A REVIEW OF ENDOCRINE REGULATION OF METABOLISM DURING LACTATION\textsuperscript{1,2}

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Summary

Lactogenesis signals the shift from uterine nutrient transfer to the fetus to neonatal nourishment at the mammary gland. Metabolic adaptations involved in this process are under endocrine regulation. Key events include an increase in blood flow to mammary tissue, a decrease in nutrient utilization by peripheral tissues and an increase in nutrient utilization by mammary tissue for milk synthesis. Deficits of certain substrates during early lactation require mobilization of those substrates from depot stores. Changes in metabolism of various tissues are related to changes in hormone receptor populations of those tissues and hormone concentrations in blood. Hormone receptors are therefore the primary mechanism by which information from the endocrine systems is linked to cellular metabolism. Endocrine changes at parturition result in dramatic changes in receptor populations of key tissues such as adipose and mammary tissues. Knowledge in this area, however, is incomplete. Relationship between hormone receptors and specific cellular metabolic pathways remains unresolved.

(Key Words: Hormones, Receptors, Metabolism, Lactogenesis, Lactation, Galactopoiesis.)

Introduction

The endocrine system regulates metabolism by a finely-tuned information delivery system that operates on several levels of mammalian organization. The net effect is maintenance of metabolic equilibrium (homeostasis) or, if the physiological state demands it, a concurrent redirection of nutrient flow to meet added metabolic requirements (homeorhesis, Bauman and Currie, 1980).

A classic example of both is the redirection of nutrient flow that occurs at parturition as the site of maternal delivery of nutrients to offspring shifts from a placental transfer at the uterus to milk synthesis, secretion and removal at the mammary gland. Several excellent reviews have outlined the magnitude of nutrient drain on the maternal unit, the key tissues involved in supporting the metabolic demands of lactation, and changes in systemic hormones associated with lactogenesis and lactation (Convey, 1974; Bauman and Currie, 1980; Thatcher et al., 1980).

The objective of this report is to relate changes in hormone concentrations and metabolic activity of tissues to changes in hormone receptor populations.

Metabolic Requirements

At parturition, the mammary gland achieves metabolic priority over other tissues to perform the synthesis and secretion of milk. Major nutrients required are water, glucose, amino acids, fatty acids, Ca and K. Negative balances of limiting nutrients occur during early lactation and may be as much as 7 kg/d of lipid, 3 kg/d of glucose, 330 g/d of amino acids and 7 g/d of Ca (Young, 1977; Bauman and Currie, 1980; Mepham, 1982; Bauman and Elliott, 1983).

The nutrient deficits are met by partitioning nutrients from body reserves either to the liver for recycling and use by the mammary gland, or

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directly to the mammary gland. The major changes involved in establishing metabolic priority of the mammary gland include: a shift in blood flow to mammary tissue, a decrease in utilization of nutrients by peripheral tissues and an increase in metabolic activity of mammary tissue. The endocrine involvement in this process is characterized by changes in hormone concentration in blood and alteration of tissue sensitivity to certain hormones by changes in receptor population or availability.

**Major Nutrients**

Glucose is utilized primarily for lactose and glycerol synthesis and generation of reducing-equivalents. Because little glucose is stored, the increased requirement is met partly through increased uptake, but primarily through gluconeogenesis from propionate, amino acids, lactate and glycerol in the liver. Glucose entry rates increase during early lactation even when intake is held constant (Bennink et al., 1972). This indicates an increase in glucose production independent of food intake, which must involve gluconeogenesis from body reserves of protein.

Amino acids needed for milk protein synthesis are also limiting factors in early lactation. Although much is understood about mammary gland utilization of amino acids (Mepham, 1982), knowledge of the quantitative release from body stores is lacking.

Long-chain fatty acids and two-carbon acetate provide the majority of energy for milk synthesis and mammary gland oxidative needs in the cow. This energy demand requires massive mobilization of fatty acids from body stores. Cows in early lactation can lose 20 to 50 kg of fat in 6 wk (Belyea et al., 1978; Bines and Hart, 1982). The synthetic pathways for triglyceride storage are de novo lipogenesis and fatty acid esterification, whereas release is through triglyceride hydrolysis (figure 1A and B). These pathways tend to be reciprocal in that lipogenesis predominates during positive energy balance and lipolysis during negative energy balance (figure 1A and B).

