

NUTRITIONAL INFLUENCES ON REPRODUCTION OF BEEF COWS

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ABSTRACT

Production of weaned calves is relatively inefficient. Many cows and heifers exposed to bulls do not become pregnant because they are not in estrus during the breeding season. Losses from less than optimal reproductive performance also results in reduced weaning weights of younger calves the next year.

Body energy reserves and nutrient intake are major regulators of reproduction of beef cows. Inadequate body energy reserves at parturition increase the interval to first estrus and ovulation, and postpartum nutrient intake can influence length of the anestrous interval in cows with thin to moderate body condition score (BCS). Nutritional restriction causes decreased secretion of gonadotropin releasing hormone and luteinizing hormone, reduces follicular growth, and decreases concentrations of estradiol in plasma. In addition to direct and indirect effects of decreased energy intake on the hypothalamus and pituitary, nutrition may influence ovarian function. Adequate body energy stores and sufficient plasma concentrations of metabolic regulators, are necessary for ovulation in postpartum cows. Complex interactions between hormones, metabolic compounds and other signals control follicular maturation, estrus, and ovulation in postpartum beef cows.

INTRODUCTION

A major determinant of profitability of beef production is reproductive efficiency. Beef cattle are frequently not pregnant at the end of the breeding season because of the absence of normal estrous cycles. The anestrous condition in postpartum cows is caused by reduced ovarian follicular growth and the absence of luteal activity (Wettemann, 1980). A major factor that regulate duration of the postpartum anestrous period are nutrient intake before and after calving. If nutrient intake is inadequate and body energy reserves are depleted, the interval from calving to the first estrus is extended (Wiltbank *et al.*, 1962; Dunn and Kaltenbach, 1980; Short *et al.*, 1990). Suckling also inhibits the resumption of normal estrous cycles after parturition (Short *et al.*, 1972; Williams, 1990).

A major goal of a beef cow feeding program should be to have a large percentage of the cows exhibiting estrous cycles early in the breeding season. The optimal amount of supplemental feed required after calving is

not well established. Factors such as forage quality and availability, the type of supplement fed, or BCS at calving, can greatly influence the response to nutrient intake. Feeding protein supplements to postpartum cows will increase intake of dry forages and thus total energy in the diet. If cows are fed diets which contain large amounts of starch, forage intake maybe reduced and total energy in the diet may be unchanged or reduced.

Relationships between body energy reserves and weight loss (before and after parturition) with the duration of the postpartum anestrous period have been established (Dunn and Kaltenbach, 1980; Selk *et al.*, 1988). The most important factor that influences pregnancy rate is body energy reserves at calving. When beef cows had a body condition score (BCS; 1= emaciated, 9= obese; Wagner *et al.*, 1988) of five or greater at calving, the number of days from calving to first estrus and ovulation was 15 to 35% less than if cows calved with a BCS of less than 5 (Richards *et al.*, 1986; Loooper *et al.*, 1997, Lents *et al.*, 2000).

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Body condition score of primiparous cows at calving influences the response to postpartum nutrient intake (Spitzer *et al.*, 1995). When young cows with a BCS of 6 were fed to gain 0.85 vs 0.44 kg/d after calving, the percentage of cows in estrus during the first 20 d of the breeding season increased from 40 to 85%. However, when cows had a BCS of 4, the greater daily gain only increased the percentage of cows in estrus from 33 to 50%.

Energy intake and body energy stores influence concentrations of energy substrates and metabolic hormones in the blood of cattle. Alterations in concentrations of substrates and metabolic hormones signal the hypothalamic-pituitary-ovarian axis as to the metabolic status of the animal. However the metabolic signals between body energy reserves and follicular maturation and ovulation have not been determined. Determination of the signal or signals by which body energy reserves control the onset of estrus cycles after calving will allow the postpartum anestrous interval to be decreased without feeding additional energy to cows.

DISCUSSION

Follicular development after parturition

The first dominant follicle (DF) occurs within 10 to 12 d after parturition in beef and dairy cows (Murphy *et al.*, 1990; Savio *et al.*, 1990; Stagg *et al.*, 1995). Thus, a lack of follicular waves after parturition is not the limiting factor for the onset of estrus and ovulation. The first postpartum DF ovulated in few (11%) beef cows (Murphy *et al.*, 1990), whereas the first DF ovulated in most (74%) dairy cows (Savio *et al.*, 1990). Beef cows with inadequate body energy reserves and/or suckling calves had several follicular waves before the first ovulation (Murphy *et al.*, 1990; Stagg *et al.*, 1995) and the number of DF before ovulation was greater with reduced postpartum nutrient intake.

