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Fetal Programming

Dam parity affects fetal growth, placental size, and neonatal metabolism in spring-born beef calves

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Abstract

To determine effects of dam parity on perinatal nutrient availability in beef cattle, data and samples were collected from 18 primiparous and 35 multiparous spring-calving Sim-Angus dams and their calves. Time to stand was recorded and neonatal vigor assessed. Jugular blood was collected from a subset of calves at 0 (post-standing and pre-suckling) 6, 12, 24, 48, and 72 h of age, and blood chemistry panels were completed. Expelled placentas were dissected, dried, and weighed. Prepartum maternal circulating glucose, non-esterified fatty acids (**NEFA**), triglycerides, and urea N were analyzed. All statistical models included the fixed effect of dam parity, and calf sex (when $P \leq 0.25$) was included for calf and placental variables. Effects of sampling hour, and parity × hour were included for calf metabolites over time using repeated measures. Multiparous dams had greater body weight prepartum ($P < 0.001$) but similar ($P = 0.25$) body condition score. Maternal circulating urea N and triglycerides were greater ($P \leq 0.05$) in multiparous dams pre-calving. Calves born to primiparous dams weighed 10% less ($P \leq 0.04$) at birth with smaller ($P \leq 0.01$) heart and abdominal girths. Cotyledonary, intercotyledonary, and total placental masses were less ($P \leq 0.05$) for primiparous dams. Dam parity did not affect ($P \geq 0.58$) calf time to stand, vigor score at 10 min, or rectal temperature. Serum glucose was greater ($P = 0.03$) at 0 h but less ($P \leq 0.04$) at all other hours in calves from primiparous dams. Calves from primiparous dams had greater ($P \leq 0.02$) serum NEFA at 6, 12, and 24 h although plasma triglycerides were greater ($P < 0.001$) at 6 h. Calves from primiparous dams had greater ($P \leq 0.04$) serum urea N at 12 h and creatinine at 12 and 24 h. Plasma insulin was greater ($P \leq 0.04$) in calves from multiparous dams at 12, 48, and 72 h, but parity did not affect ($P \geq 0.18$) serum total protein or plasma cortisol. Serum aspartate aminotransferase was greater ($P \leq 0.04$) at 6 and 24 h, creatine kinase was greater at 24 h, and gamma-glutamyl transpeptidase was less ($P \leq 0.04$) at 6, 12, and 24 h, for calves from primiparous dams. Calves born to primiparous dams had greater ($P \leq 0.02$) total bilirubin and direct bilirubin at 12 and 24 h. Data indicate that calves born to first-parity heifers had decreased perinatal nutrient availability, resulting in reduced fetal and placental growth, as well as greater energy reserve mobilization and metabolic indicators of stress as neonates.

Lay Summary

Approximately two-thirds of beef calf deaths prior to weaning occur within the first 3 wk after birth. The goal to have heifers produce their first calf by 2 yr of age likely contributes to factors that limit nutrients available for fetuses and calves immediately after birth. However, little is known about differences in heifers (first parity) and cows (later parities) regarding factors affecting calf resilience, such as fetal growth and calf metabolism shortly after birth. Our data show that calves born to first-parity heifers had altered nutrient availability, demonstrated through smaller placentas, lower birth weights, and altered metabolites in early life. Although calves had similar vigor and ability to maintain body temperature, calves born to first-parity heifers had to mobilize more energy and had lower insulin during the first 3 d post-birth. Calves born to first-parity heifers had greater indicators of stress during the first 72 h of life not associated with calving difficulties. Overall, these effects may have increased morbidity and mortality of calves born to first-parity heifers if they were in a less intensively-managed system. Better understanding of challenges faced by calves born to first-parity dams provides opportunities for their improved management.

Key words: developmental programming, gestation, metabolism, neonate, placenta, pregnancy

Abbreviations: ADF, acid detergent fiber; AI, artificial insemination; AST, aspartate aminotransferase; BCS, body condition score; BW, body weight; CK, creatine kinase; CP, crude protein; DM, dry matter; GGT, gamma-glutamyl transpeptidase; NEFA, non-esterified fatty acid; NDF, neutral detergent fiber; RIA, radioimmunoassay

Introduction

Pre-weaning calf survival is critical for economic success of cow-calf producers. A 2015 survey reported that U.S. pre-weaning beef calf death loss was 5.5% (USDA-APHIS, 2017). It has been estimated that two-thirds of beef calf pre-weaning death loss occurred between birth and 3 wk of age (USDA-APHIS, 2010), indicating that the neonatal period is crucial for calf survival. Beef calves born to primiparous dams have a greater pre-weaning mortality rate, as those born to first-parity dams have been reported as nearly twice as likely to die within 24 h of birth (7% vs. 4% calf mortality; Nix et al., 1998) and pre-weaning (3.7% vs. 2% and 10% vs. 5.5% calf mortality; Patterson et al., 1987; Berger et al., 1992). Although rates of dystocia are greater in first-parity dams (reviewed by Zaborski et al., 2009), other factors specific to pregnancies of primiparous dams likely affect perinatal nutrient availability and the neonatal calf's ability to transition successfully through the perinatal period.

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Proper fetal growth and development are necessary to prepare calves for postnatal life and are programmed in utero by nutrient availability as well as exposure to hormones and growth factors (Nathanielsz, 2006; Wu et al., 2006). The maternal environment is greatly affected by dam nutrient intake, nutrient requirements, and placental transport capacity as they interact to provide nutrients to the growing fetus (Vonnahme et al., 2015; Meyer and Caton, 2016).

Prenatal developmental alterations, in addition to postnatal nutrient availability from colostrum and milk, can affect metabolic status of neonates. Dam parity is an example of a factor that is known to affect both maternal nutrient intake and requirements, especially in systems where heifers are bred to calve at 2 yr of age. These are likely contributory factors to decreased fetal growth in primiparous dams observed in several studies (reviewed by Holland and Odde, 1992 and Wu et al., 2006). Despite this, limited research has investigated other effects of dam parity on neonatal calves, especially using current U.S. beef cattle genetics. Therefore, the objective of this study was to determine the effect of dam parity on fetal growth, placental size, vigor at birth, and neonatal blood chemistry changes for spring-born calves. We hypothesized that calves born to first-parity dams have decreased perinatal nutrient availability, resulting in less fetal growth, smaller placental size, and altered neonatal metabolism.

Materials and Methods

The University of Missouri Animal Care and Use Committee approved animal care and use in this study (protocol 8952).

Pregnant dam management and data collection

Data and samples were collected from 18 primiparous and 35 multiparous spring-calving Sim-Angus dams and their calves at the University of Missouri Beef Research and Teaching Farm in this experiment. The 53 females used in this experiment were part of a larger group of females observed for data collection that included females that conceived to natural service. The study included primiparous heifers that were calving for the first time at 2 yr of age and multiparous cows of parity 2 to 13 [5.3 ± 2.9 (SD) yr of age] that had calved for the first time as 2-yr old females. In the spring prior to study initiation, cows and heifers were all bred to a single Angus sire following a fixed-time artificial insemination (**AI**) 7-d CoSynch + controlled internal drug release estrus synchronization protocol and then were exposed to natural service by mature bulls. Heifers were managed separately from lactating cows until weaning of the previous parity's calves using standard farm operating procedures common to the lower Midwest. From mid-gestation (fall, post-weaning) to study initiation, dams were housed and nutritionally-managed similarly on tall fescue-based pastures (same grazed or harvested forage and supplement) to calve at a body condition score (**BCS**) of 5 to 5.5 (1 to 9 point BCS scale). Females that conceived to AI grazed pastures in gestational management groups (parity 1 and 2 vs. parity ≥ 3) with females bred by natural service, with both management groups grazing adjacent pastures.

