J. Dairy Sci. 100:3685–3696
https://doi.org/10.3168/jds.2016-12085

Relationships between body condition score change, prior mid-lactation phenotypic residual feed intake, and hyperketonemia onset in transition dairy cows

Francesca M. Rathbun,* Ryan S. Pralle,* Sandra J. Bertics,* Louis E. Armentano,* K. Cho,† C. Do,‡ Kent A. Weigel,* and Heather M. White*[1]
*Department of Dairy Science, University of Wisconsin-Madison, Madison 53706
†Division of Animal Breeding and Genetics, National Institute of Animal Science, Cheonan 21001, Korea
‡Division of Animal and Dairy Science, Chungnam National University, Daejeon 34134, Korea

ABSTRACT

Extensive efforts have been made to identify more feed-efficient dairy cows, yet it is unclear how selection for feed efficiency will influence metabolic health. The objectives of this research were to determine the relationships between residual feed intake (RFI), a measure of feed efficiency, body condition score (BCS) change, and hyperketonemia (HYK) incidence. Blood and milk samples were collected twice weekly from cows 5 to 18 d postcalving for a total of 4 samples. Hyperketonemia was diagnosed at a blood β-hydroxybutyrate (BHB) ≥1.2 mmol/L and cows were treated upon diagnosis. Dry period, calving, and final blood sampling BCS was recorded. Prior mid-lactation production, body weight, body weight change, and dry matter intake (DMI) data were used to determine RFI phenotype, calculated as the difference between observed DMI and predicted DMI. The maximum BHB concentration (BHB_{max}) for each cow was used to group cows into HYK or not hyperketonemic. Lactation number, BCS, and RFI data were analyzed with linear and quadratic orthogonal contrasts. Of the 570 cows sampled, 19.7% were diagnosed with HYK. The first positive HYK test occurred at 9 ± 0.9 d postpartum and the average BHB concentration at the first positive HYK test was 1.53 ± 0.14 mmol/L. In the first 30 d postpartum, HYK-positive cows had increased milk yield and fat concentration, decreased milk protein concentration, and decreased somatic cell count. Cows with a dry BCS ≥4.0, or that lost 1 or more BCS unit across the transition to lactation period, had greater BHB_{max} than cows with lower BCS. Prior-lactation RFI did not alter BHB_{max}. Avoiding over conditioning of dry cows and subsequent excessive fat mobilization during the transition period may decrease HYK incidence; however, RFI during a prior lactation does not appear to be associated with HYK onset.

Key words: hyperketonemia, body condition score, feed efficiency

INTRODUCTION

There has been a concerted effort to select for more efficient dairy cattle to reduce both feed costs and the carbon footprint of dairy production (Connor et al., 2013; Green et al., 2013; Macdonald et al., 2014; Hardie et al., 2015). Feed efficiency is commonly quantified as residual feed intake (**RFI**), which represents the difference between an individual animal's observed feed intake and their predicted feed intake (Potts et al., 2015), where their predicted intake is what they are expected to consume for their production based on a regression of milk energy, maintenance energy, metabolic BW, and BW change (Hardie et al., 2015). An animal with a negative RFI consumes less feed than predicted and is therefore more efficient (Potts et al., 2015). Although selection of animals for feed efficiency could result in positive progress in reducing feed costs and environmental impacts, the effect of this selection on other phenotypic traits, such as metabolic health, is largely unknown and further research on the correlation and co-selection of these traits is needed (Hardie et al., 2015).

Variation in feed efficiency is thought to reflect 5 major processes: feed intake, digestion of feed, metabolism (including variation in body composition, anabolism, and catabolism), activity, and thermoregulation (Herd and Arthur, 2009). Mobilization of body stores provides energy, specifically to animals in negative energy balance (**NEB**). Although changes in BW are accounted for within the RFI calculations, RFI is generally measured during a period of minimal BW and condition

Received September 30, 2016.
Accepted January 24, 2017.
[1]Corresponding author: heather.white@wisc.edu

change (Tempelman et al., 2015). In previous studies, RFI has not been measured during the transition period, the 3 wk before and 3 wk after calving, during which dairy cows enter NEB, rapidly mobilize adipose tissue as fatty acids, and often have elevated circulating ketone body concentrations (Grummer, 1993; Drackley, 1999; Duffield, 2000). Whereas ketone bodies can be used as a fuel source by some tissues, excessive production of these metabolites can lead to hyperketonemia (**HYK**) and have negative effects on animal health, production, and profitability (Baird et al., 1980; Herdt, 2000; McArt et al., 2015).

To successfully use RFI as a selection tool, an understanding of the effect of negative RFI on animal health and longevity is needed. To determine if selection based on RFI will influence subsequent lactation HYK incidence, the associations between body stores mobilization, HYK onset, and RFI were examined. The objectives of our research were (1) to determine the relationship between BCS across the transition period and HYK onset, and (2) to determine the relationship between prior lactation RFI and subsequent lactation BCS change and HYK incidence.

MATERIALS AND METHODS

All experimental protocols were approved by the University of Wisconsin-Madison College of Agricultural and Life Sciences Animal Care and Use Committee.

Transition Cow Study

Study Design and Diets. From October 9, 2014, until October 30, 2015, all primiparous and multiparous cows due to calve at the University of Wisconsin-Madison Emmons Blaine Dairy Cattle Research Center in Arlington, Wisconsin, were enrolled in the study. Five hundred seventy-one Holstein cows were enrolled into the study 28 d before their expected calving date. One cow was removed from the study due to severe mastitis and lameness. Previous lactation 305-d mature-equivalent (**305ME**) milk production and genetic merit (milk and fat yield PTA) were recorded for each cow.

Cows were fed a corn silage and wheat straw based TMR during the dry period and a corn silage- and alfalfa silage-based TMR after calving. The feed ingredients and calculated composition for the dry and lactating TMR are shown in Table 1. During the study, dry cows were housed in a freestall barn and moved to a bedded pack 3 wk before calving. After calving, fresh cows were housed on either a bedded pack or a freestall pen. In addition to being fed a TMR, fresh cows housed on the bedded pack were offered ad libitum dry hay.

Weekly TMR and hay samples were collected, frozen, and later dried at 55°C for 48 h in a forced-air oven to determine DM content and ground to pass a 1-mm screen in a Wiley mill (model #4, Thomas Scientific, Swedesboro, NJ). Ground samples were composited by month and analyzed (Dairyland Laboratories Inc., Arcadia, WI). The nutrient composition of the TMR and hay are shown in Table 2.

Blood and Milk Sampling. Blood samples were collected after the morning feeding twice weekly to achieve 4 sample time points between 5 and 18 d relative to calving (**DRTC**) for each cow. Hyperketonemia was diagnosed as blood BHB $\geq$1.2 mmol/L.

Cow-side BHB testing was completed directly after blood sampling using a Precision Xtra meter (Abbott Laboratories, Abbott Park, IL), a human electronic hand-held blood glucose and ketone body meter that has a sensitivity of 91% and a specificity of 94% for detecting HYK in bovine blood samples when compared with laboratory assays (Iwersen et al., 2009). Milk samples were collected on the same days as blood samples, during the morning milking. As a part of routine fresh cow management, cows were checked daily with a semiquantitative urine dipstick for the first 10 d postpartum. If a cow tested positive for HYK by the urine analysis on a nonsampling day, a blood sample was collected and tested with the Precision Xtra meter by farm staff. If the cow was diagnosed with a blood BHB $\geq$1.2 mmol/L, a blood and milk sample were taken that day (if the cow had not yet been milked) or the following day (if diagnosis occurred after milking) and those samples were included in the data set, resulting in 5 samples collected for some cows. After collection of a blood and milk sample, the cow was treated according to the standard treatment protocol for HYK (oral drench of 300 mL of propylene glycol once daily for 3 d).

