UNDERSTANDING PUBERTY AND POSTPARTUM ANESTRUS

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Puberty

Managerial and economic efficiencies of cattle reproduction systems that are seasonal in nature are most likely to benefit from having a compact calving season. Effective replacement heifer development is a critical segment of the integrated management program in an efficient beef cow production system. The replacement heifer represents the future profitability and genetic improvement of the cow herd. The main objective should be to raise an adequate number of heifers to reach puberty and cycle regularly at the start of the breeding season (Corah and Hixon, 1992). In order to achieve this goal, heifers must reach puberty before 12 to 13 months of age, conceive at 14 to 15 months of age, and calve at approximately 2 years of age (Schillo et al., 1992). Researchers at Montana State University concluded that heifers that conceived the earliest immediately indicated their greater productive efficiency and lifetime production potential (Paterson et al., 1987). Beef heifers that calve by 2 years of age have a greater lifetime production potential than heifers that calve at older ages (Patterson et al., 1992).The onset of puberty is the result of a series of complex developmental events that occur within the reproductive endocrine axis. In general, puberty is the process of acquiring reproductive competence. Puberty in heifers can be characterized in several ways including age at first estrus (heat), age at first ovulation, and or age at which a female can support pregnancy without any difficulty (Senger, 1999). Regardless of the criteria used to define puberty, there are several major physiological, environmental, and managerial factors that can advance or delay the age to puberty. A more thorough understanding of the physiology of puberty and factors affecting the timing of the onset of puberty in the heifer will lead to development of new and better management strategies for reducing the age to reach puberty in the heifer and enhancing the reproductive efficiency and profitability of the farm.

Physiological Mechanisms Controlling Puberty

The fundamental requirement/prerequisite for the onset of puberty and initiation of the ovarian cycle is the secretion of a gonadotropin releasing hormone (GnRH) from the hypothalamus at the appropriate frequency and quantities to stimulate gonadotropin hormone, i.e. luteinizing hormone (LH), release from the anterior pituitary (Senger, 1999, Day et al., 1998). This increase in pulse frequency of GnRH is a key factor in increasing circulating LH, follicular development, and hence synthesis and secretion of steroid hormones, predominately estradiol 17β (E2) (Figure 1). It is known that the frequency of the GnRH pulses in prepubertal heifers is much lower than the frequency of GnRH pulses in the postpubertal heifers (Senger, 1999).

The onset of puberty is not just limited by the ability of the hypothalamus and /or anterior pituitary to secrete a sufficient amount of GnRH or gonadotropin; rather it is the lack of high frequency GnRH and LH pulses that limits the onset of puberty (Day et al., 1984, 1998). Hence the question is how do the GnRH neurons acquire the ability to release GnRH in high frequency pulses? The answer to this question is related to the sensitivity of the hypothalamus to the negative feedback system created by ovarian E2 (Figure 1). In the prepubertal heifers, the hypothalamic tonic center is quite sensitive to the negative feedback effect generated by E2, thus the frequency of GnRH release and subsequently LH both remain low. During the transition from prepubertal to peripubertal, however, the hypothalamic tonic center's sensitivity to E2 decreases (Day et al., 1984, 1998). Consequently, release of GnRH from the hypothalamus and gonadotropins from the anterior pituitary increases (Figure 1). This increased level of gonadotropins results in follicular growth and development, and hence the synthesis and