Data and samples were collected only from cows and heifers that conceived to AI, calved between January 28 and February 11 (average = February 5), and gave birth to single, live calves with no maternal or offspring mortality within 72 h of parturition (1 postpartum cow death from unknown causes and 1 calf death of unknown causes removed from the dataset). This resulted in 18 primiparous and 35 multiparous dams and their calves being included in this study. No calf morbidity within the sampling period (first 3 d of life) occurred in this experiment.

After initial 1-d body weight (**BW**) was recorded [d 269 of pregnancy; 6.7 ± 3.2 (SD) d pre-calving], AI- and natural service-bred dams (n = 81 total) were allocated by gestational management group into 6 uncovered 18 × 61 m dry lot calving pens that were well-drained and limestone based (description and diagram in Duncan and Meyer, 2019). Dams remained housed in dry lots until ≥72 h postpartum and were under close observation for 18 d after study initiation. Ambient temperature (collected from a weather station located on the same farm) and calving distribution are shown in Figure 1 for the calves used in this study. Body condition score was assigned to dams by 3 trained technicians on 6.3 ± 3.2 d postpartum using a 1 to 9 scale (1 = emaciated, 9 = obese) as described by Wagner et al. (1988), and the mean BCS across technicians was used in data analysis.

While in the calving pens, summer-baled, endophyte-infected tall fescue-based grass hay [86.8% dry matter (**DM**), 6.7% crude protein (**CP**), 63.9% neutral detergent fiber (**NDF**), 34.9% acid detergent fiber (**ADF**), 10.4% ash; analyzed as described in Niederecker et al. (2018)] was fed in round bale ring feeders placed on a concrete pad in the center of each calving pen to minimize waste and mud accumulation. Dams had free access to automatic watering systems and a mineral and vitamin supplement (MLS #12 MINERA-LIX, Midcontinent Livestock Supplements, Inc., Moberly, MO). Dams were supplemented with 1.0 kg DM animal^{-1} d^{-1} of dried distillers grains with solubles (90% DM, 36.7% CP, 39.1% NDF, 19.7% ADF, 5.6% ash) at 1700 h daily in fence-line concrete bunks (described in Duncan and Meyer, 2019).

Maternal blood collection

Jugular venous blood samples were obtained from dams at initiation of study (0730 to 1000 h on d 269 of gestation, at prepartum BW collection) into 4 blood collection tubes [2 Vacutainer serum collection tubes containing no additives

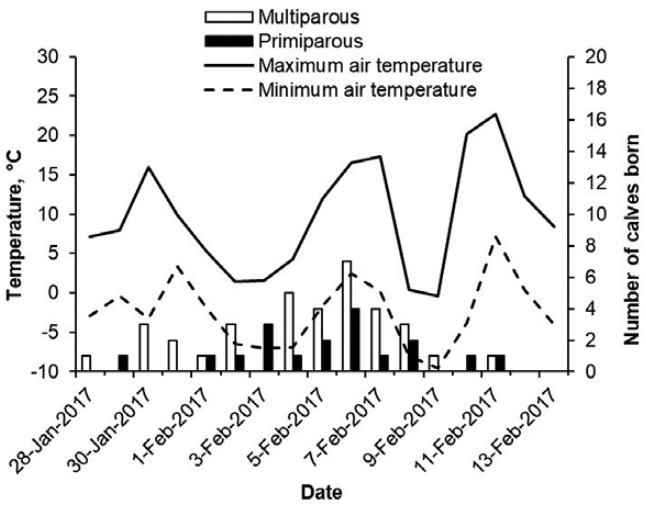

Figure 1. Ambient temperatures during calving and subsequent neonatal data and sample collection.

(10 mL draw, Becton Dickinson, Franklin Lakes, NJ), 1 Monoject plasma collection tube containing 0.10 mL of 15% K_3EDTA (10 mL draw, Covidien, Mansfield, MA), and 1 Vacutainer plasma collection tube for glucose determination containing 15 mg of sodium fluoride and 12 mg of potassium oxalate (6 mL draw, Becton Dickinson)]. All tubes were inverted as directed post-collection, and plasma tubes were placed on ice immediately. Serum tubes were allowed to clot prior to placing on ice. Samples were centrifuged within 8 h of collection at 1,500 × *g* at 4 °C for 30 min. Serum or plasma was then pipetted into 2-mL microcentrifuge tubes and stored at –20 °C until analysis.

Calving monitoring and calf data collection

Trained personnel were present through the observation period for data and sample collection. Physical signs of labor were monitored by personnel walking through calving pens at least once hourly from 600 to 2200 h, with additional checks at night occurring during periods of heavy calving. Three stadium lights were located at the back of each calving pen to allow for visualization of animals at night, and a handheld spotlight was used to visualize animals from several feet away when necessary. In periods of inclement weather and extreme cold, dams that appeared to be in labor and dams with newborn calves were moved into covered sheds until calves were dry (<12 h).

Once stage 2 of parturition was evident (appearance of amniotic membranes or calf feet), that animal was continuously monitored to observe actual time of birth. Calving assistance was provided if malpresentation was suspected, after a prolonged duration since first appearance of fetal membranes or feet (>1 h without progress), or if progress slowed during contractions based on expertise of trained personnel. Calving difficulty score ranging from 1 to 5 was assigned (1: no assistance, 2: easy pull, 3: mechanically-assisted pull, 4: abnormal presentation, and 5: caesarian-section). One calving difficulty score of 3 occurred in a primiparous dam, but all others were a score of 1.

To quantify calf vigor, time of birth (time at which entire calf, including all 4 legs, was expelled) and time of initial standing (time at which calf was standing on all 4 feet for at least 5 consecutive sec) were recorded to determine time to stand by subtraction for each calf (Dwyer, 2003). A vigor score scale modified from previous neonatal lamb studies (Matheson et al., 2011) was used to assess calf vigor at 10 min of age (Table 1). If human interference occurred before a calf stood but after the vigor score was assigned, the vigor score was used but no time to stand was calculated. If a calf took longer than 2 h to stand (n = 1), the 0 h blood sample was collected and calf was moved to a covered shed with no recorded time to stand.

Table 1. Vigor scores used to assess neonatal beef calf vigor[1]

Score	Definition
1	Very weak; lying flat on side, unable to lift head, minimal movement
2	Weak; lying flat on side, but holding head up
3	Active and vigorous; on chest and holding head up (sternal)
4	Very active and vigorous; standing on back legs and front knees (standing attempt)
5	Extremely active and vigorous; standing on all 4 feet

[1]Scores were assigned respective to vigor behaviors displayed at or prior to the time of scoring, even if the calf was not displaying that behavior at the exact time of scoring (e.g., had attempted to stand already, but was laying in a sternal position at the time of scoring = 4).

Calves were measured and processed at 20.4 ± 14.7 h of age. At this time, each calf was given visual identification (ear tag), and its umbilicus was sprayed with dilute chlorhexidine. Calf sex was recorded, and birth weight and body size were determined as described in Redifer et al. (2021), including shoulder to rump length (length from neck–shoulder junction to the end of the tailhead, following the spine), heart girth (body circumference immediately posterior to the shoulders and front legs), abdominal girth (body circumference at the umbilicus), and rear cannon bone circumference (circumference of rear leg metatarsus at the smallest point). Ponderal index was calculated using the equation ponderal index = birth weight (kg)/ shoulder to rump length $(m)^3$ as an indicator of calf shape. In human medicine, ponderal index is a measurement used to assess neonatal body shape and thinness at birth (Walther and Ramaekers, 1982). Calf heart girth:length ratio was calculated as a second indicator of shape, using both measures in cm.

Dams were monitored closely postpartum for placental expulsion. Expelled placentas were collected, rinsed of debris, refrigerated at 4 °C, and processed as previously described (Redifer et al., 2021). Briefly, cotyledons were dissected away from the intercotyledonary tissue and were counted. Dry weights of total cotyledonary and intercotyledonary tissues were determined to remove variation due to water content from rinsing. Cotyledonary and intercotyledonary dry weights were summed for each placenta to determine total placental dry weight. Average cotyledonary weight was calculated by dividing the total cotyledonary tissue dry weight by the number of cotyledons counted. Umbilical vessel diameter was measured using calipers just proximal to the first branching after the site of umbilical tearing for all 4 vessels of the umbilicus in the expelled placenta.