The adaptation to lactation by adipose tissue is exemplary of homeorhetic regulation. Even before lactation begins, in late gestation, adipose tissue synthetic rates decline (McNamara and Bauman, 1978; Vernon et al., 1981) in many species, and rates of lipolysis increase (Sidhu and Emery, 1973; Metz and van den Bergh, 1977). Lipoprotein lipase, the enzyme necessary for uptake of fatty acids from circulating triglycerides, decreases in activity at this time (Vernon et al., 1981). Exogenous prolactin has been shown to cause an increase in mammary lipoprotein lipase activity and a concomitant decrease in adipose tissue lipoprotein lipase activity (Zinder et al., 1974). Free fatty acids in blood rise dramatically at parturition as mammary fat synthesis increases (Collier et al., 1982b). The changes before and after parturition prepare the adipose tissue for the massive and extended FFA release during lactation. Lipogenesis remains low and lipolysis remains high during early lactation while the animal is in negative energy balance. When energy requirement decreases in late lactation, the adipose tissue pathways shift to increasing storage (figure 1A). These changes in adipose tissue metabolism are associated with changes in adrenergic and insulin receptor populations (figure 1A and B).

Calcium needs increase two- to threefold from late gestation to early lactation in the cow (van’t Klooster, 1976; Care et al., 1980). These needs are met both by increases in absorption of dietary Ca and by mobilization from bone. The regulation of this adaptation has been extensively studied (DeLuca, 1978; Care et al., 1980) and involves parathyroid hormone, vitamin D and calcitonin. The adaptation to lactation by Ca-metabolizing pathways is one of the best examples of efficient interaction of homeostatic and homeorhetic control systems. These endocrine systems interact at gut, kidney and bone to ensure adequate Ca supply during a period of acute need. That relatively few cows encounter parturient paresis (extreme Ca imbalance at term), is a tribute to the adequacy of the endocrine regulatory systems.

Prolactin may be involved in Ca metabolism during lactation. Prolactin can increase intestinal Ca absorption (Mainoya, 1975) and may regulate Ca metabolism independent of vitamin D (Pahuja and DeLuca, 1981).

**Mammary Blood Flow and Cardiac Output**

Because all milk precursors are derived from blood, rate of milk synthesis is dependent on rate of mammary blood flow and nutrient uptake by the mammary gland. Mammary blood flow as a percentage of cardiac output increases at lactogenesis (Linzell, 1974). Increasing mammary blood flow relative to other tissues has the net effect of diverting nutrients away from peripheral tissues toward milk synthesis and secretion and is one of the
homeorhetic adaptations occurring at lactogenesis. Likewise, increased metabolic activity of mammary tissue and decreased uptake of nutrients by peripheral tissue is an important aspect of nutrient partitioning.

Resting blood flow in the nonlactating, nonpregnant cow is related primarily to mass of tissue present (Heekin et al., 1983). Increases in mammary blood flow during pregnancy and at parturition appear to be related primarily to increases in tissue metabolic activity rather than any direct effect of a hormone on blood flow (Linzell, 1974; Burd et al., 1976, 1978; Heekin et al., 1980).
The uptake of milk precursors by the mammary gland is influenced more by rate of blood flow than by large changes in extraction rate. Research conducted mainly with the goat and cow indicates little change in arterio-venous difference with low or high flow rates or substrate concentrations (Linzell, 1974). Fasting animals, however, result in large decreases in mammary and hepatic blood flow (S. R. Davis, unpublished observation; Lomax and Baird, 1983). Decreases in hepatic blood flow are associated with reduced volatile fatty acid concentration in blood (Lomax and Baird, 1983). Thus, concentration of substrate in blood may directly or indirectly influence mammary blood flow. Hormones that increase milk synthesis indirectly cause increases in mammary blood flow (Davis et al., 1983). Thus, there is considerable autoregulation of blood flow directly at the mammary gland. The factors that control dilation and constriction of the mammary vascular bed are not well understood. However, local vascular regulation may be quite important because regulation of the degree of constriction of the precapillary arteriole would essentially regulate blood flow. Moore and Forsyth (1980) determined that local vascularity had marked effects on prolactin and estradiol receptor levels in mammary glands of rats.