Frequent pulses of LH are needed for maturation of preovulatory follicles (Roberson *et al.*, 1989; Stock and Fortune, 1993). Mean

concentrations of LH and frequency of pulses increase with time before the first postpartum ovulation (Stagg *et al.*, 1998). Recurring follicular waves and atresia of the DF may be caused by inadequate pulses of LH. Nutritionally-induced anovulation is associated with decreased secretion of LH (Wettemann and Bossis, 1999). The first DF after parturition was prolonged or ovulated when beef cows were given hourly pulses of LH (Duffy *et al.*, 2000). Treatment of nutritionally-induced anovulatory cows with one pulse of GnRH each hour will initiate ovarian luteal activity (Bishop and Wettemann, 1993; Vizcarra *et al.*, 1997).

The ability of DF to produce estradiol is limited during the postpartum anovulatory period and increases with time after parturition (Spicer *et al.*, 1986). Postpartum anovulatory follicles produced less estradiol than preovulatory follicles (Braden *et al.*, 1986). Although the amount of insulin-like growth hormone-I (IGF-I) in follicular fluid was not influenced by time postpartum or whether a follicle was estrogen active (Spicer *et al.*, 1988; Rutter and Manns, 1991), amounts of IGF binding proteins in follicles could regulate the availability of IGF-I to follicular cells. Factors that increase the postpartum interval to first ovulation probably decrease steroidogenesis in follicles.

Abnormal luteal function after the first ovulation occurs frequently in beef cows. The luteal phase after the spontaneous first postpartum ovulation is usually less than 10 d (Corah *et al.*, 1974; Werth *et al.*, 1996; Looper *et al.*, 1997). Similarly, a short luteal phase also occurs after early weaning (Odde *et al.*, 1980; Copelin *et al.*, 1987; Breuel *et al.*, 1993) or treatment with GnRH (Kesler *et al.*, 1980; Wettemann *et al.*, 1982). Short lived CL cannot maintain pregnancy since they regress before d 15 when maternal recognition of pregnancy occurs (Northey and French, 1980). A premature luteolytic signal causes short lived CL (Garverick *et al.*, 1992).

Estrous behavior usually does not occur before the first postpartum ovulation in beef (Murphy *et al.*, 1990; Perry *et al.*, 1991; Looper *et al.*, 1997) and dairy cows (Graves *et al.*, 1968; Savio *et al.*, 1990). Duration of the luteal

phase after the first estrus in beef cows is usually of normal duration (Corah *et al.*, 1974; Odde *et al.*, 1980; Looper *et al.*, 1997).

Secretion of gonadotropin

Secretion of LH is a rate limiting step for the initiation of follicular growth and estrus after calving. Pulsatile secretion of LH is associated with secretion of GnRH in cows (Gazal *et al.*, 1998; Yoshioka *et al.*, 2001) and increased frequency of exogenous GnRH pulses increased pulse frequency and mean concentrations of LH in anovulatory cows (Bishop and Wettemann, 1993; Vizcarra *et al.*, 1997).

Nutritional effects on LH secretion in ruminants are dissimilar to monogastric animals. Short term nutritional restriction or fasting reduces LH secretion in rats (Campbell *et al.*, 1977) and primates (Cameron and Nosbisch, 1991) but not in sheep and cattle (Khireddine *et al.*, 1996; Mackey *et al.*, 2000; Amstalden *et al.*, 2002a). To determine if products of rumen fermentation are involved in control of LH secretion, total rumen contents of fistulated steers (440 kg) were removed and either all the fluid and particulate material were replaced (control) or only 15% of the rumen contents were replaced (restricted; Ojeda *et al.*, 1996). Restricted steers were fed 2 kg of low quality hay each day and control steers were fed a diet of hay and soybean meal to maintain weight. Mean concentration of LH and pulse frequency and amplitude were similar in control and restricted steers before and after three days of feed restriction. Although the nutritional restriction resulted in a decrease in substrate and microbes for rumen fermentation, mobilization of body fat, and a 2-fold increase in plasma concentration of NEFA, LH secretion was unaltered.

Secretion of estrogens and progesterone during pregnancy reduce concentrations of LH in the pituitary at parturition (Nett *et al.*, 1987) and concentration of LH increase in serum within a week after calving (Ingalls *et al.*, 1973). The interval from calving until pulsatile secretion of LH is sufficient for maturation of the ovulatory follicle is influenced by factors such as body energy

reserve, nutrient intake, and suckling. During the early postpartum period a pulse of LH is secreted every 3 to 6 h (Humphrey *et al.*, 1983; Nett *et al.*, 1988) and the frequency increases to 1 to 2 pulses per h before the first ovulation (Peters *et al.*, 1981; Terqui *et al.*, 1982). Reduced pulsatile secretion of LH during the early postpartum period is probably associated with decreased GnRH secretion because the number and affinity of GnRH binding sites on the pituitary do not change during the postpartum period (Moss *et al.*, 1985) and pulsatile treatment with GnRH causes pulsatile secretion of LH.