Jugular blood was collected from 28 calves (n = 12 primiparous and 16 multiparous dams) at 0, 6, 12, 24, 48, and 72 h postnatally (±30 min for 6, 12, and 24 h; ±1 h for 48 and 72 h). This subset of calves was selected due to permissive dam temperament, known time of birth, and availability to collect blood samples at appropriate times. Blood samples collected at 0 h were obtained pre-suckling, but after standing. Calf rectal temperatures were recorded using a digital thermometer prior to blood sample collection at these sampling times. Blood samples were collected into 3 collection tubes [2 Vacutainer serum collection tubes containing no additives (10 mL draw, Becton Dickinson) and 1 Monoject plasma collection tube containing 0.10 mL of 15% K_3 EDTA (10 mL draw, Covidien, Mansfield, MA)]. Calf plasma and serum were processed as described above for maternal samples.

Circulating metabolite and hormone analysis

Prepartum maternal serum urea N, plasma glucose, and serum non-esterified fatty acid (**NEFA**) concentrations were determined using commercially-available kits as described by Niederecker et al. (2018). Neonatal calf serum NEFA was also determined at all sampling hours using these methods. Samples were analyzed in duplicate, and pooled control samples were used for all assays. The intraassay and interassay CV were 2.1% and 5.4% for serum urea N, 3.7% and 5.8% for plasma

glucose, 4.9% and 7.6% for maternal serum NEFA, and 4.3% and 3.4% for calf serum NEFA, respectively. Calf plasma triglycerides were analyzed in duplicate using a Gallery chemical analyzer (Thermo Scientific, Middletown, VA) and the Infinity Triglyceride assay reagent (Thermo Scientific). Within analytical day (intraassay) and among day (interassay) CV averaged 1.1% and 5.2%, respectively. Prepartum maternal plasma triglycerides were analyzed using the same reagent but methods described in Larson-Peine et al. (2022); the intraassay and interassay CV were 3.5 and 0.5%, respectively.

A 1-mL serum sample from each calf at each sampling hour was submitted to the University of Missouri Veterinary Medical Diagnostic Laboratory for a complete chemistry profile analysis. This was submitted after processing on the day of collection or within 48 h of sampling when collected on evenings or weekends. Serum glucose, urea N, creatinine, total protein, globulin, albumin, sodium, calcium, chloride, phosphorus, potassium, magnesium, bicarbonate, anion gap, total bilirubin, and direct bilirubin concentrations and aspartate aminotransferase (**AST**), creatine kinase (**CK**), and gamma-glutamyl transpeptidase (**GGT**) activities were determined using a Beckman Coulter AU400e Chemistry Analyzer (Beckman Coulter Inc., Brea, CA). Internal quality control and verification of performance within specific CV were conducted daily by laboratory staff. Upon delivery, samples were analyzed through the instrument's completely automated process.

Calf plasma insulin concentration at each sampling hour was analyzed by radioimmunoassay (**RIA**) in duplicate using a commercial kit (Human Insulin Specific RIA, EMD Millipore Corp., Billerica, MA). Manufacturer recommendations were followed with the exception of using bovine insulin (Sigma, St. Louis, MO) for the standards (linear range 0.156 to 4.00 ng/tube) and using 150 µL of plasma and 50 µL of buffer. Before analyzing the samples, linearity and parallelism were verified in 4 dilutions of a pooled bovine plasma sample that resulted in concentrations ranging from 0.159 to 1.72 ng/mL. Sensitivity of the RIA (90% of the zero standard binding) was 18 pg/tube. The intraassay and interassay CV were 2.0% and 1.8%, respectively. Calf plasma cortisol concentration at each sampling time was analyzed using a commercial coated-tube RIA kit (MP Biomedicals, Irvine, CA) in duplicate as described previously (Foote et al., 2016). The intraassay and interassay CV were 3.6% and 4.1%, respectively.

Statistical analysis

Dams that were extremely aggressive towards personnel were not included in some or all post-calving sampling and data collection. The calf and dam with a calving difficulty score of 3 (only score >1) were not an outlier for any parameters and included in all possible analyses except vigor. Animal and sample numbers for each parameter type vary due to dam temperament and calving time that allowed for collection data and samples; all calves needed to have birth size or vigor data to be included. Dam prepartum BW, BCS, and metabolites were included for all females with calves included in the dataset, except BW and metabolites for 1 multiparous cow that calved prior to data and sample collection (primiparous n = 18, multiparous n = 34). Gestation length was included for all calves (primiparous n = 18, multiparous n = 35), and calf size at birth was excluded for 1 calf born to a primiparous dam due to maternal temperament (primiparous n = 17, multiparous n = 35). Vigor was assessed for calves based on ability for personnel to visualize calf from time of delivery to 10 min of age (primiparous n = 11, multiparous n = 17) or time of initial standing (primiparous n = 8, multiparous n = 15). Placentas were collected post-expulsion when dam temperament allowed, and only placentas deemed complete at dissection were included in the analysis (primiparous n = 9, multiparous n = 18). Neonatal calf metabolites were included if calves had ≥4 sampling hours represented (primiparous n = 9 to 12 per sampling hour, multiparous n = 14 to 16 per sampling hour), and neonatal calf rectal temperatures were included if calves had ≥3 sampling hours represented (primiparous n = 7 to 11 per sampling time, multiparous n = 11 to 15 per sampling time).

Data were analyzed using the MIXED procedure of SAS 9.4 (SAS Institute Inc., Cary, NC) with animal as the experimental unit. Dam parity was included as a fixed effect for all measures. For calf metabolite changes over time, effects of dam parity, sampling hour, and their interaction were included as fixed effects in the model. Sampling hour was considered a repeated measure using the best-fit covariance structure (based on AIC, BIC, and BICC) specific for each variable (chosen from compound symmetry, heterogeneous compound symmetry, autoregressive, and heterogeneous autoregressive). For all calf and placental data, calf sex was included in the model when $P \leq 0.25$. Binomial data (calf sex and percent unassisted births) were analyzed with only dam parity in the model using PROC GLIMMIX (distribution = binomial). In the absence of hour × parity interactions ($P > 0.10$), significant main effects are reported for calf metabolites over time. Least square means were separated using least significant difference, with differences considered when $P \leq 0.05$ and tendencies when $0.05 < P \leq 0.10$.

Results

Dam BW, BCS, and prepartum metabolites

There was an effect of parity ($P < 0.001$) on dam prepartum BW (Table 2), where multiparous dams had greater BW than primiparous dams. Despite this, parity did not affect ($P = 0.25$) dam postpartum BCS. Plasma triglyceride and serum urea N concentrations were greater ($P \leq 0.05$) in multiparous dams than primiparous dams pre-calving, but there was no effect of parity ($P \geq 0.37$) on prepartum plasma glucose or serum NEFA concentrations.

Fetal growth and placental size

Calves born to primiparous dams had 10% lower ($P = 0.04$) birth weight than calves born to multiparous dams, despite having the same sire and similar ($P = 0.47$) gestation length and percent male calves ($P = 0.22$; Table 3). Both heart girth and abdominal girth were also less ($P \leq 0.01$) for calves born to primiparous compared with multiparous dams. Dam parity did not affect ($P \geq 0.14$) shoulder to rump length or cannon circumference. There was no effect of dam parity ($P \geq 0.14$) on calf shape as measured by ponderal index or heart girth:length. Calf birth weight as a percent of dam prepartum BW ($P = 0.13$), as well as percent of calves born unassisted ($P = 0.98$) were also not affected by dam parity in this study.

Dry total placental weight was less ($P = 0.03$) in primiparous than multiparous dams (Table 4). This was driven by both the cotyledonary and intercotyledonary tissue masses, which were also less ($P \leq 0.05$) in primiparous dams. There was no effect of dam parity ($P \geq 0.14$) on number of cotyledons or average dry cotyledonary weight.

