Effect of dry period dietary energy level in dairy cattle on volume, concentration of immunoglobulin G, insulin, and fatty acid composition of colostrum

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ABSTRACT

The objective was to investigate the effect of different dry cow feeding strategies on the volume, concentration of IgG and insulin, as well as fatty acid composition of colostrum. Our hypothesis was that different dry period diets formulated to resemble current feeding practices on commercial dairy farms and differing in plane of energy would have an effect on IgG and insulin concentration, as well as composition of fatty acid of colostrum. Animals ($n = 84$) entering parity 2 or greater were dried off 57 d before expected parturition and fed either a diet formulated to meet, but not greatly exceed energy requirements throughout the dry period (CON), or a higher energy density diet, supplying approximately 150% of energy requirements (HI). A third group received the same diet as group CON from dry-off until 29 d before expected parturition. After this time point, from 28 d before expected parturition until calving, they received a diet formulated to supply approximately 125% of energy requirements (I-med). Concentration of IgG and insulin in colostrum were measured by radial immunodiffusion and RIA, respectively. Composition of fatty acids was determined by gas-liquid chromatography. The IgG concentration was highest in colostrum of cows in group CON [96.1 (95% CI: 83.3–108.9) g/L] and lowest in group HI [72.4 (60.3–84.5) g/L], whereas insulin concentration was highest in group HI [1,105 (960–1,250) μ U/mL] and lowest in group CON [853 (700–1,007) μ U/mL]. Colostrum yield did not differ between treatments and was 5.9 (4.5–7.4), 7.0 (5.6–8.4), and 7.3 (5.9–8.7) kg in groups CON, I-med, and HI, respectively. A multivariable linear regression model showed the effect of dietary treatment group on IgG concentration was independent

of the effect of dry matter. Cows in groups CON, I-med, and HI had an average colostrum fat percentage of 5.0 (4.1–5.9), 5.6 (4.8–6.4), and 6.0 (5.2–6.8) and an average fat yield of 289 (196–380), 406 (318–495), and 384 (295–473) g, respectively. Colostrum of cows fed to exceed predicted energy requirements during the last 4 wk of the dry period (groups I-med and HI) exhibited a higher concentration and yield of de novo fatty acid and lower concentrations but similar yield of preformed fatty acid compared with cows in group CON. Feeding a controlled energy diet during the dry period increased colostrum IgG concentration in this study, whereas overall colostrum yield was not affected. Exceeding energy requirements during the period of colostrogenesis led to higher concentrations of insulin and de novo fatty acid in colostrum.

Key words: dairy, colostrum, energy, insulin, fatty acid

INTRODUCTION

Quigley and Drewry (1998) stated that “the relationship between the prepartum diet and the acquisition of passive immunity merits further investigation.” Although research efforts have led to a substantial increase in knowledge on transition dairy cow management in the last decades, these studies have largely focused on health and productivity of the dam in relation to metabolic disorders. Studies on the effect of nutrition during late pregnancy in cattle on colostrum quality have concentrated primarily on feed restriction in beef cattle. These studies targeted either severe protein restriction (Blecha et al., 1981), or a combination of both protein and energy (Olson et al., 1981; Hough et al., 1990) fed below requirements. The results of such studies are poorly applicable to dairy cows because dairy rations are generally designed to provide adequate amounts of nutrients in the prepartum TMR and dairy cows face different metabolic challenges in the peripartum period.

Received June 8, 2015.

Accepted October 25, 2015.

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Colostrum in dairy cattle has largely been regarded as a means of transferring passive immunity to the agammaglobulinemic newborn calf, as well as an excellent source of nutrients (Quigley and Drewry, 1998; Hammon et al., 2013). The fat component of colostrum plays an essential role in providing energy because energy reserves of the newborn are sparse and fat consumption increases the ability to thermoregulate (Quigley et al., 1994; Morrill et al., 2012). Besides these obvious functions, colostrum has a role in maturation of the neonatal gastrointestinal tract through provision of hormones and growth factors such as insulin (Shehadeh et al., 2006; Hammon et al., 2013). Previous studies have shown the systemic uptake of very high doses of insulin after oral administration exists in calves and rodents (Mosinger et al., 1959; Pierce et al., 1964; Shehadeh et al., 2003). On the other hand, Gruetter and Blum (1991), using radio-immunologically labeled insulin, were unable to confirm this finding at lower doses. Irrespective of a possible systemic uptake, insulin from colostrum likely plays a role as one of the components responsible for the improved oral glucose absorption in colostrum-fed calves compared with those fed milk-based formula (Steinhoff-Wagner et al., 2011).

Because of the known detrimental effects of overfeeding during the dry period on peripartum metabolism (Dann et al., 2006; Janovick et al., 2011), it is of particular interest to study the effect of different dietary energy strategies on colostrum. Circulating glucose concentrations in cows overfed energy prepartum are higher than those of cows being fed a controlled or restricted energy diet (Janovick et al., 2011; Schoenberg and Overton, 2011). In humans, research has shown that colostrum of hyperglycemic mothers had lower levels of both IgA and IgG (França et al., 2012). Other studies in human medicine have also found a relation between maternal metabolic status and both hormone (Ley et al., 2012) as well as immunoglobulin concentration of colostrum (Morceli et al., 2011; França et al., 2012). Although placentation type and therefore transfer of IgG to the human fetus are different from the bovine species, these studies provide insight in possible influences of glucose metabolism on colostrum composition in mammalian species. Dietary energy level in the dry period has been shown to affect the metabolic status of dairy cows and alter blood glucose and insulin concentrations (Rukkwamsuk et al., 1999; Janovick et al., 2011). Our hypothesis was that metabolic changes in the prepartum period could lead to similar effects in the bovine species. The objective of this study was therefore to investigate the effect of common dry period feeding strategies on colostral IgG concentration, as well as on colostrum volume, insulin concentration, and fatty acid composition of colostrum.