Concentrations of FSH increase within a week after parturition (Schallenberger *et al.*, 1982; Peters and Lamming, 1984) and are constant until ovulation (Convey *et al.*, 1983; Nett *et al.*, 1988). Postpartum anestrous beef cows have adequate FSH for development of DF (Stagg *et al.*, 1998). Similar secretion of FSH in restricted and maintenance fed heifers before the onset of nutritionally-induced anovulation, and increased concentrations of FSH in serum after the onset of anovulation (Bossis *et al.*, 1999), indicate that secretion of FSH is not limiting for follicular growth in energy restricted cattle.

Secretion of progesterone and estradiol

Plasma concentrations of progesterone are minimal at parturition (Henricks *et al.*, 1972; Smith *et al.*, 1973) and increase after the first ovulation (Lauderdale, 1986; Perry *et al.*, 1991; Werth *et al.*, 1996) or luteinization (Donaldson *et al.*, 1970; Corah *et al.*, 1974) of a follicle. The first increase in plasma concentrations of progesterone in beef cows after calving usually persist for 3 to 9 days (Perry *et al.*, 1991; Werth *et al.*, 1996; Looper, 1999). This transient increase in progesterone is usually not preceded by estrus.

Plasma concentrations of estrogens decrease rapidly after parturition (see review, Wettemann, 1980). During the postpartum anovulatory period, concentrations of estradiol may increase in plasma for a short duration, but these increases may not be

associated with growth and maturation of follicles (Murphy *et al.*, 1990; Stagg *et al.*, 1995). Concentrations of estradiol in plasma increase before the first postpartum ovulation (Echternkamp and Hansel 1973; Perry *et al.*, 1991; Stagg *et al.*, 1995).

Suckling and anovulation

Suckling prolongs postpartum anovulation and the effect is of greatest magnitude in primiparous and thin cows (Short *et al.*, 1990). (See Williams, 1990, for a detailed review of the effect of suckling on neuroendocrine control of postpartum ovarian function.) Cows develop a bond with their calf (Silveira *et al.*, 1993; Stevenson *et al.*, 1997) and the effect of sucking by a cow's calf is greater than suckling by a foster calf. Although twice daily suckling is adequate to increase the duration of the postpartum anestrous interval, twice daily milking does not prolong anovulation (Lamb *et al.*, 1999). Fewer cows with ad libitum suckling had ovulated by 80 d post partum (43%) compared with cows that had calves isolated and only allowed to suckle once per day (90%; Stagg *et al.*, 1998). However, if calves were allowed to suckle once per day and calves were adjacent to cows continuously, only 65% of the cows had ovulated by 80 d post partum. Thus, development of the cow-calf bond prolongs the postpartum anovulatory interval even with a reduced suckling stimulus.

Body energy reserves at calving influences the effect of suckling on ovarian function. If cows had a BCS greater than or equal to 5 at calving and calves were weaned at 35 d post partum, all cows ovulated by 25 d after weaning (Bishop *et al.*, 1994). In contrast only 40% of cows with a BCS less than 5 had ovulated by 25 d after weaning. Although the interval from weaning to ovulation is greater in thin cows than in cows with greater BCS, weaning is a useful management option to increase pregnancy rates in thin cows.

Potential metabolic signals

Macronutrients or their metabolites can regulate gene expression and influence growth and body functions in addition to their roles

as sources of energy. Glucose can influence expression of genes in cells independent of insulin (Jump, 2001) and low concentrations of cholesterol in cells increase the amount of low density lipoprotein receptor and synthesis of cholesterol (Brown and Goldstein, 1997). Fatty acids are also regulators of gene expression in cells and type of fat in the diet, amount consumed, and duration of consumption can influence responses in cells by alteration of transcription factors (Jump and Clarke, 1999).

Insulin

Consumption of a meal and long term dietary treatments have minimal effects on plasma glucose in cattle (Yelich *et al.*, 1996; Vizcarra *et al.*, 1998). Although plasma concentration of glucose in cattle are extremely constant compared with monogastric animals, insulin regulates utilization of glucose by bovine cells.

There are receptors for insulin in the brain, pituitary gland (Lesniak *et al.*, 1988), and ovarian tissue (Poretsky and Kalin, 1987). Insulin stimulates release of GnRH from hypothalamic fragments in vitro when glucose is available (Arias *et al.*, 1992) and infusion of insulin into the cerebroventricles of nutritionally-restricted ewes increased LH secretion (Daniel *et al.*, 2000). Insulin also stimulates steroid production by bovine ovarian cells (Spicer and Echternkamp, 1995). Systemic treatment of cows with insulin may increase follicular development (Harrison and Randel, 1986) and estradiol production by large follicles (Simpson *et al.*, 1994).