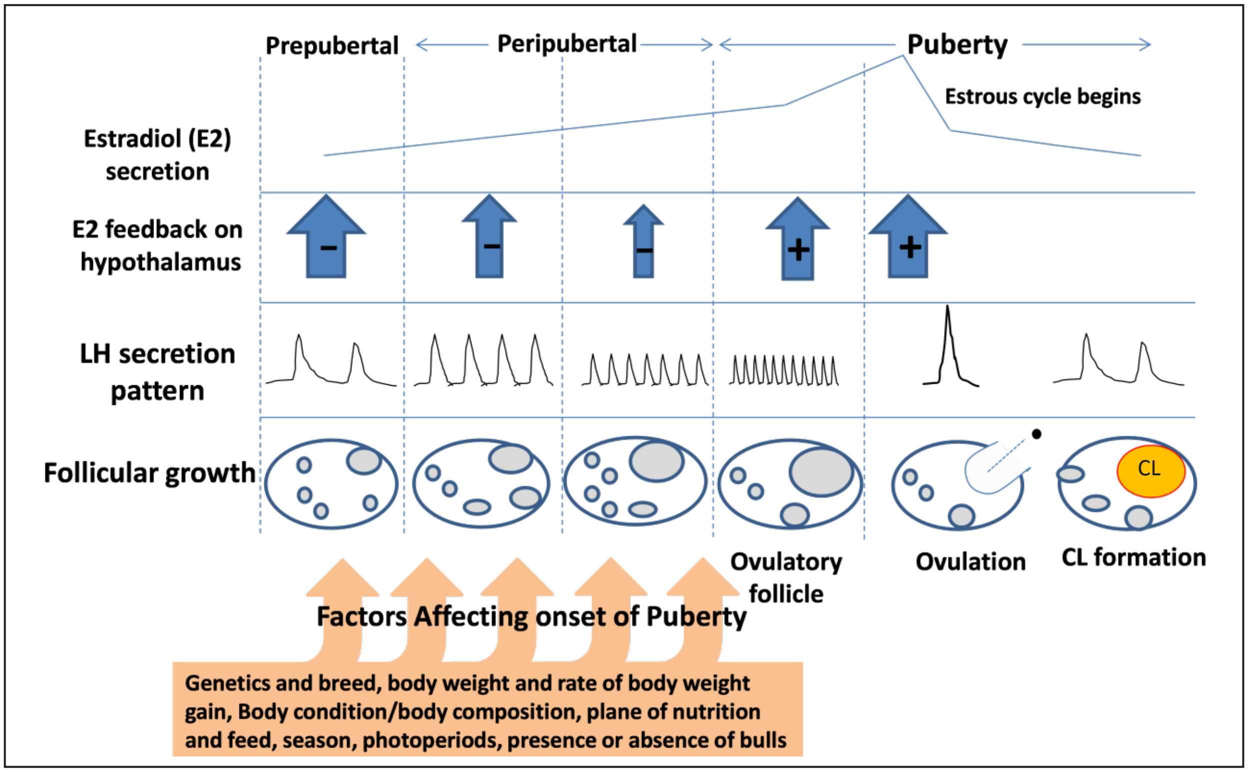

Figure 1. Endocrine and ovarian changes associated with puberty onset in the heifer and factors affecting interval to puberty onset (adapted and modified from Williams and Amstalden, 2010)
E2 = estradiol; LH=luteinizing hormone; CL=corpus luteum

secretion of a greater amount of E2. At onset of puberty, the elevated concentration of ovarian E2 causes a shift from negative feedback to a positive feedback in the hypothalamic surge center (a separate section of hypothalamus where GnRH can be discharged in relatively massive quantities) resulting in a surge of GnRH, which is responsible for triggering a surge of LH (Senger, 1999) (Figure 1). The outcomes of the surge of LH are; a) expression of behavioral estrus (heat) and, b) ovulation. The hormones involved in ovulation generate a series of physiological events that leads to further development of the reproductive tract and establishment of the estrous cycle.

The fundamental requirement for the onset of puberty is the secretion of high amplitude GnRH and pulse frequency, and ovarian E2 feedback system with the hypothalamus; however, one should also recognize that very complex sets of neural pathways, neurohormones, and peptides modulate GnRH secretion itself and mediate the effect of E2 on GnRH. In other words, these neurohormones and peptides directly or indirectly transmit information to the hypothalamic GnRH neurons and control their secretion. To name a few, neuropeptide Y and, agouti-related peptides (Allen et al., 2009), dopamine (Ahmadzadeh et al., , opioid peptides (Cosgrove et al., 1993), kisspeptin and its receptors (Kadokawa et al., 2008), have all shown to play essential roles in the secretion of GnRH and LH, and also mediating steroid feedback communication to the hypothalamus. Furthermore, as the heifer ages and grows, these factors induce or interact with various internal metabolic signals, such as glucose, propionate, leptin, ghrelin, insulin-like growth factor-1, and its transport proteins that are recognized by receptors in the central nervous system (Whittier et al., 2008).

Factors Affecting Age to Puberty

We have established that the onset of puberty is related to GnRH, LH, ovarian E2, and the sensitivity of the hypothalamus to E2, and neurohormones. However, the development of the hypothalamic-pituitary-ovarian axis occurs in a gradual fashion and during the growth of the animal. Many factors, directly or indirectly affect this gradual development and may advance or delay the pubertal onset. These factors include but are not solely limited to genetics and breed, body weight, and rate of body weight gain, body composition, plane of nutrition and feed, and certain environmental or social cues such as season, photoperiods, and presence or absence of bulls. Some of these factors play more important roles than others (Figure 1). Understanding how these factors affect the onset of puberty is the key to better management strategies and enable producers to make decisions to modify or manage these factors and reduce the interval to puberty, improve fertility at puberty, and increase profitability.

Genetics and Breed. It is well known that genetics and breed can influence age to puberty and first calving. Sire and dam effects within a breed, and heterosis, also contribute to genetic control of age at puberty. Obviously, puberty onset can be decreased by selecting a breed with younger age at puberty (e.g. Angus) or by selecting within a breed for earlier age at puberty (Patterson et al., 1997). However, regardless of breed and genetics, there are several factors that universally influence age at puberty across all breeds and genetics. The remaining discussion in this segment will further discuss these factors.

Nutrition. It is well documented that heifers have to attain a certain amount body weight, size and composition to reach puberty. The increase in body weight and degree of fatness cause a shift in metabolic status and expenditure of the animal (Senger, 1999). The apparent changes in the metabolic status, causes complex changes in metabolic hormones and accompanying metabolites that can be converted to hypothalamic neural signals leading to the onset of puberty. The impact of nutrition on metabolic hormones and metabolites is rather obvious. Therefore, it is not surprising that inadequate nutrition delays puberty and sexual maturity in heifers, reduces conception rate, and increases pregnancy losses in heifers (needs references). From a practical stand point, nutritional management involving proper rates of gain and targeted body weights present a greater opportunity to producers to decrease the time interval to onset of puberty and increase reproductive efficiency. In addition pre- and post-weaning growth rate, age at puberty, and pregnancy rates affect both the cost of raising replacement heifers and the subsequent productivity of those replacements.

