Bovine Conceptus — Maternal Interactions During the Pre- and Postpartum Periods

INTRODUCTION

Conceptus and maternal bovine endocrine systems interact throughout gestation such that pregnancy not only is maintained but that continued development and growth of the fetus are assured until its delivery from the maternal unit. This architectural achievement is brought about by a variety of regulatory agents (protein and steroid hormones, cellular receptors, prostaglandins, etc.) that program a homeorhetic response (2) of the maternal unit to permit normal fetal development. Perhaps the most vivid example of the ability of the conceptus to regulate the maternal unit is its ability to program development of mammary gland so that production of milk is synchronized closely with delivery of the mature fetus from its in utero environment (parturition). Secretion of milk at this time assures a continued source of nutrients for the newborn. However, abilities of the maternal unit to produce milk and manifest maternal behavior would not be apparent unless the conceptus exerted various controls in utero. Subsequent to growth of the maternal mammary gland and initiation of lactation regulated by conceptus, milk production to a degree represents a carryover effect of pregnancy (presence of conceptus) that continues in dairy cattle in absence of the newborn calf.

Objectives of this paper are to provide evidence that bovine conceptus influences various physiological, endocrine, and production responses of the maternal unit pre- and postpartum and to identify agents and pathways by which the conceptus may regulate, directly or indirectly, the maternal unit. This paper will be restricted to observations only in cattle with the intention of drawing the reader's attention to this species in which subtle regulatory differences between conceptus and mother differ from gestational and parturitional models described in sheep, pig, mare, and goat (14, 15, 34).

A series of symposia has been published by the American Dairy Science Association that reviews physiological, biochemical, and endocrine factors regulating function of mammary gland. Tucker (36) demonstrated with rats that pregnancy was a major stimulus of mammary cell numbers and indicated that the placenta regulated mammary cell proliferation, either directly or indirectly, via its actions on the maternal system. However, at that time secretion of placental hormones, which may stimulate bovine mammary development, had not been established. In 1974 Convey (5) reviewed changes in concentrations of hormones in bovine serum associated with development of mammary gland, late pregnancy, parturition, and lactation. Large changes in estrogens, progesterone, prolactin, glucocorticoids, and growth hormone during the periparturient period were related temporally to dynamic changes in the mammary gland associated with its transformation to a lactating unit. Review by Erb (13) of hormonal control of mammogenesis and onset of lactation in cows indicated that changing concentrations of progesterone and estrogen in blood must be involved with onset of lactation. Such an alteration in steroid balance may affect the mammary gland directly (+ or −) and alter secretion of other hormones secreted by the maternal unit (e.g., prolactin) that are associated with onset of lactation. Finally, Gorski (18) suggested that genetic differences among animals selected for milk yield probably are associated with various endocrine and biochemical factors regulating milk secretion (hormonal production rates, receptor numbers, and interactions among...
various organ systems to regulate lactation). However, there is a paucity of reports in which variability of various hormonal concentrations and their interactions have been evaluated quantitatively for groups of cows differentially selected for milk yield. Such studies are needed to evaluate changes among and within animals of various hormones in the critical periparturient period of mammogenesis, lactogenesis, and galactopoiesis. Furthermore, the influence of periparturient period on subsequent reproductive processes during the postpartum period has been neglected. The conceptus may be central to regulation of these various processes.

Service Sire Effects on Traits of the Maternal Unit

The conceptus, while residing within the uterus, has a number of effects on the maternal unit. For example, time of parturition is controlled to a considerable degree by the fetus itself. If the bovine fetus has a pituitary dysfunction, parturition can be delayed (22). Gestation length of the fetus is heritable ($h^2 \approx 0.40$ from paternal half-sib correlation), which indicates that sire of fetus (i.e., service sire) partially controls variability in gestation length.

The placenta is the major unit producing hormones during pregnancy, and the fetus plus placenta contribute to hormonal changes in maternal circulation in late gestation. As reviewed by Tucker (36), the major portion of development of mammary gland occurs during pregnancy in response to hormones secreted by the conceptus and maternal unit. It seems reasonable to the physiologist that variation in postpartum milk production and reproductive performance may be related to differences among conceptuses in their abilities to stimulate growth of mammary gland during the late prepartum period or to alter maternal endocrinology and metabolism that in turn influence galactopoiesis and reproductive cycles in the postpartum period.