MATERIALS AND METHODS

Animals, Feeding, and Management

All procedures were evaluated and approved by the Cornell University Institutional Animal Care and Use Committee (protocol no. 2011-0016). A detailed account of study animals, feeding management, and diet composition was published previously (Mann et al., 2015). Briefly, Holstein cows ($n = 84$) housed at the Cornell Teaching and Research Center entering their second or greater lactation were included in the study and enrolled between September 2012 and April 2013. All animals were housed in individual sawdust-bedded stalls equipped with feed bins. Cows were allocated to 1 of 3 dry period dietary treatment groups following a randomized block design on the day of dry off (approximately 57 d before expected parturition). Cows were blocked by expected day of calving. The treatment groups were as follows: those that were fed a TMR formulated to meet but not greatly exceed energy requirements at predicted ad libitum intake (**CON**); those that received a TMR formulated to supply 150% of energy requirements (**HI**); and an intermediate group receiving the same TMR as group CON for the first 28 d after dry off, and a TMR formulated to supply 125% of energy requirements from d 28 before expected calving until parturition (**I-med**). For all dry cow rations, predicted MP was formulated to be 1,280 g/d. Cows were fed once daily at 0900 h and adjusted to allow for a minimum of 5% refusals. All animals received the same fresh cow ration after calving. In brief, diets were formulated using the Cornell Net Carbohydrate and Protein System software (**CNCPS**, Cornell University, version 6.1). Monthly composites of all TMR as well as one composite sample of all forages were sent to Dairy One (Ithaca, NY) for wet chemistry analysis. Energy density of the diets was determined by entering forage analysis results and grain composition into CNCPS. Energy balance was estimated in CNCPS for each week and individual by entering into the software the weekly average of the animal's BW, DMI, and days carried calf.

Individual Animal Sampling

Cows calved in sawdust-bedded individual box stalls under the supervision of farm personnel. Calving ease was recorded on a scale from 1 to 5 (1 = normal/no assistance, 2 = moderate assistance, provided by farm staff, 3 = moderate assistance, but veterinarian assisted as a precaution, 4 = difficult calving, with assisted extraction, 5 = very difficult calving, with maximum veterinary assistance) by trained personnel. Calf birth

weight (platform scale, Salter Scales, Fairfield, NJ) was determined before colostrum feeding. Calves were removed from their dams within 30 min after birth and not allowed to suckle their dams. Cows were milked within 60 min after calving with a bucket milker and colostrum weight was determined on a commercial scale (model 4010, Pelouze Scale Co, Bridgeview, IL). The composite sample was mixed before, and aliquots either refrigerated at 4°C for IgG analysis, or frozen at -20°C for further analysis of insulin, fatty acid, fat %, and DM.

Blood samples were obtained 3 times weekly starting 21 d before expected parturition as described in detail in Mann et al. (2015). In brief, blood samples (10 mL) were taken before feeding (between 0600 and 0730 h) from the coccygeal vein or artery, placed on ice, separated within 1 h by centrifugation at $2,800 \times g$ for 20 min at 4°C, snap-frozen in liquid N₂, and stored at -20°C. All samples were frozen in 4 aliquots to prevent multiple freeze-thaw cycles.

Sample Analysis

The refrigerated colostrum sample was submitted within 48 h to the New York State Animal Health Diagnostic Center at Cornell University. The IgG concentration was measured via radial immunodiffusion (RID) according to standard procedures. In brief, colostrum samples were diluted with saline and set up on bovine IgG Veterinary Medical Research and Development (Pullman, WA) plates. Serial dilutions of 1:2, 1:4, 1:8, and 1:16 were made for every colostrum sample. Bovine IgG standards were used according to the manufacturer's instructions and ranged from 400 to 3,200 mg/dL. Values of the sample's ring diameter were read off the standard curve, giving a milligrams per deciliter value of IgG. The second aliquot was frozen at -20°C for later analysis. For colostrum insulin determination, frozen colostrum samples were thawed and centrifuged ($2,400 \times g$ for 20 min at room temperature) and the fat layer was removed to prepare skim milk as described by Ley et al. (2012). Insulin was measured by RIA (PI-12K Porcine Insulin RIA, EMD Millipore Corp., Billerica, MA) used for diagnostic testing and validated for bovine serological sample analysis by the Animal Health Diagnostic Center Endocrinology Laboratory. The procedure was performed according to the manufacturer instructions with the standard curve range of 3.13 to 200 µU/mL. Samples were diluted 1:40 to fall within an insulin concentration that corresponded to approximately 50% of total binding (range: 37.5–71.6). Linearity of serial dilution of 5 samples was tested and found to have an R² of 0.95 in the range of 20 to 170 µU/mL. For intraassay precision, the CV calculations

were based on 3 separate pools of colostrum tested 12 times within the assay. The % CV for the 3 samples with mean values of 19.4, 67.3, and 108.1 µU/mL was 8.1, 3.4, and 7.2%, respectively.

Plasma concentration of insulin 1, 2, or 3 d before parturition was available for a subset of 56 animals using the same RIA kit as was used for colostrum samples. The intra- and interassay CV for determination of insulin concentration in plasma was 6.9 and 5.7%, respectively.

