Effects of Genetic Selection for Milk Yield on Somatotropin, Insulin-Like Growth Factor-I, and Placental Lactogen in Holstein Cows¹

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ABSTRACT

Cows from static, low-merit control (CL) and contemporary, high-merit select (SL) lines that differed in milk yield by more than 4,000 kg/305-d lactation (SL > CL) were used to determine effects of selection for milk yield on blood serum concentrations of somatotropin (ST), insulin-like growth factor (IGF-I), and placental lactogen (PL). Cows were exposed to the same environment and management conditions and fed the same diets. Serum and milk samples were collected from primiparous (18 CL, 18 SL) and multiparous (12 CL, 18 SL) cows relative to day of lactation (from –28 to 280 d for nonpregnant cows and to subsequent calving for cows that conceived). Data were analyzed as repeated measures using mixed model procedures. Serum ST increased at calving, remained elevated for a longer interval in SL than in CL cows, and was greater in SL than in CL cows. Serum IGF-I decreased at calving, remained low through 14 DIM, and gradually returned to precalving concentrations as lactation progressed. Postpartum concentrations of IGF-I were less in SL than CL through 84 DIM and were similar through the remainder of lactation, resulting in a line by day interaction. Serum IGF-I and PL were not affected by merit during gestation. There was an interaction of merit and postconception interval on IGF-I, with the difference in IGF-I concentration between lines decreasing as gestation progressed. Change in serum IGF-I and PL appeared to be synchronous. Results indicate that selection for milk yield increased serum ST, prolonged the postpartum reduction in serum IGF-I, and did not alter serum PL. Results also indicate a positive relationship between PL and IGF-I and support the concept that PL plays a role in the regulation of serum IGF-I during gestation.

Key words: milk yield, somatotropin, insulin-like growth factor-I, placental lactogen

INTRODUCTION

Somatotropin (ST) and IGF-I are important regulators of nutrient use and tissue function (Bauman, 2000). Vascular concentrations of ST and IGF-I are coupled (positive relationship) when animals are in positive nutrient and energy balance and are uncoupled (negative or no relationship) during periods of nutrient and energy insufficiency (Vicini et al., 1991; Thissen et al., 1994; McGuire et al., 1995). The relationship between ST and IGF-I is not constant and can be influenced by several other factors including environment (Collier et al., 2005), physiological status (Vicini et al., 1991; Reist et al., 2003), and genetic merit (Knight et al., 2004).

Cows experience several endocrine alterations as they transition through each lactation cycle. The relationship between vascular ST and IGF-I during these transitions has been characterized for the contemporary cow (Abribat et al., 1990; Sharma et al., 1994) but apparently not in the same set of cows through this complete series of transitions (Reist et al., 2003). Increased genetic merit for milk yield has been associated with increased serum ST (Beerepoot et al., 1991) and decreased IGF-I (Knight et al., 2004), but other than the early lactation data from Knight et al. (2004), there appear to be no published reports on circulating ST and IGF-I concentrations in cows of different genetic merit that were sampled repeatedly during these transitions.

Placental lactogen (PL) increases during gestation, and the magnitude of this increase has been suggested to have roles in alterations of maternal and fetal metabolism that differ among species (Gootwine, 2004). There is evidence that PL exerts at least part of its effects through the IGF system (Handwerger and Freemark, 2000) and administration of bovine PL to dairy cows has increased circulating IGF-I concentrations (Byatt et al., 1992, 1997; Lucy et al., 1994); however, elucidation of the regulation of PL secretion and its functions remain incomplete (Bertolini et al., 2006). In addition, evaluations of the relationship between endogenous PL

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and IGF-I in the cow (Holland et al., 1997; Hossner et al., 1997) are scarce, have used few animals, and have not included effects of selection for increased milk yield.

The overall objective of this study was to describe lactational and physiological characteristics of Holstein cows from genetic lines that differ substantially in milk yield. Our specific objective was to determine the effects of genetic selection for milk yield on blood serum concentration profiles of ST, IGF-I, and PL and their interrelationships during lactation and gestation.

MATERIALS AND METHODS

Animal Management

Cows were from 2 genetic lines of Holsteins maintained under identical environment and management practices in free-stall facilities at the University of Minnesota Southern Experiment Station in Waseca, Minnesota. Development of the static, low-merit control line (CL) and the contemporary, high-merit select line (SL) was initiated in 1964 by Charles Young as a component of a multistate, north central regional project (NC-2; Young, 1977; Hansen, 2000). The original foundation cows were paired by genetic merit and assigned to either a low- or high-merit line. The high-merit SL cows and their female descendants were inseminated with semen from the highest PTA-milk sires ($n = 4$) available each year. From 1964 to 1991, the low-merit CL cows and their female descendants were bred with semen from sires (4 sires/yr in a 5-yr rotation) that were breed average for PTA-milk in 1964. Since 1991, breeding the low-merit CL cows and their female descendants has continued according to the original design, except semen was from sons of the original 20 low-merit CL bulls. Coefficients of inbreeding were not allowed to exceed 6.25% for low- or high-merit cows (Jones et al., 1994; Hansen, 2000). Genetic merit (PTA-milk) of the low-merit CL cows remained stable while PTA-milk for the high-merit SL cows continued to increase (Figure 1). Thus, the high-merit SL cows represent contemporary US Holsteins and the low-merit CL cows represent average US Holsteins in 1964. The primiparous (18 CL, 18 SL) and multiparous (12 CL, 18 SL) cows used in this study were born within a 4-yr period and represented offspring from 12 CL sires and 28 CL dams or 20 SL sires and 33 SL dams.