Van Vleck and Johnson (37) reviewed recent studies from Norway, Florida, New York, New Zealand, and Scotland that indicated sire of fetus influenced a proportion of variability in milk yield of the mother after delivery of the calf. Several of these studies were with lactation records collected from regional populations across many herds. Estimates of effects of sire of fetus on milk yield, measured as percentages of phenotypic variance, were variable and ranged from essentially 0 to 11.8%. Highs were from a statistical method that was not accounting for nonrandom mating in the population, e.g., Henderson Method 1. Analysis of data by Henderson Method 3 gave estimates much closer to 0 (19, 29). Adkinson et al. (1) detected effects of sire of fetus on subsequent days open by Henderson Method 1 of 1.9% and 3.2% of phenotypic variance in Holsteins and Jerseys.

A more detailed analysis of the Florida Agricultural Experiment Station herd was of 3776 observations from 1954 to 1976 (27) by Method 3. Twenty-seven variables were evaluated by the mathematical model: $Y = \mu + SOCYS + SOF(SOCYS) + F + ERROR$ ($F =$ set of fixed effects, also see Table 1). Effects of sire of fetus were divided into rankings of APPRECIABLE (milk yield, fat yield, protein yield, lactose yield, birth weight, and gestation length), MEDIUM (most milk composition percentages, days open, metritis, dystocia) and ZERO (some milk composition percentages, alive at 24 h after birth, pregnant in left or right uterine horn). Disadvantage of this mathematical model was that estimates of variances of sire of fetus also included those associated with interactions involving sire of fetus and other variables.

Table 1 depicts an analysis by least squares for Jerseys (1047 parturitions) and Holsteins (702 parturitions) in which effects of sire of cow and sire of fetus were cross classified. Weight of calf at birth was included as a continuous independent variable. In both breeds effects of birth weight on milk yield were positive and curvilinear (Figure 1). Milk production increased 103 kg with birth weights ranging from 18.6 to 29.5 kg for Jersey and 157 kg for a range of 34.5 to 45.4 kg for Holstein cows. Lactation records (305 days, 2 milkings daily) were adjusted for age of cow, which removed part of the variation from differences in size of cow. These results implied that birth weights of calves may be associated with some function of the conceptus that stimulates maternal production of milk. Perhaps birth weights were associated with placental size, placental activity, and function of the fetus. Effects of sire of fetus on milk yield were appreciable in this model for Jerseys (7%) but near 0 for Holsteins.
TABLE 1. Model, degrees of freedom, and tests of significance for least squares analysis of variance for milk yield1.

<table>
<thead>
<tr>
<th>Source</th>
<th>Jerseys</th>
<th>Holsteins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sire of fetus (SOF)</td>
<td>107*</td>
<td>55</td>
</tr>
<tr>
<td>Sire of cow (SOC)</td>
<td>41**</td>
<td>26**</td>
</tr>
<tr>
<td>Sex of fetus</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Year (Y)</td>
<td>22**</td>
<td>16**</td>
</tr>
<tr>
<td>Season (S)</td>
<td>1**</td>
<td>1**</td>
</tr>
<tr>
<td>Age of cow (LQC)2</td>
<td>3**</td>
<td>3**</td>
</tr>
<tr>
<td>Days in milk (LQC)</td>
<td>3**</td>
<td>3**</td>
</tr>
<tr>
<td>Days pregnant (LQ)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Calf birth weight (LQ)</td>
<td>2*</td>
<td>2*</td>
</tr>
<tr>
<td>Residual</td>
<td>866</td>
<td>592</td>
</tr>
</tbody>
</table>

1 All effects fixed except sire of fetus and residual.
2 L = linear, Q = quadratic, C = cubic; tests of significance refer to the combined effects of the terms indicated.

*P<.05.
**P<.01.

Results of this analysis of a single herd suggest that effects of sire of fetus might be appreciable for milk yield, fat yield, protein yield, and lactose-mineral yield, whereas effects for compositional percentages were less. These effects appeared to be influencing general function of mammary gland rather than just selective aspects of milk production. If true, this would be consistent with the hypothesis that general growth of mammary gland is affected by service sire and that cows begin their lactation after varying growths of mammary gland, possibly influenced by service sire via the conceptus but surely by the conceptus itself (since milk production normally would not ensue without pregnancy). A plot of bovine fetal growth throughout pregnancy (11) and development of the maternal mammary gland (30) reveals that growth of fetus and maternal mammary gland tissue are essentially parallel (Figure 2). A simple deduction is that fetus and placental membranes probably are regulating growth of maternal mammary gland.