The rule of thumb is to have heifers reach 60 to 65% of their projected mature weight 30 to 45 days before the breeding season. This allows for heifers to go through two to three estrous cycles before the breeding season. Research has shown that the likelihood of early conception in the initial breeding season is increased in heifers that have multiple estrous cycles before the start of the breeding season (Byerley et al., 1987). Target weight for exotic heifers is usually 65 to 70% of their projected mature weight. It should be noted that the optimum growth rates and targeted body weight of heifers of various breeds differ. By using a target weight, producers can calculate the rate of gain that is optimum for heifers before the breeding season. Diets can then be formulated based on desired rate of gains and heifers should be weighed periodically to insure that the heifers are growing properly (Hall, 1997)

Although having 60 to 65% of mature weight is generally accepted as the desired body weight at breeding, slightly lower body weights at breeding may also work in certain conditions. Using British – Continental cross bred heifers, research (Funston and Duetscher, 2004) compared the effects of either 53 or 58% of mature BW at breeding on reproductive performance and calf production. Costs of developing heifers to 53% of mature BW were lower than costs of developing heifers to 58% of mature BW without adversely affecting reproduction through the fourth pregnancy or calf production through the third gestation.

The contiguous research on effect of feeding, and various nutrition trials, on age to puberty and reproductive efficiency is extensive, and collectively indicate that the plane of nutrition can hasten or delay age to puberty and impact reproduction. For example, heifers of a similar breed composition can reach puberty several months apart when fed different diets. Feed cost accounts for 60 to 70% of the costs of raising replacement heifers. Therefore, the financial impact of puberty onset is, in part, related to age at puberty and feed costs. It is desired to achieve a younger age at puberty. Nonetheless, cost of feeding heifers to reach puberty earlier should be weighed against the income gained from increased conception rates and heavier weaning weights (Hall, 1997).

Energy is the primary limiting factor in most replacement heifer diets. In an earlier research experiment (Table 1), heifers were fed to achieve low (0.5 lb/day), medium (1.0 lb/day) or high (1.5 lb/day) average daily gain from weaning until breeding. The high-gain heifers reached puberty earlier than those in the other two groups. Moreover, 60% of the heifers in the medium- and high-gain groups conceived within the first 20 days of the breeding season, and overall conception rates were greater for the medium- and high-gain groups than the low-gain. Results of this study and other research have led to the recommendation that heifers should gain between 1.25 and 1.75 pounds per day between weaning and breeding. Depending on the size of the heifer, the desired rate of gain, and feed intake, diets will need to contain between 62 and 70% TDN.

Table 1. Effect of feed level on reproductive performance in beef heifers.

Variables	Feed Level		
	Low	Medium	High
Gain (lb/day)	0.5	1.0	1.5
Age at first estrus (days)	434	412	388
Weight at first estrus, lb	523	545	563
Conception rate first 20 days of breeding season (%)	30	62	60
Overall conception rate (%)	50	86	87

Adapted from Short and Bellows, 1971

In contrast, the effects of three heifer development strategies based upon timed nutrient limitation (High, Medium or Low-High) on primiparous heifer performance were reported by Freetly et al. (2001). The authors concluded that as long as heifers are growing and meeting a minimal BW before mating, patterns of growth may be altered in the post-weaning period without a decrease in the ability of the heifer to conceive, or a decrease in calf growth potential. However, limit-feeding heifers may decrease first-calf survival.

With a common goal of increasing the proportion of cycling heifers at beginning of breeding season, several strategies for feeding high dietary energy diets have been proposed. For instance, a diet with a greater amount of starch for 60 days before breeding may increase the likelihood of puberty of heifers that have an inadequate yearling weight (Ciccioli et al., 2005). Early work by Wiltbank et al. (1966) indicated that body weight gain during the pre-weaning period may have a greater influence on puberty onset than post-weaning gain. A more recent research trial has shown that onset of puberty is dependent upon nutritive intake between 4 and 6.5 months of age, regardless of the diet fed thereafter (Gasser et al., 2006). These authors concluded that, increasing dietary energy intake in early-weaned heifers, through feeding a high-concentrate diet from 126 to 196 d of age, decreased age at puberty regardless of the diet fed after 196 d of age (Gasser et al., 2006). Creep feeding of suckling calves is another option for enhancing postnatal growth, but increases the cost of raising heifers (Forrest, 2005). Nonetheless, where there is opportunity for accelerated growth during pre-weaning period, one should avoid the excessive rate of gain from overfeeding heifers, which may result in improper mammary gland development, premature puberty, and reproductive failure. The bottom line is that the nutritional management of heifers must promote sound development and consistent growth, and the timely onset of puberty, while being economical and profitable.

Briefly, protein availability can also affect age at puberty onset because replacement heifers poorly compensate for protein deficiencies. It is critical that protein not be deprived, especially before 7 months of age (Bagley, 1993). Bagley (1993) reported that Restriction in protein intake, which led to reduced performance, was much more difficult to overcome than energy restrictions, which reduced gains in young calves. The differences are dramatic in heifers fed low versus adequate dietary protein. For example, by the beginning of the breeding season, only 40% of the heifers fed a low protein diet (9% crude protein, CP) had reached puberty, whereas 90% of the heifers fed adequately (11% CP) had reached puberty (Hall, 1997). Even diets containing supplemental energy could not overcome a protein deficiency. At the same time, additional protein could not overcome a lack of available energy. These findings lend evidence that dietary protein is as important as dietary energy for puberty onset. Protein requirements for developing heifers are between 11 and 12% CP (Hall, 1997).