Hormone Receptors and Metabolic Pathways

Hormone receptor interactions are the processes that link changes in endocrine information in the form of circulating hormones to specific cellular metabolic pathways. The interaction of hormones and available receptor sites is a crucial step in both homeostatic and homeorhetic regulation of metabolism. Prolactin receptor numbers in mammary tissue increase with onset of lactation in all species studied to date (Nagasawa et al., 1979), in agreement with the requirement for prolactin in lactogenesis (Delouis et al., 1980). Specific actions of prolactin at mammary epithelial tissue include effects on ion transport (Falconer and Rowe, 1977; Bisbee, 1981), amino acid transport (Pocius et al., 1980), Golgi volume (Akers et al., 1981), RNA and casein synthesis (Servely et al., 1982) and lipid synthesis (Collier et al., 1977; Cameron et al., 1983). Recently, a putative second messenger for prolactin has been identified (Servely et al., 1982), and a correlation between prolactin receptor occupancy and stimulation of casein and DNA synthesis has been established (Djiane et al., 1982). Considerable research has been performed with laboratory animals establishing factors that influence association and dissociation of prolactin to its receptor. Binding of prolactin at the cell membrane has been reported as having a dissociation constant in the range of $10^{-10}$ M (Necessary and Ebner, 1983). These authors have demonstrated that dissociation of prolactin from its receptor occurs rapidly at low pH, $pK = 4.7$, suggesting that this may be the mechanism by which prolactin is dissociated from its receptor after internalization. This would permit reutilization of the receptor. Evidence is accumulating that peptide receptors have more than one association and dissociation constant, as shown in figure 2. Corin and Donner (1982) have suggested that initial binding of insulin to the plasma membrane receptor is of low affinity. Subsequently, this hormone receptor complex converts to a higher affinity and is internalized. After internalization, the hormone receptor complex is dissociated, possibly as suggested by Necessary and Ebner (1983) by altered pH conditions within a pinocytotic vesicle. Thus, there are three possible association and dissociation constants for this model, which greatly complicates interpretation of published affinity constants for various receptor preparations. Kelly et al. (1983) have reported that the affinity constant for prolactin receptor on the plasma membrane isolated from liver is twofold lower than liver microsomal and Golgi prolactin receptors. Thus, caution should be utilized in interpreting significance of affinity constants obtained.

![Figure 2. Possible affinity constants for various stages of hormone-receptor interactions. 1. Initial binding; 2. Altered affinity, irreversible binding; 3. Endocytosis, dissociation, recycling of receptor. Adapted from Corin and Donner (1982).](image-url)
<table>
<thead>
<tr>
<th>Receptor</th>
<th>Reference</th>
<th>Animal</th>
<th>Tissue</th>
<th>Physiology</th>
<th>Ligand&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Molecular wt estimate</th>
<th>Detergent&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolactin</td>
<td>Church and Ebner (1982)</td>
<td>Rabbit</td>
<td>Mammary</td>
<td>Lactating</td>
<td>oPrl</td>
<td>320,000</td>
<td>2</td>
</tr>
<tr>
<td>Prolactin</td>
<td>Shiu and Friesen (1974)</td>
<td>Rabbit</td>
<td>Mammary</td>
<td>Pregnant</td>
<td>hGH</td>
<td>220,000</td>
<td>1</td>
</tr>
<tr>
<td>Prolactin</td>
<td>Carr and Jaffe (1981)</td>
<td>Frog</td>
<td>Liver</td>
<td>Tadpole</td>
<td>oPrl</td>
<td>170,000</td>
<td>1</td>
</tr>
<tr>
<td>Prolactin</td>
<td>Jaffe (1982)</td>
<td>Rat</td>
<td>Liver</td>
<td>Virgin</td>
<td>oPrl</td>
<td>99,800</td>
<td>1</td>
</tr>
<tr>
<td>Prolactin</td>
<td>Haeuptle et al. (1983)</td>
<td>Rabbit</td>
<td>Liver</td>
<td>Pregnant</td>
<td>hGH</td>
<td>70,000</td>
<td>1</td>
</tr>
<tr>
<td>Prolactin</td>
<td>Liscia and Vonderhaar (1982)</td>
<td>Mouse</td>
<td>Liver</td>
<td>Lactating</td>
<td>oPrl</td>
<td>37,000</td>
<td>4</td>
</tr>
<tr>
<td>Growth hormone</td>
<td>Haeuptle et al. (1983)</td>
<td>Rabbit</td>
<td>Mammary</td>
<td>Pregnant</td>
<td>hGH</td>
<td>67,000</td>
<td>3, 4</td>
</tr>
<tr>
<td>Growth hormone</td>
<td>Waters and Friesen (1979)</td>
<td>Rabbit</td>
<td>Mammary</td>
<td>Pregnant</td>
<td>hGH</td>
<td>40-75,000</td>
<td>1</td>
</tr>
<tr>
<td>Growth hormone</td>
<td>Tsushima et al. (1982)</td>
<td>Rabbit</td>
<td>Liver</td>
<td>Pregnant</td>
<td>hGH</td>
<td>200,000</td>
<td>5</td>
</tr>
</tbody>
</table>

<sup>a</sup>OPrL = ovine prolactin; hGH = human growth hormone.

