Proceedings, Applied Reproductive Strategies in Beef Cattle
December 2 and 3, 2008, Fort Collins, CO

# UNDERSTANDING PUBERTY AND POSTPARTUM ANESTRUS

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## Introduction

Mammals have evolved in an environment highly dependent on nutrient intake for survival and perpetuation of the species. As some of these mammals have been domesticated, underlying physiological responses that rely heavily on nutrient supply have been carried with them. One such response is what we now call anestrus. During the period in early life before a developing female is anatomically capable of carrying, delivering and nurturing a newborn, the physiological events that are necessary for this to successfully occur are not fully coordinated. Development proceeds – driven by nutrient intake – to the point that prepuberal anestrus progresses to a highly coordinated cyclical pattern known as the estrous cycle. A similar physiological event occurs following delivery of the newborn and is termed postpartum anestrus. This paper will address the current understanding of physiological factors controlling anestrus, as well as some of the practical approaches to minimizing its impact in beef cattle production.

## Puberal "Anestrus" and Puberty

An overview of the physiological components of puberal anestrus was written by Berardinelli (2007) for a similar conference and portions of that discussion are included herein with the author's permission.

Age at puberty has a significant effect on reproductive efficiency of beef cattle herds when heifers are bred to calve as 2-yr-olds, particularly in production systems that use restricted breeding seasons (Ferrell, 1982). To achieve optimal lifetime productivity, heifers should conceive early in their initial breeding season. Future reproductive performance of heifers is dependent on the time and age that they have their first calf, since heifers that conceive early in their first breeding season have greater lifetime productivity than do their counterparts that conceive late in their first breeding season (Lesmeister et al., 1973). It is a common principle understood among ranchers that "an early calver will remain an early calver." In addition, heifers that calve as 2-yr-olds produce more calves during their lifetime than do heifers that calve for the first time as 3-yr-olds (Núñez-Dominquez et al., 1991). Furthermore, we are faced with the fact that the likelihood of early conception in the initial breeding season is increased in heifers that have experienced multiple estrous cycles before the start of the breeding season (Byerley et al., 1987). Unfortunately, failure to reach puberty at an appropriate time remains a major reason that heifers do not become pregnant during their first breeding season (Yelich et al., 1996).

Thus we are faced with two major management problems that limit reproductive efficiency in the developing heifer. They are:

1. The interval of time spent in attaining puberty after weaning (i.e. prepuberal "anestrus").
2. Low fertility associated with breeding heifers at their first estrus (i.e. puberty; Byerley et al, 1987).

To be able to modify or manage factors to reduce the time spent in the prepuberal anestrous condition and overcome reduced fertility at puberty we must first understand physiological mechanism whereby heifers attain puberty and become pregnant.

*Viable Embryos can be Produced from Young Heifer Calves.* An interesting side-bar to the discussion of heifer development toward puberty was published in 1971. Seidel et al. (1971) demonstrated that it was possible, through hormone therapy, to induce very young heifer calves to ovulate and produce viable embryos for transfer to recipients. In this work an experiment was designed to determine the response of younger calves to superovulatory treatment. Calves at birth, 1 and 2 months of age weighed approximately 38, 56 and 70 kg, respectively. All calves were given 1,500 IU PMSG, followed in 5 days with 50 mg LH i.v. and sacrificed 3 days after LH. These authors noted great differences in superovulatory response among these age groups. Apparently ovaries of neonatal calves are not capable of responding to superovulation treatment, either because of ovarian incompetence, e.g., a shortage of vesicular follicles, or because of the recent maternal hormone influence. However, a small number of the 1 and 2 month calves produced fertilized embryos that when transferred to recipients resulted in pregnancies. This early work of Seidel et al. (1971) confirms previous work (Casida et al., 1943; Marden, 1953; and Jainudeen, Hafez and Lineweaver, 1966) that calves 1 month old are capable of being superovulated and that cleaved ova can be recovered.

Therefore one can assume that the anatomical structures and general physiological processes to produce viable embryos are in place at a very young age. However, due to a lag time required to develop the physiological control mechanisms to have this system run without exogenous intervention, the heifer must wait until growth and size limitations are overcome so that pregnancy can ensue without undue risk to the dam or fetus simply due to capacity to carry a pregnancy to full term.

