ABSTRACT: This study was conducted to investigate individual metabolic and endocrine adaptation to lactation under conditions of identical housing and feeding conditions in high-yielding dairy cows. Forty-five cows were studied on a research farm under standardized but practical conditions. From wk 2 before calving until wk 14 postpartum, blood samples were collected at weekly intervals and assayed for blood chemistry and various metabolites and hormones. Body weight, BCS, and backfat thickness were also recorded weekly. Milk yield, milk composition, and feed intake and energy balance were accordingly measured during the postpartum phase. The animals were retrospectively classified according to their plasma concentration of β-hydroxybutyrate (BHB): cows in which a BHB threshold of 1 mM was exceeded at least once during the experiment were classified as BHB positive (BHB+); cows with BHB values consistently below this threshold were classified as BHB negative (BHB−). Using this classification, differences for NEFA and glucose concentrations were observed, but the mean calculated energy balance did not differ between the groups during the experimental period (−22.2 MJ of NE/d ± 4.7 for BHB+ and −18.9 MJ of NE/d ± 4.9 for BHB−). In BHB+ cows, the peripartum decrease (P < 0.05) of BW, BCS, and backfat thickness was more pronounced than in BHB− cows. Mean milk yields did not differ between groups. However, BHB+ cows had greater milk fat and lesser milk protein contents (P < 0.05), resulting in a greater (P < 0.05) fat:protein ratio than in BHB− cows. Thus, to some extent, cows were able to compensate for the negative energy balance by adjustments in performance. Milk acetone concentrations followed BHB concentrations in blood. Insulin-like growth factor-I and leptin concentrations were greater (P < 0.05) in BHB− cows during the time of observation than in the BHB+ cows. Comparing the reproductive variables recorded (first increase of progesterone, first service conception rate, number of services per conception, interval from calving to first AI, interval from first AI to conception, and days open) between the 2 groups yielded no significant differences. Our findings imply that despite comparable energy balance, there is considerable individual variation of the adaptive ability of cows during early lactation based on a variety of metabolic and endocrine variables.

Key words: body condition, dairy cow, energy supply, ketosis, metabolic profile

INTRODUCTION

The transition from pregnancy to lactation is crucial for the profitability of the dairy cow (Grummer, 1995). High-yielding cows are susceptible to metabolic diseases during the early postpartum period. A concomitant suppression of immune functions causes an increased risk for infectious diseases (Mallard et al., 1998). Moreover, metabolic disorders during early lactation are related to decreased fertility (Butler and Smith, 1989).

During early lactation, milk production increases more rapidly than DMI, and dietary intake lags behind the increase of nutrient needs (Bell, 1995). To meet the nutritional demands of milk synthesis, dairy cows need to mobilize body reserves causing negative energy balance (EB) until nutrient intake covers the demands (Nebel and McGilliard, 1993; Hattan et al., 2001). Circulating ketones [e.g., β-hydroxybutyrate (BHB)] in-
crease during periparturient lipolysis and may result in metabolic disturbances (Herdt, 2000). For the identification of cows being at risk for subclinical disorders, various threshold values of BHB have been suggested, for example by Walsh et al. (2007).

If the metabolic adaptation around parturition is impaired by environmental influences or based on the animal genetics, cows develop periparturient illnesses (Drackley et al., 2005). We aimed to characterize the individual variation in this adaptive process by recording blood metabolite concentrations, liver enzymes, hormones, BCS, BW, and resumption of ovarian activity postpartum in individual cows fed to achieve similar EB under practical farming conditions. To test the hypothesis that the course of metabolite and hormone concentrations during the postpartum period differs among animals, cows were classified according to their BHB concentrations. Differences between the groups would support the notion that factors other than nutrition and housing, namely genetic or epigenetic differences, or both, affect the individual capacity to cope with metabolic stress.

MATERIALS AND METHODS

All animal experiments were done at the research farm Hirschau of the Technical University Munich, Germany, and were approved by the local authority for animal welfare affairs.