<sup>b</sup>Detergent or denaturing agent: 1, Triton X-100; 2, Zwittergent 3-12; 3, Triton X-100/SDS; 4, Chaps; 5, SDS.
from crude membrane preparations. A number of factors have been shown to influence the number of available prolactin binding sites in various tissues. These factors include estrogen (Bohnet et al., 1977), thyroid hormones (Bhattacharya and Vonderhaar, 1979b), prolactin (Shani et al., 1982), growth hormone (Knazek et al., 1978), arachidonic acid, bradykinin and phospholipase A₂ (Dave et al., 1981), prostaglandin I₂ (Dave and Knazek, 1980) and phospholipid methylation of membranes (Bhattacharya and Vonderhaar, 1979a). Solubilization of the receptor from liver and mammary tissue has been accomplished using various detergents (table 1). As can be observed, different detergents and isolation techniques result in different molecular weight estimates, possibly due to the chemical structure of the receptor. For example, the insulin receptor has been shown to be composed of four subunits that dissociate into fragments of various molecular weights depending upon the solubilization and electrophoretic methods employed (Czech and Massague, 1982). Considerable research remains to complete the chemical characterization of the prolactin receptor, degree of heterogeneity of this receptor, if any, and events associated with binding, internalization, reutilization and the relationship of binding to cellular metabolism.

Despite the known requirement for prolactin in lactation, no published data are available on prolactin receptors in cattle. Interest in the role of prolactin during established lactation in cattle declined after reports that ergocryptine injection in lactating cattle failed to affect milk yield (Schams et al., 1972). However, there is a positive correlation between prolactin released during the milking stimulus and milk yield (Koprowski and Tucker, 1973a). Additionally, prolactin has been shown to be essential for maintenance of casein synthesis in cultured mammary tissue from lactating cattle (Ger-tier et al., 1982).

Prolactin, growth hormone and(or) placental lactogen have been implicated in controlling electrolyte, nutrient and water flux in a number of fluid pools in the mammalian system. A schematic of these sites is shown in figure 3. The sites shown are 1) gut (Mainoya, 1979, 1981), 2) kidney (Wallis and Lee, 1976), 3) placenta (Bazer et al., 1981), 4) amnion (Leontic and Tyson, 1977), 5) mammary gland (Taylor et al., 1975; Bisbee, 1981) and 6) sweat gland (Collier et al., 1982a). Of the sites shown, only receptors for prolactin in mammary gland have been partially characterized. The role of these three peptide families in partitioning nutrients among the various fluid pools during various physiological states requires further study. Considerable research is also warranted in characterizing receptor populations for these hormones. Also, there appears to be overlap of biological function of growth hormone, prolactin and placental lactogen, and to date only two classes of receptors have been identified for these hormones. Determining the relationship between structure of these peptides and affinity for their receptors as well as their biological function is central to understanding their mode of action.

Growth hormone receptors have been solubilized from liver (table 1). Molecular weight estimates for this receptor vary as well and are related to detergent or concentration of detergent used. Recently, the growth hormone receptor has been identified in ovine liver (Gluckman, et al., 1983). Because growth hormone is known to be galactopoietic in cattle (table 2), a high priority should be placed on determining the distribution and function of growth hormone and prolactin receptors.