*Physiological Control Mechanisms.* Control of reproductive processes resides in the brain centers of the hypothalamic-pituitary-ovarian axis. In the bovine, genetic factors, such as breed, sire, heterosis, and external environmental factors, such as level of nutrition and its effect on growth rate, season of birth, and social interactions (biostimulatory effect of bulls) affect age at puberty; hence, affect the time spent in prepuberal "anestrus". Genetic and environmental factors interact with internal developmental mechanisms primarily resident in the central nervous system; principally, the hypothalamic neuroendocrine system responsible for the regulating gonadotropin releasing hormone (GnRH). GnRH is the primary stimulator of luteinizing hormone

(LH) secreted by the anterior pituitary gland which in turn regulates ovarian follicular development and maturation; and is the causative agent of ovulation. During prepuberal "anestrus' or prepuberal development, GnRH secretion is depressed through the negative feedback action of low concentrations of estradiol secreted from developing antral follicles of the ovaries. This action results in infrequent pulse releases of GnRH, which in turn results in pulses of LH that occur at low frequencies (< 4 pulses/day). It is the pulsatile nature of LH secretion that is recognized by dominant follicles to determine whether they enter their final stages of development and maturation. If LH pulses are infrequent then final maturation of follicles cannot occur, hence, ovulation is suppressed. This is thought to be the physiological mechanism that causes prepuberal "anestrus" in the heifer. 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 sensed by the central nervous system.

The perception of these various signals may produce, through the action of neurotransmitters, a positive or negative effect on the system regulating GnRH pulse secretion from the hypothalamus. This perception, if positive, will advance puberty, while if negative, will delay puberty. Furthermore, it is during this period in development that the 'sensitivity' to estradiol negative feedback begins to decrease. A decrease in the negative feedback suppression on GnRH/LH release by estradiol to an unspecified "threshold" level allows the frequency of GnRH pulses to increase which in turn increases the frequency of LH pulses. This period is sometimes referred to as the puberal transition or peripuberal developmental stage of sexual maturation. There is evidence that during this period there is a reduction in estradiol receptors in the hypothalamus and pituitary gland that may be the cause of this loss of negative sensitivity to estradiol. However, it is speculated that this decrease may be due to combinations of cellular or nuclear actions of metabolic factors, neurotransmitters, and/or "on/off" switching of genes in the hypothalamus and pituitary gland that regulate the effect of estradiol. Nevertheless, the reduction in the negative feedback effect of estradiol increases GnRH pulses, which in turn increases the frequency of LH pulses (>18 pulse /day), which in turn is the appropriate endocrine signal that is responsible for the final development and maturation of a dominant antral follicle.

During final maturation of dominant follicles, estradiol is secreted in increasing quantities. This pre-ovulatory increase in estradiol triggers behavioral estrus and the pre-ovulatory release of LH which is the signal for ovulation and heralds the onset of puberty and regular occurrence of estrous cycles in the heifers. The brief discussion regarding the physiological mechanisms involved with the onset of puberty in heifers is summarized in Figure 1. This is a representation of the concepts that are associated with the onset of puberty in heifers as well as in many mammalian species. This is Jim Berardinelli's (Berardinelli, 2007) adaptation of the foregoing discussion derived primarily from data, concepts, interpretations, and principles given by Day et al. (1984), Kurz et al. (1990), Kinder at al. (1995), and Senger (2003). Figure 1 shown here as a model to depict the processes controlling puberty in heifers.