Animal care and experimental procedures were approved by the University of Minnesota Institutional Animal Care and Use Committee. Animals were observed daily for health abnormalities and treated when warranted. Cows were milked at 12-h intervals and daily yields were determined from recorded milk weights. Cows were group-fed a TMR designed to meet their nutritional needs (NRC, 1989). All nonlactating

Figure 1. Effect of selection for milk yield on PTA-milk of static, low-merit control line (CL) cows and contemporary, high-merit select line (SL) cows. The PTA-milk values for individual cows were obtained (USDA, May 2005) and summarized by line and year of birth. Data points are means (from an average of 19 CL and 23 SL cows per year). The average SE was 105 kg for CL and 150 kg for SL cows.

cows consumed the same dry-cow TMR. All cows consumed the same early-lactation TMR from calving until at least 45 DIM. After 45 DIM, they were switched to a less energy-dense TMR when milk production warranted. These rations were composed primarily of corn silage, alfalfa haylage, high-moisture corn, cottonseed, and soybean meal. Reproductive management data (insemination, dry-off, and calving dates) were recorded.

Coccygeal blood samples were collected at -28 ± 7 , -14 ± 3 , -7 ± 2 , 1, 2, 3, 7, 14, 21, and 28 DIM and at 28 ± 3 d intervals thereafter until 280 DIM (nonpregnant) or throughout pregnancy. Cows that conceived after 235 DIM were considered nonpregnant for the purposes of this study. Blood was collected into evacuated tubes (Vacutainer Beckton Dickinson and Co., Franklin Lakes, NJ) and stored overnight at 4°C. Serum was harvested ($1,200 \times g$, 15 min) and stored at -20°C until assayed. All serum samples were analyzed for ST and IGF-I, and all samples collected after conception were analyzed for PL. Samples collected on -28 , -14 , -7 , 2, 7, 21, 28, 56, 84, 168, and 280 DIM were analyzed for NEFA.

Milk samples from the morning milking were obtained at 1, 2, 3, 7, 14, 21, and 28 DIM and at 28-d intervals thereafter until 280 DIM. Milk samples (30 mL) were preserved with potassium dichromate and analyzed for fat, protein, and lactose by infrared analyses and for SCC by fluorescent detection of ethidium bromide incorporation into DNA (Minnesota DHIA, Zumbrota, MN). Body weights were determined at time of blood sampling except at 2 and 3 DIM.

Serum Analyses

Serum IGF-I concentrations were quantified by using a validated double-antibody RIA (Johnson et al., 1996)

with slight modifications. Recombinantly derived human IGF-I (H-5555, lot C00219, Bachem, Torrance, CA) was used as the standard and as the iodinated tracer. The IGF-I was iodinated as described by Cohick et al. (1989) with a slight modification. The amount of IGF-I iodinated was reduced to 1 μ g and reaction time of IGF-I and I-125 (NEZ-033H, PerkinElmer Life Sciences, Boston, MA) was increased to 5 min. The first antibody (rabbit anti-hIGF-I, UB2-495, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD) and tracer were added to the assay tubes and incubated for 24 h prior to addition of the second antibody (goat antirabbit, lot #35318, Pel-Freez, Rogers, AK). Samples were analyzed in triplicate. The minimal detectable concentration of IGF-I was 0.2 ng/mL of standard or sample added to the assay tubes. Intra- and interassay coefficients of variation were 2.7 and 3.3%, respectively.

Serum PL concentrations were quantified using a validated double-antibody RIA (Wallace, 1993). Recombinantly derived bovine PL (lot bPL 920514-10, Monsanto, St. Louis, MO) was used as standard and iodinated tracer. The PL was iodinated as described by Wallace (1993). Prior to use, the first antibody (USDA anti-bPL F56) was diluted 1:15,000 and the second antibody (sheep antirabbit, cat. #R-6503, Sigma, St. Louis, MO) was diluted 1:16. Samples were analyzed in duplicate. The minimal detectable concentration of PL was 0.5 ng/mL of standard or sample added to the assay tubes. Intra- and interassay coefficients of variation were 9.7 and 10.2%, respectively.

Serum ST concentrations were quantified using a validated double-antibody RIA (Gorewit, 1981). Recombinantly derived bovine ST (SV-3001-B, Pharmacia & Upjohn, Kalamazoo, MI) was used as the standard and as the iodinated tracer. The ST was iodinated as described by Cohick et al. (1989). Prior to use, the first antibody (rabbit anti-oGH2, AFP C0123080, National Institute of Diabetes and Digestive and Kidney Diseases) was diluted 1:20,000 and the second antibody (goat antirabbit, lot #35318, Pel-Freez) was diluted 1:75. Samples were analyzed in triplicate. The minimal detectable concentration of ST was 0.7 ng/mL of standard or sample added to the assay tubes. Intra- and interassay coefficients of variation were 3.1 and 6.8%, respectively.