Animals and Feeding Regimen

Red Holstein dairy cows (n = 45) were monitored from 2 wk antepartum (a.p.) to wk 14 postpartum (p.p.) during a period from September to May. The 305-d milk production in this herd was 7,909 ± 1,377 kg (mean ± SD) with 4.29% fat and 3.36% protein. The animals were housed in a free-stall barn, and individual feed intake was recorded electronically. A partially mixed ration consisting of roughage plus concentrate (relation 80:20 in DM) was fed ad libitum and was accessible 24 h per day. Troughs for roughage were connected to electronic balances; extra concentrate was provided by automatic feeders. Individual partially mixed ration was mixed to homogeneity, and aliquots of 88% DM) per kilogram of milk were stored at −20°C for further analyses. For the determination of DM, fresh feeds were weighed, dried for 24 h at 60°C, and were then reweighed. For the concentrate prepared weekly at the in-house mixing and milling facility at the farm, a 1-kg sample was hermetically sealed and stored cool and dry. For all further analyses, samples were milled (Brabender, Duisburg, Germany; filter width 1.1 mm) and combined afterwards into 2-wk sample pools.

Feed samples were analyzed for inorganic matter, crude fiber, crude fat, and nitrogen-free extracts according to the Weender protocol (Naumann et al., 2000). The Kjeldahl method was used to measure the CP content in the feed samples. Intestinally utilisable protein and NE₁ of the feed samples were estimated according to the German Society of Nutrition Physiology (GfE, 2001). The nutrient contents of the individual components analyzed together with their respective digestibilities were used to calculate the EB.

BW, BCS, and Ultrasonographic Measurements

Body weights were recorded weekly on electronic scales after milking from wk 1 to 14 after calving. Body condition was scored according to Edmonson et al. (1989). The B-mode ultrasonographic measurements of LM diameter (MD) and backfat thickness (BFT) were performed as described earlier (Bruckmaier et al., 1998) at 1 to 2 wk a.p. and at wk 1, 3, 5, 7, 10, 12, and 14 p.p. Muscle diameter and BFT were measured on the right side at the fourth loin vertebra. The positions for the ultrasound measurements were clipped, fluid paraffin wax was applied, and the ultrasound probe transducer (SonoVet 2000, Kretztechnik, Zipf, Austria, 5-MHz linear array transducer) was held softly against the skin and rectangular to the interface to avoid compression of the fat layer. Body weight, BCS, and ultrasonic measurements were always performed by the same person.
**Milk and Blood Samples**

Milk yield was recorded routinely by an automatic device installed in the milking parlor. Milk samples were collected twice weekly on 2 complete days (2 complete days of milking: Monday p.m., Tuesday a.m., Thursday p.m., and Friday a.m.) for 100 d to determine the average fat, protein, urea, and lactose contents via an infrared analyzer (MilkoScan-FT-60000, Foss Analytical A/S, Hillerød, Denmark). Somatic cell counts were measured with a Fossomatic-5000 (Foss Analytical A/S). Once per week, milk acetone was measured using an autoanalyzer (DAM Method, Bran + Luebbe GmbH, Norderstedt, Germany).

Blood samples were taken weekly from 2 wk a.p. until wk 8 p.p. Thereafter, blood was sampled once every 2 wk until wk 14. Blood (20 mL) was collected via jugular puncture both in EDTA-coated vacuum tubes and in NaF vacuum tubes (Greiner, Frickenhausen, Germany); samples were cooled on ice, centrifuged at 1,600 \( \times g \) at 4°C for 15 min, and the plasma was aliquoted and stored at −20°C.

**Analysis of Metabolites, Hormones, and Hepatic Enzymes**

Concentrations of BHB, NEFA, glucose, IGF-1, and leptin were assayed in blood plasma using enzymatic kit methods (BHB: No. 0907979, R-Biopharm, Darmstadt, Germany; glucose: No. 315-100, Sigma-Aldrich, Munich, Germany; NEFA: No. 994-75409, Wako, Neuss, Germany) and immunological assays (IGF-1: RIA, Daxenberger et al., 1998; leptin: enzyme immunoassay, Sauerwein et al., 2004), respectively. The activities of aspartate-aminotransferase (AST), glutamate-dehydrogenase (GLDH), and \( \gamma \)-glutamyl-transferase (GGT) were tested enzymatically; total bilirubin was measured colorimetrically using Modular Analytics (Hitachi/Roche, Mannheim, Germany).