The hypothalamus, unlike other areas in the central nervous system, expresses an insulin-dependent glucose transporter (Livingstone *et al.*, 1995). This may allow the hypothalamus to respond to increased concentrations of glucose in blood. During nutritionally-induced anestrus, cows become resistant to insulin (Richards *et al.*, 1989) and entry of glucose into hypothalamic cells may be reduced.

Early studies demonstrated that 2-deoxy-D-glucose, a glucose antagonist, induced anestrus and anovulation in cows (McClure *et al.*, 1978), and secretion of LH was reduced by treatment of ewes (Funston *et al.*,

1995b) and ram lambs (Bucholtz *et al.*, 1996) with 2-deoxy-D-glucose. Phlorizin-induced hypoglycemia prevented LH and insulin secretion after early weaning of beef cows (Rutter and Manns, 1987).

IGF-I

Insulin-like growth factor-I is produced by the liver and has effects on many cell types to regulate carbohydrate, fat, and protein metabolism. IGF-I is also produced by other tissues and can have autocrine and paracrine effects. Concentrations of IGF-I in blood of cattle are decreased during feed restriction (Richards *et al.*, 1991, 1995; Armstrong *et al.*, 1993) and concentrations of GH are increased (Bossis *et al.*, 1999). Restriction of protein and(or) energy intake reduces the increase in blood IGF-I that usually occurs in response to treatment with GH (Brier *et al.*, 1988, Ronge and Blum 1989, Armstrong *et al.*, 1993). The reduction in IGF-I in serum during nutrient restriction is associated with reduced binding of GH to hepatic membranes in restricted steers (Brier *et al.*, 1988). At least six high affinity IGF binding proteins (IGFBPs) in biological fluids can influence the functions of IGF-I (Jones and Clemmons, 1995). Degradation of IGFBPs by proteases also influences the biological activity of IGF-I (Maile and Holly, 1999).

Hypothalamic and other neural cells in rats have IGF type I receptors (Lesniak *et al.*, 1988; Hiney *et al.*, 1996) and IGF-I stimulated expression of the GnRH gene in neural cells (Longo *et al.*, 1998) and GnRH secretion (Anderson *et al.*, 1999). Body energy reserves are related to amounts of IGFBP in hypothalami of ewes (Snyder *et al.*, 1999).

Gene expression for type-1 IGF receptors and IGFBP-5 occur in the pars tuberalis and pars distalis of the ovine pituitary and are greater than expression for IGF-II, type-2 receptor and IGFBP-3 (Adam *et al.*, 2000). Treatment of ovine pituitary cells with IGF-I increases LH release (Adam *et al.*, 2000). IGFBP-2, -3, and -5 are present in bovine pituitary glands (Funston *et al.*, 1995) and the activity is associated with the stage of the estrous cycle (Roberts *et al.*, 2001).

Follicles synthesize IGF-I and systemic IGF-I could also influence ovarian function (Spicer and Echterkamp, 1995). Specifically, ovarian cell proliferation and steroidogenesis are stimulated by IGF-I (Spicer *et al.*, 1993; Spicer and Chamberlain, 1998). Steroidogenesis is stimulated by IGF-I binding to type I receptors on cells, and IGF-I is also bound to high affinity binding proteins in extracellular fluids. Concentrations of IGF-I in follicular fluid and its receptor in granulosa cells of dominant and subordinate follicles are similar, however dominant follicles have less IGFBP activity than subordinate follicles (Stewart *et al.*, 1996; Yuan *et al.*, 1998). The decrease in intrafollicular concentrations of IGFBP during terminal development of follicles (Stewart *et al.*, 1996; de la Sota *et al.*, 1996; Funston *et al.*, 1996) may increase availability of IGF-I to follicular cells. Concentrations of IGFBP-4 may determine which follicle becomes dominant during selection in cattle (Mihm *et al.*, 2000). Increased energy intake resulted in reduced concentrations of mRNA for IGFBP-2 and -4 in small follicles of heifers (Armstrong *et al.*, 2001).

Nonesterified fatty acids

Adipose tissue of ruminants is metabolized and nonesterified fatty acids (NEFA) and glycerol are released and can be used as sources of energy during negative energy balance. Concentrations of NEFA in nutritionally-induced anovulation of heifers are maximal during anestrus, decrease dramatically during realimentation, and then gradually increase before resumption of ovulation (Bossis *et al.*, 1999, 2000). Plasma concentrations of NEFA do not appear to be directly involved in nutritional regulation of ovarian function in heifers. A direct effect of NEFA on the hypothalamus and/or pituitary gland has not been established in cattle and infusion of free fatty acids did not alter LH secretion in lambs (Estienne *et al.*, 1990).