Serum NEFA concentrations were quantified spectrophotometrically (NEFA-C, Wako Chemicals, Richmond, VA) as described by Sechen et al. (1990) but volumes were adjusted for use in a 96-well plate. Intra- and interassay coefficients of variation were 4.7 and 7.5%, respectively.

Calculations and Statistical Analyses

Daily milk yields were summarized within line and parity by week of lactation (**WOL**) from 1 to 40 WOL. Milk components were summarized within line and parity from 1 to 280 DIM. Fat- (3.5% FCM) and solids- (4% SCM) corrected milk yields were calculated from milk, fat, protein, and lactose yields (Tyrrell and Reid, 1965). Yields of milk components (kg/d) were determined for each WOL using weekly milk yields and milk composition data determined within the specific week (wk 1 to 4) or within 4-wk intervals. Milk SCC were log transformed before the summaries were conducted. Daily milk yields (1 to 280 DIM) for each cow were fitted to a modified Wood's equation (Ferguson et al., 2000) and coefficients used to generate smooth curves. The smooth curves were used to identify peak milk, days to peak milk, and rates of increase (from calving to peak DIM) and decrease (from peak DIM to 280 d) in daily milk yields for each cow. Genetic merit (PTA-milk) of foundation cows and their female offspring were obtained (USDA, May 2005) and summarized by line and year of birth from 1964 to 2003.

Data from multiparous ($n = 13$ SL, $n = 10$ CL) and primiparous ($n = 17$ SL, $n = 15$ CL) cows that became pregnant prior to 235 DIM were used to evaluate effects of selection for milk yield on endocrine relationships during gestation. During gestation, serum PL, ST, and IGF-I data were analyzed from the first sample collected after conception to calving. Because the sampling scheme was based on DIM, data from the gestation period were reported as means for each 28-d interval postconception (**IPC**) and analyzed from IPC 1 to 10.

All statistical analyses were conducted with SAS programs (2001, SAS Inst. Inc., Cary, NC). Yields of milk and milk components were analyzed as a completely randomized design by the mixed model procedure for repeated measures and used first order autoregressive as the covariance structure and WOL as the repeated effect. Milk composition, BW, and serum data were analyzed by the same model but used the spatial power law for unequally spaced data as the covariance structure and DIM or IPC as the repeated effect. The models contained the variable mean, line, parity, WOL (or DIM or IPC), all interactions, and error. Results are reported as least squares means and means differed when $P < 0.05$.

Pearson correlation coefficients (PROC CORR, SAS Inst. Inc.) were used to evaluate relationships among circulating concentrations of ST, IGF-I, and PL during gestation. The relationship between maternal serum PL and calf birth weight was assessed by linear regression (PROC REG, SAS Inst. Inc.). Correlation and regression coefficients were classified as weak (absolute

Table 1. Effect of genetic merit for milk yield on yield and composition of milk and on BW during wk 1 to 40 of lactation¹

Variable	Genetic line $\times$ parity ²					<i>P</i> ³					
	CLPP	SLPP	CLMP	SLMP	SEM	Line	Parity	L $\times$ P ⁴	L $\times$ T ⁴	P $\times$ T ⁴	L $\times$ P $\times$ T ⁴
Milk, kg/d											
Unadjusted	18.9 ^a	28.3 ^b	22.1 ^a	36.1 ^c	1.2	0.001	0.001	0.053	0.001	0.001	0.605
3.5% FCM	20.1	27.7	21.7	33.5	1.1	0.001	0.002	0.063	0.001	0.001	0.382
4.0% SCM	18.7 ^a	25.6 ^b	20.1 ^a	31.2 ^c	1.0	0.001	0.001	0.041	0.001	0.001	0.317
Fat											
%	3.98	3.78	3.74	3.35	0.13	0.024	0.011	0.449	0.006	0.024	0.105
kg/d	0.74	0.95	0.75	1.10	0.04	0.001	0.073	0.115	0.039	0.001	0.445
Protein											
%	3.51 ^b	3.20 ^a	3.54 ^b	3.49 ^b	0.05	0.002	0.005	0.017	0.891	0.064	0.767
kg/d	0.62 ^a	0.85 ^b	0.72 ^a	1.15 ^c	0.03	0.001	0.001	0.006	0.001	0.001	0.692
Lactose											
%	4.77	4.78	4.46	4.60	0.05	0.184	0.001	0.218	0.001	0.001	0.041
kg/d	0.93	1.40	1.04	1.72	0.05	0.001	0.001	0.059	0.001	0.001	0.273
SCC, log ₁₀	5.05	4.94	5.08	5.12	0.09	0.757	0.283	0.461	0.001	0.002	0.447
BW, kg	537	565	644	640	15	0.414	0.001	0.288	0.001	0.006	0.058

^{a-c}Line by parity means within a row with different superscripts differ ($P < 0.05$).

¹Least squares means.

²Low-merit control line (CL) and high-merit select line (SL) primiparous (PP; $n = 18$ CLPP, 18 SLPP) and multiparous (MP; $n = 12$ CLMP, 18 SLMP) cows. Milk yield differed between lines by more than 4,000 kg/305-d lactation.

³Line = genetic line; time = week of lactation (milk and component yields) or day of lactation (milk percentage composition, BW). There were main effects of time for all variables ($P < 0.001$).

