nordlund (2004), who postulated that the effects of facilities and environment are not equal across all animals, rather they have greater impact on compromised animals or those of lower rank within the groups.

Monitoring Cow to Cow Variation in Dry Matter Intake and Metabolism on Farms

One of the challenges of monitoring opportunities for improved nutritional management and especially those related to grouping management and other nonnutritional factors is that they cause increased variation in DMI and performance, and these are very difficult to impossible to detect in pen averages. We believe that the use of some of the blood-based markers of energy metabolism (e.g., prepartum NEFA; postpartum NEFA and beta-hydroxybutyrate; BHB) provide us with opportunities to assess energy issues in transition cows. Data from a large commercial farm study that we conducted (Ospina et al., 2010) indicated that herds with more than 15% of cows over 0.3 mM NEFA prepartum, 0.7 mM NEFA postpartum, or 12 mg/dL of BHB) were at risk for higher disease, poorer reproductive performance, and in particular decreased milk yield (Table 1). Variation in plasma NEFA may be a good proxy for variation in DMI within both prefresh and fresh groups.

Table 1. Herd-level impacts of elevated prepartum and postpartum NEFA and postpartum BHB in commercial dairy farms (Ospina et al., 2010)

| Metabolite level | Herd alarm | Herd-level impact |
|--|-----------------|--|
| Prepartum NEFA (14 to 2 d precalving) > 0.3 mM | > 15% | - 1.2% 21-d pregnancy rate + 1.4% disease incidence - 529 lbs ME305 milk |
| Postpartum NEFA (3 to 14 d postcalving) > 0.6 (heifers) – 0.7 (cows) mM | > 15% | - 1.3% 21-d pregnancy rate + 1.3% disease incidence Heifers: - 640 lbs ME305 milk Cows: -1,272 lbs ME 305 milk |
| Postpartum BHB (3 to 14 d postcalving) > 10 (cows) – 12 (heifers) mg/dL | > 15% > 20%* | - 1.3% 21-d pregnancy rate + 1.3% disease incidence *Heifers: - 1,179 lbs ME305 milk Cows: -732 lbs ME 305 milk |

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

Table 2 describes three possible outcomes and potential interpretations for a herd to consider after NEFA and/or BHB evaluation in prefresh and fresh groups. Whenever NEFA are elevated in prefresh 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 metabolite concentrations. Independent of postpartum analyte values, we associate elevated precalving NEFA with negative disease, reproductive, and production outcomes (Table 1). The most likely metabolite pattern for a herd that is overfeeding energy either far-off or close-up is low NEFA values precalving but high NEFA and/or BHB values postcalving. 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 BHB independent of precalving values. Typically, when herds are overfed either far-off or close-up I see quite rapid and marked loss of BCS in the fresh cows as another observation – plasma NEFA testing in the fresh cows can help to confirm this.

Table 2. Interpretation of energy-related metabolites to assess herd-level opportunities

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

Summary and Conclusions

Success in transition cow programs depends upon excellent management in a number of different areas to optimize energy intake and minimize variation in DMI during the far-off and close-up periods. 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 in nutritional management of transition cows. In addition, management of nonnutritional factors (stocking density, grouping management, environmental control) is critical as a complement to dietary strategies for transition period success. Blood-based analytical strategies to allow herds and their consultants to assess variation in energy status in cows during both the prepartum and postpartum periods are readily available – interestingly, it appears that the major herd-level impact associated with variation in these markers is milk yield and reproduction rather than disease, which challenges the paradigm in which these analytes typically have been used in herd-level assessment.

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.
- 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.
- Cook, N. B., and K. V. Nordlund. 2004. Behavioral needs of the transition cow and considerations for special needs facility design. *Vet. Clin. Food Anim.* 20:495-520.
- 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.
- 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. 1993. Etiology of lipid-related metabolic disorders in dairy cows. *J. Dairy Sci.* 76:3882-3896.

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.

Ospina, P. A., D. V. Nydam, T. Stokol, and T. R. Overton. 2010. Association between the proportion of sampled transition cows with increased nonesterified fatty acids and B-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. Slepatis, 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.

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.

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.