

The Metabolic Profile for the Modern Transition Dairy Cow

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The transition period, the period from 3 wk prior to calving to 3 wk after calving, is the most stressful period experienced during the cow's lactation. So stressful in fact that LeBlanc et al. (2006) estimates that 75 % of all disease occurs during this period. The metabolic profile has been purported to provide a method to monitor animal health during this critical period.

INTRODUCTION

Origination of the Metabolic Profile

The need to diagnose animal disease or a method to monitor herd health was the basis for initially developing the metabolic profile, with the main purpose to indicate a herd's susceptibility to production diseases. The Compton Metabolic Profile Test was designed by Payne et al. (1970) to monitor the metabolic health of the herd with the original components being glucose, urea, inorganic phosphorus, calcium, magnesium, sodium, potassium, albumin, globulin, hemoglobin, and copper. For this test to serve its intended function it was necessary to define the limits of a *normal* profile as well as determine the sources of variation. To establish a profile along with the proper ranges for *normal* animals, a survey was conducted of 13 dairy herds encompassing 2,400 blood samples focusing on three groups: early lactation, mid-lactation, and dry period (Payne et al., 1970). A mean and standard deviation were calculated and samples from herds were then compared to the established profile to determine the health status of the animal by evaluating the number of standard deviations from the mean.

With greater emphasis on the transition period, because of its importance in ensuring a fluid transition from non-lactating to lactating status, the profile has been expanded in many instances to include non-esterified fatty acids (**NEFA**) and beta-hydroxybutyrate (**BHBA**), while removing copper and globulin. Diagnostic laboratories across the country offer varying combinations of tests with most

at least providing the option of running each test individually.

Metabolic Profile Reference Values

Just as there are differences in the tests offered by laboratories, there are differences in the reference values used by the various laboratories. Table 1 and 2 contain a compilation of metabolic profile reference values from six sources, illustrating that no profile is exactly like another. While similarities do exist, there is variation and the range for what is classified as *normal* is broader for some analytes than others. Calculating the average upper and lower limits for the selected sources results in a range that is narrower when compared to the overall range in values determined by selecting the lowest and highest value to define the range across all of the profiles from the various sources.

While a range is given for what would be classified as normal levels from each source, Penn State offers an additional suggestion of what levels would be *Cause for Concern*. These values are all set below the lower limits of the normal profile suggesting that while an animal may be outside the normal range, there is a safety margin between the lower end of normal and when an animal may actually exhibit symptoms of deficiency.

Each analyte included within the metabolic profile has been shown to play an important role in animal health due to the impact of a deficiency, toxicity, or adverse elevation. For example, Ca at insufficient levels results in hypocalcemia or milk fever as the cow is removing more Ca from the body for milk production than can be absorbed by the body from the feed or mobilized from Ca stores in the bones. Because of the extensive relationship between minerals within the body, an impact on Ca levels may affect P levels. This may be seen in cows experiencing milk fever that do not respond even after successful treatment for hypocalcemia (Goff, 2004).

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Table 1. Metabolic profile normal ranges for minerals from select sources

Source	Animal Class	Ca mg/dL	P mg/dL	Mg mEq/L	K mEq/L	Na mEq/L	Cl mEq/L
Merck ¹	Cattle ⁷	8.4-11	4.3-7.8	1.7-3	4-5.8	125-148	96-109
Zinpro ²	Cattle ⁷	8-11	5-7	1.8-3.5	3.9-5.8	135-150	97-111
TVMDL ³	Close-up	8.3-9.7	4.9-7.1	1.5-2.1	4-5	139-147	99-107
	< 14 DIM	8-10	4.9-7.1	1.5-2.1	4-5	138-146	97-105
Penn St. ⁴	Close-up	-	-	-	-	-	-
	Fresh	8.7-11	4.5-8	2-3.5	3.8-5.2	137-148	-
	Concern level, fresh	< 8	< 3.5	< 1.5	< 3, > 5.5	137-148	-
Oregon St. ⁵	Dairy ⁸	8.2-10	5.2-7.9	2-3.9	3.8-5.2	137-148	-
Puls ⁶	Cattle ⁷	8-11	4.5-7	1.8-3.5	3.9-5.8	135-150	97-111
Average Range	All	8.2-10.5	4.8-7.4	1.8-3.1	3.9-5.4	135.1-148.1	97-108.8
Range	All	8-11	4.3-8	1.5-3.9	3.8-5.8	125-150	96-111

¹Merck Veterinary Manual, 2011.