Table 2. Effect of parity on dam BW, BCS, and prepartum circulating metabolite concentrations (mean ± SEM)[1]

Variables	Parity[2]		*P*-value
	Primiparous	Multiparous	
Prepartum[3] body weight, kg	552 ± 14	661 ± 11	<0.001
Postpartum[4] body condition score	5.05 ± 0.13	5.23 ± 0.09	0.25
Prepartum[3] metabolites			
Plasma glucose, mg/dL	69.1 ± 1.3	68.8 ± 1.0	0.86
Serum non-esterified fatty acids, µEq/L	805 ± 54	744 ± 41	0.37
Plasma triglycerides, mg/L	250 ± 11	283 ± 8	0.02
Serum urea N, mg/dL	6.60 ± 0.49	7.85 ± 0.37	0.05

[1]Primiparous dam *n* = 18, multiparous dam *n* = 34.
[2]Primiparous dams were 2 yr of age, calving for the first time. Multiparous dams were 5.3 ± 2.9 (SD) yr of age, in parity 2 to 13.
[3]Determined at 6.7 ± 3.2 d (SD; range: 0 to 13 d) pre-calving.
[4]Determined at 6.3 ± 3.2 d (SD; range: 0 to 14 d) post-calving.

Table 3. Effect of dam parity on calf gestation length, size, and vigor (mean ± SEM)

Variables	Dam parity		*P*-value
	Primiparous	Multiparous	
Gestation length,[1] d	276.1 ± 0.8	275.4 ± 0.5	0.47
Calf sex, % male	38.9	57.1	0.22
Unassisted births, %[2]	94.4	100	0.98
Calf size[3]			
Birth weight, kg	32.3 ± 1.4	35.9 ± 1.0	0.04
Shoulder to rump length, cm	58.3 ± 0.9	59.9 ± 0.6	0.14
Heart girth, cm	72.4 ± 1.0	75.7 ± 0.7	0.01
Abdominal girth, cm	70.1 ± 1.2	74.4 ± 0.9	0.006
Cannon circumference, cm	12.2 ± 0.2	12.5 ± 0.1	0.16
Ponderal index,[4] kg/m^3	164 ± 6	167 ± 4	0.62
Heart girth:length[5]	1.24 ± 0.02	1.27 ± 0.01	0.14
Calf birth BW, % of dam prepartum BW	5.86 ± 0.21	5.46 ± 0.15	0.13
Calf vigor			
Time to stand,[6] min	32.3 ± 7.9	36.1 ± 5.8	0.70
Vigor score at 10 min[7]	3.25 ± 0.25	3.28 ± 0.20	0.91

[1]Primiparous dam *n* = 18, multiparous dam *n* = 35.
[2]One calf born to a primiparous dam was mechanically pulled. All others were born unassisted.
[3]Calves were weighed and measured at 20.5 ± 14.7 [SD] h of age. Primiparous dam *n* = 17, multiparous dam *n* = 35.
[4]Ponderal index = calf birth weight (kg)/ shoulder to rump length (m)^3.
[5]Ratio of heart girth (cm): shoulder to rump length (cm).
[6]Defined as time from birth to calf standing on all 4 legs for a minimum of 5 consecutive seconds. Range for all calves was 8 to 85 min. Primiparous dam *n* = 8, multiparous dam *n* = 15.
[7]Vigor scores using a scale of 1 (very weak) to 5 (extremely active and vigorous) and measured at 10 min of age. Primiparous dam *n* = 11, multiparous dam *n* = 17.

The intercotyldonary:cotyledonary mass ratio was also not affected ($P = 0.35$) by dam parity, supporting that both tissue types were greater in multiparous pregnancies. Average umbilical vessel diameter was also unaffected ($P = 0.54$) by dam parity. Lastly, placental efficiency was not affected by dam parity ($P = 0.11$), but did approach a tendency for primiparous dams to have more efficient placentas.

Neonatal calf vigor, rectal temperature, and metabolism

Vigor and rectal temperature

In this study, there was no effect of dam parity ($P \geq 0.70$) on calf time to stand or vigor score at 10 min of age (Table 3). Calf rectal temperature (Supplementary Fig. 1) was also unaffected ($P \geq 0.58$) by dam parity or its interaction with sampling hour. Rectal temperature was affected by sampling hour ($P = 0.05$), where it increased ($P = 0.06$) from 0 to 6 h of age, and then remained unchanged ($P \geq 0.32$) until 72 h.

Energy-related metabolites

There was an interaction of dam parity × hour ($P \leq 0.05$) for serum glucose, serum NEFA, and plasma triglyceride concentrations. Serum glucose (Figure 2A) was greater ($P = 0.03$) in calves born to primiparous dams at 0 h of age. Despite this, serum glucose in calves from multiparous dams was greater ($P \leq 0.04$) at 6, 12, 24, 48, and 72 h of age. In calves born to primiparous dams, serum glucose decreased ($P < 0.001$) from 0 to 6 h

Table 4. Effect of dam parity on placental size (mean ± SEM)[1]

Variables	Dam parity		*P*-value
	Primiparous	Multiparous	
Dry cotyledonary weight, g	116 ± 14	151 ± 10	0.05
Dry intercotyledonary weight, g	124 ± 8	147 ± 6	0.03
Dry total placental weight, g	240 ± 21	299 ± 15	0.03
Number of cotyledons	79.7 ± 5.8	80.2 ± 4.2	0.94
Average dry cotyledon weight, g	1.54 ± 0.20	1.92 ± 0.14	0.14
Intercotyledonary:cotyledonary mass ratio	0.94 ± 0.06	1.02 ± 0.05	0.35
Average umbilical vessel diameter, mm	7.19 ± 0.44	7.53 ± 0.32	0.54
Placental efficiency, kg calf birth BW/g placental DM	0.144 ± 0.009	0.126 ± 0.006	0.11

[1]Primiparous dam $n = 9$, multiparous dam $n = 18$. Calf birth weights for this subset: Primiparous, 31.7 ± 1.9 kg vs. Multiparous, 37.0 ± 1.3 kg; $P = 0.03$.

postnatally and then increased ($P < 0.001$) from 6 to 24 h before remaining similar ($P \geq 0.65$) for the remainder of the sampling period. In calves from multiparous dams, glucose concentration tended to increase ($P = 0.07$) from 0 to 6 h of age, then glucose increased from 6 to 24 h ($P < 0.001$) and 48 to 72 h ($P = 0.05$).

Serum NEFA (Figure 2B) were greater ($P \leq 0.02$) at 6, 12, and 24 h of age in calves born to primiparous dams compared with multiparous dams. Serum NEFA increased ($P = 0.002$) in calves born to primiparous dams from 0 to 6 h of age, tended to decrease ($P = 0.08$) from 6 to 12 h, and then decreased ($P \leq 0.04$) between 12 and 48 h before remaining similar ($P = 0.78$) between 48 and 72 h. In calves from multiparous dams, NEFA concentrations were unchanged ($P = 0.88$) from 0 to 6 h, tended to decrease ($P = 0.09$) from 6 to 12 h, and decreased ($P < 0.001$) between 12 and 24 h of age, before remaining similar ($P \geq 0.61$) until 72 h.

Plasma triglycerides (Figure 2C) were greater ($P < 0.001$) at 6 h and tended to be greater ($P = 0.06$) at 12 h in calves born to primiparous compared with multiparous dams. In calves from primiparous dams, plasma triglycerides increased ($P < 0.001$) from 0 to 6 h of age, with 0 h having lower ($P \leq 0.02$) concentrations than all other sampling times. Plasma triglycerides then decreased ($P = 0.001$) between 6 and 12 h, tended to decrease ($P = 0.10$) from 12 to 24 h, and increased ($P = 0.02$) again from 24 to 48 h of age but were unchanged ($P = 0.78$) from 48 to 72 h. In calves born to multiparous dams, plasma triglycerides at 6 h were not different ($P \geq 0.17$) from 0 or 12 h of age, but the same trend observed in primiparous was also observed in multiparous after 24 h.