Social Interaction and Season. External factors may affect the onset of puberty. Social cues such as the presence of the male, the size of the social group in which heifers are kept, and season are among those factors. Research by Roberson et al. (1991) indicated that heifer growth rate may interact with the biostimulatory influence of bulls on age at puberty in beef heifers. These researchers assigned heifers (approximately 8.5 months of age) to either bull exposure (for 175 days) or no bull exposure at all. Heifers were fed to gain at either a moderate (1.3 lb/day) or high (1.8 lb/day) growth rate. Heifers exposed to bulls attained puberty at a younger age than heifers that were not exposed to bulls. Also, the effect on puberty was greater for high than for moderate growth rate heifers. Perhaps the take home message is that the presence of bull cannot accelerate pubertal onset if heifers have not received an adequate diet and/or achieved the appropriate proper body weight. The exact physiological mechanism by which presence of bulls accelerates age to puberty in heifers is not clear. However, it is believed that pheromones shift the decrease in the negative feedback sensitivity of E2 to the left as illustrated in Figure 1 and accelerate age at puberty by increasing the frequency of LH at an earlier age (Whittier et al., 2008).

Although cattle are not seasonal breeders, seasonal conditions of the early (birth to 6 months of age) and late (6 to 12 months of age) postnatal periods appear to influence timing of puberty onset in beef heifers. Research has shown that fall-born heifers reach puberty at a younger age than spring-born heifers (in Schillo et al., 1992). Moreover, exposure to spring-summer like temperatures and long photoperiods during the second 6 months of heifers' lives reduces age at puberty regardless of season of birth. Some evidence suggests that melatonin, a pineal hormone, is involved in signaling photo stimuli into neuroendocrine systems that influence LH secretion. (Schillo et al., 1992). However, management decisions to shift calving season or photoperiod might not be achievable in different US regions or production settings.

Summary

The onset of puberty involves the capability of the hypothalamus to secrete pulses of GnRH in high frequency and high amplitude. This capability is highly related to the change in sensitivity of the hypothalamus to negative feedback of E2. In heifers, this entire physiological phenomenon is influenced by achieving appropriate body size/body weight that is related to energy metabolism and body composition. The interval from birth to onset of puberty can be influenced by many external factors such as plane of nutrition and nutrition management, genetics, and external modulators such as photoperiod, size of social groups, and presence of bulls. Manipulation of these factors by sound management considerations enables producers to develop heifers that attain puberty earlier ensuring that heifers are cycling and ready to be bred well before the breeding season begins.

Postpartum Anestrus

Reproductive efficiency is one of the most important factors impacting the profitability of the cow-calf operation. Reproductive efficiency is largely dependent on maintaining a short breeding and calving season and increasing calf uniformity. The goal of cow-calf operations is to obtain and wean one calf per cow every 12 months. Given that the gestation length is approximately 280 days, in order to maintain a 12-month calving interval, cows have to undergo uterine involution, resume ovarian function, ovulate and establish a pregnancy within 80 to 85 d after calving. However, a major limitation to the success of rebreeding after each calving is the presence of postpartum anestrus in the cow herd. In suckled beef cows, an extended postpartum anestrus is the single most important reason that cows fail to rebreed during defined breeding seasons and is recognized as a major cause of infertility (Whittier et al., 2008). Moreover, research has shown a negative relationship between postpartum interval to first estrus and overall pregnancy rate (Figure 2). This decrease in pregnancy rate is probably related

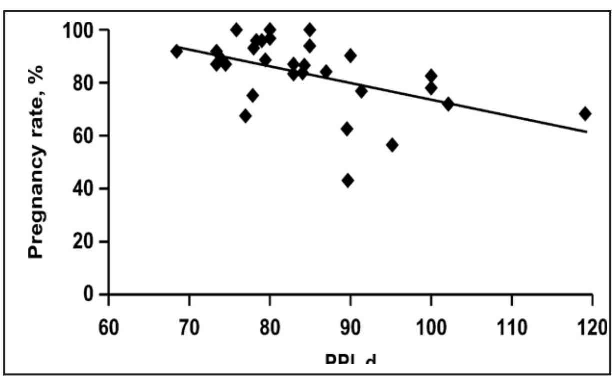

Figure 2.The relationship between length of postpartum interval to first estrus (PPI in days) and pregnancy rate (Adapted from Hess et al., 2005)

to factors that cause extended postpartum anestrus rather the than the effect of extended postpartum anestrus by itself (Hess et al., 2005).

Berardinelli (2007) described postpartum anestrus as a condition that occurs after parturition where postpartum cows fail to exhibit estrus and ovulate. This condition allows the cows to anatomically and physiologically recuperate from pregnancy and parturition. The anestrus condition is associated with the presence of inactive ovaries, and even there is follicular development, none of the growing follicles become mature enough to ovulate (Montiel and Ahuja, 2005). Consequently, ovulation does not occur while anestrus is present. Moreover, in rare occasions, if there is an ovulation, it is not associated with any signs of estrus (heat). The length (interval) of this period is measured from calving to estrus; which leads to ovulation, resumption of luteal function, and ideally conception shortly after insemination.