²Zinpro Performance Panel, 2011.

³Sprowls, personal communication.

⁴Penn State University, 2011.

⁵Oregon State University, 2011.

⁶Puls, 1989.

⁷Profile for cattle, not specific for breed.

⁸Profile specific for dairy cattle.

Table 2. Metabolic profile normal ranges for analytes from select sources

Source	Animal Class	Albumin g/dL	Urea mg/dL	Cholest. mg/dL	Glucose mg/dL	NEFA mEq/L	BHBA mg/dL
Merck ¹	Cattle ⁷	2.8-3.9	7.8-25	62-193	-	-	-
Zinpro ²	Cattle ⁷	2.7-4.7	9-20	80-230	-	-	-
TVMDL ³	Close-up	3-3.6	9.4-16.6	39-123	51-65	< 0.6	-
	< 14 DIM	3-3.6	9.4-16.6	39-123	51-65	< 0.6	-
Penn St. ⁴	Close-up	3.3-3.7	-	65-114	51-74	0.03-0.16	1.25-4.2
	Fresh	3.2-3.6	-	63-253	42-68	0.01-0.52	1.7-8.9
	Concern level, fresh	-	-	-	-	-	-
Oregon St. ⁵	Dairy ⁸	3.2-4.1	8-27	43-331	51-77	0.04-0.34	3.42-7.62
Puls ⁶	Cattle ⁷	2.7-4.7	5-20	80-230	40-80	-	-
Average	All	3-4	8.1-20.9	58.9-199.6	47.7-71.5	0.03-0.5	2.1-6.9
Range	All	2.7-4.7	5-27	39-331	40-80	0.01-0.6	1.25-8.9

¹Merck Veterinary Manual, 2011.

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Hypophosphatemia may be the diagnosed issue and the cow may require supplemental P to fully recover. Insufficient P levels at the point of impacting production are seen in limited cases in dairy cattle. While inadequate P intake may result in a reduction in lactation performance and has been purported to lead to inadequate reproductive performance (Goff, 1998), P deficiency is most likely to occur in animals consuming poor quality forages from soils deficient in P as well as excessively mature forages and crop residues that contain on a dry matter basis P content of less than 0.25 % (NRC, 2001). As more and more co-product feeds and concentrates are included in today's U.S. dairy rations, P levels are far more likely to exceed recommended levels rather than approach these deficient levels.

The minerals Na, K, and Cl are necessary to maintain osmotic pressure and for acid-base regulation. Periods of inadequate water intake and stress will impact levels and subsequently the physiological roles they serve. The final mineral included in the profile, Mg, is a necessary cation for many metabolic pathways, and interestingly shows wide variability within the normal ranges presented in Table 1, especially for the Oregon State profile. A wide range may be a result of an impact of a regional influence on metabolic disorders reported as influenced by cropping practices, soil profiles, and climatic condition variability.

Plasma proteins, including albumin, are in a state of equilibrium with amino acids and tissue proteins. Albumin is synthesized by the liver and functions to maintain the osmotic pressure within the circulatory system. Decreased albumin levels have been reported as characteristics of liver disease, kidney disease, inflammatory conditions, and malnutrition. Serum albumin levels have been shown to decrease as the severity of fatty liver increases; however serum levels alone are not an adequate diagnostic tool as albumin may be impacted by inflammation of the liver and other causes of liver disease.

Blood urea levels are one method of measuring the adequacy of dietary protein levels as well as nitrogen utilization efficiency. Monitoring levels of urea in blood, which can also be conducted in milk, may provide insight into ensuring that rumen degradable protein (**RDP**) and rumen undegradable protein (**RUP**) are coordinated with starch degradabilities to optimize rumen microbial protein synthesis, as an imbalance in protein and carbohydrate degradabilities may result in suboptimal animal health and production.