Protein-related metabolites

There was an interaction ($P = 0.002$) of dam parity × hour for serum urea N concentration (Figure 3A), where calves born to primiparous dams had greater ($P = 0.04$) serum urea N at 12 h and tended to have greater ($P = 0.08$) serum urea N at 24 h. At 72 h of age, calves born to multiparous dams tended to have greater ($P = 0.07$) serum urea N. In calves born to primiparous dams, concentrations of urea N increased ($P \leq 0.004$) between 0 and 12 h of age, remained unchanged ($P = 0.75$) from 12 to 24 h, tended to decrease ($P = 0.06$) from 24 to 48 h, and then decreased ($P = 0.004$) from 48 to 72 h. Serum urea N was least ($P \leq 0.03$) in calves from primiparous dams at 0 and 72 h of age. In calves born to multiparous dams, urea N also increased ($P < 0.001$) from 0 to 6 h of age, remained unchanged ($P \geq 0.26$) from 6 to 24 h, tended to decrease ($P = 0.06$) from 24 to 48 h, and then increased ($P = 0.02$) from 48 to 72 h.

There was also an interaction of dam parity × hour ($P = 0.01$) for serum creatinine concentration (Figure 3B), where creatinine concentration was greater ($P \leq 0.03$) in calves born to primiparous dams at 12 and 24 h than those born to multiparous dams. Creatinine decreased ($P < 0.002$) from 0 to 6 h and 12 to 48 h of age before remaining unchanged ($P \geq 0.26$) from 48 to 72 h in calves from both primiparous and multiparous dams. In calves from multiparous dams, creatinine also decreased ($P < 0.001$) between 6 and 12 h.

There was no main effect of dam parity ($P \geq 0.52$) or interaction ($P \geq 0.23$) on serum total protein or globulin concentrations (Supplementary Fig. 2A and 2B). There was an effect of sampling hour ($P < 0.001$) for serum total protein and globulin, where both increased ($P \leq 0.002$) from 0 to 24 h, and then decreased ($P \leq 0.03$) from 24 to 72 h of age. There was no interaction of dam parity × hour ($P = 0.23$) for serum albumin (Supplementary Fig. 2D), but albumin tended to be greater ($P = 0.06$) in calves from primiparous dams than multiparous. Albumin was also affected ($P < 0.001$) by sampling hour, where serum albumin decreased ($P \leq 0.03$) from 0 to 24 h and increased ($P < 0.001$) from 24 to 48 h of age.

Hormones

Plasma insulin and cortisol concentrations were measured to investigate the cause of dam parity differences in circulating glucose. There was an interaction of dam parity × hour ($P = 0.04$) for insulin (Figure 4A). Insulin was greater ($P \leq 0.04$) in calves born to multiparous dams at 12, 48, and 72 h of age compared with those born to primiparous dams. There was no effect of hour ($P \geq 0.28$) on insulin in calves born to primiparous dams. In calves born to multiparous dams, plasma insulin did not change ($P \geq 0.11$) from 0 to 12 h, then decreased ($P = 0.05$) from 12 to 24 h, and increased ($P \leq 0.04$) from 24 to 72 h of age.

There was an effect of sampling hour ($P < 0.001$) but no effect of dam parity ($P = 0.20$) or dam parity × hour ($P = 0.18$) on calf plasma cortisol concentrations (Figure 4B). Cortisol decreased ($P \leq 0.001$) from 0 to 6 h and 12 to 24 h but was unchanged ($P \geq 0.28$) from 6 to 12 and 24 to 72 h of age.

Metabolic enzymes

Activities of serum AST, CK, and GGT were affected ($P \leq 0.02$) by the dam parity × hour interaction. Serum AST activity (Figure 5A) was greater ($P \leq 0.04$) at 6 and 24 h and tended to be greater ($P = 0.08$) at 12 h of age for calves born to

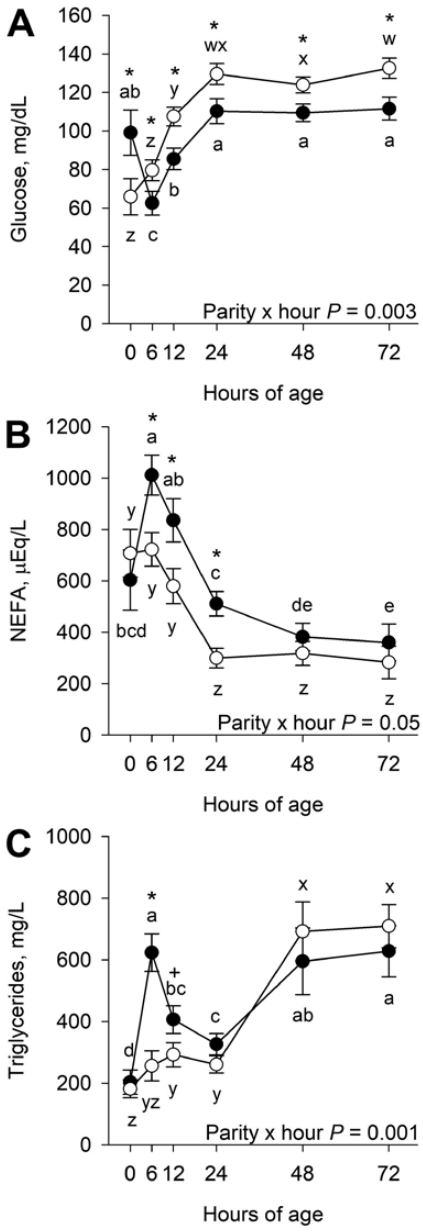

Figure 2. Effect of dam parity × hour interaction on serum glucose (Panel A), serum non-esterified fatty acid (NEFA; Panel B), and plasma triglyceride (Panel C) concentrations of neonatal spring-born beef calves. Least square means ± SEM are presented (n = 12 primiparous, n =16 multiparous). Solid circles (•) represent calves born to primiparous dams and open circles (○) represent calves born to multiparous dams. Parity means within hour *differ ($P \leq 0.05$), or +tend to differ ($P \leq 0.10$). Means differ ($P \leq 0.05$) for [abcde]calves born to primiparous dams across hours, and for [wxyz]calves born to multiparous dams across hours.

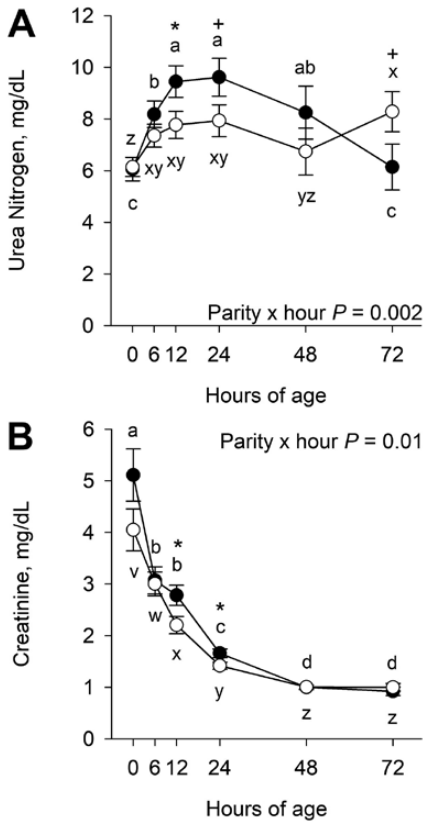

Figure 3. Effect of dam parity × hour interaction on serum urea N (Panel A) and creatinine (Panel B) concentrations of neonatal spring-born beef calves. Least square means ± SEM are presented (n = 12 primiparous, n = 16 multiparous). Solid circles (•) represent calves born to primiparous dams and open circles (○) represent calves born to multiparous dams. Parity means within hour *differ ($P \leq 0.05$), or +tend to differ ($P \leq 0.10$). Means differ ($P \leq 0.05$) for [abcd]calves born to primiparous dams across hours, and for [vwxyz]calves born to multiparous dams across hours.

primiparous dams. Serum AST from calves born to primiparous dams increased ($P \leq 0.05$) from 0 to 24 h, then decreased ($P < 0.001$) from 24 to 72 h of age. Calves from multiparous dams followed the same pattern, except that AST activity did not change ($P = 0.23$) from 12 to 24 h.