Considerable research has been conducted on the insulin receptor in laboratory animals. However, no information is available on the insulin receptor in cattle. Insulin receptor content increases in mammary tissue and decreases in adipose tissue of rodents (O'Keefe and Cuatrecasas, 1974; Flint et al., 1979) with

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**Figure 3.** Reported sites of action of prolactin, growth hormone and placental lactogen on water and electrolyte flux.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Breed</th>
<th>Stage of lactation</th>
<th>Control milk yield, kg</th>
<th>Δ Milk yield, kg</th>
<th>Δ Milk yield, %</th>
<th>GH dose, mg</th>
<th>Duration GH treatment</th>
<th>Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brumby and Hancock (1955)</td>
<td>Mixed breeds</td>
<td>Peak</td>
<td>11.0</td>
<td>7.0</td>
<td>64</td>
<td>50</td>
<td>12 wk</td>
<td>Grass + meal (oats:bran, 4:1)</td>
</tr>
<tr>
<td>Brumby and Hancock (1955)</td>
<td>Mixed breeds</td>
<td>Late (265 d)</td>
<td>7.0</td>
<td>3.0</td>
<td>43</td>
<td>50</td>
<td>4 wk</td>
<td>Pasture only</td>
</tr>
<tr>
<td>Bines et al. (1980)</td>
<td>Friesian</td>
<td>7 mo</td>
<td>18.0</td>
<td>2.3</td>
<td>12.5</td>
<td>30</td>
<td>1 wk</td>
<td>Hay concentrate</td>
</tr>
<tr>
<td>Davis et al. (1983)</td>
<td>Jersey</td>
<td>3-6 mo</td>
<td>16.2</td>
<td>3.0</td>
<td>18.7</td>
<td>40</td>
<td>4 wk</td>
<td>Complete diet</td>
</tr>
<tr>
<td>Machlin (1973)</td>
<td>Holstein</td>
<td>NRb</td>
<td>13.3</td>
<td>3.3</td>
<td>25</td>
<td>33</td>
<td>10 d</td>
<td>Complete diet</td>
</tr>
<tr>
<td>Machlin (1973)</td>
<td>Holstein</td>
<td>NR</td>
<td>14</td>
<td>5.0</td>
<td>35</td>
<td>40</td>
<td>8 wk</td>
<td>Complete diet</td>
</tr>
<tr>
<td>Peel et al. (1981)</td>
<td>Holstein</td>
<td>Peak</td>
<td>34.7</td>
<td>3.3</td>
<td>9.5</td>
<td>40</td>
<td>11 d</td>
<td>Complete diet</td>
</tr>
<tr>
<td>Peel et al. (1983)</td>
<td>Holstein</td>
<td>Early</td>
<td>28</td>
<td>4.3</td>
<td>14</td>
<td>44</td>
<td>10 d</td>
<td>Complete diet</td>
</tr>
<tr>
<td>Peel et al. (1983)</td>
<td>Holstein</td>
<td>Late</td>
<td>12</td>
<td>3.9</td>
<td>31</td>
<td>44</td>
<td>10 d</td>
<td>Complete diet</td>
</tr>
</tbody>
</table>

*aGH = growth hormone.

bNR = not reported.
onset of lactation (table 3, figure 1B). This is in agreement with increased utilization of glucose at the mammary gland and decreased utilization of glucose at adipose tissue for lipid synthesis. Instead, as shown in figure 1B, adipose tissue converts to lipolysis rather than lipogenesis to provide lipid for milk fat. Although insulin receptor numbers have been shown to increase in nonruminant mammary tissue at lactogenesis, there is no apparent effect of insulin on rates of glucose uptake or milk synthesis in ruminants (Hove, 1978). This may be related to a preponderance of low affinity binding sites for insulin in lactating mammary tissue (Inagaki and Kohmoto, 1982). The relative insensitivity of lactating mammary tissue to insulin removes a possible antagonism between systemic glucose homeostasis and glucose utilization for lactose synthesis at the mammary gland.

Clearly, much more is known about changes in concentrations of systemic hormones during lactation than is known about the interaction of these hormones with their respective receptor sites. Even less is known about the relationship of the receptors to cellular metabolism. A critical gap exists between what is known about ongoing metabolism in the cell and hormone-receptor interactions. Considerable research is needed to biochemically characterize receptor molecules and their interaction with cellular metabolic pathways.

**Hormonal Regulation of Nutrient Partitioning**

As stated previously, direct regulation of metabolism by the endocrine system occurs via two major mechanisms: changes in blood hormone concentration and changes in available receptor populations that alter tissue sensitivity and hormone metabolism.

Several extensive reviews have described changes in hormone concentrations during the periparturient period and lactation (Convey, 1974; Delouis et al., 1980; Tucker, 1981; Thatcher et al., 1982). Generally, changes in hormone concentration and receptor population fall into two groups: transitory changes occurring during the periparturient period, and the long-term changes that occur throughout lactation.

