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### Abstract

**Objectives:** To determine if a glucose precursor powder (Glucose BoosterTM, Stuhr Enterprises, LLC) added to the total mixed ration during the transition period, decreased health events, changed levels of plasma glucose and ketone bodies, and increased milk and milk component yields.

Sample Population: 106 multiparous Holstein cows and 105 multiparous Jersey cows housed at a commercial dairy.

**Procedure:** The glucose precursor powder was top dressed at a rate of 300 g/cow and then mixed into the ration just prior to the daily feeding. Blood samples were collected weekly from 21d prepartum to 21d postpartum and analyzed for glucose and beta-hydroxybutyrate using NovaMax® Plus<sup>TM</sup> meter (Nova Diabetes Care, Inc., Billerica, MA). Weekly milk and milk component yields were analyzed by Tulare and Kings Counties Dairy Herd Improvement Associations for the first 21 days in milk and then monthly milk and milk component yields to 120 days in milk. Data were analyzed using the Mixed Procedure of SAS (v. 9.4, SAS Institute 2015) separately for each breed (Holstein and Jersey) with repeated measures by cow. Least square mean comparisons were considered significant if P < 0.05.

**Results:** In the first 120 days in milk, glucose precursor powder supplementation to Holstein cows decreased the incidence of health events and ketosis (P = 0.05) and increased milk, fat, protein, fat corrected milk and energy corrected milk yield (3.3 kg/d, 0.14 kg/d, 0.092 kg/d, 4.6 kg/d, 4.4 kg/d, respectively). Plasma glucose was higher in the prepartum and postpartum fresh periods for Holstein cows fed glucose precursor powder than Holstein control cows.

**Conclusions and Clinical Relevance:** Jersey cows had a very low incidence of hyperketomia and thus did not benefit from glucose precursor powder supplementation. Supplementing Holstein cows with glucose precursor powder was beneficial to decrease health events during the transition period and increase milk production during the first 120 days in milk.

Keywords: Ketosis; Glucose Precursor; Ketosis Monitoring; Beta-Hydroxybutyrate; Health Events

### Abbreviations

BHB: Beta-Hydroxybutyrate; C: Control Treatment; DIM: Days in Milk; DMI: Dry Matter Intake; ECM: Energy Corrected Milk; FCM: Fat Corrected Milk; GP: Glucose Booster<sup>™</sup>; Stuhr Enterprises; LLC; LSM: Least Square Mean; rBST: Recombinant Bovine Somatotropin; SAS: Statistical Analysis System (v 9.4); SE: Standard Error; TMR: Total Mixed Ration

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### Introduction

Ketosis prevalence has been estimated to be as high as 60% for transition cows in Holstein herds [1,2]. Ketosis prevalence rates are high because peripartum cows experience a lag in DMI and an increase in energy demands due to the onset of lactation, resulting in negative energy balance [3]. However, the level of DMI and therefore negative energy balance varies by cow. For example, there was 30 to 40% variation in DMI in early lactation, but only 6 to 10% variation in DMI during peak milk production [4]. A study [3] estimated that at 4 DIM, energy demand was 26% greater than that provided by DMI. Even with better management, negative energy balance is unavoidable since in early lactation DMI is not sufficient for the levels of milk production that are achieved by genetically superior cows. Therefore, the risk for ketosis is increased.

On commercial dairies, BHB concentrations alone are the most common measurement used to identify ketosis [5]. However, low glucose concentrations are also an important factor in the etiology of ketosis [6-9]. Cows are considered at risk for transition diseases and ketosis starting at blood BHB concentrations greater than 1.0 mmol/L [10] and at increased risk for other diseases at blood glucose < 50 mg/dL [11].

To treat ketosis, glucose precursors such as propylene glycol, propionate and glycerol have been commonly used in commercial herds to increase blood glucose levels and lower BHB levels [12,13]. Multiple studies showed that oral boluses or drenching decreased BHB blood concentrations and increased insulin and glucose availability [14-16]. But, responses of cows to oral dosing were considered transient and oral dosing increased cost of labor and stress to cows. Feeding glucose precursors could provide a more stable and consistent increase in glucose supply rather than boluses or drenches [16]. Three studies [17-19] showed that glucose precursors mixed into either the TMR or concentrates decreased plasma BHB levels. Therefore, feeding glucose precursors may be an alternative approach to prevent ketosis during the peripartum period.

### **Objective of the Study**

The first objective of this study was to determine if TMR supplementation with GP (containing propylene glycol, glycerol, silicon dioxide, calcium propionate, niacin, cobalt carbonate and carriers (dry matter 94.75%, crude protein 0.055%, crude fat 0.22%, crude fiber 6.75%, calcium 2.24%, sodium 0.24%, ash 35.23%) during the transition period influenced plasma glucose and BHB concentrations, prevalence of health events, and milk production in multiparous Holstein and Jersey cows. The second objective was to explore relationships between plasma glucose, BHB and milk production in the control cows from the study to further understand predisposing factors for ketosis in a commercial dairy herd.

### **Materials and Methods**

All procedures involving animals were approved by the Animal Care and Use Committee of the University of California, Davis.