Calves born to primiparous dams had greater ($P = 0.01$) serum CK activity (Figure 5B) at 24 h and tended to have greater ($P = 0.06$) CK at 12 h. Serum CK increased ($P < 0.001$) from 0 to 6 h, decreased ($P \leq 0.007$) from 12 to 48 h, and remained unchanged ($P \geq 0.26$) from 6 to 12 and 48 to 72 h in calves from primiparous dams. The same pattern occurred for calves born to multiparous dams, except that 12 h tended to be greater ($P < 0.10$) than 24 h.

Serum GGT activity (Figure 5C) was greater ($P \leq 0.04$) for calves born to multiparous dams at 6, 12, and 24 h of age. Calves born to primiparous dams had GGT activity that increased ($P \leq 0.02$) from 0 to 12 h, remained unchanged ($P = 0.77$) from 12 to 24 h, decreased ($P = 0.01$) from 24 to 48 h, and remained steady ($P = 0.64$) from 48 to 72 h. Calves born to multiparous dams had the same pattern in serum GGT, except that its activity also decreased ($P < 0.001$) from 12 to 24 h of age.

Electrolytes and other blood chemistry parameters

Neonatal calf serum electrolyte concentrations are shown in Supplementary Fig. 3. Sodium, chloride, phosphorus, and magnesium concentrations were affected ($P \leq 0.05$), and calcium concentration tended to be affected ($P = 0.09$) by the interaction of dam parity × hour. Serum sodium was greater ($P = 0.002$) for calves born to multiparous dams at 0 h, but was greater ($P = 0.03$) in calves born to primiparous dams at 12 h. Calves from primiparous dams tended to have greater ($P \leq 0.10$) calcium at 0 and 24 h of age compared with multiparous. Serum chloride was greater ($P \leq 0.04$) in calves from multiparous dams at 0 and 24 h. Calves born to primiparous dams had greater ($P = 0.04$)

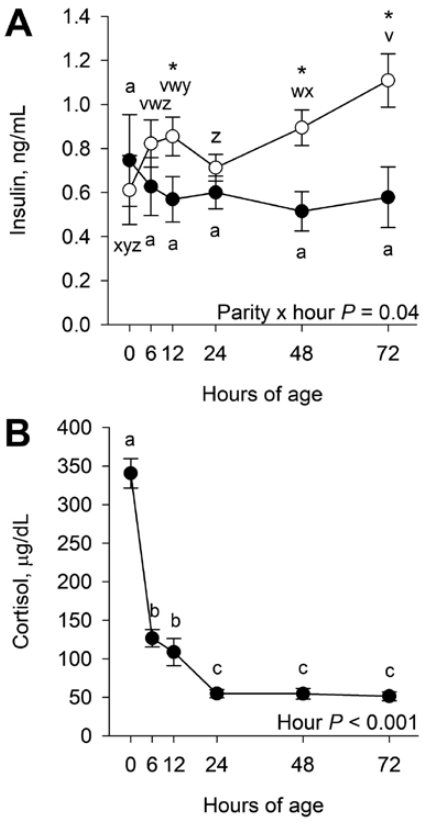

Figure 4. Effect of dam parity × hour interaction on plasma insulin (Panel A) and effect of sampling hour on plasma cortisol (Panel B) concentrations of neonatal spring-born beef calves. Least square means ± SEM are presented (n = 12 primiparous, n = 16 multiparous). Solid circles (•) represent calves born to primiparous dams (or main effect means, n = 28) and open circles (○) represent calves born to multiparous dams where there is dam parity × hour interaction. Parity means within hour *differ ($P \leq 0.05$). Means differ ($P \leq 0.05$) for [abc]calves born to primiparous dams (or hour means for main effect of hour) across hours, and for [vwxyz]calves born to multiparous dams across hours.

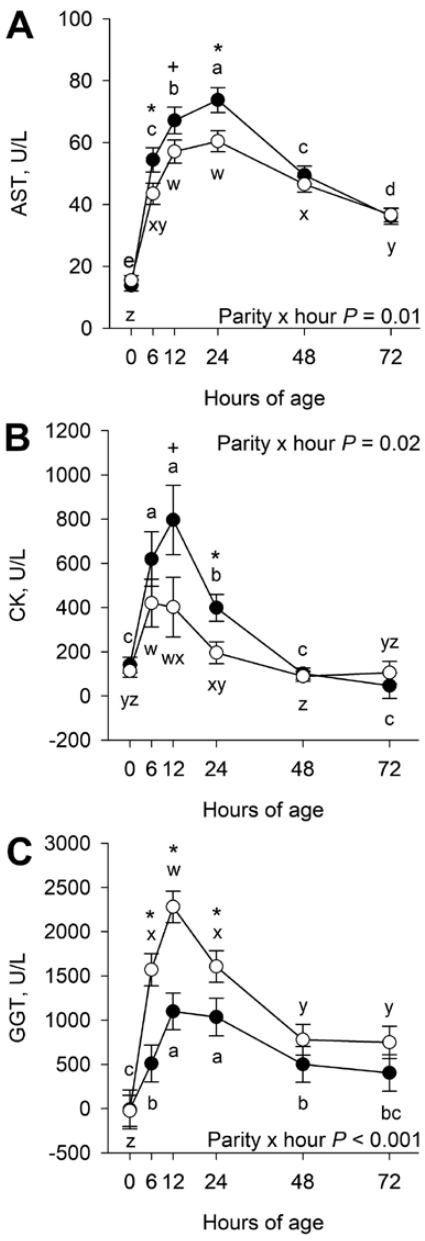

Figure 5. Effect of dam parity × hour interaction on serum aspartate aminotransferase (AST; Panel A), creatine kinase (CK; Panel B), and gamma-glutamyl transpeptidase (GGT; Panel C) activities of neonatal spring-born beef calves. Least square means ± SEM are presented (n = 12 primiparous, n = 16 multiparous). Solid circles (•) represent calves born to primiparous dams and open circles (○) represent calves born to multiparous dams. Parity means within hour *differ ($P \leq 0.05$), or +tend to differ ($P \leq 0.10$). Means differ ($P \leq 0.05$) for [abcde]calves born to primiparous dams across hours, and for [wxyz]calves born to multiparous dams across hours.

phosphorus at 0 h, but less (P = 0.01) phosphorus at 48 h, compared with multiparous. Serum magnesium tended to be greater (P = 0.10) in calves born to multiparous dams at 72 h. Serum potassium concentration was not affected (P = 0.79) by the interaction of dam parity × hour, but was affected by main effects of dam parity (P < 0.001) and sampling hour (P < 0.001). Calves born to multiparous cows had greater (P < 0.001) serum potassium than those born to primiparous. Serum chloride is the only electrolyte for which patterns of change over 72 h varied widely between calves from dam parities.

Serum bicarbonate and anion gap concentrations (Supplementary Fig. 4A and 4B) were affected ($P \leq 0.05$) by the interaction of dam parity × hour. Serum bicarbonate was greater (P = 0.01) for calves born to primiparous dams at 24 h of age compared with multiparous. Additionally, anion gap tended to be less (P = 0.08) at 12 h, but was greater (P = 0.03) at 72 h, for calves born to multiparous calves.