Service sire influenced ease of calving and frequency of dystocia in (27). A link between service sire and excretion of hormones from the maternal unit that is related to dystocia or calving ease was reported by Osinga (25). Urinary excretion of estrone (estrone to creatinine ratio and estradiol 17a to creatinine ratio) in pregnant cows was associated with stage of gestation, calf birth weight, and differences among service sire groups. Increased calving difficulty was associated with low rates of estrogen excretion. Furthermore, heritabilities were .28 and .38 for urinary excretion of estrone and estradiol 17a. Thus, fetal genotype to some degree may regulate secretion of estrogen by the conceptus.

Although genetic implications of effects of sire of fetus ultimately may prove to be of minor economic importance (37), physiological mechanisms controlling milk yield and other economically important traits are clear. Effects of sire of fetus apparently are associated with environmental influences imposed on the maternal unit by the conceptus. The physical, hormonal, and biochemical agents that manifest this effect warrant extensive investigations.
Hormonal and Physiological Responses in
the Maternal Unit Associated with
Conceptus Function During
the Periparturient Period

Hormonal production by the bovine conceptus may affect its own fetal growth and regulate maternal function to assure adequate environmental conditions (oxygen, nutrients, water, minerals) for its continued development and maturation to parturition. Furthermore, these hormonal factors are likely to stimulate directly or interact with the maternal endocrine system to regulate mammmogenesis, lactogenesis, and galactopoieses of the maternal mammary gland. Conceptus regulation of the mammary gland is important for its postnatal survival and potentially important to the dairy industry, where milk is harvested for human consumption.

Two classes of hormones have been identified as endocrine secretions of the conceptus: bovine placental lactogen (bPL) and estrogens (estrone [E1] and estrone sulfate [E1SO4]). The bovine placenta secretes a bPL (3, 17, 21); concentrations rise appreciably from 160 to 200 days of gestation and then remain high until term (3). Additionally, concentrations of bPL were higher in dairy than beef cows, and among the dairy cows those having a higher subsequent milk yield had higher concentrations of bPL (r = .6).

Concentrations of both E1 and E1SO4 in peripheral plasma of the maternal unit increased between 70 and 111 days of gestation (12, 28). Consequently, other tissues more distant to the reproductive tract are exposed to increased estrogens at this time, but excessive estrogenic activity probably is dampened by conjugation of estrogen by the uterus and conceptus before transfer into peripheral circulation. The major estrogen in plasma of the pregnant cow is E1SO4 (35). Total estrogen concentrations (E1SO4 + E1 + E2) at day 220 of gestation in Charolais cattle were correlated with birth weights .84 and subsequent preweaning growth rates .87 (31). Part of the association with growth rate may be from milk production of the dam. Estrone sulfate measurements may be a sensitive response variable indicative of conceptus function. Appreciable variability in E1SO4 concentrations in maternal peripheral plasma in late pregnancy is evident from data in Figure 3 (R. J. Collier, W. W. Thatcher, and C. J. Wilcox, unpublished). Beginning at 199 days following insemination, blood samples were collected from 10 Holstein cows at 4-day intervals until day of parturition at which time a final sample was collected. From 14 to 20 samples were collected from each pregnant cow. Figure 3 represents a family of fourth order curves (n = 10) that characterize trends of E1SO4 in the prepartum period for each cow. Data were in this form to illustrate the tremendous variability in concentrations of E1SO4 among the 10 cows. A major increase occurred approaching parturition, but concentrations ranged from 5000 to 15,000 pg/ml (3-fold) just prior to parturition. In the earlier period (76 to 48 days prepartum), concentrations of E1SO4 ranged from 250 to 7000 pg/ml (28-fold). Thus, appreciable variability existed among conceptus-maternal units in their prepartum concentrations of E1SO4 in the maternal circulation. Such variability may represent differences in hormonal production by the conceptus which, in turn, may be associated with specific responses of maternal and fetal units.