Milk samples were analyzed for fat and true protein contents by infrared analysis and SCC by flow cytometry (AgSource Milk Analysis Laboratory, Menominee, WI) using a CombiFoss 6600 FT+/FC (FOSS Electric, Hillerød, Denmark), and milk fat content was corrected to account for morning-only milk sampling (DeLorenzo and Wiggans, 1986). Yields of FCM and ECM were calculated according to NRC (2001) equations. Individual cow milk weights were also collected for the first 30 d postpartum.

BCS. Cows were body condition scored according to a 5-point scale (Wildman et al., 1982; Ferguson et al., 1994). All cows were body condition scored at 3 time points: −28 DRTC (dry BCS; **DBCS**), at calving (+1 DRTC; **CBCS**), and at the time of the last blood sample (**LSBCS**) around +18 d relative to calving.

Table 1. Calculated ingredient composition and nutrient analysis of dry and lactating cow diets[1]

Item, % DM (unless otherwise noted)	Dry		Lactating	
	Mean	SEM	Mean	SEM
Ingredient composition				
Corn silage	48.20	0.24	28.58	0.76
Lactating concentrate mix[2,3,4]			28.00	0.25
Grass hay	24.56	0.00		
Dry cow concentrate mix[4,5,6]	19.64	0.77		
Haylage			17.17	0.67
High-moisture shell corn			13.83	0.49
Wheat straw	12.50	2.75		
Linted cottonseed			5.00	0.00
Dried distillers grains			4.83	0.11
Oatlage			4.00	0.00
Dry hay			3.00	0.00
Nutrient analysis				
DM, % as fed	43.84	0.03	49.18	0.70
CP	14.46	0.03	17.43	0.03
NDF	46.40	0.20	31.89	0.23
ADF	27.70	0.47	20.80	0.19
NFC	29.60	0.20	40.18	0.24
Starch	18.72	0.72	25.66	0.11
Sugar	4.04	0.04	2.41	0.06
Fat	2.58	0.01	4.42	0.04

[1]Ration had expected fluctuations over the 12 mo of the study duration to accommodate changes in forages, commodities, and concentrates to maintain consistent chemical compositions. Means and SE portray subtle changes in formulation.

[2]Lactating cow concentrate mix was formulated to 26.50% CP (DM basis) using canola meal (18.59 ± 0.99%), soy hulls (16.09 ± 0.15%), expeller soybean meal (13.72 ± 0.13%), 47% CP soybean meal (11.21 ± 0.10%), Soy Plus (Landus Cooperative, Ames, IA; 2.85 ± 0.00%), and raw soybeans (1.33 ± 0.00%). The mix also contained 25.85 ± 0.22% fine rolled corn, 5.63 ± 0.02% calcium carbonate, 2.95 ± 0.02% sodium bicarbonate, 1.30 ± 0.02% lactating cow mineral mix, 1.16 ± 0.01% animal fat, 0.80 ± 0.01% magnesium oxide (54%), 0.73 ± 0.008% urea, 0.38 ± 0.02% potassium carbonate, and 0.19 ± 0.009% DynaMate (The Mosaic Company, Plymouth, MN).

[3]Lactating cow mineral mix did not change throughout the experiment and contained 86.97% white salt, 2.88% zinc oxide (72%), 2.40% manganous oxide, 1.75% vitamin E (50%), 1.75% Rumensin 90 (Elanco, Greenfield, IN), 1.12% selenium (0.08%), 0.90% copper chloride, 0.77% mineral oil, 0.76% biotin (2%), 0.43% iron sulfate, 0.21% vitamin AD3, 0.06% ethylenediamine dihydriodide (99%), and 0.02% cobalt carbonate.

[4]Reashure (Balchem Corporation, New Hampton, NY) was fed in both the dry and lactating TMR at a rate of 56.7 g/cow per day by addition to the mixer per pen density.

[5]Dry cow concentrate mix was formulated to 36.30% CP, DM using 78.85 ± 0.00% canola meal. The mix also contained 8.37 ± 0.09% dry cow mineral mix and 2.18 ± 0.00% calcium carbonate.

[6]Dry cow mineral mix contained 17.99 ± 0.07% calcium sulfate, 11.93 ± 0.05% white salt, 10.90 ± 0.88% OmniGen-AF (Phibro Animal Health Corp., Teaneck, NJ), 10.37 ± 0.04% magnesium oxide (54%), 9.29 ± 0.04% calcium carbonate, 8.35 ± 0.03% dicalcium phosphate (21%), 8.25 ± 0.93% magnesium sulfate, 2.06 ± 0.008% trace mineral supplement (110,000 mg/kg zinc, 99,000 mg/kg manganese, 20,000 mg/kg copper, 2,330 mg/kg iodine, 1,600 mg/kg cobalt, 660 mg/kg iron), 1.91 ± 0.009% mineral oil, 1.10 ± 0.005% vitamin E (50%), 0.69 ± 0.003% selenium yeast, 0.36 ± 0.00% Rumensin 90 (Elanco), 0.34 ± 0.00% 2% biotin, 0.04 ± 0.00% vitamin A, and 0.01 ± 0.00% vitamin D. The mix also contained either kaolin (18.71 ± 0.94%) or bentonite (10.08 ± 0.001%) as a carrier.

All cows were body condition scored within 3 d of the target by the farm manager and 1 of 2 trained research personnel at each time point. The 2 research personnel were cross trained and evaluated for consistency before being permitted to score independently. The 2 BCS recorded by the farm manager and research staff were averaged for each time point. The single time point measurements of DBCS, CBCS, and LSBCS were allocated to 5 categories: average BCS <3.0, 3.25 (range: 3.0–3.25), 3.5 (range: 3.26–3.74), 3.75 (range: 3.75–3.99) and ≥4.0. The BCS change between CBCS and DBCS, LSBCS and DBCS, and LSBCS and CBCS were calculated by subtracting the average BCS of the early time point from the later time point. The BCS change between the DBCS and LSBCS were allocated into 6 categories: ≥−1.0, −0.75, −0.5 (range: −0.74 to −0.37), −0.25 (range: −0.36 to −0.25), 0 (range: −0.24 to 0), or ≥0.25. For the BCS changes over the 2 shorter ranges of time, the ≥−1.0, −0.75, and −0.5 categories were combined into a ≥−0.5 BCS change group.