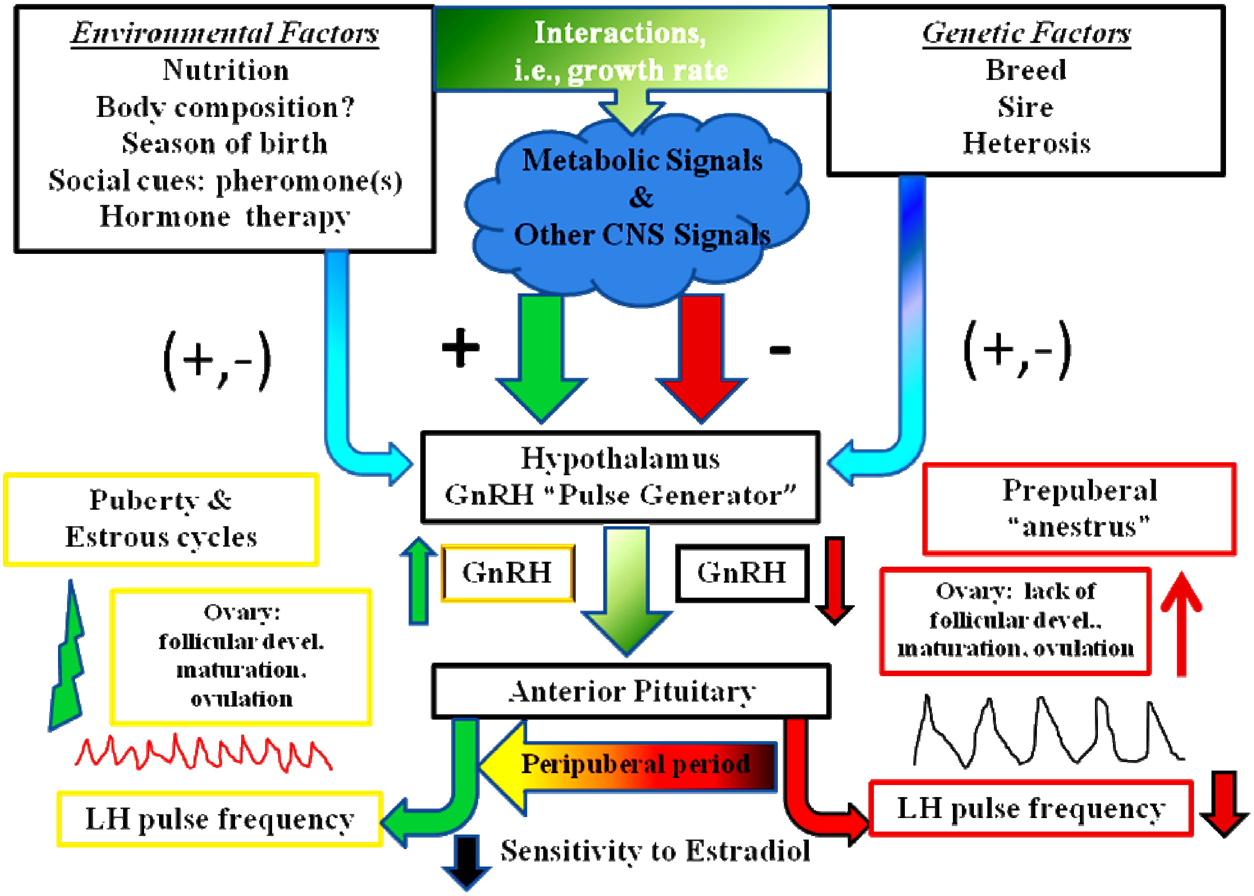


**Figure 1.** Simplified schematic of the hypothalamic-pituitary-ovarian axis and physiological model for the effect of genetic and environmental factors on attainment of puberty in heifers. Pluses and minuses are stimulatory and inhibitory effects, respectively. (Source: Model representation developed by Berardinelli, 2007.)

What are the physiological and practical consequences of management decisions related to puberty in beef heifers based upon this model? This is not an easy question to answer because even a single management change may affect more than one system involved in the model. For instance, genetic selection for increased growth rate in heifers to reach a given "target weight" sooner may affect various metabolic pathways in such a way as to have either a positive or negative affect on metabolic signals which in turn affect the sensitivity mechanism for estradiol in either a positive or negative manner. If negative, then puberty will be delayed in heifers with enhanced growth rate and reproductive efficiency of the herd may decrease. Figure 2 shows a plausible mechanism for altering age at puberty in beef heifers and is based upon studies cited in the preceding section and recent work by Gasser et al. (2006a,b,c) using a dietary regimen coupled with early weaning to induce precocious puberty in beef heifers.