One aliquot of the stored colostrum was split for fat % and DM measurements. Total fat concentration was determined at Dairy One (Dairy One Cooperative Inc., Ithaca, NY) by ether extraction (method 989.05, AOAC International, 1995). One more aliquot was analyzed for fatty acid composition as previously described (Lock et al., 2013). In brief, following extraction and methylation of lipids, GLC was used to determine the composition of fatty acid methyl esters. Yield of individual fatty acids in milk fat was calculated by correcting for glycerol content, and other milk lipid classes according to Piantoni et al. (2013). To describe the change of the concentration of major fatty acid components from colostrum samples to samples obtained at wk 2 and 4 of lactation, data of fatty acid composition previously described for these 2 time points in the same animals were used (Mann et al., 2015).

Dry matter of whole colostrum was determined according to the method described by Hooi et al. (2004) for the determination of moisture in milk. In brief, colostrum samples were thawed and warmed to 37°C in a water bath. Samples were mixed by inversion. Approximately 2.5 g of sample were weighed into dried aluminum dishes (Fisher Scientific, Waltham, PA). All samples were run in duplicate. Samples were dried at 100°C in a gravity convection oven (model 1305U, VWR, Radnor, PA). Duplicates were placed on different shelves within the oven to minimize influence of placement during drying. Samples were removed from the oven 20 h later, allowed to cool to room temperature, and weighed again. Moisture was calculated as the difference between initial weight and weight after oven drying (Hooi et al., 2004).

Analytical Approach

Because few animals entered parity 4 and 5, parity was dichotomized into parity 2 and ≥3. A variable was created to dichotomize IgG concentration as either <100 g/L or ≥100 g/L. Chi-squared tests were generated with PROC FREQ in SAS (SAS 9.3, SAS Institute Inc., Cary, NC) for treatment differences in the dependent variables IgG < or ≥100 g/L, calving scores, parity, and calf sex. Mixed effects ANOVA

were carried out with PROC MIXED for treatment differences in the dependent variables of energy balance prepartum, fat %, days dry, IgG, and insulin concentration as well as colostrum weight and fatty acid composition including enrollment block as a random effect. The assumption of equal variances was tested with Levene's test and Welch's ANOVA was performed in cases where the assumption was not met. Multiple comparisons were adjusted with Tukey's post hoc test. Because IgG concentration could be a function of the DM content of colostrum, a regression model with IgG concentration as the outcome and group as well as DM of colostrum as predictor variables was built (PROC MIXED). Two-way interactions between the predictor variables were investigated to determine if a possible group effect depended on DM of the colostrum. Enrollment block was included as a random effect. Residual analysis was performed and satisfied the assumptions of homoscedasticity and normality. Presence of highly influential observations was determined when Cook's $D > 0.5$. Repeated measures ANOVA was performed for fatty acid composition over time using PROC MIXED in SAS. Three covariance structures were tested for each variable analyzed (compound symmetry, autoregressive order 1, and unstructured). The covariance structure with the smallest Akaike's information criterion was chosen. Fixed effects were treatment group and time, and enrollment block was included as a random effect. The relationship between plasma insulin concentration at 1, 2, or 3 d before parturition and the concentration of insulin in colostrum was assessed with Pearson correlation. Results are presented as mean and 95% CI unless otherwise stated.

RESULTS

Description of Study Population and Diets

Three cows were excluded from the analysis. One was dry for 99 d, and 2 other cows had perforating teat le-

sions prepartum leading to milk leakage. Cows were dry for an average of 55.5 (± 4.4) d [CON: 56.4 (54.6–58.2), I-med: 55.0 (53.3–56.7), HI: 55.2 (53.5–56.9); $P = 0.46$]. The majority of cows were entering parity 2 ($n = 51$, 62.9%), and 30 animals were entering parity 3 or greater (37.1%). No difference was found in parity between treatment groups ($P = 0.50$). The average BW at enrollment was 672 (657–686) kg and the average BCS was 3.1 (3.05–3.16). Weight and BCS were not different among groups at enrollment ($P > 0.33$). On average, cows in group HI gained an additional 0.27 (0.18–0.36) point in BCS score, compared with group CON [0.15 (0.07–0.24), $P = 0.15$] and group I-med [0.11 (0.02–0.19), $P = 0.03$]. Weight gain in the dry period was also highest in group HI [90.4 (82.7–98.1) kg], compared with group CON [72.1 (64.3–79.8) kg, $P = 0.004$] and group I-med [71.0 (63.3–78.8) kg, $P = 0.002$]. The majority of calving ease scores in all cows were score 1 and 2 [CON: 23/25 (92.0%), I-med: 24/28 (85.7%), HI: 27/28 (96.4%)], and the distribution of all calving ease scores was not different among groups ($P = 0.62$). One animal in group I-med had twins. The mean weight of newborn calves was 44.2 ± 0.5 kg. Weight distribution by treatment group was 45.6 (44.0–47.3), 43.6 (42.0–45.1), and 43.2 (41.7–44.7) kg for CON, I-med, and HI groups, respectively ($P = 0.07$). The numbers of calves in groups CON, I-med, and HI ($P = 0.49$) were 17, 14, and 13 males and 11, 15, and 15 females, respectively. The analyzed composition of prepartum diets is summarized in Table 1. A detailed description of diet analysis and results has previously been described (Mann et al., 2015). Weekly energy balance estimates for the last 4 wk prepartum based on weekly averages of daily DMI, weekly body weight and days carried calf is presented in Table 2. Predicted MP supply, expressed as a percentage of CNCPS predicted requirements, was 118, 123, and 120% in the CON, I-med, and HI group, respectively, during the last 4 wk of gestation.