⁴Interactions of genetic line (L), parity (P), and time (T).

value < 0.5), moderate (absolute value 0.5 to 0.8), or strong (absolute value > 0.8). For all evaluations, comparisons were considered to differ when $P < 0.05$.

RESULTS

Milk Yield and Composition

Genetic selection increased milk yield such that primiparous SL cows produced more than multiparous CL cows, and this resulted in an interaction of line and parity on SCM ($P = 0.041$) and milk ($P = 0.053$) and a trend ($P = 0.063$) for this interaction on FCM (Table 1 and Figure 2A). There were effects of WOL ($P < 0.001$) and interactions of WOL with line ($P < 0.001$) and parity ($P < 0.001$) on yields of milk, FCM, and SCM because of the differences in days to peak milk, peak milk yield, and rates of change in milk yield. Daily milk yield from conception to dry-off was greater ($P < 0.001$) in SL than CL cows and did not differ ($P = 0.31$) between primiparous and multiparous cows (data not presented).

Days to peak milk occurred earlier ($P < 0.001$) for CL than SL cows (42.8 vs. 71.5 ± 2.8 d) and earlier ($P < 0.001$) for multiparous than primiparous cows (46.4 vs. 67.9 ± 2.8 d). Peak milk occurred at 35.0 and 57.9 ± 4 DIM for multiparous CL and SL cows and at 50.7 and 85.1 ± 4 DIM for primiparous CL and SL cows, respectively. The rate of increase in milk yield from calving to peak did not differ ($P = 0.20$) between CL and SL

cows (0.183 vs. 0.160 ± 0.012 kg/d, respectively) and was greater ($P < 0.001$) for multiparous than primiparous cows (0.242 vs. 0.102 ± 0.012 kg/d) cows. There was a line by parity interaction ($P = 0.021$), as the rate of increase was greater for multiparous CL than SL cows (0.274 vs. 0.210 ± 0.018 kg/d) but similar for primiparous CL and SL cows (0.093 vs. 0.111 ± 0.018 kg/d, respectively). The rate of decline (persistency) from peak milk to 280 DIM was greater ($P = 0.022$) for CL than SL cows (-0.074 vs. -0.060 ± 0.004 kg/d) and greater ($P < 0.001$) for multiparous than primiparous cows (-0.096 vs. -0.038 ± 0.004 kg/d). There was a line by parity interaction ($P = 0.030$), as the rate of decrease was greater for multiparous CL than SL cows (-0.109 vs. -0.083 ± 0.005 kg/d) but similar for primiparous CL and SL cows (-0.039 vs. -0.038 ± 0.005 kg/d).

Percentage of milk fat (Table 1 and Figure 2B) was greater ($P = 0.024$) for CL than SL cows (3.86 vs. $3.56 \pm 0.09\%$) and greater ($P = 0.011$) for primiparous than multiparous cows (3.88 vs. $3.54 \pm 0.09\%$). Percentage of milk protein (Table 1 and Figure 2C) was greater ($P = 0.002$) in CL than SL cows (3.53 vs. $3.35 \pm 0.04\%$) and greater ($P = 0.005$) for multiparous than primiparous cows (3.52 vs. $3.36 \pm 0.04\%$). Percentage of milk lactose (Table 1 and Figure 2D) did not differ ($P = 0.18$) between CL and SL cows (4.62 vs. $4.69 \pm 0.04\%$) but was greater ($P < 0.001$) in primiparous than multiparous cows (4.77 vs. $4.53 \pm 0.04\%$). Milk SCC (Table 2)

Figure 2. Effect of genetic merit and parity on least squares means for daily milk yield (A) and percentages of milk fat (B), protein (C), and lactose (D). Data are from primiparous (PP) and multiparous (MP) low-merit control line (CL) cows and high-merit select line (SL) cows. Milk yield was greater ($P < 0.001$) for SL than CL cows (32.2 vs. 20.5 ± 0.8 kg/d) and for MP than PP cows (29.1 vs. 23.6 ± 0.8 kg/d). Percentages of milk fat (3.86 vs. $3.56 \pm 0.09\%$) and protein (3.53 vs. $3.35 \pm 0.04\%$) were greater ($P < 0.05$) for CL than SL cows, but lactose (4.62 vs. $4.69 \pm 0.04\%$) did not differ ($P = 0.18$). Percentages of milk fat (3.88 vs. $3.54 \pm 0.09\%$) and lactose (4.77 vs. $4.53 \pm 0.04\%$) were greater ($P < 0.01$) and protein (3.36 vs. $3.52 \pm 0.04\%$) less ($P < 0.01$) in PP than MP cows.

averaged $111,000 \pm 1,000$ cells/mL and varied with DIM ($P < 0.001$), as SCC decreased from 450,000 during the first 3 WOL to 51,000 at 84 DIM and increased slowly to 110,000 at 280 DIM (data not presented). Milk SCC did not differ between lines ($P = 0.76$) or parities ($P = 0.28$), but there were interactions of line and DIM ($P < 0.001$) and of parity and DIM ($P = 0.002$).

There was no interaction of line and parity on any milk component except protein (Table 1), which was less ($P = 0.017$) in primiparous SL than CL cows (3.20 vs. $3.51 \pm 0.05\%$) but similar in multiparous SL and CL cows (3.49 vs. $3.54 \pm 0.05\%$). There were line by DIM interactions for milk fat ($P = 0.006$) and lactose ($P < 0.001$) percentages primarily because milk fat increased and milk lactose decreased as milk yield of multiparous CL cows decreased in late lactation.