Leptin

Concentrations of leptin in plasma are related to amounts of body fat in humans (Considine *et al.*, 1996; Ostlund *et al.*, 1996)

and rodents (Maffei *et al.*, 1995; Schneider *et al.*, 2000), but the relationship between plasma concentrations of leptin and body fat or BCS is not well established in ruminants. Nutrient intake influences amounts of mRNA for leptin in fat of cattle (Tsuchiya *et al.*, 1998; Amstalden *et al.*, 2000) and concentrations of leptin in plasma (Ehrhardt *et al.*, 2000). Concentrations of leptin in plasma of dairy cows are decreased by a negative energy balance (Block *et al.*, 2001). These effects of nutrition on plasma leptin increases the difficulty of determining the effect of body fat reserves on plasma leptin. Concentrations of leptin in plasma respond in 2 d to fasting (Amstalden *et al.*, 2000) or 4 d to reduced nutrient intake (Ciccioli *et al.*, 2003). Studies have determined positive correlations between body fat and plasma leptin in calves and dairy cows (Ehrhardt *et al.*, 2000) and ewes (Delavaud *et al.*, 2000; Thomas *et al.*, 2001) but minimal numbers of animals were sampled and in the studies with calves and ewes amount of body fat was confounded with dietary intake. We have determined that concentrations of Leptin in the plasma of gestating cows is influenced by feed intake not by body condition score (Lents *et al.*, 2005).

Since the discovery of leptin, there is much interest as to its potential function as a signal to inform brain targets about body energy stores (Spicer, 2001; Smith *et al.*, 2002). Receptors for leptin have been identified in the brain (Dyer *et al.*, 1997) and pituitary (Iqbal *et al.*, 2000) of sheep, and feed restriction increases expression of leptin receptor in hypothalamic nuclei of ewes (Dyer *et al.*, 1997). Administration of leptin into the brain of sheep reduces feed intake and suppresses LH pulse frequency (Blache *et al.*, 2000; Morrison *et al.*, 2001). However, the effect of leptin on LH secretion can not be separated from the effect of leptin on feed intake. Fasting (Tsuchiya *et al.*, 1998) of cows or heifers (Amstalden *et al.*, 2000) for 48 h decreased leptin mRNA in adipose tissue and concentrations of leptin in plasma (Amstalden *et al.*, 2000) without altering concentration or amplitude of LH pulses. Central infusion of leptin did not influence pulsatile secretion of LH in well-fed ewes (Henry *et al.*, 1999) but prevented the fasting-

induced decrease in LH pulse frequency in wethers. Exogenous leptin prevented the fasting induced suppression of plasma concentrations of LH in castrated rams treated with estradiol (Nagatani *et al.*, 2000) and LH secretion in fasted ovariectomized estradiol treated cows was increased by leptin treatment (Zieba *et al.*, 2002). Leptin has a direct inhibitory effect on the bovine ovary (Spicer and Francisco, 1997). Greater than adequate nutritional intake could result in abundant concentrations of leptin in plasma that could prevent the production of excessive amounts of estradiol by follicles (Spicer, 2001).

Nutrition and postpartum endocrine function

The influence of BCS at calving and postpartum nutrient intake on endocrine and ovarian functions was evaluated in Angus x Hereford primiparous cows (Ciccioli *et al.*, 2003). During the last third of gestation, cows were fed different amounts of protein supplement to produce cows with BCS of 4 or 5 at calving. At parturition, thin (BCS = 4.4 ± 0.1) and moderate (BCS 5.1 ± 0.1) cows were allotted to diets for gains of 0.45 kg/d (M; n=17) or 0.90 kg/d (H; n=17) for the first 70 d after calving. Cows on the H diet weighed about 45 kg more and had greater BCS than M cows after 63 d of treatment. Ovarian and reproductive functions were not influenced by BCS at calving. Duration of ovarian cycles before and after the first postpartum estrus were not influenced by BCS at calving or postpartum nutrient intake. Ninety percent of cows had short luteal phases before the first estrus and all cows had a normal luteal phase after the first estrus. The interval to first estrus and ovulation was shorter ($P < 0.01$; 100 ± 8 d) for H than M cows (120 ± 8 d). The size of the DF, determined by ultrasonography at 4 to 16 h after the onset of estrus (determined by HeatWatch), was larger ($P < 0.01$) for H (14.8 ± 0.3) than M cows (13.5 ± 0.3). Pregnancy rate from artificial insemination at 14 to 20 h after onset of first postpartum estrus was also greater ($P < 0.03$) for H (76%) than for M cows (58%).