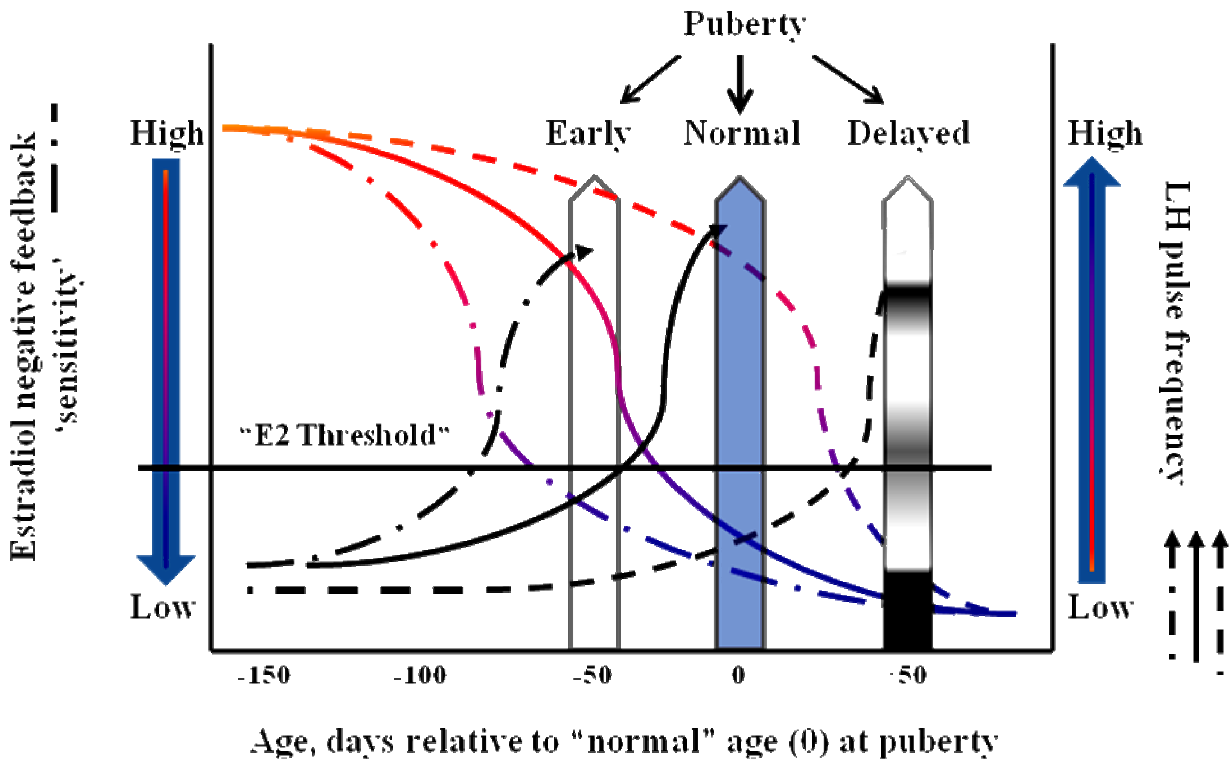


**Figure 2.** Possible mechanisms for factors that influence age at puberty by altering estradiol negative feedback sensitivity mechanism relative to a minimum "threshold" level of sensitivity below which a heifer transitions into puberty. Management options that move the point at which estradiol negative feedback effect crosses the "threshold" level moves age at puberty left or right of the "normal" age at puberty. (Source: Illustration based on work by Gasser et al. (2006a,b,c) developed by Berardinelli, 2007).

Based upon the findings of Gasser et al. (2006a,b,c) it is clear that maturation of the hypothalamic-pituitary-ovarian axis is complete many months before the "normal" age at puberty in beef heifers. The constraining factor appears to be related to the sensitivity/threshold of the system to the negative feedback effects of estradiol. Furthermore, they concluded that maturation of this system is dependent upon nutritive intake between 4 and 6.5 months of age, regardless of the diet fed thereafter (Gasser et al., 2006d). Thus, the expected outcomes of management decisions based upon this model depends upon "shifting" the timing of the occurrence in the decrease in sensitivity to the negative feedback effects of estradiol given a constant maturation threshold set before weaning. Differences in genotype may be postulated to occur as a result of either a genetic shift in the timing of the decrease in estradiol feedback or the genes themselves which are responsible for the system itself, may interact with other factors to change the timing of the shift. Increasing or decreasing plane of nutrition will accelerate or delay the shift in the timing of the decrease in the negative feedback of estradiol, respectively.

Fall-born heifers tend to reach puberty earlier than spring-born heifers; an effect mediated by photoperiod during the first 6 months of age (Schillo et al., 1982). Thus, photoperiod during the 4 to 6.5 months of age during the maturation of the system would be expected to shift the timing of the decrease in sensitivity to estradiol to the right if heifers are born in the spring and to the left is they are born in the fall. This notion remains to be tested.

Exogenous progestins, progesterone-like compounds, have been shown to accelerate age at puberty (Kinder et al., 1994). The mechanism for this effect is unknown but would be expected to shift the decrease in estradiol negative feedback to the left in the Figure 2. However, careful examination of the characteristics of the experimental heifers, in the studies cited in the review by Kinder et al. (1994) indicated that progestin treatment was given within 40 to 30 days of the “normal” age for various breeds. This is during the peripuberal period when sensitivity to the negative effect of estradiol is naturally decreasing. Attempts to use progestin treatment on younger aged heifers have met with limited success (Berardinelli et al., 1978). Perhaps exogenous progesterone treatments during the peripuberal period accelerates the decrease in estradiol negative feedback sensitivity or reduces the so-called “threshold level” for estradiol during the peripuberal period.

Does accelerating age at puberty provide a direct benefit to producers for developing replacement heifers, i.e., why keep shifting the curve to the left in Figure 2? The main reason for reducing age at puberty in heifers is to allow them to exhibit more that one estrous cycle before the beginning of fixed breeding season, whether in spring or fall. It is well-know that breeding heifers at their first estrus (puberty) results in significantly lower pregnancy rates than breeding heifers at a later estrus (Byerley et al., 1987). Perhaps this is the reason that short-term progestin-induction of puberty results in lower fertility in younger and lighter heifers than in older and heavier heifers. Nevertheless, management practices that shift the curve to the left in Figure 2 decrease age at puberty and allow for a majority of replacement heifers to be bred early in a fixed breeding season to calve as 2-yr-olds early in their first calving season. This in turn gives one the opportunity to increase reproductive efficiency of a beef cattle herd.