Glucose is another analyte with usefulness relating to dietary adequacy. Although ruminants do not absorb large amounts of glucose from their digestive system, they do synthesize significant amounts of glucose in their liver from the volatile fatty acids, particularly propionic acid, absorbed from the rumen as well as from amino acids. During the prepartum transition period a large proportion of the maternal glucose supply is utilized by the near term fetus and then, after parturition, the mammary gland will commence utilizing the largest proportion of the glucose supply requiring rapid hepatic changes (Drackley et al., 2001). While glucose is regulated closely under homeostatic controls, a deficiency in dietary carbohydrates or starch content may result in deficient glucose levels. As another example of the importance to view the full system (i.e. monitoring all cow symptoms), prior to making a decision to rectify deficient glucose levels, it is necessary to know when the blood sample was taken in relationship to feeding as glucose levels decrease post-prandially.

The liver is under greater stress post-calving as the cow is requiring greater amounts of energy to maintain milk production, resulting in mobilization of body fat. This fat that reaches the liver is transported by very low density lipoproteins that contain a large amount of cholesterol. The measurement of cholesterol in the blood can be used as an indirect measure of liver function in producing very low density proteins, hence another method to monitor animal health and well-being when used as an additional tool as part of an overall thorough exam.

THE TRANSITION PERIOD IN DAIRY CATTLE

Although there may be some discussion between research groups, a widely accepted definition of the transition period includes the period from wk 3 prepartum until 3 wk postpartum (Grummer, 1995). It is during this period that the dairy cow goes through significant physiological changes in transitioning from a pregnant, non-lactating status to a non-pregnant, lactating status following parturition. Researchers have increasingly focused on this time frame, since the fate of the ensuing lactation resides in negotiating the physiological changes without incident. A particular deterrent to researchers investigating this area has been the rapid change in physiological state occurring within the 2 wk prior to 2 wk after calving (Drackley, 1999); however research is warranted based upon the estimate by LeBlanc et al. (2006) that 75 % of disease incidence

occurs within one month after calving. Some of the diseases experienced in the month postpartum include: displaced abomasum, milk fever, retained placenta, metritis, mastitis, and ketosis. Many of these maladies may result from underlying factors or a combination of factors including decreased dry matter intake of up to 30 % in the week prior to calving (Bertics et al., 1992), immunosuppression (Kehrli et al., 1989a,b), calving dystocia, or environmental factors.

In response to the onslaught of challenges, both metabolically and physiologically, faced by the cow as she completes the dramatic change from a non-lactating to a lactating state, many management strategies have been implemented during this transition period in an attempt to mitigate the negative impact of the maladies and their underlying causes. Some of these strategies include reducing stocking density to prevent overcrowding and competition at the feedbunk (Friend et al., 1977; Huzzey et al., 2006), *steaming up* or feeding a higher concentrate ration containing components of the postpartum ration in the weeks leading up to parturition (Grummer, 1995), feeding a ration formulated utilizing the dietary cation-anion difference (**DCAD**; Block, 1984), reducing the number of pen moves thereby decreasing the need for reestablishment of social hierarchy (Schirrmann et al., 2011), separating heifers from cows, and monitoring body condition score prior to dry off (Gearhart et al., 1990). While the implementation of these added management strategies has proven to be beneficial in decreasing disease incidence, some animals may still experience at least one of the issues typically associated with the transition period.