**Classification of Animals**

To allocate the cows studied herein to groups in which adaptation to early lactation led to either hyper- or normoketonaemic conditions, we used the plasma concentrations of BHB with a threshold value of 1 mM as suggested by Huszenicza et al. (2006). Cows that had BHB values \(>1\) mM at least once during the 16-wk observation period were considered as BHB positive (BHB+, \( n = 21 \)), whereas those cows with BHB values \(<1\) mM throughout the entire experiment were classified as BHB negative (BHB−, \( n = 24 \)).

**Reproductive Performance**

Ovarian cyclic activity was evaluated by determining the progesterone concentrations (Prakash et al., 1988) in milk samples collected from each cow twice per week beginning wk 2 p.p. Progesterone concentra-

tions exceeding 1.2 ng/mL for at least 1 wk and declining thereafter below 0.5 ng/mL were regarded as indicative of a corpus luteum developed in consequence of a preceding ovulation (Schopper et al., 1989).

**Statistical Analyses**

Data are presented as means ± SEM. The MIXED models procedure (SAS Inst., Cary, NC) program package used included animal, group, and time as class variables. Animal was the repeated subject. The compound symmetry matrix structure was used. Statistical significances (\( P < 0.05 \)) between group and time and of interactions between both were tested by LSD. The \( \chi^2 \) test was used to analyze disease frequency and nominal reproduction data in BHB groups.

Incomplete test-day records and test-day records of cows under a medical or preventive treatment, which might have influenced metabolic or endocrine status, were omitted. In total, records of 45 cows from wk 2 a.p. to 14 p.p. were available for calculations.

**RESULTS**

**Milk Yield and Composition**

The mean 100-d lactation milk yield recorded during the experimental period was 3,086 ± 78.0 kg; there was no difference between the BHB− and BHB+ groups. Milk production started with 28 kg/d and then increased (\( P < 0.05 \)), reaching peak values of 35.3 ± 1.5 kg at wk 7 in the BHB− group and 33.7 ± 1.2 kg in wk 9 in the BHB+ group (Figure 1A). Thereafter, milk yield declined (\( P < 0.05 \)) for both groups to about 31 kg/d until wk 13. For milk fat and protein content, the timely changes are shown in Figure 1B and C. Cows of the BHB+ group had greater (\( P < 0.05 \)) milk fat contents than those of the BHB− group during lactation in wk 2, 3, 4, 5, 7, and 9 p.p. Mean milk protein percentage was greater (\( P < 0.05 \)) in the BHB− group in wk 4, 6, and 9. All milk constituents were greatest (\( P < 0.05 \)) in wk 1 p.p. and then decreased, reaching relatively constant values until wk 6 and 7 p.p. (fat), or slightly increased thereafter (protein; \( P < 0.05 \)). As presented in Figure 1D, the fat:protein ratio was greater (\( P < 0.05 \)) in the BHB+ than in the BHB− group during the trial in wk 2 to 9, 12, and 14 p.p. (\( P < 0.05 \)). The fat:protein ratio values peaked in wk 4 with 1.8 in BHB+, and in wk 2 with 1.4 in BHB−, respectively. No group differences were detected for lactose (4.7%) and urea concentrations (248.0 mg/L) in milk and for somatic cell counts (235 × 10⁶ cells/mL).

**Feed Intake and Energy Balance**

Mean total DMI was least (\( P < 0.05 \)) at about 13 kg/d during the first week p.p. and then increased (\( P < 0.05 \)) steadily until wk 10 to 11 without detectable differences between the 2 BHB groups (Figure 2A). At the
end of wk 14, DMI was about 19.5 kg/d in both groups. The intake of NE\textsubscript{1} was also least ($P < 0.05$) in the first week postcalving with 92.9 MJ of NE\textsubscript{1}/d in BHB\textsuperscript{+} and 87.2 MJ of NE\textsubscript{1}/d in BHB\textsuperscript{−}, increased ($P < 0.05$) rapidly within wk 4 p.p., and peaked at wk 11 p.p. at 133.4 MJ of NE\textsubscript{1}/d in BHB\textsuperscript{+} and in wk 10 at 134.1 MJ of NE\textsubscript{1}/d in BHB\textsuperscript{−} cows. During the period after calving, NE\textsubscript{1} intake was not different between BHB\textsuperscript{+} and BHB\textsuperscript{−} cows from wk 3 to 11 of lactation. At the end of the experimental period, both groups had mean NE\textsubscript{1} intakes of 132.9 ± 9.6 MJ/d. The calculated EB, presented in Figure 2B, started with a nadir at about −42 MJ/d in the first week after calving and increased ($P < 0.05$) thereafter. By wk 14, BHB− cows had reached positive EB values, whereas BHB\textsuperscript{+} cows still had an energy deficit of −4.8 NE\textsubscript{1} (MJ/d). However, EB was not different between the 2 groups during the experimental period.