#### Animal housing and care

Multiparous Jersey and Holstein cows at a commercial dairy in Tulare, California were systematically enrolled at approximately 245 to 255d of pregnancy into either C (odd numbered ear tags) group or GP (even numbered ear tags) groups. Both breeds were moved into a C or GP treated dry lot pen for the prepartum period. During the trial, the dairy agreed to not drench or supplement cows with any other glucose precursor product. Approximately 12 to 24h before calving, cows were moved to a maternity pen bedded with straw. Following parturition, cows were moved to a dry lot hospital pen for 1 to 2d during which supplementation stopped. Cows were then moved to either a C or GP free stall fresh cow postpartum pen and supplementation resumed for the GP pen until 18 - 24 DIM. At 18 - 24 DIM,

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supplementation stopped and cows were randomly assigned to one of 4 milking pens for the postpartum follow up period to 120 DIM. At 80 DIM, Jersey cows were treated with rBST every 14d, while Holstein cows did not receive rBST.

All cows were fed once daily in the prepartum and fresh postpartum periods. The GP supplemented prepartum pen was fed at 0530h followed by the C prepartum pen at 0540h. The GP treated fresh postpartum pen was fed at 0600h followed by the C postpartum pen at 0615h. Both prepartum pens were fed from the same wagon load, and both fresh postpartum pens were fed from the same wagon load. To prevent cows from eating before GP was mixed into the TMR, stanchions were closed prior to feeding in both the prepartum and postpartum fresh pens. Supplemented GP was added to the ration at a rate of 300 g/cow/d. Using a push-up blade on a tractor, the TMR and GP supplement were then mixed and pushed up to the feed bunk. Stanchions were then opened and cows were allowed to eat. The C prepartum and postpartum fresh pens were fed normally. Cows in the postpartum follow up pens. Residual feed intakes were measured every other day and residuals left in the feed bunk were less than 3%. Weekly milk tests were performed during the postpartum fresh period and then monthly during the postpartum follow-up period by Tulare County Dairy Herd Improvement Association. Milk fat and protein percents were analyzed using a Bentley Instruments ChemSpec 150 (Chaska, MN).

### Data and sample collection

All cows were bled at enrollment in the prepartum pen to obtain initial plasma glucose and BHB concentrations. Blood samples were taken weekly thereafter at the morning feeding and were collected from the coccygeal vein (vacutainer needles 20Gx1" and Vacutainer Plus PST Plastic Venous Blood Collection Plasma Tubes; Becton, Dickinson and Company, Green Hemogard Closure, 3.0 mL). Blood samples were centrifuged within 1 h of collection for 20 minutes at  $2000 \times g$ ,  $10^{\circ}C$  and the separated plasma was placed into microcentrifuge tubes (Costar<sup>®</sup> 2.0 mL Microcentrifuge Tube) for glucose and BHB analyses. These tests were performed using the NovaMax<sup>®</sup> Plus<sup>™</sup> blood glucose and ketone monitoring system (Nova Diabetes Care, Inc., Billerica, MA). Ketosis was defined as  $\geq 1.0 \text{ mmol/L}$  plasma BHB and < 50 mg/dL plasma glucose.

In commercial herds, it is common to use a meter to perform cow side tests to identify ketosis, so NovaMax<sup>®</sup> Plus<sup>™</sup> meters were used to monitor changes in glucose and BHB levels. The NovaMax<sup>®</sup> meter has been used in previous research monitoring glucose and BHB levels [20-22]. Performance of the meter was tested against other meters for glucose monitoring [11]. They found that none of the meters estimated blood glucose levels accurately. We used the Nova Max Plus meter as an indicator of low blood glucose only (< 50 mg/dL) and therefore a risk factor for ketosis. The Nova Max Plus meter also was evaluated for diagnosing ketosis by measuring BHB level [21]. They determined the Nova Vet meter was acceptable but the Nova Max Plus meter was not. The Nova Vet meter uses the same method to measure BHB but, included a calibration step to calibrate the meter to different concentrations of BHB in cow blood which involves a 1.25 slope adjustment. The Nova Max Plus meter does not include this step since it is for human use. Since they did not use the slope correction for the Nova Max Plus meter it did not perform well in their analyses. If the slope adjustment is used, our BHB ≥ 1.0 mmol/L plasma BHB definition of ketosis becomes 1.25 mmol/L which agrees with other definitions of ketosis [23,24]. Dairy producers are unlikely to go to the extra step of using the correction factor, therefore, the BHB numbers presented in this paper are uncorrected.

Daily TMR samples were collected prior to GP being added to the ration. Samples were collected by grab sampling 10 times down the feed lane, 6 m apart, to fill a gallon plastic bag. A 60 g subsample from daily samples was pooled by week and sent to Analab for analysis (Agriking, Fulton, IL). Samples of TMR were analyzed for DM, acid-detergent fiber, neutral-detergent fiber, crude protein, fat, ash, and lignin using wet chemistry analyses [25] (methods 935.29, 973.18, 2002.04, 990.03, 920.39, 942.05, 973.18, respectively). Starch was measured using near-infrared spectrometry based on predictive equations developed by Analab. Mineral analyses for calcium, phosphorus,

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magnesium, potassium, sulfur, sodium, chloride, iron, copper, manganese, and zinc were done using an inductively coupled plasma-mass spectrophotometry [25] (methods 985.01 for Ca, P, Mg, K, Na, Fe, Cu, Mn and Zn, 923.01 for S and 915.01 for Cl).

During the first 60 DIM, negative health events and all reproduction and milk production data were collected from DairyComp5 herd management software (Valley Ag Software, Tulare, CA). Daily feeding data were recorded using FeedWatch feed management software (Valley Ag Software, Tulare, CA).