Early pregnancy in suckled beef cows can be drastically limited by the proportion of suckled cows not exhibiting regular estrous cycles (anestrus) at the beginning of the breeding season (Short et al., 1990). The incidence of anestrus at the initiation of the breeding season can be significant in the cow-calf operations. In a multi-state experiment utilizing the records from 851 postpartum cows (Lucy et al., 2001), 53% of cows were still anestrous by 7 days before the beginning of the breeding season (range 17-67%). In other experiments the incidence of anestrus ranged from 44% (Gasser et al., 2006) to 46% (Stevenson et al., 2003).

Physiological Mechanisms Controlling Anestrus

The mechanisms controlling postpartum anestrus reside in the hypothalamic-pituitary-ovarian axis, and interactions of this axis with other central nervous systems centers that are involved with lactation/suckling, metabolism, and maternal behavior (Short et al., 1990). Production of large amounts of steroids by the placenta, especially E2 and progesterone, during late pregnancy exerts strong negative feedback effects on the hypothalamus, resulting in a decreased release of GnRH (Short et al., 1990). The resumption of normal postpartum ovarian cycles is regulated mainly by the rate of recovery of the hypothalamic-pituitary axis and normal secretions of GnRH and LH. Failure of postpartum dominant follicles to undergo final maturation is related to the absence of appropriate GnRH and LH pulses, which is necessary for final follicular maturation and subsequent ovulation. The lack of adequate GnRH pulse frequencies is largely because of two main interrelated factors; 1) increased sensitivity of the hypothalamic GnRH pulse-generator to the negative feedback effect of E2, which results in absence of GnRH pulses and subsequently LH remains low, and 2) suckling stimulus which causes the release of endogenous opioid peptides from the hypothalamus that indirectly inhibits GnRH release. In normal circumstances, as the postpartum interval progresses, the hypothalamic tonic center sensitivity to E2 decreases. Consequently, the release of GnRH from the hypothalamus and gonadotropins from the anterior pituitary increases. This increased level of gonadotropin results in follicular growth and maturation, ovulation, and continued cyclicity (Yavas and Walton, 2000). However, the recovery of hypothalamic-pituitary axis and initiation of ovarian activity and ovulation may be delayed, hence increasing the duration of postpartum anestrus in cattle.

Anestrus is a result of many interacting factors; managerial, physiological, pathological and nutritional factors. These factors include age, breed, pre- and postpartum nutrition, body condition at calving, milk yield, suckling, calving season, presence or absence of the bull, delayed uterine involution, dystocia and general health status influence duration of postpartum anestrus (reviewed in Yavas and Walton, 2000). Although the above factors affect postpartum anestrus, perhaps nutrition and the presence of suckling calves affect the resumption of postpartum cyclicity the most (Short et al., 1990, Webb et al., 2004, Hess et al., 2005, Yavas and Walton, 2000). Under-nutrition contributes to prolonged postpartum anestrus, particularly among cows that are heavily dependent on forages to meet their nutrition requirements. Nutrition may interact with genetics of the breed, or environmental and other management factors that influence the duration of anestrus (Montiel and Ahuja, 2005). The following section briefly describes the interaction between nutrition and postpartum anestrus condition as well as influence of calf suckling in prolonging postpartum acyclicity.

Nutrition and Postpartum Anestrus

The nutrition/reproduction interaction involves several complex biological pathways. The hypothalamus, pituitary, and/or the ovaries can be affected by nutritional deficiencies. Regardless of the mechanism, it is clear that the reproductive success in beef cows is highly related to body energy reserves and metabolic responses to nutrition. These responses involve signaling molecules and hormones that regulate the partitioning of energy and nutrients and the reproductive axis (Chagas et al., 2007). As beef producers, we must understand the nutrition/reproduction axis to fully appreciate how our cows respond to proper nutritional management to produce a live and healthy calf on a yearly basis (Lamb, 2000).

It is generally accepted that cows maintained on an increasing plane of nutrition before parturition usually have a shorter postpartum interval to first ovulation than cows on a decreasing plane of nutrition. Furthermore, energy restrictions during the prepartum period appear to lower body condition at calving and result in prolonged postpartum anestrus, as well as lowered pregnancy rates at the end of breeding season (Lamb, 2000).

The interaction between nutrition and reproductive function has been extensively reviewed (Short et al., 1990, Webb et al., 2004, Montiel and Ahuja, 2005, Hess et al., 2005). The possible mechanism by which under-nutrition may inhibit resumption of postpartum cyclicity in cows is related to the inhibition of GnRH and LH secretion. The inhibition of GnRH and LH secretion impair proper follicular development, ovulation, and corpus luteum formation (Schillo, 1992). As previously mentioned, a hypersensitivity to the negative feedback effects of E2 (Short et al., 1990) contributes to the continuation of postpartum anestrus. Interestingly, nutritionally compromised cows also seem to remain more sensitive to the negative feedback effects of E2 (Keisler and Lucy, 1996; Wettemann et al., 2003), and may remain acyclic for approximately 100 d (Williams, 1990).