RFI: Data Compilation

Phenotypic RFI data were pooled from 14 nutrition studies carried out between 2007 and 2014 at the Emmons Blaine Dairy Cattle Research Center (Arlington, WI) and the Dairy Cattle Instructional Center (Madison, WI) of the University of Wisconsin-Madison Integrated Dairy Facilities. Individual intakes were recorded via electronic gates (RIC system, Insentec, Markenesse, the Netherlands) or were recorded manually via weigh-backs in a tiestall barn. All experiments providing phenotypic RFI data were summarized (Tempelman et al., 2015) or reported (Weld and Armentano, 2016) previously. Five studies used only 1 ration and the remaining studies used multiple rations; however, it is important to note that ration within experiment was accounted for when assembling animal cohort groups during RFI calculations, and this allows for comparing and compiling RFI values determined across different experiments, experiment stations, and countries (Tempelman et al., 2015) and that RFI is repeatable across high- and low-starch diets (Potts et al., 2015). Experiment and parity of RFI origin was recorded for each cow in the transition cow study. Repeatability of RFI between lactations has been estimated to be 0.2 (Connor et al., 2013) and between 0.1 and 0.35 (Tempelman et al., 2015). Determination of RFI was by the first step of the 2-step modeling process, as thoroughly described previously (Hardie et al., 2015; Tempelman et al., 2015). A model for DMI was fitted based on parity, DRTC, milk energy, metabolic BW, BW change, ration within experiment, and time. The RFI was the unaccounted-for difference between predicted DMI and the observed DMI (Hardie et al., 2015; Tempelman et al., 2015). All RFI data were collected between 50 and 200 DRTC to minimize BW change and reduce error in calculating RFI introduced by extensive body tissue mobilization (Tempelman et al., 2015). Calculation of RFI was based on actual DMI collection for 56 consecutive days during the 50 to 200 DRTC period. Not all cows on the current study were previously enrolled in an RFI study. Additionally, primiparous cows were not previously eligible for an RFI study as all were done during a lactation. Out of the 570 cows enrolled in the study, 214 multiparous cows had a phenotypic RFI.

Statistical Analysis

All statistical analyses were performed in SAS (version 9.4; SAS Institute Inc., Cary, NC) and significance was declared at $P \leq 0.05$ and a tendency was declared at $0.05 < P \leq 0.10$. Least squares means were separated by Tukey's studentized adjustment when $P \leq 0.05$ when appropriate. Descriptive statistics were calculated by the FREQ and MEANS procedures. Daily milk yield and weekly milk composition (wk 1 = 5 to 7 DRTC; wk 2 = 8 to 14 DRTC; and wk 3 = 15 to 18 DRTC) data were analyzed using the MIXED procedure in a model that accounted for the fixed effect of diagnosis [not hyperketonemic (**nonHYK**) vs. HYK], time (week or DRTC), the subsequent interaction, and the random effect of cow. When the diagnosis by time interaction was significant, means were separated by SLICE analysis.

Lactation number, BCS, RFI, previous lactation 305ME, and genetic merit data were analyzed using the MIXED procedure with linear and quadratic orthogonal contrasts when appropriate. In each model the effect of maximum BHB ($\mathbf{BHB_{max}}$) concentration out of all samples for each cow was the dependent variable and cow was designated as a random effect. The main effect of RFI experiment of origin and relative parity (parity during the transition period minus the parity when RFI was calculated) and the associated interaction was included in the model and removed if not significant. The relationship between BCS and BCS change was conducted using the MIXED procedure with linear and quadratic orthogonal contrasts with cow as a random effect. Relationships between BCS time point and changes were analyzed with PROC CORR. The effect of prior lactation RFI on HYK incidence was examined by grouping cows into quartiles based on RFI using PROC RANK. The effect of RFI quartile on BHB_{max}, BCS, and milk parameters was examined using a mixed model similar to the above model.

Table 2. Nutrient composition of corn silage and haylage based lactating cow TMR and ad libitum hay[1]

	TMR		Hay	
Component[2]	Mean	SEM	Mean	SEM
DM, % as fed	48.54	0.39	85.07	0.23
Nutrient, % DM				
CP	17.06	0.10	12.89	0.23
NDF	31.12	0.20	60.33	0.35
Lignin	3.47	0.20	7.18	0.21
ADF	22.92	0.17	46.05	0.31
AD-ICP	1.14	0.02	1.17	0.02
ND-ICP	2.77	0.06	3.30	0.09
Starch	25.76	0.19	0.72	0.05
Ether extract	4.83	0.04	1.77	0.04
Ash	7.14	0.04	7.61	0.07
Sugar[3]	3.26	0.15	4.88	0.11

[1]Ad libitum hay was offered to fresh cows housed on a bedded pack in addition to the TMR.

[2]AD-ICP = acid detergent insoluble CP; ND-ICP = neutral detergent insoluble CP.

[3]Water soluble carbohydrates.

RESULTS

Hyperketonemia Descriptive Statistics

Of the 570 cows enrolled in the study, 112 (19.7%) were diagnosed with HYK. There were 465 (81.6%) multiparous and 105 (18.4%) primiparous cows enrolled in the study. Of the multiparous cows, 103 (22.2%) were diagnosed with HYK and of the primiparous cows, 9 (8.6%) were diagnosed with HYK. The average DRTC at the first positive test was 9.06 ± 0.86 d and the average BHB concentration at the first positive test was 1.53 ± 0.14 mmol/L.

Maximum blood BHB was different ($P = 0.0003$) by lactation number and was greater ($P \leq 0.0001$) for cows in lactation 2, 3, 4, and 5 compared with cows in lactation 1 with a quadratic ($P \leq 0.0001$) pattern (Table 3). Mean BHB_{max} for all lactation groups was below the threshold for HYK diagnosis; however, incidence of HYK followed the same quadratic pattern as the BHB_{max} concentrations (Table 3). Diagnosis as HYK or nonHYK was not altered ($P > 0.1$) by milk PTA (−270 vs. −318 ± 164, nonHYK vs. HYK), fat PTA (−19 vs. −18 ± 5.8, nonHYK vs. HYK), or previous lactation 305ME (36233 vs. 36554 ± 1252, nonHYK vs. HYK).

Milk Composition and Yield

From 5 to 30 DRTC, cows diagnosed with HYK produced more milk ($P < 0.0001$) than nonHYK cows (Table 4; Figure 1). We found no diagnosis by DRTC interaction ($P = 0.9974$). Milk fat content was greater ($P = 0.0001$) and milk protein content was less ($P < 0.0001$) in cows diagnosed with HYK compared with nonHYK cows, although we observed no difference ($P > 0.1$) in milk fat or protein yield. Fat-corrected milk and ECM were greater ($P < 0.0001$) in cows diagnosed with HYK compared with nonHYK cows (Table 4). Log-transformed SCC was decreased by time ($P < 0.0001$) and was greater ($P = 0.04$) for nonHYK cows compared with HYK cows, although we noted no difference ($P > 0.1$) between weekly means.