### Statistical analysis

Because cows were randomly sorted among 4 milking pens in the postpartum follow up period and they did not remain in the same pen throughout all periods, cow was considered to be the experimental unit of interest. To be included in the statistical analyses, cows had to be in the C or GP treated prepartum pen for a minimum of 14d prior to being moved to the maternity pen and had to be in the postpartum pens for at least 14d after calving. In total, 211 cows were included in the analyses (control Holstein 54 cows, GP Holstein 51 cows; control Jersey 52 cows, GP Jersey 54 cows). From statistical model evaluation, residuals were normally distributed and there were homogeneity of variance. Significant differences were at *P* values of  $\leq 0.05$ , while tendencies were at P values  $0.05 < P \le 0.10$ . All data were expressed as LSM with SE except for ingredient and nutrient contents of the TMR.

The effect of GP supplementation on plasma concentrations of BHB and glucose, body condition score, pen DMI, milk composition, FCM, ECM and milk, fat and protein yield (response variables in table 2 and figure 1) were analyzed using the Mixed procedure of SAS (v. 9.4, SAS Institute 2015). Negative DIM values were used to designate the prepartum period and DIM = 0 was used to indicate the day the cow calved. The model used was  $Y_{nilpt} = \mu + T_n + P_1 + C(T_n)_i * P_1 + B_p + S_i + X_t + e_{nilpt}$  where  $Y_{nilpt} =$  response variable,  $\mu$  = overall mean response;  $T_n =$  fixed effect of treatment where n = C or GP;  $P_1 =$  period of trial (l = prepartum, fresh postpartum, and postpartum follow up periods);  $C(T_n)_i * P_1 =$  interaction term for individual cow  $C_i$  (i = 0 to 211) nested within treatment group  $T_n$  by period of trial  $P_1$ ;  $B_p =$  random effect of parity (p = 2 to 7);  $S_i$  = random effect of previous lactation total 305 d milk for each cow i (i = 0 to 211);  $X_t$  = random effect of DIM (t = -28 to 120) and  $e_{nilpt} =$  residual error. Holstein and Jersey cow data were analyzed separately to account for breed differences.

Using a similar model, milk, milk fat and milk protein yields at a specific average DIM ( $\pm$  7**d**) for C and GP Holstein cows were compared using the Analysis of Variance procedure of SAS (Figure 1). The model used was  $Y_{np} = \mu + T_n + B_p + e_{np}$  where  $Y_{np} =$  response variable (milk, fat or protein yield on a given test day)  $\mu$  = overall mean response;  $T_n$  = fixed effect of treatment where n = C or GP;  $B_p$  = parity (p = 2 to 7) and  $e_{np}$  = residual error.

Data from Holstein C cows, only, were used to examine effects of glucose and BHB plasma concentrations in the first week of lactation on total milk yield in the current lactation at 120 DIM compared to previous lactation total milk yield (Figure 2). Only Holstein C cows who successfully made it past 120 DIM without missing a test date were included (43 cows). Cows were categorized by plasma glucose and BHB levels using the following criteria: Category 1 was < 50 mg/dl glucose, < 1.0 mmol/L BHB, 2 was  $\geq$  50 mg/dl glucose, < 1.0 mmol/L BHB, 3 was < 50 mg/dl glucose,  $\geq$  1.0 mmol/L BHB and 4 was  $\geq$  50 mg/dl glucose,  $\geq$  1.0 mmol/L BHB. The Univariate procedure of SAS was used to estimate means and SE for each category, current and past milk, fat and protein yields.

### **Results and Discussion**

There were no differences in TMR nutrient composition or ingredients between treatments for the prepartum and postpartum periods indicating that the TMR were fairly uniform across mixer wagon loads (Table 1). Estimated DMI (Table 2) from prepartum and fresh pens were pen averages that included both Jersey and Holstein cows therefore individual DMI differences between breeds could not be determined.

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Items, % DM basis	Prepar	rtum <sup>3</sup>	Postpartum Fresh⁴		
(Unless otherwise noted)	Mean	SD <sup>5</sup>	Mean	SD	
Nutrients <sup>6</sup>					
DM	57.6	2.34	53.1	1.47	
СР	15.4	0.845	16.9	0.758	
ADF	26.6	1.92	24.5	1.69	
NDF	38.4	2.68	35.9	1.84	
Lignin	4.8	0.71	4.8	0.41	
Fat	2.6	0.23	3.5	0.30	
Starch	13.9	1.35	17.7	1.39	
Ash	9.6	0.69	9.2	0.59	
NE <sub>1</sub> , MJ/kg	6.6	0.22	6.8	0.18	
Ingredients					
Corn Silage	38		30		
Alfalfa Hay	27		19		
Corn	4.6		14		
Oat Straw	4.0		1.6		
Beet Pulp Pellets	5.4		5.3		
Soy Hulls Pellets	3.8		4.1		
Wheat Mill Run	3.4		3.2		
Canola Meal	3.2		4.3		
Dry Corn Distillers Grains	2.5		1.2		
Molasses Cane	0.13		0.51		
Whole Cottonseed			7.1		
Soybean Meal			5.4		
Soy Best <sup>1</sup>			1.6		
Blood Meal			0.75		
Supplement <sup>2</sup>	8.85		2.65		

 Table 1: Nutrients, energy and ingredients in total mixed ration provided to all cows

 (control and glucose precursor powder supplemented cows) in the prepartum and postpartum fresh pens.

 1: Soy Best (Soy Best, West Point, NE).