Concentrations of glucose and insulin in plasma during the last three weeks of

nutritional treatment (weeks 8 to 10 post partum) and the three weeks after treatment when all cows received the same diet, were influenced by treatment x week ($P < 0.01$). During treatment, concentrations of glucose were 5 to 10 mg/dL greater in H than M cows. However by 2 wk after treatment, concentrations of glucose in plasma of H and M cows were not significantly different. Similarly, concentrations of insulin in plasma during treatment were 40 to 50% greater in H than M cows, but were not different 1 wk after cessation of the nutritional treatment.

Concentrations of IGF-I in plasma during the last three weeks of treatment and the first three weeks after treatment were influenced by treatment ($P < 0.01$). Cows on H treatment had greater plasma concentrations of IGF-I on week 2 and 3 before the end of treatment and on the first week after treatment. Effect of greater nutrient intake on IGF-I plasma decreased with time after treatment.

Leptin concentrations in plasma were 2.6-fold greater ($P < 0.01$) in H than M cows during the last three weeks of nutritional treatment. However, within 4 d after the end of nutritional treatment, concentrations of leptin in plasma were similar for M and H cows. At the end of treatment, H cows had about a 0.75 greater BCS than M cows. This indicates that leptin is associated with feed intake and not amount of body fat. Concentrations of insulin, IGF-I and leptin were greater in H than M cows during nutritional treatment, but were not significantly different by 1 or 2 wk (approximately 90 d post partum) after the end of treatment. Ovulation and estrus occurred in most cows after the end of treatment; only 32% of H cows were in estrus by 80 d postpartum. Concentrations of insulin, IGF-I and leptin during 7 wk before the first postpartum estrus were not influenced by time. Changes in concentrations of these hormones and glucose and NEFA, occurred more than 7 wk before ovulation. Similarly, when nutritionally-induced anovulatory heifers were realimented, concentrations of glucose and insulin were similar in control ovulatory and realimented anovulatory heifers during at least three weeks before ovulation of realimented heifers (Bossis *et al.*, 2000). In

realimented heifers, concentrations of IGF-I and NEFA in plasma were greater at 3 wk before ovulation than during the consumption of the restricted diet, and concentrations continued to increase until ovulation.

The stable concentrations of insulin, IGF-I and leptin in plasma of primiparous cows during the seven weeks before the first postpartum estrus indicates that immediate changes in these constituents may not stimulate the first postpartum ovulation. These hormones could be metabolic signals by which nutrient intake and body fat stores regulate ovulation but have a delayed effect, a permissive role, and/or the effect could be mediated by alterations in binding proteins or specific receptors, so absolute changes in concentrations of hormones may not be necessary for the response to occur.

Nutrient intake, BCS and plasma Insulin and IGF-I

The roles of nutrient intake and BCS on concentrations of insulin and IGF-I in plasma of gestating cows were determined (Lents *et al.*, 2005). Commencing at 2 to 4 months of gestation, cows ($n=73$) were fed one of four diets for 109 d. High (H) cows received a 50% concentrate diet in a drylot, and moderate (M), low (L) and very low (VL) cows grazed native range pasture and received 2.5, 1.5 or 0.5 kg of a 42% CP supplement each day. After 109 d of treatment, all cows grazed a common pasture and received 1.5 kg of a 42% CP supplement daily. By 109 d of treatment, BCS were 6.7^a, 4.8^{bc}, 5.0^b and 4.7^c (Means without a common superscript differ; $P < 0.05$), for H, M, L and VL cows, respectively. On d 123, after cows were on the same diets for 14 d, BCS were 6.4^a, 4.8^b, 4.8^b and 4.5^c (Means without a common superscript differ; $P < 0.05$) for H, M, L and VL cows, respectively. Body condition scores of cows ranged from 4 to 7.5 on d 109 and 3.5 to 7.5 on d 123. The relationship between BCS and concentration of insulin in plasma on d 109, after cows had access to feed, was best fit by linear regression with $R^2=0.34$ ($P < 0.001$). However, concentrations of insulin in plasma after cows were fasted (no water and feed for 18 h) were not as strongly related

to BCS ($R^2=0.10$). On day 123 of the experiment, after cows were on the same diets for 14 d, concentration of insulin in plasma were not influenced by BCS after either feeding or fasting. These results indicate that concentrations of insulin in plasma of gestating cows are influenced by nutrient intake more than by BCS.