Table 1. Analyzed composition of diets

Component ¹	Treatment group			
	Controlled	Intermediate	High	Fresh
DM ² (%)	56.4 $\pm$ 3.8	49.8 $\pm$ 3.1	44.7 $\pm$ 3.9	46.8 $\pm$ 3.1
MP ³ (g/d)	1,490 (1,272–1,738)	1,520 (1,241–1,808)	1,520 (1,223–1,774)	2,650 (1,673–3,009)
CP (% of DM)	14.2 $\pm$ 1.6	13.9 $\pm$ 0.7	12.5 $\pm$ 0.9	17.8 $\pm$ 0.9
NDF (% of DM)	48.4 $\pm$ 5.0	42.2 $\pm$ 4.5	41.0 $\pm$ 4.2	35.4 $\pm$ 2.3
ADF (% of DM)	30.1 $\pm$ 4.2	28.5 $\pm$ 3.2	26.5 $\pm$ 3.3	21.3 $\pm$ 4.4
Starch (% of DM)	15.0 $\pm$ 2.5	20.1 $\pm$ 3.6	23.7 $\pm$ 2.6	21.2 $\pm$ 2.3
Fat (% of DM)	2.7 $\pm$ 0.2	2.9 $\pm$ 0.2	3.1 $\pm$ 0.1	4.1 $\pm$ 0.3

¹Chemical composition is presented as average of 11 monthly composites $\pm$ SD (except DM).

²Average $\pm$ SD of 36 weekly DM measurements.

³Prediction of MP supply for average DMI (range given for $\pm$ SD in DMI) in each treatment group for the last 7 wk before calving and for overall average intakes postpartum (Cornell Net Carbohydrate and Protein System v. 6.1).

Table 2. Energy balance in percent of requirement as estimated by the Cornell Net Carbohydrate and Protein System (v. 6.1) for each week in the last month prepartum¹

Week prepartum	Treatment group ²			P-value
	Controlled	Intermediate	High	
4	115 (108–122) ^a	128 (121–135) ^b	156 (149–163) ^c	<0.0001
3	107 (102–113) ^a	133 (127–139) ^b	147 (141–153) ^c	<0.0001
2	102 (96–107) ^a	126 (120–131) ^b	135 (129–140) ^b	<0.0001
1	91 (86–97) ^a	113 (108–119) ^b	123 (117–128) ^b	<0.0001

^{a–c}Means in the same row with different superscripts differ ($P < 0.05$).

¹Enrollment block included as random effect, data presented as LSM (95% CI).

²Cows were fed a TMR ad libitum to supply approximately 100, 125, and 150% of energy requirements in the controlled, intermediate, and high energy diet, respectively, during the last 4 wk before expected calving.

Results of Colostrum Analysis

Differences in IgG concentration, insulin concentration, colostrum yield, DM, and fat % and yield are summarized in Table 3. Cows in group CON had the highest concentration of IgG and cows in group HI had the lowest concentration [96.1 (83.3–108.9) vs. 72.4 (60.6–84.1) g/L, $P = 0.03$]. Insulin concentration was highest in group HI [1,105 (965–1,244) μ U/mL] and lowest in group CON [853 (700–1,007) μ U/mL, $P = 0.09$]. Values for IgG concentration [88.2 (76.2–100.2) g/L] and insulin [1,054 (907–1,202) μ U/mL] for group I-med were in between those of the other groups. The correlation between insulin concentrations in plasma on d 1, 2, or 3 before parturition and concentrations in colostrum was $\rho = 0.54$ ($P < 0.0001$, Figure 1). When regarding IgG concentration as either below or above 100 g/L, 40.0, 21.4, and 10.7% of cows in group CON, I-med, and HI had a colostral IgG concentration above 100 g/L, respectively ($P = 0.04$). The results of the regression analysis are shown in Table 4. No interaction was found between group and DM for the outcome of IgG concentration ($P = 0.44$); therefore, the effect of group was independent of the effect of DM. For every

increase in 1% of DM, the model showed an increase in concentration of IgG by 2.9 g/L.

Fatty acid concentration and yield of colostrum samples are summarized in Tables 5 and 6. Feeding a controlled energy diet during the dry period increased the concentration, but not yield, of preformed fatty acid, whereas the concentration of de novo fatty acid was lower in comparison with cows that received a higher energy diet during the whole dry period (group HI) or during the last 4 wk of the dry period alone (group I-med), respectively. This difference was caused by an increase in C10:0, C12:0, and C14:0 fatty acid in groups I-med and HI in comparison with group CON. The overall yield of de novo fatty acid in colostrum was approximately 50% higher in both groups I-med and HI compared with group CON (Table 6).

Figure 2 shows the results of repeated measures analysis of preformed, mixed, and de novo fatty acid concentration in colostrum samples as well as samples in wk 2 and 4 of lactation. The concentration of preformed fatty acid increased and the concentration of mixed fatty acid decreased in all 3 groups in wk 2 and 4. The concentration of de novo fatty acid in group CON remained relatively stable, whereas the concen-

Table 3. Effect of treatment group for the outcomes colostral IgG and insulin concentration, fat concentration, and yield, as well as colostrum yield and DM¹

Measurement	Treatment group ²			Overall mean	P-value
	Controlled	Intermediate	High		
IgG (g/L)	96.1 ^a (83.3–108.9)	88.2 ^{ab} (76.2–100.2)	72.4 ^b (60.3–84.5)	83.9 (76.6–91.1)	0.02
Insulin (μ U/mL)	853 ^a (700–1,007)	1,054 ^{ab} (907–1,202)	1,105 ^b (960–1,250)	1,010 (924–1,096)	0.04
Fat (%)	5.01 (4.12–5.90)	5.61 (4.77–6.41)	5.96 (5.15–6.78) ³	5.55 (5.07–6.01)	0.25
Fat yield (g)	289 (196–380)	406 (318–495)	384 (295–473) ³	393 (307–412)	0.08
Yield (kg)	5.94 (4.46–7.42)	7.00 (5.6–8.4)	7.27 (5.87–8.67)	6.77 (5.95–7.59)	0.40
DM (%)	26.52 (24.94–28.10)	25.84 (24.29–27.34)	25.73 (24.23–27.22)	26.01 (25.13–26.89)	0.74

^{a–c}Means in rows with different superscripts differ ($P < 0.05$; Tukey's test).