## Bringing Science and Practice Together

Progress has been made in understanding the physiological processes that control age at puberty. As a result, genetic, nutritional and hormonal systems have evolved to reduce age at puberty and thereby increase the percentage of heifers pregnant during their first breeding season and enabling them to remain in the herd for subsequent breeding seasons. A few of these are briefly outlined below:

*Progesterone Therapy.* An example of the beneficial effects of exogenous progesterone treatment during the peripuberal period on accelerating the decrease in the negative feedback of estradiol may be seen in the use of intravaginal progesterone releasing devices (CIDRs) for estrus synchronization in heifers which has become common in recent years. Lucy et al. (2001) reported a positive response in pregnancy rate seen in anestrous and cyclic cows as well as in prepuberal and cyclic heifers. The improved rate of pregnancy reported by Lucy et al (2001) in prepuberal beef heifers treated with the CIDR was noteworthy because prepuberal heifers in the untreated control or PGF2$\alpha$

alone treatments never attained pregnancy rates that were similar to those of the CIDR+PGF2$\alpha$-treated heifers.

*Biostimulation by the Male.* The biostimulatory effect of bulls on age at puberty in heifers may be an important management tool if we understood the underlying mechanism and the agents responsible for this effect. The biostimulatory effect of bulls to decrease prepuberal "anestrus" in heifers appears to be associated with growth rate of heifers (Roberson et al., 1991). In general, if heifers are fed to meet a growth rate of greater than 1.8 lb/d and are exposed to bulls during this period then one may expect a decrease in age at puberty. However, heifers fed to achieve a lower growth rate do not appear to be influenced by the biostimulatory effect of bulls (Berardinelli et al, 1978; Roberson et al., 1987). Apparently, the biostimulatory effect of bulls in this case is mediated by a priming pheromone; an air-borne chemical signal produced by bulls which accelerated puberty in heifers (Izard and Vandenbergh, 1982). The nature of the chemical signal is unknown. However, based upon the model, the assumed pheromone would shift the decrease in the negative feedback sensitivity of estradiol to the left as illustrated in Figure 2 and accelerate age at puberty by increasing the frequency of LH at an earlier age.

*Genetic Progress.* Genetic predication by means of expected progeny differences (EPD) for traits that relate to fertility and indirectly to puberty in heifers are being used widely in the cattle industry today. Early work done at Colorado State University by Dr. Jim Brinks (Smith et al., 1989) showed a strong correlation between bull scrotal circumference and age at puberty in siblings and offspring. The science behind this trait has been explored and is now a key part of sire selection programs in beef programs (BIF, 2002). Therefore scrotal circumference has become an indicator trait for the genetic hastening of the physiological events described above. Additionally, more recent EPDs for Heifer Pregnancy and Stayability have evolved as genetic tools to further enhance identification of animals with genes that likely interact in some way with the brain centers of the hypothalamic-pituitary-ovarian axis which result in escape from anestrus to move the events described in Figure 2 above to the left.

*Potential of Fetal Programming for Heifer Fertility from Dam Nutrition.* A three-year study published by Martin et al. (2007) reported an apparent positive impact of nutritional plane during gestation on fertility of the heifer offspring. Heifers born to cows supplemented with protein were heavier at weaning, prebreeding, first pregnancy diagnosis, and before their second breeding season. Despite similar ages at puberty and similar proportions of heifers cycling before the breeding season, a greater proportion of heifers from protein supplemented dams calved in the first 21 d of the heifers' first calving season, and pregnancy rates were greater compared with heifers from non-supplemented dams. Collectively, these results provide evidence of a fetal programming effect on heifer postweaning body weight and fertility. More details from this research will be presented by Dr. Funston later in this symposium.

*Early Nutrition of the Developing Heifer*. In the 2007 paper written by Berardinelli (Berardinelli, 2007), he concluded that there is the possibility that we could theoretically accelerate age at puberty in heifers by many months if we understood the development of the sensitivity mechanism for estradiol during the first 120 to 190 days of life. Target weight at puberty may not be the most appropriate management tool for reducing prepuberal "anestrus" in heifers. It may be that growth rate from 4 months of age through weaning, and the nutritive value of the diet as they progress through this developmental period, is more important. In the future this concept may become an important management consideration for developing heifers to attain puberty well before the breeding season.