Recent Research Regarding the Metabolic Profile

With the many changes that have occurred over time, including the genetic advancement of dairy cattle (Chen, 2009) which resulted in increased milk production as well as changes in feeding strategies and management; it is imperative to have tools available to assist in disease management and prevention. Non-esterified fatty acids and BHBA have received a majority of the attention when considering what blood parameters can be monitored within the transition period to determine animal health as well as to predict potential disease issues. Ospina et al. (2010) evaluated the association between NEFA and BHBA levels and disease incidence. The data support previous observations that as NEFA levels increase, there is an increased risk of disease incidence. The authors further reported that a 15 % herd alarm level (proportion of

sampled animals above a certain threshold) for prepartum NEFA levels at or above 0.27 mEq/L leads to a 3.6 % increase in displaced abomasum and clinical ketosis concomitantly with a 1.2 % decrease in pregnancy rate and a loss of 282 kg in mature equivalent 305-d milk yield. Postpartum NEFA levels of ≥ 0.70 mEq/L were defined as the critical herd alarm level resulting in 1.7 % increase in displaced abomasum and clinical ketosis; while a postpartum NEFA level ≥ 0.60 mEq/L resulted in a 0.9 % decrease in pregnancy rate and a 593 kg decrease in projected mature equivalent 305-d milk yield for cows (Ospina et al., 2010). The utilization of BHBA analysis for monitoring health has shown better results when used postpartum (Ospina et al., 2010). The study by Ospina et al. (2010) revealed a critical herd level of 20 % of animals having BHBA levels at or above 12 mg/dL resulted in a herd level effect of 1.8 % increase in displaced abomasum and clinical ketosis, 0.8 % decrease in pregnancy rate, and 358 kg decrease in projected 305-d milk yield.

Time relative to calving (prepartum vs. postpartum), as shown in Opsina et al. (2010), appears to have an impact on metabolites. Another physiological issue influencing metabolites is age as measured by lactation number. Quiroz-Rocha (2009) sampled cows from -7 d prepartum to 7 d postpartum and not only looked at BHBA, but also included multiple other analytes. Their results support the fact that prepartum and postpartum analyte levels differ for each component measured (BHBA, fatty acids, cholesterol, glucose, urea, Ca, P) based on the time relative to calving. Further analysis was conducted by the authors based on the number of lactations and the effect on biochemical analytes, revealing limited patterns exist for the relationship between lactations and biochemical analytes. First lactation animals had greater levels of glucose, Ca, and P postcalving than all other lactations; while third lactation and greater cows had higher BHBA levels than second lactation animals and also had the lowest levels of Ca in the week postpartum.

PHOSPHORUS ENVIRONMENTAL ISSUES

One element receiving more and more scrutiny is P. As the impact of excessive levels of P on certain locations within the environment are realized, as well as the availability of affordable feed ingredients containing high levels of P, more emphasis is placed on ensuring that the ration is formulated to meet the cow's demands, without feeding excess P.

Overfeeding of P in lactating cow diets is a cause of concern due to the increased land base required to apply manure to cropland based on P agronomic rates compared to the traditional N based application rates to reduce the possibility of excess P entering surface water. Increasing the amount of P above NRC recommendations was not shown to have deleterious effects on milk yield or major effects on milk fat, milk protein, or the incidence of health problems in cows fed from parturition to 165 days in milk (DIM; Lopez et al., 2004). These results agreed with those of Wu et al. (2000) who reported that feeding excess P to early lactation cows is not necessary since the cow has the ability to mobilize a minimum of 500-600 g of P from the skeletal system in early lactation.

Supplementing P above requirements for early lactation cattle leads to increased fecal and urinary excretion (Knowlton and Herbein, 2002). In 1999, Sansinena et al. reported that nutritionists in the Mid-South were formulating rations for high-producing cows at 0.52 % P, DM basis (Range: 0.35 % to 0.72%) and low producing cows at 0.45 % P, DM basis (Range: 0.30 % to 0.68%). At that time almost half of the respondents indicated the need to provide a safety margin above NRC recommendations as the reason for feeding the higher levels of P. This practice was not restricted to the Mid-South region as surveys have shown that 34 % of farms in the northeast United States were feeding above the P guidelines set by the NRC, with the majority of these farms following the recommendations of their consulting nutritionist (Dou et al., 2003). A survey of 54 farms in Wisconsin revealed an average feeding level of 4.1 g P/kg, a level above the NRC recommended level of 3.8 g P/kg (Powell et al., 2006).