<sup>2</sup>: Prepartum Supplement: Calcium carbonate, calcium chloride, magnesium sulfate 7H20, calcium sulfate dihydronate, magnesium oxide, vitamin E, white salt, Rumensin 90.7 (Elanco<sup>®</sup> Greenfield, IN), Prequel 21 (Virtus Nutrition LLC Corcoran), Alimet (Novus International, Inc Saint Charles, MO), Celmanax SCP (Arm and Hammer Animal Nutrition Princeton, NJ), Diamond V XPC (Diamond V Cedar Rapids, Iowa), Clarifly 0.67% (Central Garden and Pet Company, Schaumburg, IL), Biochlor (Arm and Hammer Animal Nutrition Princeton, NJ), Animate (Phibro Animal Health Corporation Teaneck, NJ), Reashure Choline (Balchem Corporation New Hampton, NY), PDS L55 Mintrex Premix (Progressive Dairy Solutions, Inc. Oakdale, CA).

Fresh supplement: Magnesium oxide, Vitamin E, oytershell ground, sodium bicarbonate, white salt, Zinpro4 Plex C (Diamond V Cedar Rapids, Iowa), Rumensin 90.7 (Elanco<sup>®</sup> Greenfield, IN), Prequel 21 (Virtus Nutrition LLC Corcoran), Alimet (Novus International, Inc Saint Charles, MO), Celmanax SCP (Arm and Hammer Animal Nutrition Princeton, NJ), Diamond V XPC (Diamond V Cedar Rapids, Iowa), Clarifly 0.67% (Central Garden and Pet Company, Schaumburg, IL), PDS L45 TM (Progressive Dairy Solutions, Inc. Oakdale, CA).

<sup>3</sup>: Cows were in prepartum pens from approximately 14 days prior to calving to calving.

<sup>4</sup>: Cows were in fresh pens from approximately calving to 21 DIM.

<sup>5</sup>: SD is standard deviation.

<sup>6</sup>: DM is dry matter, CP is crude protein, ADF is acid detergent fiber, NDF is neutral detergent fiber, NE<sub>1</sub> is net energy of lactation.

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	Prepartum <sup>3</sup>		n <sup>3</sup> PostpartumFresh <sup>4</sup>		Postpartum Follow-up <sup>5</sup>			P value <sup>6</sup>		
	С	GP <sup>7</sup>	С	GP	С	GP	SEM	Treatment	Period	Treatment*Period
Jersey Cows										
Plasma Glucose, mg/dL	65	61	54	55	-	-	0.97	0.09	< 0.01	
Plasma BHB, mmol/L	0.6	0.5	0.7	0.7	-	-	0.020		< 0.01	
Milk, kg/d	-	-	29.4	29.9	32.4	33.3	0.77		< 0.01	
Fat, kg/d	-	-	1.36	1.41	1.47	1.46	0.040	0.05		
Fat, %	-	-	4.53	4.77	4.37	4.40	0.091		0.02	
Protein, kg/d	-	-	1.16	1.18	1.17	1.20	0.027			
Protein, %	-	-	4.03	4.03	3.63	3.61	0.035		< 0.01	
FCM <sup>1</sup> , kg/d	-	-	34.6	36.8	36.8	38.2	0.91	0.06	0.1	
ECM², kg/d	-	-	36.0	37.7	37.7	38.9	0.90	0.1		
Holstein cows										
Plasma Glucose, mg/dL	65	67	55	57	-	-	1.2	0.09	< 0.01	
Plasma BHB, mmol/L	0.5	0.5	0.9	0.9	-	-	0.020		< 0.01	
Milk, kg/d	-	-	36.4	40.7	47.4	49.8	1.1	< 0.01	< 0.01	
Fat, kg/d	-	-	1.59	1.82	1.38	1.46	0.049	< 0.01	< 0.01	0.02
Fat, %	-	-	4.39	4.46	2.95	2.93	0.079		< 0.01	
Protein, kg/d	-	-	1.25	1.37	1.35	1.42	0.036	< 0.01	0.02	
Protein, %	-	-	3.49	3.37	2.90	2.87	0.038	0.04	< 0.01	
FCM, kg/d	-	-	41.3	47.4	42.5	45.5	1.3	< 0.01		0.03
ECM, kg/d	-	-	41.7	47.5	43.3	46.3	1.3	< 0.01		0.04

Table 2: Jersey and Holstein cow least square mean plasma glucose, plasma beta-hydroxybutyrate

(BHB) and milk production during different periods of lactation from control cows

(C) and cows supplemented with glucose precursor powder (GP).

<sup>1</sup>: Fat corrected milk (3.5% fat): (0.4324 × kg of milk) + (16.216 x kg of fat).

<sup>2</sup>: Energy corrected milk (3.5% fat, 3.2% protein): (0.3246 × kg of milk) + (12.86 × kg of fat) + (7.04 × kg of protein).

<sup>3</sup>: Prepartum period was approximately 14 days prior to calving.

<sup>4</sup>: Fresh period was approximately 0 - 21 DIM.

<sup>5</sup>: Follow-up period was approximately 21 - 120 DIM. Cows were not supplemented during this time.

<sup>6</sup>: Only P values  $\leq 0.1$  were shown.

<sup>7</sup>: GP Cows were only supplemented with a glucose precursor powder during the prepartum and fresh periods.