**BW, BCS, and Ultrasonographic Measurements**

Body weight decreased ($P < 0.05$) rapidly after parturition up to wk 6 and 4 in BHB\textsuperscript{+} and BHB\textsuperscript{−} cows, respectively. The cows lost BW (Figure 3A) to a nadir of 614 kg in wk 11, and to 656 kg in BHB\textsuperscript{+} and BHB\textsuperscript{−} cows, respectively. Overall, BHB\textsuperscript{+} cows had greater ($P < 0.05$) reductions of BW after calving, with group differences in wk 6, 7, and 10. At the end of wk 14, the BW difference between the 2 groups was about 48 kg.

Body condition score was decreased ($P < 0.05$) in both groups until wk 3 by about 0.9 points (Figure 3B). Thereafter, the cows of the BHB\textsuperscript{+} group lost more ($P < 0.05$) condition than the BHB\textsuperscript{−} animals, with differences established for wk 7 and 12. The ultrasound measurements of MD and BFT of BHB\textsuperscript{+} and BHB\textsuperscript{−} cows from wk 2 a.p. until wk 14 p.p. are presented in Figure 3C and D. After calving, the cows lost ($P < 0.05$) subcutaneous fat rapidly until wk 10 in BHB\textsuperscript{+} and wk 7 in BHB\textsuperscript{−}, respectively. Similarly, MD was greatest ($P < 0.05$) before calving and was then decreased, but again, no differences were seen between the 2 groups.

**Metabolites, Hormones, and Enzyme Activities**

As expected, the cows grouped into BHB\textsuperscript{+} and BHB\textsuperscript{−} were clearly distinguishable by the time course of the BHB concentrations in blood throughout the study (Figure 4A), but showed no differences with regard to EB (Figure 2B). In the BHB\textsuperscript{+} group, the concentrations were greater ($P < 0.05$) from 1 wk until wk 10 p.p. than in the BHB\textsuperscript{−} animals. The timely changes
were only marginal in the BHB− group, whereas in the BHB+ group, the concentrations increased (P < 0.05) after calving reaching peak values in wk 2 to 5 and decreased thereafter.

The classification according to ketotic load was also confirmed by the concentrations of acetone measured in milk (Figure 4B). In BHB+ cows, the concentrations were about 2-fold greater (P < 0.05) during wk 1 to 5 than in BHB− cows. Thereafter, the milk acetone concentrations from BHB+ animals decreased (P < 0.05) and reached similar concentrations as seen in the BHB− group by wk 10.

For NEFA, increasing values toward calving were observed in both groups (Figure 4C). At parturition, BHB+ animals had about 2-fold greater (P < 0.05) NEFA values than the BHB− cows and maintained these concentrations during the following 4 wk. In BHB− cows, maximal NEFA values were reached during the first week of lactation but decreased (P < 0.05) thereafter. At wk 12, both groups had reached almost equal concentrations that were falling below the a.p. values.

Glucose concentrations were greater (P < 0.05) in BHB− than in BHB+ cows at 2 wk a.p. (Figure 4D) and in wk 0, 2 to 5, and 7 p.p. The nadir of glucose concentrations was reached at wk 2 in BHB+ cows and 1 wk earlier in BHB− animals; the a.p. concentrations were again reached by wk 10 in both groups.

For IGF-1 (Figure 5A), there was a steep decrease (P < 0.05) of the concentrations until calving in both groups. In BHB− animals, the concentrations remained at this level and then increased (P < 0.05) slowly. In contrast, BHB+ cows had further decreasing concentrations until wk 2 and then increased (P < 0.05) again. Differences between groups were limited to wk 1 to 8 after calving. By the end of the study, both groups had reached about 50% of the IGF-1 concentrations recorded 2 wk a.p.