Feeding P above the recommended level has a direct effect upon the P concentration of the organic fertilizer produced by the cows. Increasing P intake from 82 g/d to 112 g/d (0.41 % to 0.56 % of diet DM) resulted in a 48.6 % increase in fecal P excretion, while a decrease in P intake from 82 g/d to 60 g/d (0.41 % to 0.30 %) resulted in a 22.7 % decrease in fecal P excretion in multiparous lactating cows fed 20 kg DM/d (Morse et al., 1992). At feeding levels of 0.31, 0.39 and 0.47 % of diet dry matter, Wu et al. (2001) found for every 0.08 % increase in P in the diet, fecal P excretion increased by approximately 20 grams. Utilizing a model, Weiss and Wyatt (2004) created an equation that concurs with Wu et al. (2001) that fecal excretion of P increases linearly as intake of P increased.

In response to environmental concerns and the research demonstrating that NRC recommendations were adequate to support reproductive and productive performance, many nutritionists have decreased their use of supplemental P in lactating cow rations. At the same time, there has been increased scrutiny on the transition cow and metabolic profile samples that have been collected in an attempt to identify potential herd level issues. On occasion some field reports have indicated that P levels in sera samples were at the low end of normal range, leading to questions regarding whether reproduction was being negatively impacted and what should the *normal* P level be in the transition cow.

METABOLIC PROFILE RESEARCH

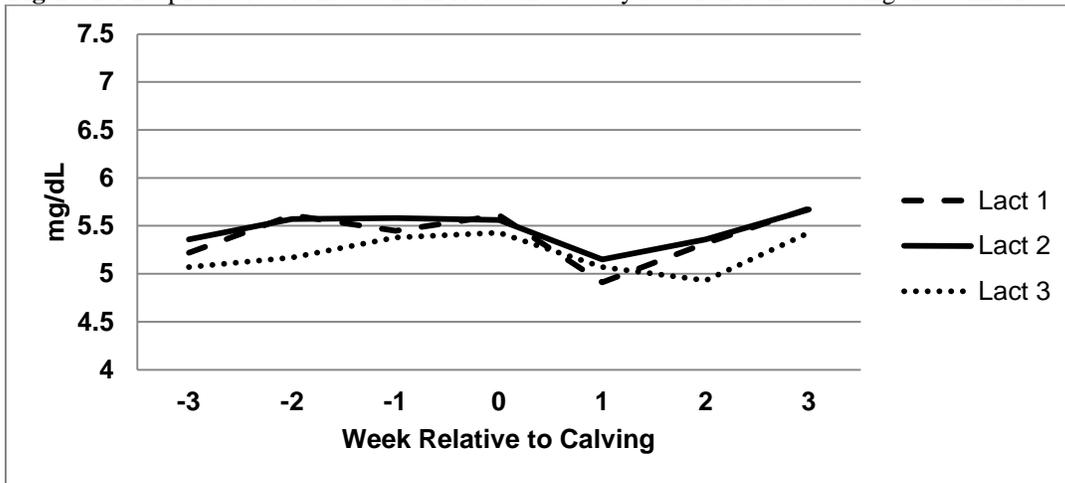
Utilizing 8 commercial Holstein herds and 8 commercial Jersey herds in the Southern High Plains, blood samples were collected in summer (Holstein and Jersey) and winter (Holstein only) from cows within the transition period (3 wks prepartum to 3 wks postpartum). Samples were placed on ice until processed, then serum was stored frozen (-20°C) until analysis was conducted for Ca, P, Mg, Na, Cl, K, glucose, blood urea nitrogen, cholesterol, albumin, NEFA, and BHBA at the Texas Veterinary Medical Diagnostic Laboratory, Amarillo, Texas. Herd records were collected and health events were extracted from herd records including dystocia, still births, twins, retained placenta, hypocalcemia, ketosis, and mastitis. Cows that were overconditioned or underconditioned and evidence of lameness was noted at sampling.

Although there were many differences noted by week relative to calving, season, breed, and disease status only select data will be discussed in the following sections.