The accumulative evidence of effects of conceptus on the maternal unit, possibly by the hormones it produces, led to an experiment which was designed to evaluate pre- and postpartum endocrine changes in two genetically diverse groups of Jersey cows selected for milk yield (9, 10, 33). The control group (C) of five cows and two heifers was sired by and bred to bulls which had zero estimated breeding values. A selected group (S) of seven cows was sired by bulls with a predicted difference (PD) for milk yield of 406 kg and bred to bulls which had zero estimated breeding values. A selected group (S) of seven cows was sired by bulls with a predicted difference (PD) for milk yield of 406 kg and bred to bulls with a PD of

Figure 3. Prepartum concentrations of E1SO4 in peripheral plasma of 10 Holstein cows.

Measurements in the maternal circulation would not give a clear estimate for sire of fetus alone since effects of sire of cow and sire of fetus were confounded. Collections of blood were by jugular venipuncture between 0700 to 1000 h on alternate days from -35 to -14 days prepartum and +14 to +28 days postpartum, and daily from -14 to +14 days. Examined were hematocrit (Hct) and concentrations of protein in plasma (PP), E₁, E₂, E₁SO₄, P₄, glucocorticoids (GC), LH, Prl, and 13, 14 dihydro-15 keto PGF₂α (PGFM).

Overall pre- and postpartum trends among all 14 cows for P₄, E₁, E₁SO₄, Prl, and PGFM up to day 10 postpartum are in Figure 4. Each curve is the regression pooled within cow fitted during pre- and postpartum periods with day of parturition a common reference point. This composite graph illustrates the synchrony of changes in concentrations of hormones around parturition. Hormonal interrelationships in Figure 4 include the gradual fall in prepartum P₄ and rise in E₁ that were associated with a prepartum increase in Prl. Prolactin remained elevated between day -5 prepartum to +3 postpartum. Concentrations of estrogens in plasma (E₁ and E₁SO₄) declined abruptly in association with delivery of the conceptus (calf and placenta). Low basal concentrations of P₄, E₁, E₁SO₄, and E₂ were detected by 1 day after parturition and for approximately 14 days postpartum.

The gradual decrease of concentrations of P₄ in plasma and increases in E₁ during the last 2 wk of pregnancy agreed with (5, 14). These changes indicated alterations in conceptus function or maturation leading to the impending processes of parturition. Gradual decreases in concentrations of P₄ were correlated negatively (−.64) with a slight but significant increase in concentrations of PGFM prepartum. This prepartum increase in PGFM may reflect release of PGF₂α that leads to final regression of the corpus luteum and the precipitous decrease in P₄ 1 to 2 days before parturition. The major increase in concentrations of PGFM in plasma during the periparturient period occurred 1 to 4 days postpartum with concentrations returning to basal concentrations by day +15. These temporal changes agreed closely with those reported by Edqvist et al. (8). The tissue producing prostaglandin F₂α is not known since we monitored only the metabolite of PGF₂α in the peripheral circulation. A uterine source is suspected since the increase was coupled closely with delivery of calf and placenta, and the postpartum decrease was correlated positively (+.65) with uterine regression.

Differences between C and S groups (9, 10) for prepartum P₄ (C<S) and E₁ (C>S) were associated with differences in concentrations of Prl in plasma (C>S; Figure 5). Interrelationships of concentrations of P₄ and E₁ with Prl are important relative to understanding the synchrony of hormonal changes associated with parturition and lactogenesis. During the periparturient period concentrations of Prl rose and
fell, which agreed with changes reported by others (7, 20). Prolactin concentrations were associated with plasma E₁ (r = .27; P<.01) and P₄ (r = -.44; P<.01) concentrations within animals, as well as among animals (E₁ and Prl, r = .65, P<.01; P₄ and Prl, r = -.26, P<.10). Concentrations of E₁ and Prl of cows in group C were higher prepartum and began to increase earlier, whereas concentrations of Prl in the S cows remained lower, and the increase was synchronized more closely to the last 3 days of gestation (Figure 5). Padmanabhan and Convey (26) demonstrated that E₂ increased basal and thyrotropin releasing hormone-induced release of Prl by bovine pituitary cells in culture. Associations and differences are consistent with the positive association of free estrogens with Prl and the negative relationship with P₄. The greater rise in Prl at parturition (ΔPrl) for S cows (181 vs. 136 ng/ml) and the correlation of this rise among the 14 cows with postpartum milk yield (r = .52; P<.10) indicates that the dynamics of Prl secretion may be involved with the processes of mammogenesis and lactogenesis in dairy cows.