BCS

Expectedly, single time point BCS were correlated ($P \leq 0.0001$) with each other: DBCS and LSBCS (r = 0.62), DBCS and CBCS (r = 0.65), CBCS and LSBCS (r = 0.77). Change in BCS patterns were not correlated with a single time point BCS measurement. The change in BCS over the entire period (DBCS to LSBCS) was negatively correlated with the DBCS ($P \leq 0.0001$; r = −0.52) and positively correlated the LSBCS ($P \leq 0.0001$; r = 0.35), but not correlated with the CBCS ($P = 0.18$; r = 0.06). The change in BCS from DBCS to CBCS was inversely correlated with the DBCS ($P \leq 0.0001$; r = −0.51), correlated with the CBCS ($P \leq 0.0001$; r = 0.32), and weakly correlated with the LSBCS ($P = 0.02$; r = 0.10). Between calving and the last sample, the BCS change was not related to the DBCS ($P = 0.27$; r = −0.05), but was inversely correlated with the CBCS ($P \leq 0.0001$; r = −0.35) and correlated with the LSBCS ($P \leq 0.0001$; r = 0.34). The DBCS affected ($P \leq 0.001$) the BCS change across the transition period linearly ($P \leq 0.001$), with incrementally greater BCS losses for cows with greater DBCS (DBCS 5 = −0.87 ± 0.06 BCS loss, 4 = −0.76 ± 0.06 BCS loss, 3 = −0.58 ± 0.05 BCS loss, 2 = −0.48 ± 0.05

Table 3. The effect of lactation number on maximum BHB (BHB_{max}; mmol/L) concentration for cows tested 4 times between 5 and 18 d relative to calving[1]

Item	n[2]	BHB_{max}	SEM	Minimum[3]	Maximum[4]	HYK incidence,[5] %	*P*-value[6]		
							Lact	L	Q
Lactation							0.0001	0.031	0.0001
1	105	0.60[b]	0.12	0.3	2.6	8.6			
2	192	0.80[a]	0.11	0.4	4.3	16.7			
3	144	0.85[a]	0.10	0.3	2.6	25.0			
4	63	0.98[a]	0.11	0.3	3.8	28.6			
5	34	0.94[a]	0.12	0.4	3.6	32.4			
≥6	32	0.75[ab]	0.12	0.4	2.1	18.8			

[a,b]Means without common letters differ ($P < 0.05$).

[1]Blood samples were collected twice weekly from each cow after morning milking and quantified using the Precision Xtra meter (Abbott Laboratories, Abbott Park, IL). Cows were treated upon diagnosis of hyperketonemia (HYK), defined as blood BHB ≥1.2 mmol/L.

[2]The number of animals (n) within each group.

[3]Minimum BHB_{max} within group.

[4]Maximum BHB_{max} within group.

[5]HYK incidence calculated as cows with blood BHB ≥1.2 mmol/L divided by total number of cows within the group.

[6]Significance of effects for lactation group (Lact) and linear (L) and quadratic (Q) orthogonal contrasts.

BCS loss, and 1 = −0.33 ± 0.08 BCS loss). Similarly, the DBCS affected ($P \leq 0.001$) the changes in BCS from −28 DRTC to calving linearly ($P \leq 0.001$), with a DBCS of 5 to 1 resulting in incrementally greater losses (DBCS 5: −0.55 ± 0.06 BCS loss, 4: −0.40 ± 0.05 BCS loss, 3: −0.27 ± 0.05 BCS loss, 2: −0.16 ± 0.05 BCS loss, and 1: −0.018 ± 0.07 BCS loss). The DBCS did not alter ($P = 0.38$) the change in BCS from calving to the last sample.

Out of the 3 single time point BCS measurements, BHB_{max} was only altered ($P < 0.0001$; quadratic $P = 0.0025$) by differences in DBCS (Table 5). Cows with a DBCS of ≥4.0 had greater ($P \leq 0.05$) BHB_{max} than all other BCS groups. We found an effect ($P \leq 0.0001$) of BCS change between LSBCS (+18 DRTC) and DBCS (−28 DRTC) that exhibited a linear ($P \leq 0.0001$) pattern with increasing BCS loss over the transition period, resulting in increased BHB_{max} and HYK incidence (Table 6). The effect ($P = 0.0002$) of BCS change between DBCS and calving was quadratic ($P = 0.018$) with loss of 0.5 or more BCS units resulting in the greatest BHB_{max}. Change in BCS from calving to LSBCS affected ($P = 0.03$) BHB_{max} linearly ($P = 0.0066$).

RFI

Of the 214 cows with RFI, the relative parity difference between this transition cow study and the study of RFI origin was 1 for 102 cows, 2 for 58 cows, 3 for 42 cows, 4 for 11 cows, and 5 for 1 cow. We found no effect ($P > 0.1$) of RFI experiment of origin, relative parity (between the transition cow experiment and the RFI experiment), or the interaction of BHB_{max} or RFI. When RFI was categorized into quartiles, no effect of RFI quartile on BHB_{max} was observed (Table 7). The RFI mean for quartiles 1, 2, 3, and 4 were −1.71 ± 0.088, −0.48 ± 0.039, 0.38 ± 0.038, and 1.93 ± 0.160 kg/d, respectively. Within these quartiles, the respective blood BHB means were 0.95, 0.92, 1.02, and 0.94 ± 0.087 mmol/L and were not different ($P = 0.82$). Means of BHB_{max}, milk yield, milk fat concentration, BCS,

Table 4. Weekly least squares means of milk yield and composition for cows with or without hyperketonemia (HYK or nonHYK, respectively)

	Diagnosis[1]			*P*-value[2]		
Item	nonHYK	HYK	SEM	HYK	Week	HYK × W
Yield, kg/d						
Milk	41.01	44.65	0.65	0.0001	0.0001	0.636
Week 1	36.30	40.76	1.28	0.0017		
Week 2	41.59	45.27	1.03	0.0012		
Week 3	45.14	47.90	1.03	0.0152		
FCM[3]	42.34	47.17	0.69	0.0001	0.0013	0.565
Week 1	39.70	45.63	1.38	0.0001		
Week 2	43.19	47.89	1.09	0.0001		
Week 3	44.13	48.00	1.09	0.0013		
ECM[4]	45.78	50.14	0.72	0.0001	0.0323	0.545
Week 1	43.62	49.13	1.44	0.0005		
Week 2	46.56	50.81	1.14	0.0007		
Week 3	47.18	50.47	1.14	0.0086		
Composition						
Milk fat, %	4.27	4.52	0.06	0.0001	0.0001	0.487
Week 1	4.64	5.00	0.12	0.0047		
Week 2	4.29	4.47	0.09	0.0685		
Week 3	3.90	4.08	0.09	0.0621		
Milk protein, %	3.60	3.40	0.02	0.0001	0.0001	0.202
Week 1	4.04	3.88	0.03	0.0001		
Week 2	3.54	3.30	0.03	0.0001		
Week 3	3.21	3.03	0.03	0.0001		
logSCC[5]	1.86	1.80	0.03	0.0396	0.0001	0.823
Week 1	2.10	2.01	0.05	0.1063		
Week 2	1.81	1.76	0.04	0.3358		
Week 3	1.68	1.63	0.04	0.3398		

[1]Diagnosis defined as either healthy (blood BHB <1.2 mmol/L) or HYK (blood BHB ≥1.2 mmol/L) based on blood samples collected between 5 to 18 d relative to calving and analyzed with the Precision Xtra Meter (Abbott Laboratories, Abbott Park, IL).

[2]Significance of effects for HYK, time (Week), and the interaction of HYK by week (W).

[3]4.0% fat-corrected milk calculated as defined in the NRC (2001).

[4]Energy-corrected milk calculated as defined in the NRC (2001).

[5]$\log_{10}$ of SCC in cells/mL.