Week Relative to Calving

When sera from Holstein cows within the transition period during the summer were evaluated for P on a week-by-week basis (week zero = -3 d precalving to 3 d post-calving), week 1 was the only week where serum P values differed (Lager et al., 2011). This would mean that P levels decrease around 10 d postpartum (Figure 1). There was not an effect of number of lactation, which differs from Quiroz-Rocha (2010), who found that first lactation animals had greater P levels than both second and third lactation cows, but concurs with their data that no differences exist prior to calving. However a

Figure 1. Phosphorus levels in sera from Holstein cows by lactation number during the summer.



similar decrease was found by Grünberg et al. (2009) from d 1 to d 14 when sampling on 2 wk intervals in a study looking at the correlation between liver P levels and serum P levels. Further, our group collected samples from summer and winter to provide seasonal analysis and it was discovered that P levels are impacted by season. Kume et al. (1986) reported that when cows were kept in a hot environment P levels decreased; however, an opposite trend was noted by Calamari et al. (2007).

Magnesium data from this project allows for an interesting comparison when compared to the profiles displayed previously. Values range from 1.48 to 1.84 mEq/L for cows in the summer. This falls below the normal range for two of the selected profiles from states on opposite sides of the contiguous United States, so if regional differences exist due to differences in agronomic practices, soil profiles, climatic conditions, or forage types remains to be investigated. The lowest value for Mg occurred in second lactation animals at 10 d postpartum.

Breed Differences

Samples were collected from Holstein and Jersey dairy cattle to allow for a comparison between breeds. Limited work has been done to assess the current metabolic profile in Jersey cattle, despite increasing interest in the breed; thus allowing for the opportunity to determine if establishment of a separate profile is necessary for diagnostic use, in much the same manner as it has been for Holstein cattle. Differences were seen in many of the profile analytes, although while the Holstein data set showed an interaction between the number of lactations,

week, and if the cows experienced a disorder for Ca, there was not an interaction when all samples were compiled nor was there an interaction when comparing breeds.

Seasonal Differences

Although there are several seasonal differences that occur, discussion will be limited to cholesterol. Cholesterol is necessary for hormone and vitamin D synthesis. In summer cholesterol was negatively impacted when cows experienced disorders; thus cholesterol would be an asset within the context of the full profile during the summer since it would be a determinant of animal health. Also, at decreased levels cholesterol may be used as an indicator of fatty liver as the liver is impaired in its ability to secrete lipoproteins, the blood carriers for cholesterol (Merck, 2011). Since cholesterol was impacted by season, it is necessary to view the profile in its entirety when determining herd status.

Animal Health

Albumin has seen increased interest as a part of determining animal health since it decreases when inflammation is occurring and also can be affected by liver disease. Combined data collected from Holstein cows in two seasons displayed no effect of the number of lactations on overall albumin levels; however when looking at week-to-week variation there are significant changes that occur. Park et al. (2010) was able to document changes in albumin, urea, NEFA, and triglycerides at varying stages by collecting samples at regular intervals from approximately 80 d prepartum to 90 d postpartum.

Although the authors used a small number of cows, variation was still evident. Albumin levels in our study decreased to the lowest point around 10 d postpartum in summer with first lactation cows impacted by two disorders having an albumin level of 2.79 g/dL. Based on the profiles in Table 1, this level would be considered within the normal range for two of the six profiles; however the agreeing profiles are based upon similar data, thus the animals experiencing two disorders would be declared abnormal if the remaining profiles were considered and would raise an alarm.

CONCLUSION

The metabolic profile is a useful tool that has evolved over time. This evolution or adaptation is necessary to account for changes in feeding management and animal genetics. The key is ensuring that the reference values match the stage of lactation as noted by Quiroz-Rocha et al. (2009). Because of the prevalence of disease within the periparturient period, a reference profile based on mid-lactation cows will limit the interpretation of data from cows within the transition period. By understanding the fluctuations that occur in serum biochemical analytes over the course of lactation, especially within the transition period, the value of the metabolic profile as a tool to differentiate between normal and compromised animals will be enhanced. With recent data displaying an impact of breed and season on the metabolic profile, as well as the documented variability within the transition period, it may be necessary to account for each factor as well as be cognizant of when a sample is collected to insure results are interpreted accurately.

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