Ratios of variances among cows to within cows for all hormonal and physiological measurements were ranked in decreasing magnitude (9). Responses with the largest ratios would be responses having the highest probabilities of discriminating one cow from another with our sampling scheme and experimental design. Ratios for P₄ (3.92), E₁ (2.0), Hct (1.08), and E₁SO₄ (1.00) indicated that these components varied at least as much among animals as they did within animals. These are four factors associated with pregnancy via the conceptus (E₁ and E₁SO₄), or pregnancy via the maternal unit (P₄ or CL of pregnancy), or a physiological response (HCT, water metabolism, etc.), possibly manipulated by the endocrinology of pregnancy. From this standpoint, prepartum P₄ was correlated with birth weight of the calf (r = -.52; P<.10) and prepartum E₁ with milk yield (r = -.72; P<.05). Thus, variability in these hormonal responses among cows was associated with important postpartum production traits.

Hormonal and physiological responses differed between cow groups representing these two genetically diverse gene pools (maternal and conceptus). Although measurements were from the maternal system, selection criteria allowed us to assume that differences between the two groups reflected genetic influence of sire of cow and service sire. The study provided evidence that these effects were transmitted partially to the dam via the fetus she bore. The link between the dam and her fetus may be through production of estrogens by the conceptus and other products of the conceptus not measured such as bPL. Differences in certain maternal responses, such as Hct, P₄, and Prl, may be attributed directly to the maternal unit or indirectly to influences of the conceptus acting on the maternal unit (vascular bed, ovary, and pituitary). Relationships between estrogens (produced by the conceptus) and prepartum maternal response (Hct, P₄, and Prl) were characterized and may account for part of the postpartum variability in milk yields previously attributed to sire of the conceptus. Genetically different conceptuses appear to contribute to differences in hormonal milieu during the periparturient period. The source of free estrogens (E₁ and E₂) during the last 2 wk of pregnancy is intriguing. Walker and Peaker (38) demonstrated that production of E₂ by goat mammary gland accounted for over 90% of the rise in estrogen in the last 2 wk of pregnancy. It is not known whether the mammary gland of the dairy cow produces E₁ and E₂ due to sulfatase cleavage of conjugated estrogens, which contribute to the rise approaching parturition. However, mean concentrations of prepartum E₁ among cows were correlated negatively (-.72) with their mean daily milk yields for 23 days postpartum. Furthermore, E₁ and E₁SO₄ concentrations were correlated .37 within and .59 among cows.

Synchrony of hormonal changes in the periparturient period (Figure 4) appears to be essential for initiating lactogenesis (5). As described previously, the major increase in concentrations of PGFM occurred 1 to 4 days postpartum, and concentrations were maintained above basal concentrations until approximately 2 wk postpartum. Measurable quantities of the parent PGF₂α may stimulate secretion of Prl (Figures 4 and 5) and GH (5) since both are secreted in response to exogenous administration of PGF₂α (23). Source of PGF₂α secretion in the postpartum period, its possible role in lactogenic and galactopoietic processes, and the influence of such an agent on metabolism of certain tissues, such as adipose and muscle, warrant further investigation in dairy cattle.
The reproductive system and its "reawakening" during the early postpartum period may be linked to temporal changes in PGFM. This was evaluated in 18 Holstein cows in which concentrations of PGFM and P₄ were measured concurrently in peripheral plasma on alternate days from parturition to 50 days postpartum (G. L. Lewis, W. W. Thatcher, R. J. Collier, unpublished). Regressions pooled within cows for concentrations of PGFM and P₄, until 20 days postpartum, are in Figure 6. A subtle but perhaps important rise in P₄ (> 1 ng/ml) did not occur (X = 15.7 days; range, 10 to 20 days) until concentrations of PGFM had decreased to below 100 pg/ml.

Frequency of ovulations from the postpartum ovary adjacent to the previous pregnant horn increases as diameter of the horn decreases (24). The uterus appears to exert a local effect on the ovary, and as the diameter of the uterine horn returns to near normal, which occurs first in the previous nonpregnant horn, ovulation occurs. It seems feasible that reestablishment of normal reoccurring estrous cycles, in nonsuckled dairy cows, may be dependent upon removal of uterine inhibition; the agent regulating this inhibition may be PGF₂α acting physiologically at the ovarian level or via the hypothalamus and pituitary. A postpartum rise in P₄ that may be critical to hypothalamic regulation does not occur until after a major decrease in concentrations of PGFM. Nevertheless, inhibition of ovarian function represents an additional indirect carryover effect of the conceptus on a postpartum reproductive response in dairy cattle.