*Number and Size of Antral Follicles during the Prepuberal Period.* Berardinelli (2007) cited recent work from Dr. J. J. Ireland's laboratory at Michigan State University that indicates the possibility that individual heifers might best be classified by the numbers of antral follicles that are 3 mm or greater by ultrasonography. This is because over a number of follicular waves cows appear to repeat the same number of either low or high numbers of 3 mm and greater follicles. Higher numbers of antral follicles are associated with many reproductively important events including pregnancy rates following in vitro fertilization; greater numbers of transferable embryos; shorter calving intervals; and fecundity (see Burns et al., 2005; Ireland et al. 2007). As yet there is no research on classification of follicular numbers and age at puberty in heifers.

Additionally, if antral follicle numbers are important in many reproductive processes they may be important in the process that underlies puberty. Furthermore, it may be that scrotal circumference of bulls, genetically related to age at puberty in heifers, may be related to antral follicles numbers in heifers, i.e., selection for one may be selection for the other. Future research may lead to management options related to puberty that might include follicular numbers of antral follicles in developing heifers. The end result of any management strategy during this developmental period is to ensure that a majority of heifers attain puberty at least one cycle length before the breeding season.

## Postpartum Anestrus

Berardinelli (2007) described postpartum anestrus as a condition that occurs after parturition in the female bovine that allows the dam to anatomically and physiologically recuperate from pregnancy and parturition. The length (interval) of this period is measured from calving to estrus, ovulation, resumption of luteal function, or conception. Under reasonable management conditions, postpartum anestrus last for 35 to 75 days in cows that are 3-yr-old or older. However, cows that calve as 2-yr-olds generally have intervals that can last much longer, from 50 to 125 days, even under good management conditions.

Failure of cows to rebreed after calving significantly decreases reproductive efficiency of beef cattle production (Short et al., 1994). Extended postpartum anestrus is the single most important reason that cows fail to rebreed during defined breeding seasons. This problem is exacerbated by primiparous cows because they require significantly more time after calving to resume estrus/ovulatory activity than multiparous cows (Short et al., 1994). The end result of this problem is that, in general, cows that calve late in the breeding season wean substantially smaller calves, and, in particular, primiparous cows that calve late in their first calving season tend to calve later in the next and subsequent calving seasons, reducing their lifetime productivity (Lesmiester et al., 1973). Economically this means that cows that have extended anestrus and fail to rebreed after calving must be culled and replaced by heifers to maintain herd size: if replacement rate exceeds 15% then one can expect significantly less net income from a beef cow-calf operation (Werth et al., 1991).

## Incidence of Anestrus

Anderson (2006) explained that early conception in a cow herd is 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 is significant in the beef cow-calf operations. In an experiment that included 851 postpartum cows from six states (Lucy et al., 2001), 53% of cows were anestrous 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., 2003) to 46% (Stevenson et al., 2003). Strategies to improve reproductive rate in beef cattle may be maximized when methods are used that successfully synchronize a fertile estrus in anestrous beef cows.

Factors regulating anestrus have been reviewed extensively (Short et al., 1990; Yavas and Walton, 2000; Rhodes et al., 2003; Stevenson et al., 1997). Anestrus is initiated by the presence of a suckling calf; weaning at birth results in the resumption of estrous cycles in about 14 days (Williams, 1990). Nutritional status greatly influences the length of the anestrous period. Reduced body energy reserves or inadequate energy or protein intake before or after calving can delay the return to estrus. In a summary by Stevenson and coworkers (2003), these authors identified three key issues (body condition, parity, and days postpartum) that were associated with the incidence of anestrous and pregnancy failure.

*Body Condition.* The degree of fatness (body condition score or BCS) of a female's body has been shown to be an accurate indicator of her energy and/or nutritional status. Body condition at calving influences the length of the postpartum interval (time from calving to first estrus). Short and coworkers (1990) reviewed several studies examining the influence of different nutritional regimens. Cows that calve with a body condition score less than 5 (1 = emaciated and 9 = obese) have longer postpartum intervals than cows calving with a body condition score 5 or greater (Figure 3). Increasing energy supplementation reduced the length of the anestrous period in thin (BCS < 5) cows but not heavier conditioned cows (Short et al., 1990). Stevenson and coworkers (2003) demonstrated that the proportion of cows initiating estrous cycles (cycling cows) increased linearly by approximately 18% per unit as BCS increased from 3.5 to 6.0 at the onset of the breeding season (Figure 4). Thus, to minimize the length of the anestrous period, cows should calve in a BCS of 5 or greater.