¹Data presented as least squares means (95% CI), enrollment block included as random effect.

²Cows were fed a TMR ad libitum to supply approximately 100, 125, and 150% of energy requirements in the controlled, intermediate, and high energy diet, respectively, during the last 4 wk before expected calving.

³One animal removed due high concentration and yield of fat leading to extreme observation (Cook's D > 0.5).

Figure 1. Relationship between plasma insulin on d 1 to 3 prepartum with colostral insulin concentration (n = 56). Pearson correlation coefficient $\rho = 0.54$, $P < 0.0001$.

tration of these fatty acid dropped in groups I-med and HI, especially in wk 2.

DISCUSSION

Differences in IgG Concentration

In this study, cows fed a controlled energy diet during the dry period had a higher concentration of IgG in colostrum compared with cows fed higher energy density diets. Colostral immunoglobulins are derived from those circulating in plasma and are actively taken up by the mammary gland through binding to the neonatal FcRn receptors (Zhang et al., 2009). Lower concentrations in colostrum could therefore be caused by a decreased circulating level in the blood of the dam, a change in transfer capability, a difference in the rate of water inclusion or any combination of these as discussed in more detail below.

Jennbacken et al. (2013) describe that high concentrations of glucose caused a reduction in secretion of

immunoglobulin from B-1 lymphocytes in an in vitro cell culture experiment. Lower IgG concentrations in colostrum or milk of prepartal hyperglycemic mothers have recently been reported (Morceli et al., 2011; França et al., 2012). Smilowitz et al. (2013) hypothesized that this difference is due to an impairment of B-cell function or a difference in circulating prolactin, which has a lower concentration in blood samples from women with mild hyperglycemia due to insulin-dependent diabetes (Botta et al., 1984). Several authors have reported higher blood glucose concentrations prepartum in cows overfed in the dry period (Janovick et al., 2011; Graugnard et al., 2012). To our knowledge, the biological significance of this difference and potential effects on B cell activity have not been investigated in the bovine species to date. Furthermore, we did not assess plasma concentrations of IgG or B cell function in the dams in the present study, which limits our ability to evaluate differences in circulating blood concentrations of dams as a possible source of differences in colostral IgG concentration.

Human B lymphocytes are equipped with prolactin receptors and prolactin may play a role in regulating the immune response according to research carried out by Russell et al. (1985). Prolactin concentrations in study animals and the possible effects on B-cell function were not assessed in the present study, and data on a possible dietary influence on prolactin concentration or onset of increased concentrations in dairy cows are lacking.

Colostral IgG concentration varies widely between individual animals (Kehoe et al., 2007; Morrill et al., 2012), suggesting differences in the total mass transferred. Moreover, individual concentration and mass differences of IgG1 within quarters of individual cows exist (Baumrucker and Bruckmaier, 2014), further adding to the potential variability in IgG colostral mass. Concerning possible differences in transfer of immunoglobulins, Baumrucker et al. (2010) reported large differences in individual cows capacity to transfer

Table 4. Effect of treatment group and colostral DM on the outcome IgG concentration (g/L) based on a multivariable linear regression model, with enrollment block included as a random effect

Explanatory variable	Group ¹	LSM (95% CI)	β (95% CI)	P-value
Group	Overall	—	—	0.05
	Controlled	93.4 (80.9 to 105.6)	19.9 ² (2.8 to 36.8)	0.03
	Intermediate	90.0 (77.8 to 102.2)	16.5 ² (−0.29 to 33.2)	0.05
	High	73.5 (61.9 to 85.2)	Referent	—
DM (%)	—	—	2.9 ³ (1.1 to 4.7)	0.003

¹Cows were fed a TMR ad libitum to supply approximately 100, 125, and 150% of energy requirements in the controlled, intermediate, and high energy diet, respectively, during the last 4 wk before expected calving.

²Change in IgG concentration compared with group HI (= referent group).

³Change in IgG concentration for every increase in 1% of DM.

IgG₁ that could be attributable to endocrine or genetic differences. Differences in rate of transcytosis via the FcRn receptor and individual variability in the onset of colostrogenesis may play a role (Baumrucker and Bruckmaier, 2014). We are currently unaware of a potential mechanism influencing IgG transfer capabilities in cows fed different planes of energy during the dry period.

In a study including over 900 colostrum samples, Pritchett et al. (1991) described that weight of first milking colostrum was most highly correlated with IgG concentration. In contrast, Quigley et al. (1994) found the correlation between IgG concentration and colostrum volume to be small ($r = -0.19$). We addressed this possible influence of a simple dilution both by determining the DM content of colostrum samples and by using a multivariable linear regression model to account for both effects at once and to assess a possible interaction. Cows in the high energy group had on average a 1.3 kg higher colostrum yield and

0.80% lower DM compared with the controlled energy group. Group had an effect on IgG concentration that was independent of the effect of colostrum DM, and no interaction was found between yield and group as independent variables. Also, the mean increase in colostrum IgG concentration per 1% increase in DM as predicted by the model was 2.9 g/L. The numerical difference of an average of 0.80% DM between the controlled and high energy group would therefore theoretically only explain a total average difference of approximately 2.3 g. The authors of a recent study based on 700 cows in Ireland found that each increase in 1 kg of colostrum yield decreased the IgG concentration by 1.7 g/L (Conneely et al., 2013), which supports the magnitude of IgG concentration difference per increase in colostrum yield that we observed.