Table 5. The effect of BCS at −28 d relative to calving (DRTC), at calving (+1 DRTC), and at the last sample collection (+18 DRTC) on maximum BHB (BHB_{max}; mmol/L) concentration for cows tested 4 times between 5 and 18 DRTC[1]

BCS	n[2]	BHB_{max}	SEM	Minimum[3]	Maximum[4]	HYK incidence,[5] %	*P*-value[6]		
							BCS	L	Q
−28 DRTC							0.0001	0.0002	0.0025
<3.0	28	0.86[b]	0.09	0.4	1.7	21.4			
3.25	129	0.83[b]	0.04	0.4	2.2	12.4			
3.5	297	0.84[b]	0.03	0.3	3.8	17.8			
3.75	81	0.96[b]	0.05	0.3	3.6	22.2			
≥4.0	35	1.28[a]	0.08	0.3	4.3	45.7			
+1 DRTC							0.494	0.909	0.812
<3.0	49	0.91	0.08	0.4	2.1	26.5			
3.25	227	0.86	0.03	0.4	3.8	16.7			
3.5	269	0.89	0.03	0.3	4.3	20.1			
3.75	23	1.05	0.10	0.4	2.6	30.4			
≥4.0	2	0.85	0.36	0.8	0.9	0.0			
+18 DRTC							0.785	0.458	0.780
<3.0	121	0.92	0.05	0.4	3.3	24.8			
3.25	333	0.88	0.03	0.3	3.8	18.9			
3.5	110	0.87	0.05	0.3	4.3	16.4			
3.75	6	0.77	0.20	0.4	1.4	16.6			
≥4.0	0								

[a,b]Means without common letters differ ($P < 0.05$).

[1]Blood samples were collected twice weekly from each cow after morning milking and quantified using the Precision Xtra meter (Abbott Laboratories, Abbott Park, IL). Cows were treated upon diagnosis of hyperketonemia (HYK), defined as blood BHB ≥1.2 mmol/L.

[2]The number of animals (n) within each group.

[3]Minimum BHB_{max} within group.

[4]Maximum BHB_{max} within group.

[5]HYK incidence calculated as cows with blood BHB ≥1.2 mmol/L divided by total number of cows within the group.

[6]Significance of effects for BCS category (BCS) and linear (L) and quadratic (Q) orthogonal contrasts.

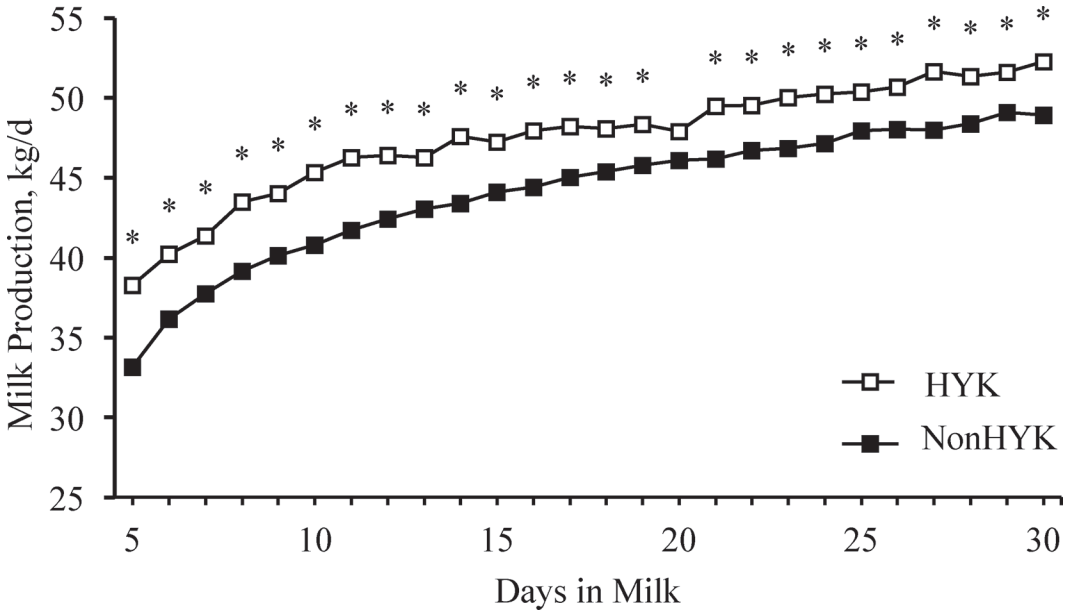

Figure 1. Daily least squares means of milk production (kg/d) from 5 to 30 d relative to calving for cows diagnosed as not hyperketonemic (nonHYK, blood BHB <1.2 mmol/L) or hyperketonemic (HYK, blood BHB ≥1.2 mmol/L) based on blood samples collected between 5 and 18 d relative to calving and analyzed with the Precision Xtra meter (Abbott Laboratories, Abbott Park, IL). An asterisk (*) indicates means differ $P \leq 0.05$.

Table 6. The effect of the change in BCS between 3 time points, −28 d relative to calving (DRTC), calving (+1 DRTC), and at the last sample collection (+18 DRTC), on maximum BHB (BHB_{max}; mmol/L) concentration for cows tested 4 times between 5 and 18 DRTC[1]

BCS change	n[2]	BHB_{max}	SEM	Minimum[3]	Maximum[4]	HYK incidence,[5] %	*P*-value[6]		
							BCS	L	Q
−28 to +18 DRTC							0.0001	0.0001	0.104
≥1.0	19	1.34[a]	0.11	0.5	3.3	52.6			
−0.75	29	1.07[ab]	0.09	0.3	3.6	34.5			
−0.5	148	0.96[b]	0.04	0.3	4.3	25.7			
−0.25	246	0.86[bc]	0.03	0.3	2.6	17.5			
0	97	0.73[c]	0.05	0.4	1.9	6.2			
≥0.25	14	0.76[bc]	0.13	0.4	1.1	0.0			
−28 to +1 DRTC							0.0002	0.001	0.018
≥−0.5	58	1.12[a]	0.07	0.3	3.6	37.9			
−0.25	190	0.92[b]	0.04	0.3	4.3	22.6			
0	232	0.81[c]	0.03	0.3	2.8	13.4			
≥0.25	67	0.86[bc]	0.06	0.4	2.6	14.9			
+1 to +18 DRTC							0.0307	0.0066	0.944
≥−0.5	40	1.04[a]	0.08	0.4	3.3	30.0			
−0.25	255	0.92[ab]	0.03	0.3	4.3	20.8			
0	235	0.85[bc]	0.03	0.3	2.6	18.7			
>0.25	34	0.74[c]	0.09	0.4	1.9	5.9			

[a–c]Means without common letters differ ($P < 0.05$).

[1]Blood samples were collected twice weekly from each cow after morning milking and quantified using the Precision Xtra meter (Abbott Laboratories, Abbott Park, IL). Cows were treated upon diagnosis of hyperketonemia (HYK), defined as blood BHB ≥1.2 mmol/L.

[2]The number of animals (n) within each group.

[3]Minimum BHB_{max} within group.

[4]Maximum BHB_{max} within group.

[5]HYK incidence calculated as cows with blood BHB ≥1.2 mmol/L divided by total number of cows within the group.