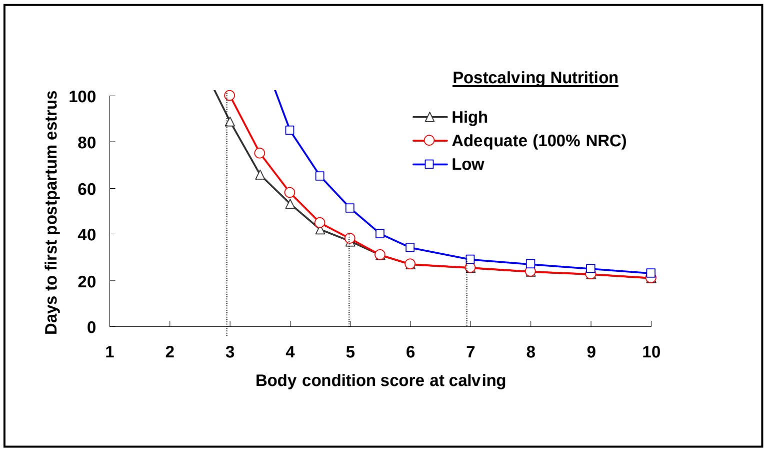


**Figure 3.** Days to first postpartum estrus on the basis of body condition scores assessed at parturition and postcalving feeding regimen. Those cows with a body condition score 5 or greater are less likely to respond to improved postcalving nutrition but thinner cows may benefit from increased nutritional regimens postcalving. Source: Short et al. (1988).

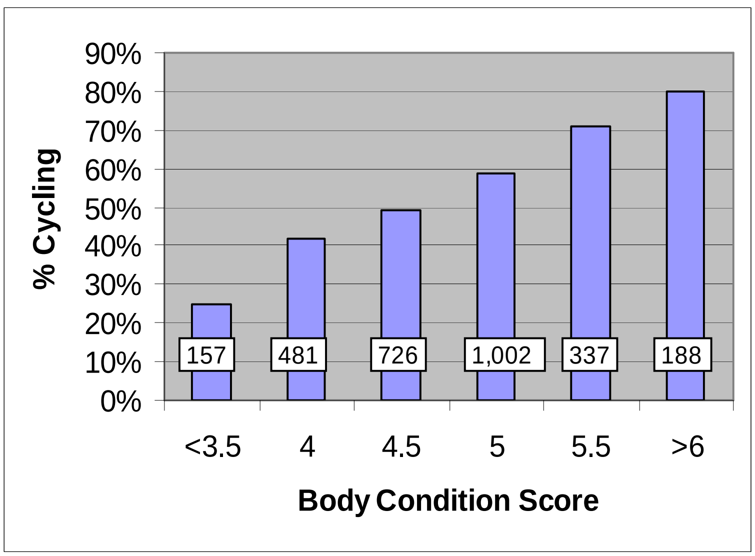


**Figure 4.** Proportion of suckled cows that were cycling on the first day of the breeding season on the basis of body condition score assessed at that time. Cycling status was estimated by concentrations of progesterone in blood serum of cows sampled during 7-10 days before the breeding week. (Numbers shown in blocks on each bar are the number of cows included in each condition score noted.) Source: Stevenson et al. (2003).

*Parity.* Most beef producers understand the influence of parity on anestrus. Two-year old suckled beef cows simply require more time postpartum to initiate estrous cycles because they need additional energy to support both lactation and growth (Short and Adams, 1988). Fewer 2-year-old cows were cycling, despite calving up to 3 weeks earlier, compared to the multiparous cows (Stevenson et al., 2003). Cycling activity increased linearly from 9% (30 days) to a peak of 70% at 81-90 days postpartum (Figure 5). The delay in estrus is the result of altered nutrient partitioning after calving. The priority system for energy use in cows is as follows; first, maintenance of essential body functions; second, growth; third, lactation; and finally, reproduction and initiation of estrous cycles. Most cows complete their physical growth at approximately 4 years of age. Mature cows, then, have no growth requirement and nutrients are more readily partitioned to lactation and reproduction. It is not surprising then, that cows are most productive from 4-10 years of age.