**Hormone and Receptor Changes During the Periparturient Period.** Hormone changes during this period may be the key events that establish the basic pattern of receptor populations in various target tissues for the entire lactation. This would set the stage for regulating nutrient flow during lactation primarily by changing hormone secretion rates. Evidence to support this has been gathered in both laboratory and domestic animals. Changes in blood hormone concentrations known to occur in the periparturient period include hormones of conceptus origin (estrogens and placental lactogen) and hormones of maternal origin (prolactin, glucocorticoids, prostaglandins, progesterone, etc.).

**FUNCTION**

<table>
<thead>
<tr>
<th>Tissues</th>
<th>Adaptation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose metabolism</td>
<td>Adipose tissue</td>
</tr>
<tr>
<td></td>
<td>Mammary tissue</td>
</tr>
<tr>
<td></td>
<td>Reduced insulin binding</td>
</tr>
<tr>
<td></td>
<td>Lack of insulin requirement for lactose synthesis</td>
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<tr>
<td></td>
<td>Increased numbers of low affinity insulin receptors</td>
</tr>
<tr>
<td>Lipid metabolism</td>
<td>Adipose tissue</td>
</tr>
<tr>
<td></td>
<td>Mammary tissue</td>
</tr>
<tr>
<td></td>
<td>Increased numbers of β-adrenergic receptors</td>
</tr>
<tr>
<td></td>
<td>Increased prolactin binding</td>
</tr>
<tr>
<td>Milk synthesis</td>
<td>Mammary tissue</td>
</tr>
<tr>
<td></td>
<td>Increase in prolactin receptors</td>
</tr>
<tr>
<td></td>
<td>Increase in glucocorticoid receptors</td>
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<tr>
<td></td>
<td>Decrease in progesterone receptors</td>
</tr>
<tr>
<td></td>
<td>Increase in low affinity insulin receptors</td>
</tr>
</tbody>
</table>
insulin and oxytocin). Changes in receptor populations of various tissues are shown in table 3.

The decline in progesterone concentration before parturition is due to the luteolytic action of prostaglandin $F_2\alpha$ of uterine origin. This decline in progesterone is associated with reduced progesterone receptors in mammary tissue (Shymala and McBlain, 1979; table 3) and increased synthetic activity of mammary tissue.

Mammary glucocorticoid receptor numbers increase at lactogenesis as shown in table 3 and as described by Goresit and Tucker (1976). This may be due to the increase in glucocorticoids at parturition or a decrease in progesterone. Progesterone competes for the glucocorticoid receptor and the decline in progesterone is associated with increased numbers of available glucocorticoid receptors (Collier and Tucker, 1978). Insulin receptors increase in mammary tissue and decrease in adipose tissue at parturition (O'Keefe and Cuatrecasas, 1974; Flint et al., 1979; table 3), apparently in association with the decline in progesterone (Flint et al., 1980). Inagaki and Kohmoto (1982) reported that affinity of mammary insulin receptors differed between lactating and pregnant animals. Mammary tissue displayed predominantly high affinity binding during estrous cycles and early gestation and low affinity binding in late gestation and lactation. Presently, it is not known whether these binding components are nonidentical subunits of different receptors or a single species of receptor that converts from a low affinity to high affinity state. The latter possibility was recently proposed by Corin and Donner (1982), who determined that hepatic insulin receptors convert from low to high affinity state subsequent to insulin binding.

Adrenergic receptor population increases in adipose tissue at lactogenesis (Jaster and Wegner, 1981; figure 1B). Although endocrine regulation of this phenomenon is not understood, the metabolic result is a greatly increased epinephrine-stimulated fatty acid release. The decrease in insulin receptor numbers and increase in epinephrine receptors of adipose tissue are linked to an altered cellular metabolism favoring lipolysis rather than lipogenesis. Mammary gland prolactin binding increases dramatically at parturition in those animals producing placental lactogen (Holcomb et al., 1976) and at midgestation in those animals that do not produce a placental lactogen (Djiane et al., 1977). Thus, increase in prolactin binding in species producing a placental lactogen is believed to be due to the decline in placental lactogen at parturition, removing it as a competitor for the prolactin receptor. Estrogen has also been shown to cause increases in mammary gland prolactin receptors (Bohnet et al., 1977), and periparturient rise and fall in estrogen may be involved in regulating prolactin receptor numbers in various tissues. Prolactin also rises and falls during the periparturient period and has been shown to cause increases in its own receptor (Nagasawa et al., 1979).