Reproductive Performance

Conception occurred at 112 ± 14 , 129 ± 16 , 94 ± 12 , and 123 ± 13 DIM for multiparous SL and CL cows and primiparous SL and CL cows, respectively, and was not affected by parity, line, or their interaction. Three SL primiparous cows carried twins, but there was no indication that their endocrine profiles differed from cohorts that carried a single fetus; therefore, data from these 3 cows were included in the analyses.

BW

Cow BW (Table 1 and Figure 3A) did not differ between CL and SL (590 vs. 602 ± 10 kg) cows but was greater ($P < 0.001$) for multiparous than primiparous cows (642 vs. 551 ± 10 kg). There was no interaction of

Table 2. Effect of genetic merit for milk yield on circulating NEFA, somatotropin (ST), IGF-I, and placental lactogen (PL) concentrations¹

Variable	Genetic merit $\times$ parity ²					P^3						
	CLPP	SLPP	CLMP	SLMP	SEM	Line	Parity	Time	$L \times P^4$	$L \times T^4$	$P \times T^4$	$L \times P \times T^4$
Lactation ⁵												
NEFA, $\mu\text{Eq/L}$	234	323	355	406	20	0.001	0.001	0.001	0.360	0.006	0.001	0.204
ST, ng/mL	3.3	4.6	3.8	4.7	0.3	0.001	0.333	0.001	0.426	0.378	0.947	0.141
IGF-I, ng/mL	156	142	106	93	6	0.040	0.001	0.001	0.991	0.001	0.007	0.133
Gestation ⁵												
ST, ng/mL	2.2	3.2	2.5	3.2	0.2	0.001	0.412	0.203	0.503	0.066	0.601	0.252
IGF-I, ng/mL	158	164	142	123	5	0.364	0.001	0.001	0.087	0.001	0.671	0.962
PL, pg/mL	231	193	196	217	30	0.799	0.853	0.001	0.339	0.022	0.719	0.382

¹Least squares means.²Low-merit control line (CL) and high-merit select line (SL) primiparous (PP; $n = 18$ CLPP, 18 SLPP) and multiparous (MP; $n = 12$ CLMP, 18 SLMP) cows. Cows that became pregnant ($n = 15$ CLPP, 17 SLPP, 10 CLMP, and 13 SLMP) were used for the gestation data. Milk yield differed between lines by more than 4,000 kg/305-d lactation.³Line = genetic line; time = day of lactation or interval postconception.⁴Interactions of genetic line (L), parity (P), and time (T).⁵Blood samples were collected at -28 ± 7 , -14 ± 3 , -7 ± 2 , 1, 2, 3, 7, 14, 21, and 28 d postpartum and at 28 ± 3 d intervals thereafter until 280 d postpartum (nonpregnant) or throughout pregnancy. Data for the lactation phase were summarized through 280 d. Data for the gestation phase were summarized as means for each ($n = 10$) 28-d interval postconception.

line and parity on BW but there were interactions of WOL within line ($P < 0.001$) and parity ($P = 0.006$). There was a trend ($P = 0.058$) for an interaction of line, parity, and DIM for BW because BW of the primiparous SL cows was greater than BW of the primiparous CL cows from -28 to 28 DIM and because there were interactions of line and DIM ($P < 0.001$) and of parity and DIM ($P = 0.006$). By 56 DIM, BW of primiparous SL and CL cows did not differ. The nadir of BW occurred at 29.8 and 35.4 DIM for multiparous CL and SL cows and at 16.6 and 38.6 DIM for primiparous CL and SL cows, respectively. Multiparous SL and CL cows lost similar amounts of BW (51 ± 6 kg) from calving to BW nadir while primiparous SL and CL cows lost 45 and 12 ± 6 kg, respectively. There was no difference in BW between lines during gestation, but BW of multiparous cows was greater ($P < 0.001$) than BW of primiparous cows and there was an interaction ($P = 0.05$) of parity and IPC, as BW of primiparous cows increased more rapidly than BW of multiparous cows (data not reported).

Serum NEFA

Serum NEFA concentrations (Table 2 and Figure 3B) increased after calving and peaked at 7 DIM for all 4 line-parity combinations. Postpartum alterations in NEFA concentrations were less ($P < 0.001$) in primiparous CL cows than in the other 3 groups. Serum NEFA concentrations were greater ($P = 0.001$) in SL than CL cows (364 vs. 294 ± 14 $\mu\text{Eq/L}$), greater ($P < 0.001$) in multiparous than primiparous cows (381 vs. 278 ± 14 $\mu\text{Eq/L}$), and greater ($P < 0.001$) during 0 to 28 DIM than during the prepartum period or after 28 DIM.

There were interactions of DIM with line ($P = 0.006$) and with parity ($P < 0.001$) because NEFA remained elevated for a longer postpartum interval in SL cows, and magnitude of the difference between multiparous and primiparous cows varied during prepartum, early postpartum, and late postpartum intervals. These differences were due primarily to the peak postpartum NEFA concentration being less ($P < 0.001$) in primiparous CL cows than in the other line-parity combinations.