Conceptus-Maternal Interrelationships

Figure 7 summarizes various pathways by which the conceptus may influence the maternal unit for variation in such postpartum traits as milk yield and reproductive performance. However, these two components (conceptus and maternal unit) are not independent. If we consider variability in milk production among and within cows, sire of cow and dam of cow each contribute 50% of the genotype of an individual to produce milk. While the individual is in utero, dam of the cow does not confer any measurable environmental influence (i.e., estimates for milk yield of maternal additive genetic variance are close to 0, E = 0, Figure 7) that ultimately affects milk yield of the individual as a mature animal.

The major stimulation for mammary gland growth and lactogenesis during the natural life cycle is pregnancy (36). Thus, presence of the conceptus in the uterus of the individual is responsible for the cow beginning lactation and producing milk.

Potential effects of the conceptus can be classified into a series of genetic and environmental components. The conceptus itself (fetus and placenta) received 50% of its genotype for any trait from its sire (sire of fetus) and 50% from its dam (defined here as individ-

![Figure 6](image1)

Figure 6. Pooled with cow least squares regressions of 13,14-dihydro, 15-keto prostaglandin F₂α and progesterone in the postpartum period of 18 Holstein cows.

![Figure 7](image2)

Figure 7. Conceptual diagram of conceptus-maternal interrelationships in cattle.
ual). However, the individual or maternal unit also provides the in utero environment (oxygen, nutrients, minerals, water, etc.) for continued development of the conceptus until delivery. Likewise, the conceptus regulates the maternal unit environmentally by influencing the partitioning and mobilization of maternal nutrients for its own development (2). Maternal effects on birth weight are estimated by the maternal correlation (Figure 7) for birth weight of .50 (i.e., maternal heritability of .25).

In a series of statistical methods and mathematical models, estimates of effects of sire of fetus have been variable (37). Furthermore, several analyses from our laboratory have detected interactions of sire of cow with sire of fetus on milk yield (29). Concern exists for interpretation of various statistical models in estimating effects of sire of fetus. Ability of the service sire to exert an effect (positive or negative) on the maternal unit (as demonstrated by variation in postpartum milk yield) via the conceptus is dependent on the maternal unit responding to the various inhibitory or stimulatory agents produced by the conceptus in utero. Variability among maternal units or individuals for such factors as amount of target tissue (e.g., mammary alveolar cells), responsiveness of alveolar cells, and pool size and responsiveness of supporting tissues (e.g., adipose tissue) and nutrients, is critical in manifesting these conceptus effects. To reduce possible bias due to nonrandom mating, a logical mathematical model in the statistical analyses of production and reproduction data is one in which sire of cow and other factors (notably herd-year-season effects) are fixed. In field data (e.g., Dairy Herd Improvement milk yield records) this has resulted in estimates of variances of sire of fetus of 1% or less for milk yield and days open (37). The approach, by reducing genetic differences among mates of sires, doubtless would reduce interactions of fetal sire by cow, part of which would be genetic in the classic sense but the remainder of which would be environmental (e.g., physiological). Hence, these types of adjustments may underestimate the physiological impact of conceptuses on their dams since genetic (sire of cow) differences among dams have been minimized. At present, there seems to be no alternative statistical analytical approach with field data. Interactions of fetal sire by cow (dam of fetus) appear to be logical physiologically. Certain maternal units may differ from others in factors or conditions essential for maximum milk production. Such maternal units may respond more dramatically to stimulation by conceptus (e.g., hormonal) during pregnancy than others, or respond to one conceptus type (fetal sire) that provides a better array and quantity of stimulatory or inhibitory agents.

It is possible to delineate potential agents produced by the conceptus and maternal unit and to speculate on possible pathways by which they influence milk yield of the maternal unit (Figure 7). Experiments designed to induce lactation by hormonal injections have been useful to illustrate roles of such hormones as P₄, E₂, Prl, and Gc (6). However, these systems do not consider the impact of the placenta (bPL, etc.), and, generally, lactation responses have not been equivalent to those of a natural lactation following a normal pregnancy. Two classes of hormones (estrogens and bPL) are produced by the conceptus during late pregnancy and appear to regulate the maternal unit. Although the ultimate response in Figure 7 is milk yield, sites of hormonal actions may be at various locations for the maternal unit (hypothalamic, pituitary, ovarian, adrenal, mammary gland, uterus, and other metabolically important tissues such as adipose, liver, etc.). Identified in Figure 7 are several tissue sites and hormonal agents where interrelationships have been detected that ultimately may influence milk yield as a consequence of their regulation in the periparturient period.