Glucose, non-esterified fatty acids, and amino acids: There are several metabolites and hormones that may link nutritional status with postpartum anestrus. Glucose is one of the most important metabolic substrates required for proper function of reproductive processes in beef cows. It has been hypothesized that low blood glucose, as a result of underfeeding and low energy diets, may be linked to reduced progesterone concentrations (Villa-Godoy et al., 1988) and lower fertility (McClure, 1970). Low blood glucose may be detected by the hypothalamus; such that if glucose is not available in proper concentrations, GnRH secretion will be impaired (Hess et al., 2005). Therefore, it is advantageous to ensure proper nutrition, in order to increase gluconeogenesis and potentially stimulate GnRH secretion (Randel, 1990). It is also argued that the lack of glucose or glucogenic precursors (i.e. acetate) in energy deficient animals leads to increased concentration of ketone bodies (β-hydroxybutyrate) and greater production of non-esterified fatty acids (NEFA, as a result of greater amount of fat mobilization). There is evidence that both of these metabolites affect LH secretion. (see Hess et al., 2005).

The role of amino acids (AA) and low dietary protein on the reproductive performance in beef

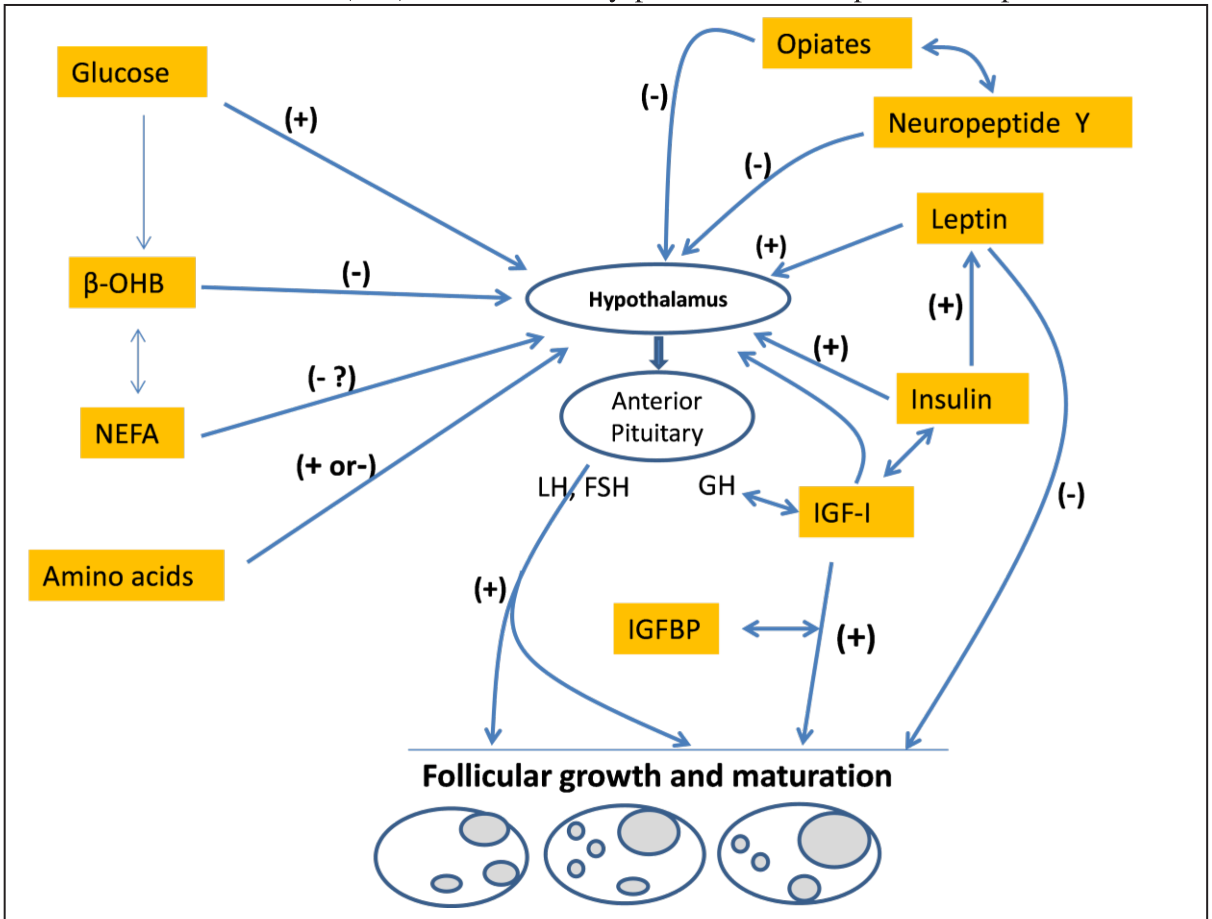

Figure 3. Interaction between metabolites, neuro hormones, and hypothalamic-pituitary-ovarian axis. Potential mechanisms by which metabolites interact with various hormones, peptides and neurohormones that affect gonadotropin secretion and follicular development (simplified from Hess et al., 2005)
B-OHB= Beta hydroxybutyrate; NEFA=non-esterified fatty acids; IGFBP=insulin like growth factor binding proteins

cattle is not clear. Hess et al. (2005) proposed that increased supplies of metabolizable AA, or perhaps specific AA imbalances, are detected by the hypothalamic region responsible for GnRH release. Reduced protein intake from 150 days prepartum to 40 days postpartum, increased the postpartum interval to first estrus, to first service and to conception and decreased the number of animals that showed estrus and conceived (Sasser et al., 1988). Nonetheless, research on effects of low protein diets on reproduction is often confounded with energy deficiency or general poor nutrition. The effect of dietary protein on postpartum interval and reproductive performance may be more of a concern when the supply of protein is inadequate, and cows are consuming low quality forages. The mechanism by which dietary protein affects reproduction is not clear. It is possible that increase or deficiencies of certain amino acids are detected by the regions of the brain responsible controlling GnRH and LH secretion (Hess et al., 2005). It has been shown that excitatory amino acids glutamate and aspartate are the major excitatory neurotransmitters in the central nervous system and play an important role in the regulation of gonadotropin secretion in many species (Keisler and Lucy, 1996). Nonetheless, more investigation is required to determine whether a dietary crude protein deficiency alone reduces the reproductive performance of beef cattle.