Endocrine Profiles

Serum ST concentrations were affected ($P < 0.001$) by DIM, as concentrations increased immediately postpartum, remained elevated through 7 DIM, and gradually decreased as lactation progressed (Figure 3C). Overall concentrations of ST (Table 2) were greater ($P < 0.001$) in SL than CL cows (4.7 vs. 3.6 ± 0.2 ng/mL) and did not differ ($P = 0.33$) between multiparous and primiparous cows (4.2 vs. 4.0 ± 0.2 ng/mL). Serum ST concentrations during gestation (IPC; Figure 4A and Table 2) were similar ($P = 0.41$) for multiparous and primiparous cows (2.9 vs. 2.7 ± 0.2 ng/mL, respectively) but were greater ($P < 0.001$) in SL than CL cows (3.2 vs. 2.3 ± 0.2 ng/mL). This was true whether the data for SL multiparous cows during IPC 4 and for primiparous SL cows during IPC 5 were included or excluded. There was a trend ($P = 0.066$) for an interaction of line and IPC because there were no differences between lines during IPC 9 and 10.

Serum IGF-I concentrations decreased ($P < 0.001$) at calving, remained reduced for varying intervals among the line-parity combinations, and gradually returned

Figure 3. Effect of genetic merit and parity on least squares means for BW (A) and serum NEFA (B), somatotropin (ST; C), and IGF-I (D). Data are from primiparous (PP) and multiparous (MP) low-merit control line (CL) cows and high-merit select line (SL) cows. Body weight was similar for SL and CL (602 vs. 590 ± 10 kg) cows and greater for MP than PP (642 vs. 551 ± 10 kg) cows. Peak serum NEFA was less ($P < 0.05$) in CLPP than in CLMP, SLPP, and SLMP cows (369 , 842 , 692 , and 954 ± 45 $\mu\text{Eq/L}$, respectively). Serum ST was greater ($P < 0.001$) in SL than in CL cows (4.7 vs. 3.6 ± 0.2 ng/mL) throughout lactation. Serum IGF-I was greater ($P < 0.001$) in PP than in MP cows (149 vs. 100 ± 5 ng/mL) and greater ($P = 0.04$) in CL than SL cows (131 vs. 117 ± 5 ng/mL).

to precalving concentrations as lactation progressed (Figure 3D). Overall concentrations of IGF-I (Table 2) were greater ($P = 0.040$) in CL than SL cows (131 vs. 117 ± 5 ng/mL) and greater ($P < 0.001$) in primiparous than multiparous cows (149 vs. 100 ± 5 ng/mL). There were interactions of DIM and line ($P < 0.001$) and of DIM and parity ($P = 0.007$) on IGF-I, as the postpartum increase in IGF-I was more rapid in CL than in SL cows and more rapid in primiparous than in multiparous cows. Concentrations of IGF-I began to increase at 2, 14, 14, and 21 DIM for primiparous CL, multiparous CL, primiparous SL, and multiparous SL cows, respectively.

Serum IGF-I concentrations (Table 2 and Figure 4B) during gestation (IPC) were similar ($P = 0.36$) for SL and CL cows (150 vs. 144 ± 5 ng/mL) but greater ($P <$

0.001) in primiparous than multiparous cows (161 vs. 133 ± 5 ng/mL). There was a trend for a line by parity interaction ($P = 0.087$), as serum IGF-I concentrations were greater in multiparous CL than SL cows (142 vs. 123 ± 5 ng/mL) and similar for primiparous SL and CL cows (164 vs. 158 ± 5 ng/mL, respectively). There was an overall increase ($P < 0.001$) in serum IGF-I with IPC (primarily from IPC 4 to 9) and there was an interaction ($P < 0.001$) of line and IPC, as the postconception increase in serum IGF-I was greater in CL than in SL cows.

There was no effect of line ($P = 0.80$) or parity ($P = 0.85$) on PL concentrations during gestation but there was an interaction ($P = 0.022$) of line and IPC, as PL concentrations increased more in CL than in SL cows in late gestation (Table 2 and Figure 4C). Serum PL

Figure 4. Effect of genetic merit and parity on least squares means for serum somatotropin (ST; A), IGF-I (B), and placental lactogen (PL; C) concentrations and on the relationship between serum PL and IGF-I during 28-d intervals postconception (IPC; D). For panels A, B, and C, data are from primiparous (PP) and multiparous (MP) low-merit control line (CL) cows and high-merit select line (SL) cows. Serum ST concentrations were greater ($P < 0.001$) in SL than in CL cows (3.2 vs. 2.3 ± 0.2 ng/mL). Serum IGF-I concentrations were greater ($P < 0.001$) in PP than MP (161 vs. 133 ± 5 ng/mL) cows and did not differ ($P = 0.36$) between lines (150 vs. 144 ± 5 ng/mL). Serum PL concentrations increased ($P < 0.001$) from 3 to 9 IPC and did not differ ($P = 0.80$) between lines (213 vs. 205 ± 22 pg/mL) or parities (212 vs. 206 ± 22 pg/mL). For panel D, data represent overall means by IPC for PL and IGF-I.

concentrations increased ($P < 0.001$) from IPC 3 to 8, remained relatively stable from IPC 8 to 9, and decreased from IPC 9 to 10. The overall IGF-I and PL serum profiles were very similar during gestation (Figure 4D). Serum PL increased by IPC 4 and serum IGF-I increased by IPC 5.