[6]Significance of effects for BCS change (BCS) and linear (L) and quadratic (Q) orthogonal contrasts.

and BCS change by RFI quartiles are provided in Table 7. Milk yield during the transition experiment lactation was greater ($P = 0.003$) for cows within the first, third, and fourth RFI quartiles in a quadratic pattern ($P = 0.01$). A similar quadratic pattern ($P = 0.006$) in milk yield was observed in milk production data collected during the studies in which RFI was measured, with milk volume yield being the greatest for the first RFI quartile compared with the second quartile, but not different than the third or fourth quartile (46.8, 42.8, 43.5,

Table 7. The effect of residual feed intake (RFI[1]; kg/d) quartile during prior lactations on maximum BHB (BHB_{max}; mmol/L) concentration for cows tested 4 times between 5 and 18 d relative to calving (DRTC)[2]

Variable	Quartile[3]				SEM	*P*-value[4]		
	1	2	3	4		RFI	L	Q
BHB_{max}	0.95	0.92	1.02	0.94	0.09	0.82	0.94	0.98
Milk yield, kg/d	51.3[a]	46.9[b]	50.7[a]	51.5[a]	1.10	0.003	0.33	0.01
Milk fat, %	4.06	4.30	4.22	4.21	0.11	0.49	0.46	0.26
BCS								
−28 DRTC	3.53	3.38	3.45	3.43	0.05	0.06	0.15	0.13
+1 DRTC	3.24	3.12	3.15	3.11	0.08	0.06	0.03	0.23
+18 DRTC	2.98	2.94	2.89	2.87	0.08	0.10	0.01	0.80
BCS change								
−28 to +18 DRTC[5]	−0.43	−0.32	−0.44	−0.43	0.04	0.04	0.44	0.10
−28 to +1 DRTC	−0.21	−0.16	−0.22	−0.23	0.03	0.52	0.44	0.48
+1 to +18 DRTC	−0.22	−0.15	−0.22	−0.21	0.02	0.09	0.85	0.19

[1]RFI recorded for 56 d between 50 and 200 DRTC of a prior lactation.

[2]Blood samples were collected twice weekly from each cow after morning milking and quantified using the Precision Xtra meter (Abbott Laboratories, Abbott Park, IL). Cows were treated upon diagnosis of hyperketonemia (HYK), defined as blood BHB ≥1.2 mmol/L.

[3]Quartile of RFI (n; mean; minimum, maximum): 1 (53; −1.71; −4.12, −0.98); 2 (54; −0.48, −0.97, −0.05); 3 (54; 0.38; −0.04, 0.89); 4 (53; 1.93; 0.91, 7.04).

[4]Significance of effects of RFI quartile and linear (L) and quadratic (Q) orthogonal contrasts.

[5]Means could not be separated by Tukey's studentized adjustment.

45.6 ± 1.1 kg/d, respectively) during the mid-lactation periods examined.

At calving and at LSBCS, BCS decreased linearly ($P = 0.03$ and 0.01) as RFI quartile increased (Table 7). Body condition score at −28 DRTC tended to be different ($P = 0.06$) by RFI but lacked a statistical pattern. Change in BCS from −28 to +18 DRTC differed ($P = 0.04$) by RFI quartile and tended ($P = 0.10$) to follow a quadratic pattern, with cows in quartiles 1, 3, and 4 losing the greatest body condition. The loss in body condition from calving to +18 DRTC tended ($P = 0.09$) to be different by RFI quartile; however, we found no effect of RFI on the BCS change from −28 DRTC to calving.

DISCUSSION

Hyperketonemia

Incidence of HYK in this study was 19.7%, which is lower than previously reported subclinical ketosis (**SCK**) incidences of 40 to 60% (Emery et al., 1964; Simensen et al.; 1990, McArt et al., 2011), which could be a product of the precision management and nutrition of the research farm or the reduced frequency of sampling in the current study compared with previous (McArt et al., 2012). However, cows in the current study were monitored from 1 to 10 DRTC by the farm staff during daily fresh cow health checks, which likely reduced missed HYK cases. Furthermore, the average BHB concentration at the first positive test was low (1.53 mmol/L), which would support that cases were detected quickly before progression. Given that cows were treated upon diagnosis, our study was not designed to examine severity of HYK; rather, BHB_{max} severed as a quantitative indicator of phenotype for each cow. Mean BHB_{max} for all lactation groups was below the threshold for HYK, but the incidence of HYK within 1st, 2nd, 3rd, 4th, and 5th lactation animals was 9, 17, 25, 29, and 32.4% respectively, which is consistent with previous literature supporting increased HYK incidence as cow parity increases (Andersson and Emanuelson, 1985; Duffield et al., 1997; Vanholder et al., 2015). The quadratic response resulting in lower BHB_{max} in 6th and greater lactation animals likely represents selection bias that has resulted in culling of cows that consistently have transition cow metabolic disorders.

Milk Composition and Yield

Greater milk yield was observed in the first 30 d of lactation for cows diagnosed with HYK compared with nonHYK cows. A recent study in the Netherlands found that cows diagnosed with HYK at a single time point during the second week of calving produced more milk at the first test day than nonHYK cows (Vanholder et al., 2015). Greater milk production in cows that develop HYK may be due to increased risk for HYK onset in cows with greater genetic merit for milk yield; however, in the present study, neither the previous lactation milk production nor the genetic merit for milk volume or fat yield influenced HYK onset. The greater milk yield seen in cows diagnosed with HYK compared with nonHYK cows beginning at 5 DRTC, combined with the later average d of HYK onset (9 DRTC), may suggest that higher-producing cows became hyperketonemic due to the high energy demand for milk production during the current lactation.

If left untreated, onset of HYK in the first or second weeks of lactation can negatively affect milk yield (Duffield et al., 1997, 2009; McArt et al., 2012). We may not have observed a reduction in milk yield after HYK onset due to the low BHB concentration at the first positive test in our study and the immediate treatment after diagnosis, which has been shown to ameliorate the reductions in milk yield compared with cows that are not treated after diagnosis (McArt et al., 2011). Greater milk fat and lower milk protein percentages in cows diagnosed with HYK in the present experiment are consistent with previously published literature (Duffield et al., 2009; Vanholder et al., 2015). Both ECM and FCM were increased in cows diagnosed with HYK, which is a function of the observed increase in both milk yield and milk fat content.

Log-transformed SCC was greater in nonHYK cows compared with cows diagnosed with HYK. These results are inconsistent with previously reported literature. In a large study in the Netherlands, no relationship between HYK and SCC was found (Vanholder et al., 2015). Additionally, a recent meta-analysis reported that cows diagnosed with SCK were more likely to get clinical mastitis and more likely to have a high SCC, but these results must be interpreted cautiously due to the small number of studies that reported SCC data along with SCK incidence (Raboisson et al., 2014). Although we did detect a significant difference in the logSCC average across all 3 wk between nonHYK and HYK cows, it may be difficult to draw conclusions from these results because the difference was small (1.86 and 1.80, respectively) and was not seen when comparing groups of cows within individual weeks.

BCS

Although BCS is a subjective measure, monitoring BCS and BCS change across the transition to lactation is common practice on dairy farms and serves as an indicator of body fat stores and mobilization. Within the

current study, dry cows with a BCS of 4.0 or greater had greater BHB_{max} concentrations than dry cows with lower BCS. Similarly, previous research has noted a 1.6 times greater risk of HYK onset in cows with a precalving BCS of 4 or greater (Duffield et al., 1998). Other studies have reported that HYK risk increased at a precalving BCS of 3 (Bernabucci et al., 2005) or 3.25 (Vanholder et al., 2015). Increased risk for HYK was also reported in Norwegian dual-purpose breed dairy cows that had a BCS of 3.5 or greater at calving (Gillund et al., 2001); however, no effect of BCS at calving was observed in the current study.