Leptin concentrations decreased (P < 0.05) until wk 2 p.p.; reduced concentrations were observed in BHB+ cows at wk −1, 4 to 6, and 10 compared with BHB− animals (Figure 5B). When taking all measurements of both leptin and BFT into account, a correlation of \( r = 0.31 \) (P < 0.001) was observed; for individual time points considered as representative for the a.p. or p.p. situation (i.e., for wk −2 a.p. and wk 5), significant correlations were limited to the a.p. stage (r = 0.38, P = 0.03).

The activities of the enzymes AST, GGT, and GLDH were greater (P < 0.05) from wk 1 to 14 p.p. than before calving. Significant differences between the BHB+ and the BHB− group were established for AST and GGT; the time courses for these 2 enzymes are shown in Figure 6 and demonstrate greater (P < 0.05) activities in BHB+ cows in wk 2 and 4 (AST) and wk 3 to 8 (GGT), respectively. For GLDH, an analogous difference was limited to 1 time point only [i.e., to wk 4 p.p. (P < 0.05)]. Total bilirubin concentrations increased (P < 0.05) from parturition until wk 1, when maximal values were reached. In BHB− cows, the concentrations were greater (P < 0.05) than in BHB+ around parturition and in wk 4 (P < 0.05).

### Animal Health and Reproductive Performance

There was no difference between BHB groups for the occurrence of clinical cases of mastitis, endometritis, retained placenta, lameness, and metabolic diseases (taking hypocalcemia, ketosis, and acidosis together) based on \( \chi^2 \) analysis. The variables recorded in the 2 BHB groups to evaluate reproductive performance are shown in Table 1. The interval from calving to the onset of ovarian activity was studied in 45 cows and was below 100 d in all cases. Five cows were not inseminated for reasons of lameness or elevated somatic cell count in milk in the previous lactation. Thus, 40 cows were included for the analysis of the interval from parturition to conception. Each of these 40 cows was insemi-
nated at least once. There was no difference between groups for any reproductive endpoint.

**DISCUSSION**

The hypothesis was tested that the course of metabolic, endocrine, and reproductive variables during the p.p. period differs considerably among animals despite similar housing and feeding management, in particular energy balance, thus indicating that the capability to cope with metabolic stress varies between individual cows. Compared with other studies, we neither used a feed restriction model nor dietary-induced ketonemia. The cows were at a rather high body condition level (BCS of about 4.2) 2 wk a.p. The incidence of metabolic diseases (20% of all animals) in this experiment was probably attributable to overconditioning during the dry period. Overfeeding during the dry period causes overcondition at calving and depression of appetite thereafter, thereby aggravating the negative EB (Rukkwamsuk et al., 1999). Overfeeding during the far-off period (drying-off to d 25 a.p.) has a more negative effect on a.p. metabolism than differences in nutrition 3 wk a.p. (Dann et al., 2006). The metabolic demands in this period require that the liver synthesizes more glucose from noncarbohydrate precursors. A reduction in the ruminal production of propionic acid, the main precursor of glucose in ruminants, will result in hypoglycaemia. This leads to a mobilization of free fatty acids and glycerol from the fat stores (Holtenius and Holtenius, 1996; Andrews, 1998). The level of increased serum concentrations of NEFA appears to be causally linked to these problems, and feeding strategies to decrease or avoid this dramatic increase are desirable for optimal health and performance in dairy cows (Gerloff, 2000). In case of excess NEFA associated with an elevated formation of acetyl-coenzyme A, fatty acids are used for ketogenesis. Extreme lipid mobilization from adipose tissue exceeds the metabolizing capacity of the liver, leading to an increased accumulation of triglycerides (Herdt, 1988). The affected cows display fat infiltration and degeneration of the liver (Moore and Ishler, 1997).

The adipose tissue thus has a critical role in the development of fatty liver and ketosis, because these changes in liver composition and metabolism arise both from excessive lipolysis in adipose tissue and altered secretion of adipose tissue-derived hormones, which modulate hepatic metabolism (Vernon, 2005). The postpartal mobilization of fat was associated with increasing milk fat and decreasing milk protein contents as a consequence of the energy deficit. The fat:protein ratio allowed for an identification of the cows with elevated ketone body concentrations. Cows with fat:protein ra-

**Figure 3.** Body weight, BCS, backfat thickness, and diameter of the LM recorded from 2 wk before calving until wk 14 postpartum (p.p.) in cows grouped according to their blood concentrations of 8-hydroxybutyrate (BHB). -Δ- = BHB+ group (BHB concentrations ≥1 mM) and -●- BHB− group (BHB values ≤1 mM). Data are given as least squares means ± SEM. *Differences between the 2 BHB groups at a particular sampling week (P < 0.05).
tios >1.3 in the first week of lactation are at risk for ketosis or are already affected with it (Heuer et al., 1999). Milk yields were similar in BHB− and BHB+ cows, although there were differences in milk composition associated with the metabolic profile.