There was an interaction of dam parity × hour ($P \leq 0.03$) for both total and direct bilirubin concentrations (Supplementary Fig. 4C and 4D). Calves born to primiparous dams had greater ($P \leq 0.02$) total bilirubin and direct bilirubin at 12 and 24 h of age. Despite this, direct bilirubin was greater (P = 0.04) for calves from multiparous dams at 6 h.

Discussion

Fetal and placental growth

Beef calves born to primiparous dams are generally smaller than those born to multiparous dams, which has been demonstrated both in planned gestational feeding experiments (Bellows et al., 1982; Doornbos et al., 1984) and analysis of large datasets (Knapp and Lambert, 1940; Dawson et al., 1947; Burris and Blunn, 1952; Koch and Clark, 1955; Bourdon and Brinks, 1982). In the current study, calves born to first-parity

heifers weighed 10.0% less than those born to multiparous cows, which is comparable to the 10.5% and 7.4% reductions observed by Bellows et al. (1982) and Doornbos et al. (1984), respectively. Other calf size data indicate that girth may have been decreased to a greater degree than skeletal size. Despite this, similar ponderal index and heart girth:length supports that calves born to first-parity dams were likely smaller overall rather than having disproportionate growth, which is in agreement with work of Bellows et al. (1982).

Differences in birth weight were not due to gestation length in the current study, although gestation length differences due to parity have been variable in beef cattle (Knapp and Lambert, 1940; Reynolds et al., 1980; Bellows et al., 1982; Bourdon and Brinks, 1982). Although the distribution of male calves was uneven between parity groups, calf sex was tested in all calf data statistical models as described in the statistical analysis methods. For size measures, calf sex was only included in the final model for heart girth, indicating that calf sex did not greatly affect fetal growth in this study. Additionally, use of a single AI sire prevented differential fetal growth due to selection of sires for heifers versus cows. Previously it has been suggested that intrauterine growth restriction in first-parity females can be attributed solely or predominantly to maternal BW (Reynolds et al., 1980) because calf birth weights are positively correlated with dam BW (reviewed by Holland and Odde, 1992). In the current study, however, calf birth weight as a percentage of cow BW approached a tendency for primiparous dams to have larger calves per BW. Prepartum maternal (gravid) BW were 16% less in first-parity heifers compared with birth weights that were 10% less, which supports that their maternal weight difference was greater than that of their calves. It has also been hypothesized that the competition of nutrient partitioning between maternal growth and pregnancy may result in decreased fetal growth for calves born to heifers, especially given the immature size (85% of mature BW recommended) at which beef heifers calve under current U.S. management recommendations for Bos taurus-based females (Holland and Odde, 1992; Wu et al., 2006). Although greater prepartum plasma triglycerides and serum urea N of multiparous females may indicate greater relative nutrient intake, similar NEFA and BCS pre-calving suggest that first-parity females were not mobilizing greater body stores to support late pregnancy. Less long-chained fatty acids of dietary origin and carbon skeletons of amino acids may have been available to support fetal growth and colostrogenesis in first-parity dams, but more sampling of late pregnant primiparous and multiparous dams under similar nutritional management is necessary to answer this question more definitively. First-parity females are likely to consume less forage due to their smaller body size despite their additional requirements for growth, but cows also have greater maintenance requirements given their larger body size. More controlled feeding experiments are necessary to attempt to discern the role of intake versus requirements in parity differences, as they cannot be determined in the current study.

Given that first-parity livestock (Wu et al., 2006) and human (Shah, 2010) females give birth to offspring with lower birth weights, the first use of the uterus and adaptation to pregnancy may not allow for optimal fetal growth. In the current study, placental growth was disproportionately impaired compared with fetal growth. Placental mass was 20% less in primiparous vs. multiparous dams, whereas birth weight of the subset of calves whose placenta was successfully collected was 14% less, leading to a greater placental efficiency for primiparous dams that approached a tendency. Others have previously reported that primiparous Belgian Blue (Van Eetvelde et al., 2016) and Holstein (Kamal et al., 2017) dams have less placental mass than multiparous cows, and placental efficiency also was greater for first-parity Belgian Blue dams (Van Eetvelde et al., 2016). More efficient placentas of pregnant heifers would indicate that the fetal growth is greater than expected given the size of the placenta, suggesting that other uteroplacental mechanisms allow for greater nutrient transport. Blood flow to the uteroplacenta or transporters within these tissues may play a role, but they have not been compared by parity in cattle to our knowledge.

Neonatal calf vigor, metabolism, and stress

Calves likely experienced cold stress after birth in the current study based on ambient temperatures shown in Figure 1, as the minimum daily temperatures were below the estimated lower critical temperatures for neonatal calves (Carstens, 1994). Given that smaller calves are more likely to be affected by cold stress due to surface area:body mass, calves born to primiparous females were likely at a disadvantage. Although ambient temperatures varied within this short study, cold stress likely affected all aspects of early neonatal calf physiology, including vigor at birth, ability to maintain body temperature, and energy requirements for thermogenesis of all calves. Thus, results of the current study may differ for calves born in the fall calving season or a more thermoneutral climate.

Dam parity did not appear to affect calf vigor at birth in the current study in contrast to previous observations in ruminant neonates. Offspring born to first-parity dams were less vigorous in sheep (Dwyer, 2003; Dwyer et al., 2005) and dairy cattle (Edwards, 1982) studies, but limited data are available for beef cattle. Reduced vigor has been reported in calves from assisted deliveries (Barrier et al., 2012; Homerosky et al., 2017b), suggesting that vigor differences in many studies may be caused by difficulty of labor. Therefore, the lack of parity difference in our study may be driven by the low rate of dystocia in our primiparous dams (1 of 18). Variation in ambient temperatures during the calving period (Figure 1) likely also influenced the range in time to stand (8 to 85 min) observed in the current study, and possibly negated any advantage of calves born to multiparous dams.

Despite lower birth weight of calves born to primiparous dams, it does not appear that calves from primiparous dams had more difficulty maintaining body temperature in the cold temperatures compared with calves from multiparous dams in the current study. Furthermore, rectal temperatures indicate that calves born to both parity groups experienced cold stress at birth, but increased body temperature in the first 6 h of life. This is likely because the cold ambient conditions of calving (Figure 1) caused heat loss immediately after birth, but use of brown adipose tissue and increased metabolism allowed for thermogenesis (Carstens, 1994). The pattern observed for rectal temperature differs from that observed for fall-born calves by our lab (Larson-Peine et al., 2022) but is similar to other spring-born calf data (Hadorn et al., 1997; Egli and Blum, 1998).

Even though calves born to primiparous and multiparous dams had similar vigor and rectal temperatures in this study,

their metabolic status diverged in the early neonatal period while they experienced cold stress. In general, neonatal calf serum chemistry changes over time were similar to those reported by our lab in fall-born beef calves (Larson-Peine et al., 2022), and calves born to multiparous cows had a more similar pattern to these previously reported values when dam parity differences occurred.

Calves born to first-parity dams appeared to mobilize more energy stores during cold stress, as demonstrated by greater NEFA at 6 to 24 h of age. This lipolysis may have been necessary to provide energy following rapid depletion of glycogen immediately after birth. Because fetal ruminants have low circulating glucose and lactose consumption from colostrum does not typically meet glucose needs of the neonate, the increase of glucose observed postnatally also comes from glycogenolysis and gluconeogenesis, and ability for the latter increases after colostrum consumption (Hammon et al., 2013). Pre-suckling, serum glucose was greater in calves born to primiparous dams, suggesting greater glycogenolysis immediately after birth. These calves born to primiparous dams then had less circulating glucose after colostrum consumption in this study, which may indicate that they had access to less colostrum and early milk postnatally (and therefore less lactose intake), had less glycogen storage prenatally, or had impaired gluconeogenic pathways due to poor fetal development or signaling from colostrum. If one or all of these mechanisms affected calves born to first-parity dams cannot be determined from this dataset, but future research in this area is warranted due to the importance of glucose metabolism in neonatal calves (Hammon et al., 2013). In the current study, calves from first-parity heifers had elevated plasma triglycerides for a short time after colostrum consumption, possibly due to greater lipid concentration of colostrum from heifers (Kume et al., 2003; Dunn et al., 2017). Despite this, their elevated NEFA indicate mobilization of fat stores, likely to maintain body temperature given decreased circulating glucose post-suckling. Brown adipose tissue uses NEFA and glucose as substrates, and muscle can also use NEFA for thermogenesis (Carstens, 1994). Greater serum urea N in calves born to primiparous dams may also suggest greater deamination of amino acids for gluconeogenesis (Hammon et al., 2013), but the neonate's high rate of protein synthesis may limit amino acid catabolism (Girard et al., 1992).