Except for ST and PL in CL cows, all correlations between pairs of the 3 hormones within line ($n = 237$ CL and 284 SL), within parity ($n = 297$ primiparous and 224 multiparous), or overall ($n = 521$) were significant ($P < 0.05$) and all were weak (correlation coefficients were between -0.28 and 0.42). All correlations between ST and IGF-I were negative, with an overall $r = -0.23$ ($P < 0.001$), and all correlations between ST and PL were negative, with an overall $r = -0.13$ ($P = 0.003$). In contrast, all correlations between PL and IGF-I were positive, with an overall $r = 0.29$ ($P < 0.001$). There was no overall relationship ($P > 0.27$) between serum PL and calf birth weight when assessed for any

of the serum PL concentrations between IPC 7 and IPC 10. This was also true for all the line, parity, and line by parity subgroups [$P = 0.11$ for primiparous CL cows, with a range of 0.19 to 0.95 (mean P of 0.53) for all other subgroups].

DISCUSSION

Genetic merit of the SL cows has increased steadily since 1964 while genetic merit of the CL cows has remained relatively static. These results are consistent with those of Jones et al. (1994) and indicate that perpetuation of the CL cows with semen from sons of the original CL bulls has not altered this relationship. Contemporary primiparous cows now produce more milk than multiparous cows did in 1964. Results from a single year or single lactation of a long-term breeding project are subject to potentially large environmental and management effects, which may mask the true magni-

tude of differences attributable to genetics. Nevertheless, the difference in milk yield between our 2 lines continues to increase, and the large difference between these lines dwarf expected year-to-year differences in well-managed herds (Jones et al., 1994).

The increase in days to peak milk and in peak and total milk yields of SL cows are consistent with previous evaluations of effects of selection for milk yield (Kelm et al., 2000; Kay et al., 2005). The rate of increase in milk yield was greater and persistency reduced in multiparous CL cows when compared with multiparous SL cows. These differences appear to be attributable to factors other than genetic selection because they were not observed in our previous studies (Kay et al., 2005; B. A. Crooker, personal communication) or in the general US Holstein population (Kelm et al., 2000). Effects of WOL and parity on milk composition were similar to those expected in well-managed herds. Milk fat and protein percentages were less in SL than in CL cows. This is consistent with previous evaluations of increased milk yield on fat and protein content (Kelm et al., 2000) but has not been observed in all of our previous studies (Kay et al., 2005). Yields of milk components were greater in SL cows because of their greater milk yield. Although increased milk yield is associated with increased SCC and greater prevalence of subclinical and clinical mastitis (Hansen, 2000; Kelm et al., 2000), the low (<110,000 cells from 84 to 280 DIM) and similar SCC for SL and CL cows in this study support the notion that this relationship can be minimized by proper management.

Consistent with our observation that young SL heifers increase their BW more rapidly than CL heifers (Baumgard et al., 2002; Weber et al., 2005), precalving BW was greater for primiparous SL than CL cows. These differences decreased rapidly after calving, and by 56 DIM, BW of primiparous SL and CL cows did not differ. In contrast, BW profiles of multiparous SL and CL cows were similar throughout the study. Profiles of BW during early lactation are not ideal indicators of energy balance because DMI increases as BW decreases. Changes in serum NEFA concentrations, another indirect indicator of energy balance, were consistent with changes in BW of the CL and SL cows. The NEFA and BW profiles indicate that during early lactation, energy balance of primiparous CL cows was greater than that of SL cows and that primiparous SL cows mobilized more tissue than primiparous CL cows. These profiles also indicate that energy balance did not differ substantially between multiparous SL and CL cows, which is consistent with our direct evaluations of energy balance in multiparous SL and CL cows (Crooker et al., 2001).

A positive relationship exists between genetic merit for milk yield and circulating ST concentrations in lactating cows but not in nonlactating cows (Knight et al., 2004; W. J. Weber, unpublished data) or growing heifers (Baumgard et al., 2002; Weber et al., 2005). These results support a physiological role for ST in directing nutrients toward the mammary gland during lactation. The greater ST concentrations in high-merit cows could be a consequence of increased sensitivity to ST-releasing hormone, a reduced clearance of ST from the blood, a reduced negative feedback of IGF-I, or a combination of these factors (Knight et al., 2004). Although there are reports of this positive relationship in growing calves (Lovendahl et al., 1991; Woolliams et al., 1993), there appears to be a consensus that measurements of endogenous ST concentrations in calves or nonlactating cows do not provide an accurate estimate of merit for milk yield (Baumgard et al., 2002; Lovendahl and Klemetsdal, 2004; Weber et al., 2005; Taylor et al., 2006). The episodic release of ST makes results from analysis of single daily samples tenuous, but results from the current study support the existence of a positive relationship between circulating ST and genetic merit in lactating cows and are consistent with results obtained from a more thorough evaluation (samples every 15 min for 7 h) of ST profiles in cows from these 2 lines (W. J. Weber, unpublished data).