Perhaps more important to metabolic health is BCS change throughout the transition period, because it indicates the degree of body fat mobilization by the cow (Wright and Russel, 1984; Otto et al., 1991; Overton and Waldron, 2004). In the current transition cow study, cows that lost 1 BCS unit or more through the transition period had greater BHB_{max} concentrations. Furthermore, BHB_{max} was linearly decreased as BCS loss decreased. Similarly, a loss of one BCS unit has been reported to double HYK risk (Duffield et al., 1998), and any BCS loss precalving was demonstrated to increase fatty acids and BHB postcalving compared with animals that maintained BCS (Sheehy et al., 2017). Together, these data support the importance of guarding against BCS loss across the transition period and to avoid excessive precalving body condition. Improving management of dry cow BCS, and minimizing BCS loss during the transition period, could reduce HYK incidence in dairy cattle.

RFI

Given that mobilization of body stores contributes to energy pools postpartum, both changes in BCS and DMI can influence RFI. Although metabolic BW and BW change are accounted for during the RFI calculations, most experiments examining feed efficiency are conducted during a state of minimal BW change (Tempelman et al., 2015). By accounting for BW change during RFI measurements, the goal is to keep feed efficiency phenotypically independent of body tissue mobilization during that period (Tempelman et al., 2015). Although this is effective during the measurement period, it is currently unknown if feed efficiency influences mobilization of body stores during negative energy balance, such as during the transition to lactation, and if this would extrapolate to differences in metabolic health. If selection of dairy cows based on RFI is employed, influences on subsequent lactation body tissue mobilization and metabolic health could be phenotypically dependent on RFI.

One of the objectives of the current experiment was to determine if there was an effect of feed efficiency in prior lactations on body tissue mobilization and metabolic health in subsequent lactations. In beef animals, both growing heifers (Kelly et al., 2010b) and postpartum cows (Lawrence et al., 2011) with low RFI had higher fatty acid concentrations, though the opposite was observed for BHB in beef heifers (Kelly et al., 2010a). Some studies have shown that beef cattle with lower RFI had lower amounts of carcass fat, which may indicate that RFI is related to lipid metabolism (Herd et al., 2003; Nkrumah et al., 2007). The more severe NEB experienced by dairy cattle postpartum further emphasizes the need to understand the relationship between RFI and metabolic disorders. In this study, we observed no effect of prior lactation phenotypic RFI on BHB_{max}. This lack of relationship could indicate that selection of animals based on RFI will not influence onset of HYK in subsequent lactations. Given that the between lactation repeatability of RFI is not as great as the within-lactation repeatability (Connor et al., 2013; Tempelman et al., 2015), it could also mean that RFI during mid lactation is not a good indicator of subsequent lactation metabolic health, even if a relationship between feed efficiency and metabolic health exists. If this is the case, determining the influence of RFI on metabolic health will be difficult considering the challenges of determining RFI during NEB. It is also possible that we may have lacked power to overcome animal variability and detect effects of RFI on subsequent lactation HYK with the limited number of animals on the study that had phenotypic RFI values.

Within our study, prior lactation RFI was associated with differences in BCS and BCS change; however, these differences were within a tight range of both BCS and BCS change, which were well within what is expected during the transition to lactation period. Although BCS is not an indicator of BW, relative BCS change and BW change during NEB can both suggest body stores mobilizations. The BCS differences between RFI quartiles may indicate that although RFI is phenotypically independent from BW change during the RFI measurement period; that independence may not be maintained in subsequent lactations, specifically during the transition to lactation period. Although BCS at −28 d was greater (3.5) within the lowest RFI quartile, it was not at or above the 4 BCS cutoff that increased risk of HYK, which supports the lack of association between RFI and subsequent BHB concentrations. Given the early onset of HYK postpartum, it is more likely that the onset of HYK may influence RFI during that lactation, instead of the reverse; however, we were not able to quantify RFI later in the transition cow study

lactation. Further research examining the relationship between HYK and RFI, specifically in the transition and early lactation periods of the same lactation, are still needed; however, at this point it does not appear that selecting for improved feed efficiency will increase incidence of HYK in subsequent lactations.

CONCLUSIONS

Within the current research, HYK incidence was lower than previously reported; however, this is likely a reflection of the intense management of transition cows at the research facility. Cows diagnosed with HYK had greater milk production than nonHYK cows, which may support increased risk for HYK in higher-producing cows. Animals with a BCS of 4 or greater before calving, or those that lost more body condition over the transition period, were more likely to develop HYK, emphasizing the importance of avoiding over-conditioning of cows in the dry period and excessive BCS loss throughout the transition period. The lack of relationship between RFI and HYK supports the selection for feed efficient cattle without the increased risk of HYK onset in subsequent lactations.

ACKNOWLEDGMENTS

This work was conducted with the support of the Cooperative Research Program for Agriculture Science and Technology Development (Project No. PJ012078) Rural Development Administration, Jeonju-si, Jeollabuk-do, Republic of Korea; USDA Hatch grant number MSN180013 from the Wisconsin Agricultural Experiment Station (Madison); and graduate student funding from Vita Plus Corporation (Madison, WI). Residual feed intake data was supported by the National Institute of Food and Agriculture, USDA (Washington, DC), under award number 2011-68004-30340, sub-award RC100236UW. Appreciation is extended to Sandy Trower and the staff at the University of Wisconsin-Madison Blaine Dairy Cattle Center for animal care and trial management.

REFERENCES

Andersson, L., and U. Emanuelson. 1985. An epidemiological study of hyperketonaemia in Swedish dairy cows; Determinants and the relation to fertility. Prev. Vet. Med. 3:449–462.

Baird, G. D., M. A. Lomax, H. W. Symonds, and S. R. Shaw. 1980. Net hepatic and splanchnic metabolism of lactate, pyruvate and propionate in dairy cows in vivo in relation to lactation and nutrient supply. Biochem. J. 186:47–57.

Bernabucci, U., B. Ronchi, N. Lacetera, and A. Nardone. 2005. Influence of body condition score on relationships between metabolic status and oxidative stress in periparturient dairy cows. J. Dairy Sci. 88:2017–2026.

Connor, E. E., J. L. Hutchison, H. D. Norman, K. M. Olson, C. P. Van Tassell, J. M. Leith, and R. L. Baldwin. 2013. Use of residual feed intake in Holsteins during early lactation shows potential to improve feed efficiency through genetic selection. J. Anim. Sci. 91:3978–3988.

DeLorenzo, M. A., and G. R. Wiggans. 1986. Factors for estimating daily yield of milk, fat, and protein from a single milking for herds milked twice a day. J. Dairy Sci. 69:2386–2394.

Drackley, J. K. 1999. Biology of dairy cows during the transition period: The final frontier? J. Dairy Sci. 82:2259–2273.

Duffield, T. 2000. Subclinical ketosis in lactating dairy cattle. Vet. Clin. North Am. Food Anim. Pract. 16:231.

Duffield, T. F., D. F. Kelton, K. E. Leslie, K. D. Lissemore, and J. H. Lumsden. 1997. Use of test day milk fat and milk protein to detect subclinical ketosis in dairy cattle in Ontario. Can. Vet. J. 38:713–718.

Duffield, T. F., K. D. Lissemore, B. W. McBride, and K. E. Leslie. 2009. Impact of kyperketonemia in early lactation dairy cows on health and production. J. Dairy Sci. 92:571–580.

Duffield, T. F., D. Sandals, K. E. Leslie, K. Lissemore, B. W. McBride, J. H. Lumsden, P. Dick, and R. Bagg. 1998. Efficacy of monensin for the prevention of subclinical ketosis in lactating dairy cows. J. Dairy Sci. 81:2866–2873.