Milk acetone concentrations represented in this paper were in agreement with Reist et al. (2000). The periodic sampling of milk for the determination of acetone is getting more common in herd-health monitoring programs and is most suitable for diagnosis of clinical and subclinical ketosis in the first 6 wk of lactation.

Both groups had decreased DMI in early lactation. The EB did not differ between the BHB+ and BHB− groups, and both groups failed to achieve a positive EB by wk 14 of lactation. Total DMI followed a curve similar to the reports of Ingvartsen and Andersen (2000). As a consequence of the overfeeding in the dry period, total DMI was low in both groups in the present study.

The consequences resulting from the decreased DMI are reflected by energy intake. The total intake of energy by cows after calving is usually below the energy requirements, even for healthy cows (Bell, 1995). The NE\textsubscript{1} intake was fractionally less in BHB+ than BHB−. In agreement with Drackley et al. (2005), it appears that changes in DMI a.p., and not the absolute DMI per se, are more closely related to poor intake and fatty liver after calving. These data emphasize the importance of good management that keeps cows healthy and comfortable before calving. In this way, increased DMI indicates the overall comfort and well-being of the cows rather than revealing the underlying reasons.

The negative EB challenges the metabolic adaptation of the cow. The least values were observed between 2 and 12 d p.p. The balance between energy from feed intake and energy requirements is mostly attained at approximately 72 d p.p. (Jorritsma et al., 2003). If negative EB is prolonged beyond this time or has an extended magnitude, or both, successful metabolic adaptation is less likely.

The least BW and the greatest BCS losses p.p. were found in the BHB+ group. Thus, we assume that BHB+ cows mobilized a greater amount of body tissue as a support of lactation. This interpretation is based on differences in milk composition, which imply altered nutrient partitioning (Zulu et al., 2002). Our data on MD give some indication that mobilization of body tissue comprised not only fat but also muscle tissue. Muscle protein serves as a source for glucoplastic amino acids to supply the increased needs for glucose during early lactation. Body condition score losses were present in both groups, although the BCS loss in BHB+ was

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**Figure 4.** Timely changes in the concentrations of 4 metabolites recorded from 2 wk before calving until wk 14 postpartum (p.p.) in cows grouped according to their blood concentrations of β-hydroxybutyrate (BHB). -Δ- = BHB+ group (BHB concentrations ≥1 mM) and -●- = BHB− group (BHB values ≤1 mM). Concentrations of BHB, NEFA, and glucose are in blood, and concentrations of acetone are in milk. Data are given as least squares means ± SEM. *Differences between the 2 BHB groups at a particular sampling week (P < 0.05).
greater. In agreement with Kunz et al. (1985), Busato et al. (1998), and Heuer et al. (1999), cows with a high BCS a.p. were more likely to develop an elevated ketone body status p.p. than cows in moderate to low body condition. This might be due to a greater mobilization rate of NEFA from fat depots in overconditioned than in thin cows.

Generally, greater plasma NEFA and BHB and lower plasma glucose concentrations are associated with decreased reproductive performance, indicating that the balance of lipogenic and glycogenic compounds is important for reproductive function (Knegsel et al., 2005). The increase observed in glucose concentrations was greater for BHB+ cows and remained elevated for a longer period. Nevertheless, BHB was the criterion used for classification; the values in both groups during the first 14 wk of lactation mirrored the detrimental situation of fresh cows and the measurable results of utilization of body fat as a source of energy for milk production (Dann et al., 2005).

In general, enzyme activities increased p.p. Significantly differing enzyme activities between both groups indicate differences in potential tissue damage and liver function, which are known to be impaired during energy deficits and ketosis (Mills et al., 1986).