The immediate postpartum reduction in IGF-I concentration is consistent with previous reports that serum IGF-I concentrations during the first week of lactation are approximately 35% of prepartum concentrations (Radcliff et al., 2003; Reist et al., 2003; Taylor et al., 2003) and increase slowly toward prepartum concentrations as DIM increases. The decrease in serum IGF-I concentrations as parity increased has been reported (Wathes et al., 2003). Similar to the report of Knight et al. (2004), serum IGF-I in our high-merit SL cows was less than that in low-merit CL cows. This difference persisted through the first 84 DIM, after which IGF-I concentrations were similar between lines for the remainder of the lactation. Serum IGF-I did not differ between lines when summarized by IPC but there were line by IPC and line by parity interactions, as multiparous CL cows had greater IGF-I concentrations than multiparous SL cows during IPC 7 to 9. The lack of a main effect of line during gestation may be a result of the fact that sampling was relative to DIM rather than day of gestation. Although our study was not designed to evaluate differences between pregnant and nonpregnant cows, this comparison indicates serum IGF-I concentrations were greater in pregnant cows in late lactation (data not presented).

Relationships among ST administration, serum IGF-I, and milk yield are well established (Bauman, 2000),

but relationships among genetic merit for milk yield and endogenous serum ST and IGF-I during lactation and gestation require additional examination. Serum IGF-I is responsive to nutrient supply (Vicini et al., 1991; McGuire et al., 1995), and Thissen et al. (1994) have suggested that IGF-I can serve as an indicator of nutrient status. It has been suggested that negative energy and nutrient balance are responsible for the early postpartum reduction in serum IGF-I (Vicini et al., 1991; Radcliff et al., 2006). Our 2 indirect assessments of energy balance (BW and serum NEFA profiles) indicate that multiparous CL and SL cows returned to positive energy balance at relatively similar DIM. The more rapid postpartum increase in serum IGF-I in primiparous CL than SL cows could be attributed to their apparent more rapid return to positive energy balance; however, serum IGF-I also increased more quickly in multiparous CL than SL cows despite their apparent similarity in energy balance. These results support the concept that nutritional status is not the only factor responsible for the prolonged duration of reduced serum IGF-I in the contemporary, high-merit cow (Kim et al., 2004; Radcliff et al., 2006).

Although the similar positive nutritional status, similar serum IGF-I concentrations, and greater serum ST concentrations in SL cows in late lactation and gestation could be interpreted as an indication that the relationship between serum ST and IGF-I is attenuated, these results could be influenced by the fact that samples were collected relative to DIM rather than day of gestation. Examination of other endocrine signals, such as insulin (Rhoads et al., 2004), and of components known to influence the somatotrophic axis (Kim et al., 2004) is needed to delineate the relationships among genetic merit for milk yield, ST, and IGF-I during lactation.

The observed PL profiles are consistent with previous reports (Wallace, 1993; Hossner et al., 1997; Bertolini et al., 2006) that serum PL increased after 60 d of gestation, peaked at 215 d of gestation, and decreased gradually until parturition. The negative correlations between ST and IGF-I and between ST and PL during gestation are a result of the relatively constant ST concentration and the increase in IGF-I and PL during this interval. The positive correlation between PL and IGF-I, the nearly identical PL and IGF-I serum profiles, and the earlier gestational increase in PL support the concept that PL may play a role in regulating serum IGF-I in the pregnant cow (Hossner et al., 1997; Handwerger and Freemark, 2000). Indeed, when exogenous recombinant bovine PL was administered to cows, serum IGF-I increased (Byatt et al., 1992, 1997; Lucy et al., 1994). The correlation between PL and IGF-I in our study was weak, which indicates PL is one of several

factors involved in the regulation of serum IGF-I concentrations during gestation. A negative relationship between serum PL and IGF-I has been reported in nulliparous beef heifers (Hossner et al., 1997). These nulliparous heifers were on pasture and losing body condition as gestation progressed (Hossner et al., 1997). It is likely that their reduced nutritional status also contributed to the decrease in serum IGF-I and the negative relationship between serum IGF-I and PL as gestation progressed.

Genetic merit for milk yield had no effect on serum PL concentration. To our knowledge, this is the first direct evaluation of the effects of genetic merit on serum PL in dairy cows. Previous evaluation of our genetic lines indicated the SL cows have larger mammary glands than the CL cows (Petersen et al., 1985). Our results indicate that although serum PL concentrations have been associated with mammary development and function in other species (Gootwine, 2004), they are not related to the increased mammary size and greater milk yield achieved by the dairy cow through the past 40 yr of genetic selection. Although the study was not designed to evaluate effects of twinning on serum PL and our number of calves was relatively small to assess effects of PL on calf birth weight, our limited observations indicate there was no obvious effect of twinning on serum PL and no relationship between serum PL and birth weight.

CONCLUSIONS

Selection for milk yield increased milk yield, decreased milk fat and protein content, and increased milk component yields. During lactation, contemporary high-merit cows had greater increases in ST than the static low-merit cows and these results support a physiological role for ST in directing nutrients toward the mammary gland. Despite the apparent similarity in energy status, selection for milk yield prolonged the postpartum reduction in serum IGF-I in multiparous cows, which indicates that nutritional status as well as other factors influence serum IGF-I in early lactation. Selection for increased milk yield has not increased serum PL in the pregnant cow. All correlations among circulating concentrations of ST, IGF-I, and PL were significant but weak. The earlier gestational increase in serum PL relative to IGF-I and the positive correlation between serum PL and IGF-I during gestation support the concept that PL plays a role in the regulation of serum IGF-I in the dairy cow.

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