Insulin, IGF-I: A number of studies have shown that the effect of nutrition on reproduction, i.e. follicular growth is mediated through insulin. Insulin, in combination with glucose, affects GnRH secretion (reviewed in Webb et al., 2004 and Hess et al., 2005). Moreover, insulin may affect synthesis and secretion of IGF-I, which also play a role in follicular development. Clearly, the plane of nutrition can change IGF-1and IGF binding proteins (IGFBP) concentrations. Reduced nutrient intake of cyclic beef cows resulted in decreased concentrations of IGF-I and plasma LH (Richards et al., 1991, Bossis et al., 1999). Increased duration of anovulation was also associated with decreased concentrations of IGF-I and IGFBP-3 in follicular fluid (Prado et al., 2002). Thus, it appears that insulin, IGF-I and IGFBPs play a role in mediating metabolic event that are related to reproduction.

Leptin and neurohormones: Leptin, is a 16-kD product of the *o*-gene, and plays a major role in communicating nutritional status to the central nervous system and the hypothalamic-pituitary-gonadal reproductive axis of mammals (Zieba et al., 2005). The expression and secretion of leptin is highly correlated with body fat mass and acutely affected by changes in feed intake (Zieba et al., 2005). Moreover, exogenous leptin stimulated the secretion of LH in fasted, but not in normal-fed, cows (Amstalden et al., 2003). Research appears to indicate that leptin stimulates the hypothalamic–adenohypophyseal axis mainly in nutritionally stressed animals (Zieba et al., 2005). Assuming that cows are metabolically stressed during the early postpartum period and that cows lose body fat during this period, it is possible that leptin is one of the mediators of nutritional status to the hypothalamic-pituitary axis and hence may influence the duration of nutritional postpartum anestrus. It is know that endogenous opioid peptides (EOP) influence LH secretion in cattle (Reviewed in Williams, 1990, Kiesler and Lucy, 1996).In other species evidence suggests that neuropeptide Y (NPY) may serve as a direct endocrine link by which the nutrient status of the animal is communicated to the central nervous system and the hypothalamus, which regulates GnRH secretion. Neuropeptide Y is secreted from the hypothalamus and has been associated with a number of physiological processes in the brain, including food intake and the regulation of energy. Moreover, Kiesler and Lucy (1996) argued in favor of the existence of a functional relationship between the opiates and NPY. However, the relationship between, postpartum nutrition, the length of postpartum anestrus and NPY is not well known. It seems that the EOP-NYP system cannot be solely responsible for mediating the effect of postpartum nutrition on reproduction.

Body Condition Score, Parity, and Postpartum Anestrus

The nutritional status of the cows, as evaluated by BCS, reflects the body reserves available for basic metabolism, growth, lactation and activity (Wright et al., 1987). Body condition is indicative of the immediate past and current nutritional status of the animal and can be used as a management tool to evaluate the nutritional and reproductive status of a herd (Stevenson et al., 2003). For instance, the rapid loss of body reserves during the early postpartum period may be indicative of fat mobilization due to insufficient amounts of dietary energy intake.

Does BCS influence postpartum anestrous period? A review of multiple studies in which postpartum nutritional treatments were imposed and body condition were assessed at calving revealed that cows with body condition scores of < 5 (1 = emaciated and 9 = obese) are at a greater risk for prolonged intervals to return to first estrus than cows with a greater body condition (Short et al., 1990). Stevenson et al. (2003) demonstrated that as body condition score increased from 3.5 to 6.0 at the onset of the breeding season, the proportion of cows cycling increased linearly by 18 ± 2% for each unit increase in body condition score. In addition, ovulatory responses to GnRH, following progestin exposure before PGF2α, increased as BCS increased, especially in older cows. Table 2 (Houghton et al., 1990) demonstrates the importance of BCS at calving on return to estrous cycles in suckled beef cows. Cows calving in poor condition (BCS < 5) had longer intervals to estrus than cows calving with BCS ≥ 5. Obviously, the chance of having a shorter calving interval is less for cows that have BCS < 5. Lake et al. (2005) argues that although cows in BCS of 4 at calving seemed capable of maintaining BCS during lactation, the overall decrease in pregnancy rate indicates cows should be managed to achieve a BCS >4 before parturition to improve reproductive success (Lake et al., 2005). From a practical stand point, BCS at breeding is less useful a management tool, than BCS at calving because it is virtually impossible to improve BCS of cows once the breeding season has started (Hess et al., 2005).

Table 2. Influence of body condition on return to estrous cycles in beef cows

BCS	Days Postpartum to estrus (days)
3	88.5
4	69.7
5	59.4
6	51.7
7	30.6

Body condition score at parturition was positively correlated with follicular development in early postpartum and pituitary LH content at 30 days postpartum (reviewed in Yavas and Walton, 2000), and influenced concentrations of circulating IGF-1, LH pulse frequency, and postpartum interval after weaning (Bishop et al., 1994). Moreover, body weight at resumption of cyclicity postpartum was negatively correlated to the postpartum interval (Sasser et al, 1988).