A recent study described the absence of an effect of dry period nutrition on colostrum IgG concentration (Nowak et al., 2012) in dairy cattle. In this study, NDF content of the prepartum diets was 52% of DM in

Table 5. Colostrum fatty acid concentration (g/100 g of fatty acid) of cows fed different dry period treatment diets (n = 80)

Item	Treatment ¹			SEM	P-value
	CON (n = 25)	I-med (n = 27)	HI (n = 28)		
Fatty acid concentration (g/100 g)					
Summation by source ²					
De novo	20.6 ^a	22.6 ^b	22.4 ^b	0.38	0.001
Mixed	50.1	52.4	52.2	0.94	0.16
Preformed	29.4 ^a	25.0 ^b	25.4 ^b	1.07	0.001
Selected individual fatty acid ³					
4:0	1.38	1.35	1.42	0.07	0.71
6:0	0.88	0.91	0.94	0.02	0.27
8:0	0.49	0.51	0.53	0.01	0.15
10:0	1.37 ^a	1.52 ^b	1.51 ^{ab}	0.04	0.03
12:0	2.43 ^a	2.73 ^b	2.67 ^{ab}	0.07	0.01
14:0	13.0 ^a	14.3 ^b	14.0 ^b	0.26	0.002
14:1 <i>cis</i> -9	1.11	1.29	1.26	0.08	0.14
16:0	46.8	49.2	49.0	0.83	0.07
16:1 <i>cis</i> -9	3.00	3.14	3.21	0.14	0.54
17:0	0.48 ^a	0.43 ^b	0.43 ^b	0.01	0.004
18:0	5.05	4.27	4.44	0.30	0.15
18:1 <i>trans</i> -4	0.007	0.006	0.006	0.0004	0.85
18:1 <i>trans</i> -5	0.006	0.006	0.006	0.0003	0.99
18:1 <i>trans</i> 6-8	0.13	0.12	0.13	0.006	0.45
18:1 <i>trans</i> -9	0.09	0.08	0.08	0.01	0.14
18:1 <i>trans</i> -10	0.14	0.12	0.11	0.007	0.12
18:1 <i>trans</i> -11	0.48 ^a	0.38 ^b	0.34 ^b	0.03	0.002
18:1 <i>cis</i> -9	16.3 ^a	13.1 ^b	13.5 ^b	0.67	0.002
18:1 <i>cis</i> -11	0.55 ^a	0.47 ^b	0.48 ^b	0.02	0.002
18:1 <i>cis</i> -12	0.12 ^a	0.12 ^a	0.14 ^b	0.01	0.02
18:2 <i>cis</i> -9, <i>cis</i> -12	2.01	2.02	1.95	0.07	0.25
18:2 <i>cis</i> -9, <i>trans</i> -11	0.24 ^a	0.20 ^b	0.17 ^b	0.01	<0.0001
18:3 <i>cis</i> -9, <i>cis</i> -12, <i>cis</i> -15	0.18	0.17	0.18	0.01	0.06

^{a,b}Main effects of treatment in the same row with different superscripts differ ($P \leq 0.05$).

¹Cows were fed a TMR ad libitum to supply approximately 100, 125, and 150% of energy requirements in the controlled, intermediate, and high energy diet, respectively, during the last 4 wk before expected calving.

²De novo fatty acids originate from de novo synthesis in the mammary gland (<16 carbons), preformed fatty acids originate from extraction from circulating plasma fatty acid (>16 carbons), and mixed fatty acids originate from both sources (C16:0 + *cis*-9 C16:1).

³A total of approximately 70 individual fatty acids were quantified and used for calculations (summation by yield). Only selected fatty acids are reported.

the higher energy group and 56% in the lower energy group. Although there might be a lack of comparability between forage sources and methods of analysis between the cited and our own study, both values are above our target value of 46% of NDF for the controlled energy diet. Starch concentrations were not reported in the study of Nowak et al. (2012). We assume that both experimental diets in the cited experiment would classify as controlled energy diets when compared with values of our own study. Furthermore, the concentration of CP as percentage of DM was 11.4 and 11.5%, respectively, which is below the recommended minimal target for CP of 12.0% for dry cows (Lean et al., 2013). Diet formulation in our current study successfully ensured that cows were not deficient in protein during the dry period (Mann et al., 2015). Predicted MP amounts were not different among groups and were on average well above the recommended average of 1,300 g of predicted MP (Ji and Dann, 2013; Van Saun and

Sniffen, 2014). Predicted MP amounts were not reported in the study of Nowak et al. (2012), but could have been deficient based on CP and NDF concentrations. Average IgG concentrations measured by ELISA were below 35 g/L in both groups. This difference in overall IgG concentrations could have been due to laboratory methods, but sample handling or differences in study animals, nutrition, and management could also play a role. We measured IgG with RID, which is considered the gold standard for this analysis (Bielmann et al., 2010; Bartier et al., 2015) in unfrozen, refrigerated samples and which is used as the reference method for validation of other tests such as colostrometry, turbidimetric immunoassay, Brix refractometry (Quigley et al., 2013), and newer methods such as quartz crystal microbalance (Crosson and Rossi, 2013). Gelsinger et al. (2015) recently described significant differences in measurements of IgG in colostrum depending on the laboratory method. Samples measured by ELISA yield-

Table 6. Colostrum fatty acid yield of cows fed different dry period treatment diets (n = 80)