On day 109 of gestation the relationship between BCS and plasma concentrations of IGF-I were best fit by a quadratic equation ($P < 0.001$) with $R^2=0.36$ for samples collected after cows had access to feed, and $R^2=0.27$ ($P < 0.001$) after an 18 h fast. After all cows were on the same diet for 14 d (d 123) BCS had little influence on concentration of IGF-I in plasma samples after feeding ($R^2=0.07$) or after an 18 h fast ($R^2=0.03$). Similar to the relationship between BCS and concentrations of insulin in plasma, concentrations of IGF-I in plasma of gestating cows are influenced by nutrient intake more than by not BCS.

Nutritional effect on postpartum follicular growth

Mature Angus x Hereford cows were fed amounts of supplemental protein during the last 4 mo of pregnancy so they would have a BCS of 4 or 5 at calving (White *et al.*, 2008). Follicular growth was monitored by ultrasonography to measure growth of the DF between day 27 and 33 or day 47 to 53 post partum. When diameter of the DF increased less than 0.75 mm in 24 h, it was aspirated using a transvaginal ultrasound-guided needle. Concentrations of IGF-I, estradiol and IGFFBPs were quantified in follicular fluid. Proestrus DF were aspirated from postpartum cows with normal estrous cycles at 48 h after treatment with prostaglandin $F_{2\alpha}$. BCS at calving did not influence any of the postpartum follicular characteristics. Time of aspiration of DF was classified as either less than (short) or greater than 35 d (long) before the first estrus and ovulation. Follicles from short cows were aspirated an average of 42 d post partum and estrus and ovulation occurred about 55 d post partum. Follicles from long cows were aspirated about 39 d post partum and estrus and ovulation occurred about 85 d post partum. Diameters of the aspirated DF were

similar (12.8 ± 0.6 mm) for short, long and proestrus follicles. Concentrations of IGF-I in follicular fluid were not influenced by estrus/ovulation classification and averaged 25.4 ± 3.6 ng/mL. Concentration of estradiol in the fluid from proestrus follicles was greater (435 ± 79 ng/mL) than concentration in follicles of short (95 ± 56 ng/mL) or long cows (72 ± 59 ng/mL). Amounts of IGFBP-3 and -4b were greater in the DF of short than long cows. In addition, the amounts of IGFBP-3 and -4b in short cows were similar to amounts in proestrus follicles. Amounts of IGFBP-2 and -4a were not different in follicles from short, long and proestrus cows. Follicular fluid concentrations of IGF-I were not different between DF and first subordinate follicles (Stewart *et al.*, 1996). Changes in amounts of IGFBP in follicles during several weeks before the first postpartum estrus and ovulation may result in similar total concentration of IGF-I within follicles, but may result in different biological effects on follicular growth and maturation.

Postpartum nutrient intake of primiparous beef cows influenced concentrations of IGF-I and insulin in plasma and in dominant DF, and may be related to follicular function (Rubio, 2005). Nutritionally induced changes in follicular fluid IGFBP may also induce changes in postpartum follicular growth. Postpartum protein intake and BCS of cows at calving influenced the size of the dominant follicle at the first postpartum estrus in mature suckled beef cows (Lents *et al.*, 2008). Concentrations of IGF-I in plasma, and pregnancy rate, were greater in the plasma of cows with greater BCS at calving. Cows that gained weight after calving had larger dominant follicles. Cows should be managed to calve in moderate BCS and maintain body weight after calving to decrease the interval to first estrus, increase follicular development, and maximize pregnancy rate.

Short term nutrient restriction does not have a major effect on mature cows. However, severe acute nutrient restriction of young beef heifers alters availability of metabolic fuels and reduces growth and size of the dominant follicle (Lents *et al.*, 2013). Frequency of LH pulses prior to luteolysis are suppressed indicating that gonadotropic support of early follicle growth is compromised. Concentrations

of IGF-I are reduced and likely further limited size of the dominant follicle during restriction. These preovulatory events result in an absence of the ovulatory surge of LH leading to ovulatory failure in approximately 40 to 70% of heifers.

CONCLUSIONS

Body energy reserve at calving is the most important factor that influences the interval from parturition to the first estrus and ovulation in beef cows. Postpartum nutrient intake can modulate the duration of the postpartum anestrous interval, however, even if thin cows gain great amounts of weight after calving, ovulation occurs later than for cows that calve in good body condition and maintain body weight.