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### Responses of plasma glucose and BHB to GB supplementation

For both Holstein and Jersey cows, average plasma BHB were higher and average plasma glucose were lower in the fresh period than in the prepartum period (Table 2). The decrease in average plasma glucose and increase in plasma BHB in the fresh period reflect the cow's response to the energy demands and negative energy balance associated with the onset of lactation. Holsteins supplemented with GP had a tendency for higher average glucose than C in the prepartum and postpartum fresh periods which supports the tendency for a reduction in ketosis cases in glucose precursor supplemented Holsteins (Table 3). Therefore, Holstein cows responded to GP supplementation with a reduced percentage of ketosis cases.

Health Event, prevalence %	С	GP
Total events <sup>1</sup>		
Holstein	30	15
Jersey	12	12
Displaced abomasum		
Holstein	3.7	2.0
Jersey	0	0
<b>Retained placenta</b>		
Holstein	3.7	0
Jersey	0	0
Mastitis		
Holstein	11	7.8
Jersey	0	3.7
Ill <sup>2</sup>		
Holstein	1.9	0
Jersey	0	0
Culled		
Holstein	11	2.0
Jersey	0	1.9
Death		
Holstein	0	0
Jersey	1.9	0
Do not breed		
Holstein	5.6	0
Jersey	1.9	5.6
Ketosis <sup>3</sup>		
Holstein	65	34
Jersey	26	31

**Table 3:** Prevalence of negative health events during the first 60 DIM for control cows

 (C) and glucose precursor powder supplemented cows (GP).

<sup>1</sup>: Total health events were relative to total cows on each treatment and did not include

clinical or subclinical ketosis. Cows that had multiple events were only counted once.

<sup>2</sup>: Cows reported as ill included fever, down, etc.

<sup>3</sup>: Ketosis was defined as ≥ 1.0 mmol/L plasma BHB, < 50 mg/dL plasma glucose and cows that had multiple events were only counted once

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The tendency for increased plasma glucose in response to GP supplementation in Holsteins may be due to slower absorption of glucose precursors when they are fed in a TMR. Cows did not receive a large dose in a short time period as in drenching therefore glucose levels may be more consistent when glucose precursors are fed. Other studies supplementing propylene glycol or glycerol in the TMR have not consistently resulted in an increase in glucose concentration or decrease in BHB concentrations. A study [17], used either 0.43 kg or 0.86 kg of glycerol top dressed and hand-mixed into the daily ration of Holstein cows and did not observe an effect on plasma glucose or BHB when tested at 7, 14, and 21 DIM. Another study [26], also supplemented Holstein cows with 400 g/d of powdered propylene glycol from 14 d prepartum to 14 d fresh, but only observed a difference between treatment glucose concentrations at 70 DIM. However, a third study [13] observed that BHB concentrations did decrease with feeding 250 g/d of glycerol to Holsteins from 0 to 21 DIM. Studies providing propylene glycol or glycerol in a drench show a rapid increase in glucose concentrations. For example, 300 or 600 mL of propylene glycol or glycerol were infused into the rumen and plasma glucose concentrations peaked within 90 minutes for Holstein cows at 19 to 33 DIM [27]. A similar peak in glucose precursors supplemented in the TMR is associated with tendencies or no response in glucose concentration. In this study, Holsteins supplemented with GP had more substrate available to decrease ketogenesis and increase ketolysis.

Jersey cows responded differently than Holstein cows to GP supplementation. Control Jerseys had higher average glucose than GP Jerseys in the prepartum period (Table 2) and there was little difference in the percentage of ketosis cases in GP Jerseys compared to C Jerseys (Table 3). The difference in BHB concentrations as well as the greater energy demands for milk yield in Holsteins as opposed to Jerseys increased the risk of health events in early lactation, which is supported by the fact that 30% of C Holsteins had a health event in the first 60 DIM compared to only 12% of C Jerseys. There is limited data comparing Holsteins and Jerseys in the transition period but, in a study [29] with both Holstein and Jersey cows it was found that both breeds decreased in glucose and increased in BHB levels following the onset of lactation. Results from this study also suggest that Jersey cows have a less extreme negative energy balance than Holsteins and thus BHB levels were lower for Jersey cows.

#### Differences in prevalence of health events in response to GP supplementation

None of the Holstein cows in this study exhibited classic signs of clinical ketosis. Holstein cows supplemented with GP had lower total health events, lower prevalence of ketosis, retained placenta and culled cows. Reasons for culling included mastitis, illness, low milk production, and other unnamed issues. The decrease in culled GP supplemented Holsteins may have been related to the reduction in ketosis (Table 3) and corresponding increase in milk yield and components (Figure 1). Therefore, GP supplementation was beneficial for Holsteins.

There were little or no differences in the prevalence of health events between C and GP treated Jerseys and results from GP treated Jerseys in this study did not show beneficial responses. There were limited data on GP supplementation effects on Jerseys since most research has been performed with Holsteins.

#### Increases in milk, fat and protein production in response to GB supplementation

Holstein cows supplemented with GP had higher milk, fat and protein, FCM and ECM yields in the fresh and the follow-up periods to 120 DIM (Table 2 and figure 1). Holstein GP cows produced 2.4 kg/d more milk, 0.08 kg/d more fat, 0.07 kg/d more protein, 3.0 kg/d more FCM, and 3.0 kg/d more ECM in the first 120 DIM than C Holstein cows. Percentage of protein was lower indicating that protein yield did not increase proportionally to milk yield and percentage fat did not change indicating that milk fat yield increased proportionally to milk yield.