Secretion of prostaglandin $F_2\alpha$ by the uterus increases dramatically during the periparturient period in cattle (Thatcher et al., 1982). What effects it or its metabolite, 13, 14-dihydro-15-keto prostaglandin $F_2\alpha$, has on metabolism or receptor populations remains unresolved.

In addition to causing changes in receptor populations, hormonal changes during the periparturient period result in initiation of milk synthesis and mobilization of body stores of substrates required for milk synthesis. The relationship between changing receptor populations and change in activity of metabolic pathways in the tissues involved requires considerable additional research. The timing of metabolic changes in adipose tissue and mammary tissue in ruminants has only been studied in goats (Chilliard et al., 1977, 1978). Changes in peptide receptor populations during gestation and lactation in domestic animals have not been studied to date.

Hormonal Changes During Lactation. Two major adaptations occur in hormone concentrations during lactation. These are changes in basal concentration, (i.e., insulin and growth hormone) and changes in secretion in response to the milking stimulus (i.e., prolactin).

The suckling or milking stimulus results in release of prolactin, adrenocorticotropic hormone, oxytocin and, in some animals, growth hormone (Tucker, 1981). In vitro, prolactin is essential for maintaining mammary synthesis of casein (Gertler et al., 1982). The relative increase in glucocorticoids after milking is not related to stage of lactation or milk yield (Tucker, 1981). Feeding a synthetic glucocorticoid, 9-fluoroprednisolone acetate, during lactation gave variable results (Head et al., 1976; Swanson and Lind, 1976).

Hormones that appear to be related to milk yield in cattle are prolactin, growth hormone, insulin and thyroxine. Basal prolactin concen-
trations are correlated to milk yield in cattle; however, the correlation is low compared with the correlation between milking stimulus release and milk yield (Koprowski and Tucker, 1973a). Secretion and clearance rates of prolactin did not differ between high and low yielding cattle (Hart et al., 1980). These same investigators, however, did find an increase in metabolic clearance and distribution space of prolactin between 30 and 150 d of lactation.

Insulin concentrations are related negatively to milk yield (Koprowski and Tucker, 1973b) and low yielding cattle have a higher insulin secretion rate throughout lactation than high yielding cattle (Hart et al., 1980). Low insulin concentrations during early lactation are presumably related to energy balance rather than stage of lactation per se. Available glucose is preferentially shunted towards mammary metabolism.

Growth hormone concentrations during lactation are related to stage of lactation (Koprowski and Tucker, 1973b) and distribution space of growth hormone is larger in high yielding cattle compared with low yielding cattle (Hart et al., 1980). Injection of growth hormone in cattle results in increased milk yield (table 2). It is noteworthy that the absolute increase in milk yield in early and late lactation is quite similar although the percentages differ (table 2). An improvement of gross efficiency of feed conversion to milk by growth hormone has been shown in several studies (Brumby and Hancock, 1955; Machlin, 1973; Bines et al., 1980; Peel et al., 1981). The increase in gross efficiency of feed conversion in growth hormone-treated animals does not appear to be due to any change in partial efficiency of metabolizable energy utilization for milk synthesis (Tyrell et al., 1982). It is probable that the effect of growth hormone is to preferentially partition nutrients to the mammary gland at the expense of other tissues. This hypothesis is supported by the observation that mammary blood flow as a percentage of cardiac output increases in growth hormone-treated dairy cows (Davis et al., 1983).

Thyroxine injections or thyroprotein feeding have also been shown to cause increases in milk yield (Blaxter et al., 1949). The galactopoietic effects of feeding thyroprotein, however, last only 2 to 4 mo and subsequent yields are lower than expected, resulting in no clear increase in milk yield over the entire lactation (Thomas et al., 1957) while additional feed must be given (Thomas, 1953). In contrast, animals given growth hormone display no increase in feed intake despite increased milk yield (Peel et al., 1981). Thyroxine concentrations are negatively correlated with milk yield (Shaw et al., 1975) and thyroid secretion rates are reduced during lactation. This suggests that lowered thyroid hormone secretion rates during lactation may reduce peripheral metabolism that would allow preferential utilization of substrate by mammary tissue. Metabolic rate of mammary tissue is clearly not directly related to systemic thyroid hormone concentrations.

**Literature Cited**


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