Although first-parity dams are generally thought to have less colostrum production (McGee and Earley, 2019), better understanding of parity effects on colostrum yield and nutrient composition would aid in interpreting metabolic differences observed here. Greater insulin of calves born to multiparous cows was expected due to greater serum glucose, but likely also indicates greater nutrient intake from colostrum overall (Hammon et al., 2013). Lower serum GGT concentrations in calves born to primiparous dams may indicate that they consumed less colostrum (Perino et al., 1993), further suggesting decreased colostrogenesis in first-parity heifers despite the lack of parity difference in passive transfer as determined by serum total protein. Conversely, insulin secretion or regulation may have been developmentally-impaired in calves born to primiparous dams, as has been observed in intrauterine growth restricted offspring of multiple species (reviewed by Mohan et al., 2018).

Calves born to first-parity heifers had multiple indicators of metabolic stress as neonates, despite a lack of dam parity effect on neonatal plasma cortisol in this study. Many of these variables suggest increased trauma or are often associated with dystocia, even though assistance at parturition was necessary for only one calf in the current study. Duration of labor was not measured in this dataset, but increased calving difficulty for first-parity heifers relative to cows is well-established (Bellows et al., 1982; Berger et al., 1992; Zaborski et al., 2009), and length of parturition was greater for heifers in one study (Doornbos et al., 1984). Laster and Gregory (1973) reported that calf mortality within 24 h of birth was greater for calves born to heifers compared with cows when parturition was unassisted, and hypothesized that longer duration of calving and/or births that were more difficult without needing assistance caused this increase in death. In the current study, parturition itself may have caused the differences observed, or other stress-related differences may have existed that did not result in altered cortisol at the pre-suckling sampling time.

In the current study, calves born to primiparous dams had greater circulating glucose at 0 h than calves born to multiparous dams, despite age at this pre-suckling sampling being unaffected by parity (P = 0.77, data not shown). Homerosky et al. (2017a) also observed this parity difference at 10 min of age in beef calves. Neonatal glucose is known to increase rapidly after birth in ruminants (Comline and Silver, 1972), as elevated cortisol signals for increased fetal endogenous glucose production shortly before birth (Fowden and Forhead, 2022). Calves born with assistance during parturition due to dystocia had elevated glucose prior to consuming colostrum previously (Bellows and Lammoglia, 2000; Civelek et al., 2008; Vannucchi et al., 2015). Calf circulating glucose and cortisol concentrations at birth have also been positively correlated both in previous studies (Massip, 1980; Vannucchi et al., 2015), and in our current study despite the lack of difference in cortisol due to parity (r = 0.50, P = 0.02). In addition to cortisol, catecholamines, along with glucagon, stimulate hepatic gluconeogenesis (Fowden and Forhead, 2022). Fetal catecholamine production increases during parturition, and can be further stimulated by hypoxia or hemorrhage (Sperling et al., 1984). Although catecholamines decrease postnatally, cortisol increases shortly after birth (Nagel et al., 2019). Thus, calves born to first-parity dams in the current study likely had elevated pre-suckling glucose due to stress response. The sampling scheme in this study may have missed the stress response responsible for the glucose alterations. This hyperglycemia pre-suckling likely contributed to the later hypoglycemia of calves born to primiparous dams (Vannucchi et al., 2015), and negative correlations between circulating glucose and cortisol existed at all other sampling hours except 24 h (r = –0.39 to –0.60, $P \leq 0.06$) for neonatal calves in the current study.

Other indicators of physiological stress were evident post-suckling in calves born to first-parity dams. Serum AST and CK enzyme activities were greater within the first 24 h of life, suggesting muscle damage or ischemia (Russell and Roussel, 2007). Previously, Pearson et al. (2019) observed calves whose birth was classified as a difficult assist had greater AST and CK at 24 h compared with unassisted and easy assist categories. Additionally, both AST and CK were greater for calves with measures associated with trauma at birth (Pearson et al., 2019). Serum creatinine was also greater for calves born to primiparous dams at 12 h, which may itself also indicate trauma (Perrone et al., 1992) given that smaller calves were unlikely to have greater muscle mass. Calves born to

primiparous dams also had elevated total and direct bilirubin at 12 and 24 h in this study, suggesting greater red blood cell breakdown and/or competitive binding of albumin by NEFA that decreased bilirubin metabolism in the liver (Hadorn et al., 1997).

Effects of dam parity on acid-base and electrolyte balance in this study were variable, as some measures show inconsistent trends (e.g. anion gap is greater for each parity, depending on the sampling time). These data suggest that calves born to first-parity females were not necessarily suffering from metabolic acidosis. Moreover, electrolyte concentrations may be related to maternal electrolyte balance, as dam parity affected plasma calcium and phosphorus, as well as colostrum sodium and potassium in dairy cows in another study (Kume et al., 2003).

Potential impacts for calf survival

Although there was no early calf morbidity and mortality for calves in the current dataset, this would be unlikely in a less intensive management system, as collection of research data ensured nearly continuous monitoring of calves. Calves born to first-parity heifers have greater death losses pre-weaning (Patterson et al., 1987; Berger et al., 1992; Nix et al., 1998), and intrauterine growth restriction likely contributes to the increased pre-weaning mortality of calves born to primiparous dams, as development or maturity at birth may be impaired (Perry et al., 2019). Further research is necessary to determine if first-parity beef heifers are able to partition nutrients adequately during pregnancy to allow for fetal growth to meet calves' genetic potential and improve calf survival. Given that calves born to heifers have often been smaller at birth even in controlled nutrition studies, greater nutrient intake alone may not provide for maximal fetal growth.

When born into cold conditions, smaller size at birth further challenges calves born to primiparous dams. Possible management strategies to ensure survival of calves born to first parity dams may include providing more shelter from precipitation and wind and supplementing colostrum to support calves in negative energy balance. Limited data have compared calves born to heifers and cows born into more thermoneutral conditions, so this is necessary to determine if spring-born calves are of greater concern than fall-born calves of primiparous dams.

Producers reported in one study that they check heifers more frequently than cows during the calving season (Dargatz et al., 2004). Our data support this management strategy, especially given that calves born to first-parity dams in our study showed more signs of stress than expected given the limited dystocia. If calves born to heifers begin life more metabolically-stressed, monitoring them more closely during the early neonatal period is also warranted to minimize mortality with swift intervention for signs of metabolic acidosis or disease.

Conclusion

Data from the current study indicate that calves born to first-parity heifers had altered nutrient availability during both the prenatal and neonatal periods. Calves born to primiparous dams weighed less at birth, likely due in part to their smaller placentas. Although they had similar vigor and ability to maintain body temperature as calves born to multiparous cows, neonatal calves born to primiparous dams had greater energy reserve mobilization and lower insulin, despite greater circulating triglycerides. Calves born to first-parity dams also had greater metabolic indicators of stress during the first 72 h of life even though minimal dystocia existed in this group of animals. Overall, these effects may have increased morbidity and mortality of calves born to first-parity heifers had they been in a less intensive management system. Therefore, these data add to the literature not only possible mechanisms by which calves born to primiparous dams are born at greater risk, but also provide opportunity for their improved management.

Supplementary Data

Supplementary data are available at *Journal of Animal Science* online.

Acknowledgments

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Conflict of Interest Statement

Authors have no conflict of interest to disclose.

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