Decreased pulsatile secretion of GnRH is the major cause of reduced pulsatile secretion of LH and extended postpartum anovulatory intervals in beef cows (Figure 1). With inadequate secretion of LH, DF do not become estrogen active and secrete insufficient estradiol to induce an ovulatory surge of LH and estrus. Adequate nutrient intake results in increased concentration of insulin, IGF-I and leptin in plasma and increased body fat reserves. If fat stores are sufficient (BCS greater than 5) and nutrient intake is not adequate, mobilization of fat can occur and alter plasma concentrations of insulin, IGF-I and leptin. Secretion of growth hormone by the anterior pituitary stimulates synthesis of IGF-I by the liver except during inadequate nutrient intake when GH receptors on the liver are inadequate and the growth hormone-IGF-I system is disconnected. Under these circumstances, tissue-specific synthesis of IGF-I may have important autocrine or paracrine effects. A stimulatory role of leptin in control of GnRH secretion in cattle is not established, however, insulin and IGF-I may enhance GnRH secretion. Leptin, IGF-I and insulin may have direct effects on the pituitary to increase secretion of LH and on the ovary to regulate steroidogenesis.

Although concentrations of insulin, IGF-I and leptin in plasma are relatively constant during the 7 wk before the first postpartum estrus and ovulation, this does not mean they are not metabolic signals that regulate

reproduction. The hormones could a) influence early follicular or oocyte development and have delayed effects, b) have a permissive role to facilitate the effect of other hormones or factors, or c) have effects that are modulated by amounts of binding proteins or specific receptors. It is probable that unidentified compounds produced by adipose tissue have stimulatory or inhibitory effects on hypothalamic, pituitary or ovarian function since adequate body energy reserves, as well as secretion of insulin and IGF-I, are a prerequisite for postpartum ovulation.

Suckling has an inhibitory effect on pulsatile GnRH secretion during the early postpartum period and in thin cows. If cows have adequate body energy reserves and nutrient intake, the suppressive effect of suckling on GnRH secretion is greatly diminished by 30 d post partum.

Both body fat reserves and nutrient intake regulate ovulation in beef cows. Effects of BCS and nutrient intake on concentrations of IGFBPs, as well as receptors for IGF-I and leptin, must be evaluated in the hypothalamus, pituitary and ovary to elucidate metabolic signals that control postpartum ovulation in beef cows.

IMPLICATIONS

The interval from calving to conception greatly influences profitability of beef production. Inadequate body fat stores at calving and reduced postpartum nutrient intake increase the interval from calving until ovulation. Suckling suppresses ovulation during the early postpartum period in cows with moderate body fat stores and the suppression is longer in thin cows. Restricted suckling or early weaning of calves can be used to improve reproductive efficiency in very thin cows. Insulin, IGF-I and leptin may be metabolic signals or permissive cues, however, other interactive factors must be involved. Determination of metabolic signals by which body energy stores and nutrient intake regulate the interval from calving to first ovulation will allow development of management strategies to increase pregnancy rates in beef cows.

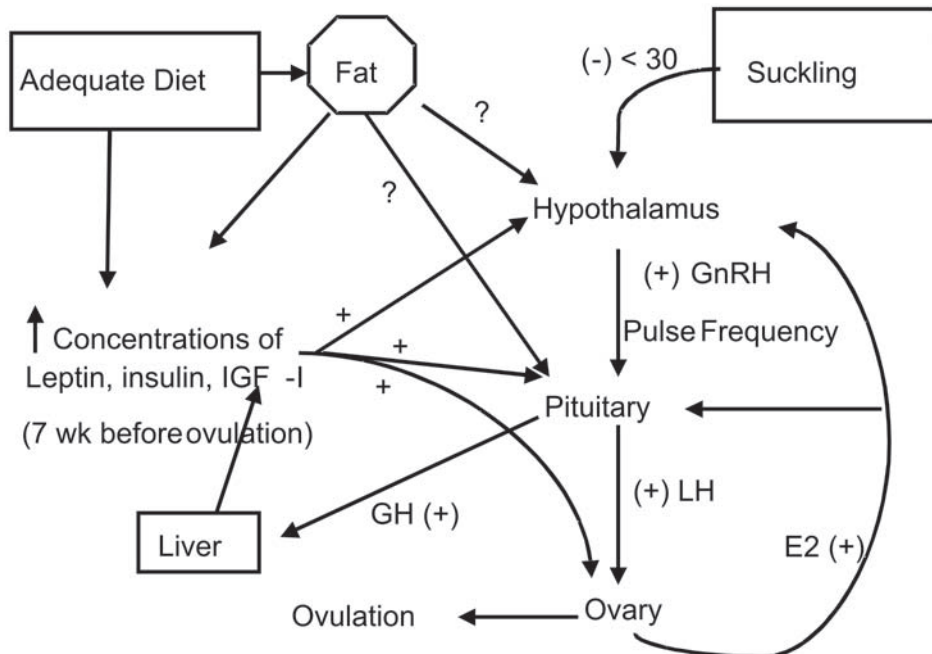


Figure 1. Control of reproductive function in postpartum beef cows.

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