Insulin-like growth factor-1 is known to be markedly influenced by energy intake in dairy cows (Ronge et al., 1988). A negative EB decreases IGF-I concentrations (Lucy et al., 1992) and may thus explain for the decrease in IGF-I concentration around parturition. Decreased IGF-1 concentrations are in turn related to impaired luteal activity, slower follicular growth, and altered production of sex steroids (Spicer et al., 1990; Lucy et al., 1992). Negative EB during the early weeks of lactation and a delayed EB nadir are associated with longer intervals to the first ovulation p.p. (Beam and Butler, 1998). In our study, the concentrations of IGF-1 were clearly distinguishable between the BHB groups, whereas no differences in EB could be established for these groups. Considering the other differences established between the 2 groups, BHB seems to be more sensitive and thus more suitable to characterize the metabolic situation relevant for reproduction. The fertility records of the cows studied herein were accept-

**Figure 5.** Timely changes in the concentrations of IGF-I and of leptin recorded from 2 wk before calving until wk 14 postpartum (p.p.) in cows grouped according to their blood concentrations of β-hydroxybutyrate (BHB). -●- BHB+ group (BHB concentrations ≥1 mM) and -●- BHB− group (BHB values ≤1 mM). Data are given as least squares means ± SEM. *Differences between the 2 BHB groups at a particular sampling week (P < 0.05).

**Table 1.** Key variables of reproduction recorded in cows grouped according to their concentrations of β-hydroxybutyrate (BHB) in blood

<table>
<thead>
<tr>
<th>Item</th>
<th>BHB−</th>
<th>BHB+</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days from calving to first ovulation</td>
<td>46.0 ± 28.3</td>
<td>40.9 ± 24.1</td>
<td>0.59</td>
</tr>
<tr>
<td>Days from calving to first service</td>
<td>64.4 ± 16.4</td>
<td>75.3 ± 29.1</td>
<td>0.151</td>
</tr>
<tr>
<td>Days from first service to conception</td>
<td>27.6 ± 41.5</td>
<td>38.0 ± 55.5</td>
<td>0.531</td>
</tr>
<tr>
<td>Days from calving to conception</td>
<td>91.2 ± 40.4</td>
<td>115.47 ± 74.4</td>
<td>0.228</td>
</tr>
<tr>
<td>Services per conception</td>
<td>1.90 ± 1.11</td>
<td>1.94 ± 1.18</td>
<td>0.907</td>
</tr>
<tr>
<td>First-service conception rate, %</td>
<td>52.4</td>
<td>42.1</td>
<td>0.941</td>
</tr>
<tr>
<td>Rate of cows failing to conceive, %</td>
<td>15.8</td>
<td>9.5</td>
<td>0.550</td>
</tr>
</tbody>
</table>

1 BHB+ group: concentrations ≥1 mM; BHB− group: BHB values ≤1 mM.
2 n = 40.
3 n = 35.
able in general (Ruegg, 2001) but give some indication for problems resulting from lipid mobilization and ketone body formation in the BHB+ group.

Drackley et al. (1992) suggested that intrahepatic factors altered by early negative EB and extensive tissue mobilization act in support of mechanisms that increase ketogenesis. However, the fact that cows respond differently to the homeorhetic needs of early lactation even though their EB was not different emphasizes individual animal variation. The effect of other potential stressors was considered as being the same for all animals; nevertheless, it was not specifically addressed in this study. The variability observed within a given setup in feeding and management (Hachenberg et al., 2007) is thus likely to be attributable to genetic, epigenetic, or rumen bacterial metagenomic regulation or all three. As an example, heritability values have been reported for ketosis (Henricson et al., 1977). In addition, variations in rumen microbial populations and metabolism as recently reviewed by Firkins et al. (2007) might contribute to the range of responses observed for various metabolites, enzymes, and hormones.

In conclusion, the timely changes of the concentrations of metabolites and hormones during the p.p. period remarkably differ among animals kept under similar and highly standardized conditions on a research farm. This indicates that the ability to cope with metabolic stress varies between individual cows. When aiming to characterize the adaptive capability, the intricate estimation of EB will not provide the information required. Instead, blood analyses, in particular of BHB, seem more appropriate to reflect the individual situation. Considering these findings, the identification of cows with high or low adaptive capabilities seems promising to investigate the underlying causes.

**LITERATURE CITED**