Previous studies with GP supplementation did not report large increases in milk, milk fat, or milk protein yield for Holsteins. There was a significant decrease in plasma BHB concentrations and an increase in glucose with ruminal infusions of propylene glycol but, there

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was no change in milk yield [30]. In another study [31] there was no response in milk yield to supplementation of propylene glycol given by oral drenching and [32] had no response in milk yield with propylene glycol supplied in the diet. But, in other studies [13,33] there was an increase in milk yield in cows fed glycerol and propylene glycol. Since increased milk yield is associated with a greater supply of glucose to synthesize lactose, it is expected that increasing glucose supply should increase milk yield. However, increased protein is also needed to increase synthesis of alpha-lactalbumin as a cofactor for lactose synthesis. The decrease in protein yield may be due to higher demands for alpha-lactalbumin to keep up with increased glucose for lactose synthesis. Studies which do not observe an increase in milk yield with increased glucose precursor supplementation may not have adequate protein in the TMR to support increased lactose synthesis or may provide glucose over such a short period of time, i.e. drenching, that the mammary gland cannot respond with an increase in lactose synthesis.

Both C and GP Holsteins had a fat: protein inversion following peak production (Figure 1). This resulted in a significant interaction between treatment and period in milk fat yield, which then caused an interaction for FCM and ECM. The fat: protein inversion in post peak production could be due to many possible factors. However, since both C and GP Holsteins were in the same pen and in the same stage of lactation during the inversion, it was unlikely that it was related to GP treatment during the transition period.

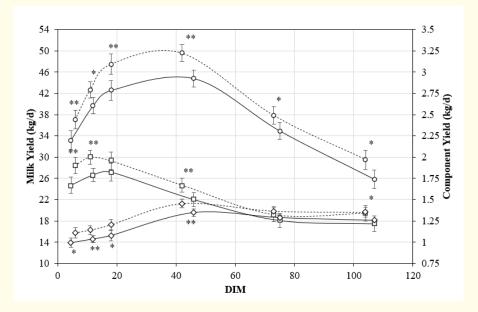


Figure 1: Changes in milk yield and milk component yield in control or glucose precursor powder (GP) treated Holstein cows. Control cows are represented by (→) and GP cows by (--). Cows given GP were supplemented for approximately 14 d before parturition to 21 d after parturition. Weekly and monthly milk (◇), milk fat (○) and milk protein yield (□) are shown as LSM ± SEM. Differences between GP and control milk, milk fat, or milk protein yield are represented by \* for 0.05 < P < 0.1 and \*\* for P < 0.05.</p>

Jerseys supplemented with GP did not differ in milk and protein yield from C Jerseys. Fat yield for GP supplemented Jerseys was greater than C Jerseys in the postpartum period by 0.05 kg/d. Associated with an increase in fat composition was a tendency for GP treated Jerseys to have higher FCM and ECM. During the postpartum follow up period, there was no difference in fat yield or fat percentage for Jerseys in the GP versus C group. There was an increase in fat yield while Jerseys were supplemented with GP but, Jerseys were treated with rBST at 90 DIM. Therefore, the impact of rBST and treatment cannot be separated from GP supplementation results in the postpartum follow up period.

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### Early lactation plasma metabolites effects on control Holstein cow milk production

Cows with the greatest BHB (categories 3 and 4) were those who had higher previous lactation milk yield (Figure 2). Cows that had lower previous lactation milk yields (categories 1 and 2) also had lower BHB levels. Therefore, previous lactation milk yield may influence current BHB levels. Current milk production was highest in category 1 and 4 cows to 120 DIM. These cows also had the highest milk production during the first 3 wk of lactation and therefore higher energy demands. Category 1 cows, which had low BHB and low glucose, may have supported higher milk production by utilizing glucose and glucose precursors, such as glucogenic amino acids, more effectively than category 3 cows. Category 4 cows were likely in 'compensated ketosis' in which body fat was being utilized for energy, BHB was being produced by liver, but peripheral tissues were able to utilize BHB for energy sparing glucose to support a higher level of milk production. Thus milk production and health did not suffer. Milk yield was lowest in category 2 and 3 cows. Category 2 cows did not have high energy demands for lactation as glucose did not appear to be used effectively for milk yield and body stores were not being mobilized. These cows may be lower genetic merit, or may have limited production capacity due to recovery from disease, etc. Category 3 cows seemed to be utilizing body fat stores to supply energy for lactation but might have been lacking in Krebs Cycle intermediates to utilize BHB effectively and thus were developing ketosis either in response to another disease or an environment that limited feed intake. In figure 2, 51% of the blood samples taken were in category 2, followed by 39% in category 3, 7% in category 4, and 3% in category 1. Therefore, the sample sizes of the extreme categories were low. Generally, high producing cows and older cows are noted as being at a higher risk of ketosis [1]. But in this study, there was no relationship between parity and plasma BHB or glucose. The lack of significance of parity is likely due to the fact that the majority of cows were parity 2 or 3 and very few cows were greater than parity 3.