The length of postpartum anestrus period is influenced by parity. In general, two-year-old cows (first lactation) required more time to overcome postpartum anestrus than older cows, even when they calved before the cow herd. This is, in part, related to the fact that two-year-old cows require greater energy needs to sustain both lactation and their own growth. However, body growth and lactation combined have greater energy priority than reproduction (Short et al., 1990). Older cows have no growth requirement, thus nutrients are more likely to be prioritized for milk synthesis and initiation of estrous cycles. Because of this priority system, young, growing cows generally produce less milk and are in a state of prolonged postpartum anestrus longer after calving (Stevenson, 2004).

In two suckled beef cow groups, multiparous cows had a greater percentage of cows return to cyclicity than primiparous cows (74.1 vs 53.4%, respectively). This data provides further evidence that first-calf heifers tend to have greater difficulty resuming their estrous cycles after calving than mature cows. Therefore, it is imperative to ensure that pre-calving management allows first-calf heifers sufficient resources to recover following calving, and yield acceptable fertility results (Lamb, 2000).

Thorough reviews by Hess et al. (2005) summarized that under practical conditions and from a nutritional stand point, much of the variation in reproductive performance of beef cows may be accounted for by differences in energy intake and body condition. After reviewing the scientific literature from 1990 to 2000, these authors concluded that 1) prepartum nutrition is more important than postpartum nutrition in determining the duration of postpartum anestrus; 2) energy is the primary nutrient regulating reproduction in female beef cattle and inadequate dietary energy during late pregnancy lowers reproduction even when dietary energy is sufficient during lactation; 3) a BCS ≥ 5 will ensure that body reserves are adequate for postpartum reproduction; 4) severity and duration of negative energy balance during the early postpartum extends the postpartum anestrus period and negatively affects reproductive performance. In the future, based on this area of research, short-term nutritional manipulations (i.e. addition of supplemental dietary fat) may be designed to shorten the postpartum anestrus interval, and improve pregnancy rates during the breeding season.

Suckling and Postpartum Anestrus

It has been known that suckling is one of the main factors influencing the length of the postpartum anestrus period (reviewed in Yavas and Walton, 2000). If suckling is continuously practiced during lactation, it blocks ovulation, elongates period of postpartum anestrus, and contributs to a lesser reproductive efficiency. Following the replenishment of LH stores, which occur approximately 20 days postpartum, the absence of LH pulses becomes suckling-dependent (Nett, 1987). Once anterior pituitary LH stores have been replenished, therefore, complete weaning, temporary (48 to 96 h) weaning, or partial weaning (restricted suckling once or twice a day) increased the frequency of LH pulses followed by ovulation (Shively and Williams, 1989).

Williams and Amstalden (2010) argue that the maternal-offspring bond is the primary feature of postpartum anestrus. Formation of a selective maternal bond by the cow combined with the physical interaction of the calf in the inguinal region appears to be responsible for neural changes that create the anestrus state (Williams and Griffith, 1995). It has been hypothesized that suckling induced suppression of GnRH/LH is mediated through a complex neuroendocrine system involving endogenous opioid peptides, i.e. β-endorphin (reviewed in Yava and Walton, 2000). Regardless of these complex physiological mechanisms, a better understanding of how suckling increases the postpartum anestrus period has lead scientists to develop several management protocols to reduce those effects. These management practices (Williams and Amstalden, 2010) include but are not limited to a) temporary calf removal (48-h calf removal) which should be combined with some methods estrous synchronization; b) once-daily suckling, which appears to be more beneficial with first-calf heifers. Lamb (2000) indicated that in managing postpartum anestrus, all the other management alternatives should be considered and dealt with before resorting to this option i.e. temporally weaning. The potential economic and management disadvantages should be carefully weighed against the potential advantages of increased fertility.

Summary

Postpartum anestrus is a major reason that cows fail to rebreed during defined breeding seasons, and is recognized as a major cause of infertility. The resumption of normal postpartum ovarian cycles is regulated mainly by the rate of recovery of the hypothalamic-pituitary axis and normal secretion of GnRH and LH. Therefore, since anestrus is a result of many factors that include age, breed, pre- and postpartum nutrition, body condition at calving, milk yield, suckling, calving season, presence or absence of the bull, delayed uterine involution, dystocia, and the general health status of the cow, all of these can greatly influence the duration of postpartum anestrus. Understanding the managerial and physiological processes factors listed above enable producers, managers, and veterinarians to tackle these issues and minimize the impact of anestrus. Producers, veterinarians, nutritionists, and farm consultants should not only focus on overall fertility, but also review *up-stream* factors such as postpartum management practices, nutritional regimens, health status; BCS at calving, presence of calves and calf management. It is still quite common to find farms that have no standard operating procedures or strategies to alleviate postpartum anestrus problems. Moreover, implementation of a sound systematic breeding protocol can reduce the number of anestrous cows in the herd and shorten the postpartum anestrous period. Combinations of progestins, GnRH, and prostaglandin F2α are quite effective to induce estrus and ovulation, in anestrous suckled cows and peripubertal heifers.

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