Emery, R. S., N. Burg, L. D. Brown, and G. N. Blank. 1964. Detection, occurrence, and prophylactic treatment of borderline ketosis with propylene glycol feeding. J. Dairy Sci. 47:1074–1079.

Ferguson, J. D., D. T. Galligan, and N. Thomsen. 1994. Principal descriptor of body condition score in Holstein cows. J. Dairy Sci. 77:2695–2703.

Gillund, P., O. Reksen, Y. T. Grohn, and K. Karlberg. 2001. Body condition related to ketosis and reproductive performance in Norwegian dairy cows. J. Dairy Sci. 84:1390–1396.

Green, T. C., J. G. Jago, K. A. Macdonald, and G. C. Waghorn. 2013. Relationships between residual feed intake, average daily gain, and feeding behavior in growing dairy heifers. J. Dairy Sci. 96:3098–3107.

Grummer, R. R. 1993. Etiology of lipid-related metabolic disorders in periparturient dairy-cows. J. Dairy Sci. 76:3882–3896.

Hardie, L. C., L. E. Armentano, R. D. Shaver, M. J. VandeHaar, D. M. Spurlock, C. Yao, S. J. Bertics, F. E. Contreras-Govea, and K. A. Weigel. 2015. Considerations when combining data from multiple nutrition experiments to estimate genetic parameters for feed efficiency. J. Dairy Sci. 98:2727–2737.

Herd, R.M., J.A. Archer, and P.F. Arthur. 2003.Reducing the cost of beef production through genetic improvement in residual feed intake: Opportunity and challenges to application. J. Anim. Sci. 81(E. Suppl. 1):9–17.

Herd, R. M., and P. F. Arthur. 2009. Physiological basis for residual feed intake. J. Anim. Sci. 87(E. Suppl.):64–71.

Herdt, T. H. 2000. Ruminant adaptation to negative energy balance—Influences on the etiology of ketosis and fatty liver. Vet. Clin. North Am. Food Anim. Pract. 16:215.

Iwersen, M., U. Falkenberg, R. Voigtsberger, D. Forderung, and W. Heuwieser. 2009. Evaluation of an electronic cowside test to detect subclinical ketosis in dairy cows. J. Dairy Sci. 92:2618–2624.

Kelly, A. K., M. McGee, D. H. Crews, A. G. Fahey, A. R. Wylie, and D. A. Kenny. 2010a. Effect of divergence in residual feed intake on feeding behavior, blood metabolic variables, and body composition traits in growing beef heifers. J. Anim. Sci. 88:109–123.

Kelly, A. K., M. McGee, D. H. Crews, T. Sweeney, T. M. Boland, and D. A. Kenny. 2010b. Repeatability of feed efficiency, carcass ultrasound, feeding behavior, and blood metabolic variables in finishing heifers divergently selected for residual feed intake. J. Anim. Sci. 88:3214–3225.

Lawrence, P., D. A. Kenny, B. Earley, D. H. Crews, and M. McGee. 2011. Grass silage intake, rumen and blood variables, ultrasonic and body measurements, feeding behavior, and activity in pregnant beef heifers differing in phenotypic residual feed intake. J. Anim. Sci. 89:3248–3261.

Macdonald, K. A., J. E. Pryce, R. J. Spelman, S. R. Davis, W. J. Wales, G. C. Waghorn, Y. J. Williams, L. C. Marett, and B. J.

Hayes. 2014. Holstein-Friesian calves selected for divergence in residual feed intake during growth exhibited significant but reduced residual feed intake divergence in their first lactation. J. Dairy Sci. 97:1427–1435.

McArt, J. A. A., D. V. Nydam, and G. R. Oetzel. 2012. Epidemiology of subclinical ketosis in early lactation dairy cattle. J. Dairy Sci. 95:5056–5066.

McArt, J. A. A., D. V. Nydam, P. A. Ospina, and G. R. Oetzel. 2011. A field trial on the effect of propylene glycol on milk yield and resolution of ketosis in fresh cows diagnosed with subclinical ketosis. J. Dairy Sci. 94:6011–6020.

McArt, J. A. A., D. V. Nydam, and M. W. Overton. 2015. Hyperketonemia in early lactation dairy cattle: A deterministic estimate of component and total cost per case. J. Dairy Sci. 98:2043–2054.

Nkrumah, J. D., D. H. Keisler, D. H. Crews, J. A. Basarab, Z. Wang, C. Li, M. A. Price, E. K. Okine, and S. S. Moore. 2007. Genetic and phenotypic relationships of serum leptin concentration with performance, efficiency of gain, and carcass merit of feedlot cattle. J. Anim. Sci. 85:2147–2155.

NRC. 2001. Nutrient Requirements of Dairy Cattle. 7th rev. ed. Natl. Acad. Sci., Washington, DC.

Otto, K. L., J. D. Ferguson, D. G. Fox, and C. J. Sniffen. 1991. Relationship between body condition score and composition of ninth to eleventh rib tissue in Holstein dairy cows. J. Dairy Sci. 74:852–859.

Overton, T. R., and M. R. Waldron. 2004. Nutritional management of transition dairy cows: Strategies to optimize metabolic health. J. Dairy Sci. 87(Suppl):E105–E119.

Potts, S. B., J. P. Boerman, A. L. Lock, M. S. Allen, and M. J. VandeHaar. 2015. Residual feed intake is repeatable for lactating Holstein dairy cows fed high and low starch diets. J. Dairy Sci. 98:4735–4747.

Raboisson, D., M. Mounie, and E. Maigne. 2014. Diseases, reproductive performance, and changes in milk production associated with subclinical ketosis in dairy cows: A meta-analysis and review. J. Dairy Sci. 97:7547–7563.

Sheehy, M. R., A. G. Fahey, S. P. M. Aungier, F. Carter, M. A. Crowe, and F. J. Mulligan. 2017. A comparison of serum metabolic and production profiles of dairy cows that maintained or lost body condition 15 days before calving. J. Dairy Sci. 100:536–547.

Simensen, E., K. Halse, P. Gillund, and B. Lutnaes. 1990. Ketosis treatment and milk-yield in dairy-cows related to milk acetoacetate levels. Acta Vet. Scand. 31:433–440.

Tempelman, R. J., D. M. Spurlock, M. Coffey, R. F. Veerkamp, L. E. Armentano, K. A. Weigel, Y. de Haas, C. R. Staples, E. E. Connor, Y. Lu, and M. J. VandeHaar. 2015. Heterogeneity in genetic and nongenetic variation and energy sink relationships for residual feed intake across research stations and countries. J. Dairy Sci. 98:2013–2026.

Vanholder, T., J. Papen, R. Bemers, G. Vertenten, and A. C. B. Berge. 2015. Risk factors for subclinical and clinical ketosis and association with production parameters in dairy cows in the Netherlands. J. Dairy Sci. 98:880–888.

Weld, K. A., and L. E. Armentano. 2016. Milk fat secretion in lactating dairy cattle is influenced by soybean particle size and fatty acid profile. J. Dairy Sci. 99(E. Suppl. 1):337.

Wildman, E. E., G. M. Jones, P. E. Wagner, R. L. Boman, H. F. Troutt Jr., and T. N. Lesch. 1982. A dairy cow body condition scoring system and its relationship to selected production characteristics. J. Dairy Sci. 65:495–501.

Wright, I. A., and A. J. F. Russel. 1984. Partition of fat, body-composition and body condition score in mature cows. Anim. Prod. 38:23–32.