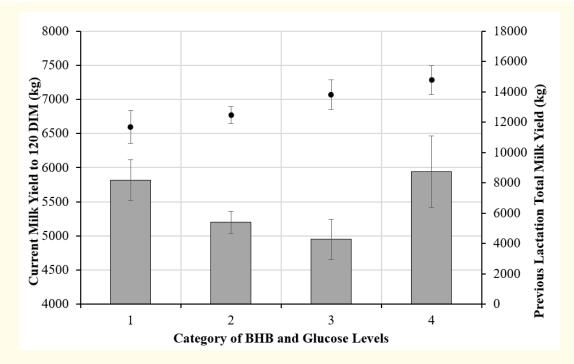


Figure 2: Relationship between previous lactation milk yield (), plasma glucose and beta- hydroxybutyrate (BHB) levels during the first week of the current lactation and current lactation milk yield to 120 days in milk (columns) for control Holstein cows only. Cows were separated into 4 categories by glucose and BHB concentrations as either 1 (< 50 mg/dl glucose, < 1.0 mmol/L BHB), 2 (≥ 50 mg/dl glucose, < 1.0 mmol/L BHB), 3 (< 50 mg/dl glucose, ≥ 1.0 mmol/L BHB), or 4 (≥ 50 mg/dl glucose, ≥ 1.0 mmol/L BHB). Values are means ± SE.</p>

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There was a tendency for milk yield to decline with BHB greater than 1.0 mmol/L and glucose less than 50 mg/dl. In other studies, Holstein cows with BHB levels  $\geq$  1.0 to 1.4 mmol/L produced 5.5 to 7.0% less milk yield than cows with lower BHB concentrations [10,34]. However, these studies did not use glucose concentrations. Results from this study showed there was a 13% decrease in daily milk yield in early lactation and 17% decrease in total milk yield for the first 120 DIM for cows in category 3 compared to those in category 4. Therefore, cows having glucose levels above 50 mg/dL potentially negated issues associated with hyperketomia. Currently, glucose concentrations are not used as an indicator of ketosis. While current literature does not consistently show that low glucose was an indicator of ketosis, glucose does play a role in development of ketosis [9,35] and low glucose is associated with lower milk yield.

Previously, research has focused on increased fat: protein ratio to identify cows that potentially have ketosis [36]. In this study, BHB levels were associated with an increased ratio and increased milk fat percentage was only associated with cows in category 3 (4.89% milk fat) which was higher than all other categories by 0.62%. Therefore, cows with greater than 1.0 mmol/L BHB had higher fat: protein ratios (1.50) and cows that had BHB less than 1.0 mmol/L had a ratio of 1.30. However, cows in category 4 had lower milk protein percentage explaining why both category 4 and category 3 were identified with increased fat: protein ratios. Therefore, using fat: protein ratio to identify ketosis can result in false positive results and should not replace glucose monitoring.

#### Developing a ketosis monitoring program

Fifty percent of the ketosis cases were identified within 7 DIM. Of those Holsteins, 43% were chronic and continued to exhibit low glucose and high BHB. Week 1 blood values also had the greatest effect on milk yield within the current lactation. Therefore, the first week of lactation was the most effective time to begin monitoring cows for ketosis. In addition, glucose was a better indicator of ketosis rather than fat:protein ratio. Since glucose test strips are typically much less expensive than BHB strips in cow side testing kits, glucose could be used as a prescreening test. If cows were < 50 mg/dl glucose, a BHB test can be used to more efficiently identify category 3 cows. These guidelines could be used to generate an economically efficient monitoring program.

### Conclusion

Supplementation with GP in the prepartum and fresh period had beneficial health and production effects for Holstein cows up to 120 DIM demonstrating that reducing ketosis by supplying GP in the TMR can increase milk, protein and fat yield even after the fresh period. Based on the results of this study, ketosis should be monitored in the first week of lactation by identifying cows with glucose less than 50 mg/dL, and then follow with a BHB test to identify ketotic cows in commercial herds.

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#### **Conflict of Interest**

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### **Bibliography**

- 1. Duffield TF., *et al.* "Use of test day milk fat and milk protein to detect subclinical ketosis in dairy cattle in Ontario". *Canadian Veterinary Journal* 38 (1997): 713-718.
- 2. McArt JAA., *et al.* "A field trial on the effect of propylene glycol on milk yield and resolution of ketosis in fresh cows diagnosed with subclinical ketosis". *Journal of Dairy Science* 94 (2011): 6011-6020.