Item	Treatment ¹			SEM	P-value
	CON (n = 25)	I-med (n = 27)	HI (n = 27) ²		
Colostrum fatty acid yield (g)					
Summation by source ³					
De novo	55.5 ^a	86.4 ^b	80.2 ^{ab}	9.90	0.03
Mixed	132	193	187	21.8	0.04
Preformed	79.8	95.2	91.2	12.3	0.58
Selected individual fatty acid ⁴					
4:0	3.79	5.14	5.14	0.68	0.19
6:0	2.37	3.44	3.35	0.41	0.08
8:0	1.31	1.95	1.87	0.23	0.06
10:0	3.68 ^a	5.78 ^b	5.37 ^{ab}	0.65	0.03
12:0	6.51 ^a	10.4 ^b	9.54 ^{ab}	1.18	0.03
14:0	35.1 ^a	55.0 ^b	50.6 ^{ab}	6.40	0.04
14:1 <i>cis</i> -9	2.75 ^a	4.74 ^b	4.37 ^b	0.43	0.004
16:0	125	181	176	20.7	0.05
16:1 <i>cis</i> -9	7.87 ^a	11.1 ^{ab}	11.2 ^b	1.04	0.04
17:0	1.30	1.64	1.53	0.19	0.34
18:0	14.1	16.5	16.0	2.32	0.71
18:1 <i>trans</i> -4	0.02	0.02	0.02	0.003	0.42
18:1 <i>trans</i> -5	0.02	0.02	0.02	0.002	0.40
18:1 <i>trans</i> 6-8	0.36	0.46	0.45	0.06	0.39
18:1 <i>trans</i> -9	0.24	0.29	0.29	0.03	0.48
18:1 <i>trans</i> -10	0.36	0.45	0.40	0.03	0.55
18:1 <i>trans</i> -11	1.30	1.44	1.21	0.20	0.70
18:1 <i>cis</i> -9	43.5	49.8	48.5	6.71	0.72
18:1 <i>cis</i> -11	1.50	1.75	1.72	0.22	0.61
18:1 <i>cis</i> -12	0.33	0.44	0.48	0.06	0.11
18:2 <i>cis</i> -9, <i>cis</i> -12	5.46	7.78	6.80	0.52	0.14
18:2 <i>cis</i> -9, <i>trans</i> -11	0.64	0.74	0.61	0.09	0.51
18:3 <i>cis</i> -9, <i>cis</i> -12, <i>cis</i> -15	0.50	0.65	0.62	0.07	0.31

^{a,b}Main effects of treatment in the same row with different superscripts differ ($P \leq 0.05$).

¹Cows were fed a TMR ad libitum to supply approximately 100, 125, and 150% of energy requirements in the controlled, intermediate, and high energy diet, respectively, during the last 4 wk before expected calving.

²One animal was removed due to extreme observation (Cook's D > 0.5).

³De novo fatty acids originate from de novo synthesis in the mammary gland (<16 carbons), preformed fatty acids originate from extraction from circulating plasma fatty acid (>16 carbons), and mixed fatty acids originate from both sources (C16:0 + *cis*-9 C16:1).

⁴A total of approximately 70 individual fatty acids were quantified and used for calculations (summation by yield). Only selected fatty acids are reported.

Figure 2. Least squares means of repeated measures ANOVA showing the sum by source of the concentration (g/100 g of fatty acids) of preformed (>16 carbons), mixed (C16:0 + *cis*-9 C16:1), and de novo fatty acids (<16 carbons) of colostrum and milk in wk 2 and 4 postpartum, respectively. Error bars represent standard error. Enrollment block was included as a random effect. Cows were fed a TMR ad libitum to supply approximately 100, 125, and 150% of energy requirements in the controlled (CON), intermediate (I-med), and high (HI) energy diet, respectively, during the last 4 wk before expected calving.

ed concentrations that were approximately 50% lower compared with those measured by RID. Therefore, when comparing colostral IgG concentration between different studies, such as between the study by Nowak et al. (2012) and our own, the laboratory method used to generate the results should be taken into account.

The absorption of immunoglobulin is linearly and positively related to concentration in colostrum (Stott and Fellah, 1983; Godden et al., 2009; Osaka et al., 2014). Although the physiologic capacity of IgG absorption might be limited (Besser et al., 1985), higher concentrations of IgG in colostrum are likely always advantageous. Moreover, in a study by Hopkins and Quigley (1997), the efficiency of absorption did not change significantly as immunoglobulin intake increased. In our study, the proportion of animals with very high colostrum IgG concentration (≥ 100 g/L) was 4 times higher in animals fed the controlled energy diet compared with the high energy diet. In a recent study on US dairy farms by Morrill et al. (2012), 29.4% of all colostrum samples from 67 farms across 12 states had IgG concentrations <50 g/L and were considered inadequate. Given the fact that colostral IgG concentration is highly variable on modern dairy farms (Conneely et al., 2013), achieving the highest possible concentration is important to optimize newborn health.

Differences in Fatty Acid Composition

The fat component in colostrum plays a major role in supplying energy to the newborn (Quigley and Drewry, 1998). Colostral fat can be derived through de novo synthesis in the mammary gland (4–16 carbons) from acetate and BHB, from the feed and microbial activity in the rumen of the cow, and from dietary lipids and adipose tissue lipolysis (Mansson, 2008). The average colostral concentration of fat of 5.55% was lower compared with results by Kehoe et al. (2007) reporting an average of 6.7% based on 55 samples from 55 farms in Pennsylvania. According to Quigley et al. (1994), the fat content of bovine colostrum is variable. Differences could have been due to prepartum dietary composition, particularly fat content, but diet information was not available for the study by Kehoe et al. (2007). Fat content was numerically different for the 3 groups such that cows in both groups receiving higher energy density diets in the close-up period showed higher concentrations of fat in colostrum compared with the controlled energy group. This was also reflected in the numerically higher colostral fat yield. Current literature suggests that overfeeding in the dry period increases expression of several genes involved in fatty acid uptake and de novo lipogenesis. The expression of *LPL*, *ACACA*, *FASN*, and *DGAT2* in adipose tissue was upregulated in response to