Various hormones (6, 36) regulate cell numbers of mammary gland (P₄, estrogens, placental lactogens, Prl, Gc, growth hormone [GH], and insulin) and lactogenesis (Prl, GH, GC, and P₄ removal). Prepartum concentrations of bPL are associated positively with milk yield (3), and also it is likely that bPL has other regulatory effects (metabolic and endocrine) on the maternal unit (2) that have yet to be investigated extensively in cattle. Two studies detected relationships during gestation between concentrations of estrogens and subsequent milk yield. Terqui et al. (31) detected a positive correlation between total estrogens (conjugated plus free) in earlier stages of gestation (day 220) and subsequent preweaning growth rates in Cnarolais cattle (r = .87), whereas Eley et al. (9) reported negative correlations for E₁ (r =
-.72) and E$_1$SO$_4$ ($r = -.55$) in the immediate prepartum period and subsequent milk yield in dairy cows. This apparent difference (positive and negative correlations) may be related to the nature of measurements (milk yield vs. preweaning growth rates) and stage of gestation (220 days vs. 265 days to 279 days). At 220 days of gestation, total estrogens may be indicative of placental size, whereas measurements immediately prepartum may be influenced both by size and activity of the placenta since free (5, 9) and conjugated (Figure 3) estrogens are increasing at this later time. Estrogens also were related to various maternal hormones that regulate the mammary gland (9). For example, prepartum concentrations of E$_1$ were associated with Prl ($r = .65$), both within and among cows, and dynamics of Prl secretion in the periparturient period (Figure 4) were associated with subsequent milk yield ($r = .51$). Control of the parturition process by the conceptus influences the maternal endocrine system as well. The prepartum increase in free estrogens is associated temporally with gradual decreases in P$_4$ of plasma and the final demise of the CL (Figures 4 and 7) via prostaglandin F$_2$α secretion. Likewise, maternal concentrations of P$_4$ in the prepartum period were correlated negatively with Prl ($r = -.46$). Thus, a decrease in P$_4$ prepartum is directly (via removal of inhibition to lactogenesis; 6) and indirectly (by its relationship to Prl secretion) related to timing of lactogenesis. Chronic and acute changes in P$_4$ during the prepartum period may be associated with variation in subsequent milk yield. This is supported by Eley et al. (9), who reported that Control cows had different P$_4$ secretory patterns prepartum than Selected cows of higher milk yield.

A thorough understanding of how PGF$_2$α might affect the maternal unit in the postpartum period is needed. Concentrations of PGFM in plasma are increasing and still are elevated postpartum at which time concentrations of Prl are dynamic (Figure 4). From a pharmacological standpoint, injections of PGF$_2$α stimulate secretion of both Prl and Gc. Collectively, these interrelationships emphasize that the conceptus unit not only influences the potential of the dam to produce milk by its possible effects on mammary gland growth and lactogenesis but also influences its ability to maximize realization of that potential by exerting carryover effects postpartum in which various metabolic responses of the maternal unit are directed towards supporting the demands of lactation. Furthermore, the periparturient hormonal cascade, which results in birth of the fetus and initiation of lactation, is a closely integrated process between conceptus and maternal units.

A final point is warranted regarding the external environment. Proper management systems (16, 39) allow cattle more nearly to achieve their genetic potential for milk production. Future management systems also need to consider well-being of the conceptus and its potential effects that may be beneficial to the dam. A hostile physical environment (e.g., climate) exerts negative effects directly on the cow (32), as well as indirectly via the conceptus (4), which adversely affect milk yields.

As new knowledge is acquired, management specialists, physiologists, geneticists, nutritionists, and endocrinologists may incorporate various regulatory controls on conceptus function to improve efficiency of such traits as postpartum milk yield and reproductive efficiency. This will supplement genetic improvement already achieved in milk production through sire selection and use of artificial insemination. However, an interdisciplinary approach needs to be fostered in meeting these challenges.

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