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- 3. Bell AW. "Regulation of organic nutrient metabolism during transition from late pregnancy to early lactation". *Journal of Animal Science* 73 (1995): 2804-2819.
- 4. Drackley JK. "Biology of dairy cows during the transition period: The final frontier?" Journal of Dairy Science 82 (1999): 2259-2273.
- 5. Oetzel GR. "Monitoring and testing dairy herds for metabolic disease". *Veterinary Clinics North America Food Animal Practice* 20 (2004): 651-674.
- 6. Duffield TF. "Subclinical ketosis in lactating dairy cattle". Veterinary Clinics North American Food Animal Practice 16 (2000): 231-253.
- 7. Fukao T., *et al.* "Pathways and control of ketone body metabolism: on the fringe of lipid biochemistry". *Prostaglandins Leukotrienes Essential Fatty Acids* 70 (2004): 243-251.
- Whitaker DA., et al. "Subclinical ketosis and serum beta-hydroxybutyrate levels in dairy cattle". British Veterinary Journal 139 (1983): 462-463.
- 9. Xia Z., *et al.* "Concentrations of plasma metabolites, hormones, and mRNA abundance of adipose leptin and hormone-sensitive lipase in ketotic and nonketotic dairy cows". *Journal of Veterinary Internal Medicine* 26 (2012): 415-417.
- Ospina PA., *et al.* "Association between the proportion of sampled transition cows with increased nonesterified fatty acids and betahydroxybutyrate and disease prevalence, pregnancy rate, and milk production at the herd level". *Journal of Dairy Science* 93 (2010): 3595-3601.
- 11. Lopes RB., *et al.* "Technical note: Glucose concentration in dairy cows measured using 6 handheld meters designed for human use". *Journal of Dairy Science* 102 (2019): 9401-9408.
- 12. Kristensen NB. and Raun BML. "Ruminal and intermediary metabolism of propylene glycol in lactating Holstein cows". *Journal of Dairy Science* 90 (2007): 4707-4717.
- 13. Chung YH., *et al.* "Effects of feeding dry glycerin to early postpartum Holstein dairy cows on lactational performance and metabolic profiles". *Journal of Dairy Science* 90 (2007): 5682-5691.
- Goff JP. and Horst RL. "Oral glycerol as an aid in the treatment of ketosis/fatty liver complex". *Journal of Dairy Science* 84.1 (2001): 153.
- 15. Miyoshi S., *et al.* "Effects of propylene glycol drenching on energy balance, plasma glucose, plasma insulin, ovarian function and conception in dairy cows". *Animal Reproductive Science* 68 (2001): 29-43.
- 16. Nielsen NI and Ingvartsen KL. "Propylene glycol for dairy cows A review of the metabolism of propylene glycol and its effects on physiological parameters, feed intake, milk production and risk of ketosis". *Animal Feed Science and Technology* 115 (2004): 191-213.
- 17. DeFrain JM., *et al.* "Feeding glycerol to transition dairy cows: effects on blood metabolites and lactation performance". *Journal of Dairy Science* 87 (2004): 4195-4206.
- 18. Fisher LJ., *et al.* "Preliminary evaluation of the addition of glucogenic materials to the rations of lactating cows". *Canadian Journal of Animal Science* 51 (1971): 721-727.
- 19. Fisher LJ., et al. "Effects of propylene glycol or glycerol supplementation of the diet of dairy cows on feed intake, milk yield and composition, and prevalence of ketosis". Canadian Journal of Animal Science 53 (1973): 289-296.
- Wu Z., et al. "Effect of feeding calcareous marine algae to Holstein cows prepartum or postpartum on serum metabolites and performance". Journal of Dairy Science 98 (2015): 4629-4639.

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- 21. Bach KD., *et al.* "Technical note: Comparison of 4 electronic handheld meters for diagnosing kyperketonemia in dairy cows". *Journal of Dairy Science* 99 (2016): 9136-9142.
- 22. Suarez-Mena FX., *et al.* "β-Hydroxybutyrate (BHB) and glucose concentrations in the blood of dairy calves as influenced by age, vaccination stress, weaning, and starter intake including evaluation of BHB and glucose markers of starter intake". *Journal of Dairy Science* 100 (2017): 2614-2624.
- 23. Iwersen M., *et al.*, "Evaluation of an electronic cowside test to detect subclinical ketosis in dairy cows". *Journal of Dairy Science* 92 (2009): 2618-2624.
- 24. Voyvoda H and Erdogan H. "Use of a hand held meter for detecting subclinical ketosis in dairy cows". *Research in Veterinary Science* 89 (2010): 344-351.
- 25. American Association of Analytical Chemists. "Official Methods of Analysis" 14<sup>th</sup> edition. Association of Official Analytical Chemists, Washington, DC (1984).
- 26. Mikula R., *et al.* "Effects of propylene glycol supplementation on blood biochemical parameters in dairy cows". *Bulletin Veterinary Institute Pulawy* 52 (2008): 461-466.
- 27. Piantoni P and Allen MS. "Evaluation of propylene glycol and glycerol infusions as treatments for ketosis in dairy cows". *Journal of Dairy Science* 98 (2015): 5429-5439.
- 28. Studer VA., *et al.* "Effect of prepartum propylene glycol administration on periparturient fatty liver in dairy cows". *Journal of Dairy Science* 76 (1993): 2931-2939.
- 29. Guretzky NA., *et al.* "Lipid Metabolite Profiles and Milk Production for Holstein and Jersey Cows Fed Rumen-Protected Choline during the Periparturient Period". *Journal of Dairy Science* 89 (2006): 188-200.
- 30. Bjerre-Harpøth V., *et al.* "Effect of propylene glycol on adipose tissue mobilization in postpartum over-conditioned Holstein cows". *Journal of Dairy Science* 98 (2015): 8581-8596.
- 31. Pickett MM., *et al.* "Effects of propylene glycol or fat drench on plasma metabolites, liver composition and production of dairy cows during the peri parturient period". *Journal of Dairy Science* 86 (2003): 2113-2121.
- 32. Emery RS., *et al.* "Detection, occurrence and prophylactic treatment of borderline ketosis with propylene glycol feeding". *Journal of Dairy Science* 47 (1964): 1074-1079.
- 33. Lomander HJ., *et al.* "Supplemental feeding with glycerol or propylene glycol of dairy cows in early lactation-Effects on metabolic status, body condition, and milk yield". *Journal of Dairy Science* 95 (2012): 2397-2408.
- 34. Chapinal N., *et al.* "The association of serum metabolites in the transition period with milk production and early-lactation reproductive performance". *Journal of Dairy Science* 95 (2012): 1301-1309.
- 35. Asl AN., *et al.* "Prevalence of subclinical ketosis in dairy cattle in the Southwestern Iran and detection of cutoff point for NEFA and glucose concentrations for diagnosis of subclinical ketosis". *Preventative Veterinary Medicine* 100 (2011): 38-43.
- 36. Čýejna V and Chládek G. "The importance of monitoring changes in milk fat to milk protein ratio in Holstein cows during lactation". *Journal of Central European Agriculture* 6 (2005): 539-546.

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