overfeeding in the close-up period (Ji et al., 2012). The potential upregulation of genes involved in milk fat de novo synthesis could explain the observed difference in fatty acid composition with an increased concentration and trend for higher yield of de novo fatty acid in group I-med and HI compared with group CON. The greater concentration of *cis*-9 C18:1 in group CON supports the greater relative contribution of fatty acid from adipocytes (Rukkwamsuk et al., 2000) to colostrum fatty acid in this group, whereas the total yield of preformed fatty acid was similar in all groups. This suggests that the observed differences in the treatment groups are caused by differences in synthesis rates of de novo fatty acid rather than differences in uptake of preformed fatty acid. Garcia et al. (2014) described the effect of supplementing fat during the dry period on colostrum fatty acid profile. Cows receiving supplemental fat during the dry period had increased concentrations of C18:0, but de novo synthesis of short- to medium-chain fatty acid was not affected by treatment. This is in contrast to our study where we observed differences in de novo fatty acid concentration in groups overfed energy during the close-up period. This could be due to treatments differing in concentrations and composition of fat supplements in the study by Garcia et al. (2014), but not in overall prepartum energy intake, and that differences in energy may be necessary to affect fatty acid synthesis in the mammary gland during the dry period.

Based on a recent study where all animals were fed the same prepartum hay-based diet, milk fatty acid composition of Holstein cattle changed over time in milk harvested starting at 24 h after parturition (Contarini et al., 2014). Lower amounts of short-chain SFA and higher amounts of long-chain SFA were found in milk from animals on the day of parturition compared with those samples that were obtained during the next 4 d, and 5 mo later, respectively. In contrast, colostrum samples from our study exhibited a lower concentration of preformed fatty acid, but increased concentration of de novo fatty acid and fatty acid from both sources (C16:0 and *cis*-9 C16:1) compared with samples obtained during wk 2 of lactation. Concentration of preformed fatty acid increased substantially from concentrations found in colostrum. Differences could be due to energy level during the dry period as in the present study all animals were fed to either meet or exceed estimated energy requirements and would have limited mobilization of adipose tissue prepartum, whereas restriction of energy during the dry period could lead to a higher concentration of preformed fatty acid from body fat mobilization as was previously shown (Dann et al., 2006) and which could have been the case in the study by Contarini et al. (2014). However, estimation of energy balance for this study was not available.

Differences in Insulin Concentration

Increasing evidence in the current literature suggests that insulin is important in mammalian gut maturation (Buts et al., 1988; Shulman, 1990; Shehadeh et al., 2006). Malven et al. (1987) found that the ratio of colostrum: blood concentration of insulin in the immediate prepartum period was 41:1. Higher serum fasting glucose during pregnancy in women was associated with higher insulin concentrations in milk (Jovanovic-Peterson et al., 1989; Ley et al., 2012). Jovanovic-Peterson et al. (1989) also found that intravenously injected insulin appeared in milk with a lag time of 30 to 50 min. Several authors have documented a higher blood insulin concentration in cows being overfed energy prepartum (Dann et al., 2006; Janovick et al., 2011; Schoenberg and Overton, 2011), but to the best of our knowledge this is the first study describing the effect of prepartum energy on insulin concentration in colostrum. When investigating the relationship of circulating concentrations of insulin with those in colostrum, we chose to use the 1 to 3 d prepartum sampling time point for plasma based on the greatest insulin uptake rate within the last few days before calving in dairy cows (Malven et al., 1987). The moderate positive correlation between plasma insulin concentration at this time and colostrum insulin concentration could be interpreted such that insulin uptake in colostrum is driven by a gradient, and that higher circulating concentrations of insulin would lead to higher concentrations in colostrum. However, the exact mechanism and control of insulin transport into the bovine mammary gland and rate of degradation during the colostrum phase require further research.

Because the aim of this study did not include follow-up of the calves and measurements of intestinal development and nutrient uptake capability, we are unsure at this time of the biological significance of the observed difference in insulin concentration in cows being fed diets differing in energy levels during the dry period.

CONCLUSIONS

In this study, feeding a dry period diet that was formulated to either meet or exceed energy requirements for Holstein affected the fatty acid composition of colostrum, as well as colostrum IgG and insulin concentrations. Cows overfed energy during the entire dry period exhibited lower colostrum concentrations of IgG, and higher concentrations of insulin compared with cows fed a controlled energy diet. The composition of fatty acid revealed that the concentration of de novo fatty acid was increased in cows that exceeded energy intake above predicted requirements during the whole duration of the dry period or the close-up period

alone compared with those fed a controlled energy diet. Prepartum dietary strategies influence the composition and quality of bovine colostrum. Further research is needed to study the possible effect of the differences in colostrum components caused by different dry period feeding strategies on IgG uptake, gut maturation, and metabolism of the newborn calf.

ACKNOWLEDGMENTS

This study is supported by the Agriculture and Food Research Initiative competitive grant no. 2012-67015-30230 from the USDA National Institute of Food and Agriculture and the American Association of Bovine Practitioners Research Assistantship 2013. We thank the Endocrinology Laboratory of the Animal Health Diagnostic Center, College of Veterinary Medicine, Cornell University for their assistance with sample analysis. We acknowledge the technical assistance of Courtney Preseault and Carolina Ferreira, Michigan State University, for fatty acid analysis and the help of Gladys Birdsall and the staff from the Cornell University Teaching and Research Center in Harford, New York, with sample collection.

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