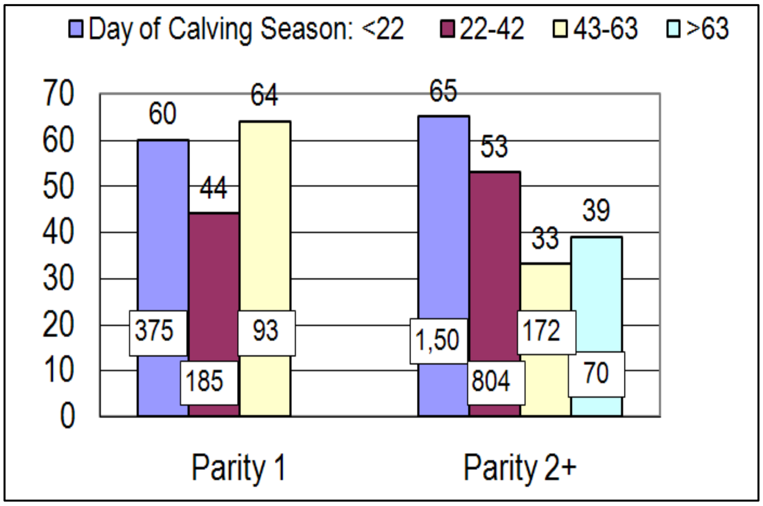


**Figure 5.** Proportion of primiparous (parity 1) and multiparous (parity 2+) suckled cows that were cycling on the first day of the breeding season, based on when they calved during the first (< 22 days), second (22-42 days), or third or more (> 63 days) 3-week period of the calving season. Cycling status was estimated by concentrations of progesterone in serum of cows sampled during 7 to 10 days before the breeding week. Source: Stevenson et al. (2003).

*Days Since Calving.* Time is an essential component of the postpartum period. Stevenson and coworkers (2003) demonstrated that the proportion of cows cycling on the first day of the breeding season was influenced by calving date. Regardless of parity, the proportion of cows cycling increased in a curvilinear fashion (Figure 6). Days postpartum averaged 86 ± 0.7 for primiparous and 68 ± 0.3 for multiparous cows. The percentage of cycling cows decreased after 90 days postpartum due mostly to the reduced cyclicity of the primiparous cows (85% of the cows at this time). The proportion of cows initiating estrous cycles increased by approximately 7% for every 10-day interval from calving. Thus, more cows had initiated estrous cycles when they had longer periods of time between calving and the breeding season.

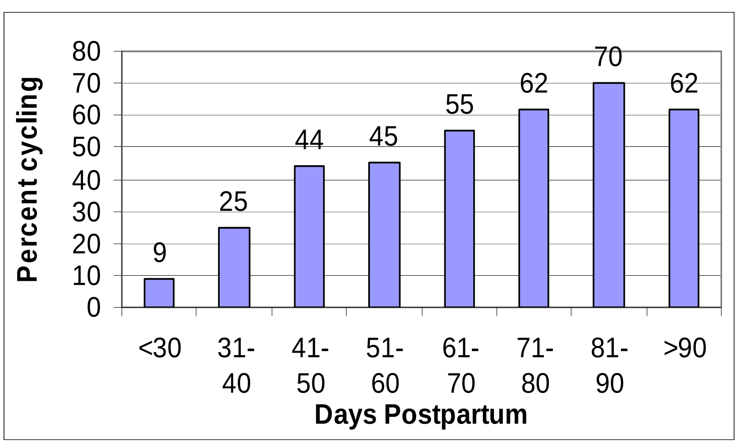


**Figure 6.** Proportion of suckled cows that were cycling on the first day of the breeding season on the basis of days since calving. Cycling status was estimated by concentrations of progesterone in blood serum of cows sampled during 7 to 10 days before the breeding week. Source: Stevenson et al. (2003).

Interestingly, the influence of time on cyclicity on the first day of the breeding season differed between primiparous and multiparous cows. For primiparous cows, the percentage of cows cycling at the onset of the breeding season did not differ among the first three 21-day calving intervals (Figure 5) but was lower for those very late-calving primiparous females. In contrast, cyclicity was higher for multiparous cows calving in the first 6 weeks of the calving season (> 50%) compared with those that calved after 6 weeks (< 40%). Early calving appears critical for both primiparous and multiparous cows.

### Physiological Mechanisms Controlling Anestrus

Short et al. (1990) published a review of the mechanisms involved in control of anestrus and infertility in the bovine. This work outlines four broad causes of infertility following calving. General infertility may include a myriad of components that decrease fertility by 20 to 30% for any estrus regardless of whether it occurs after calving or at any other reproductive state. Fertilization rates in cattle have been shown to be high. However, there seems to be some type of a biological ceiling in place that controls the reproductive processes that determine the number or quality of embryos that are successfully fertilized which progress to fetal development. It appears that there is a sort of screening process to enhance the likelihood of a successful pregnancy since the cost of pregnancy to the dam is so high in both nutritional demand and time invested. The components of general infertility may include genetic factors (Martin et al., 1992), asynchrony of endocrine events during maternal recognition of pregnancy (Bazer et al., 1998) or other yet-to-be identified factors which serve as screening safeguards in biology to assure survival of a viable neonate.

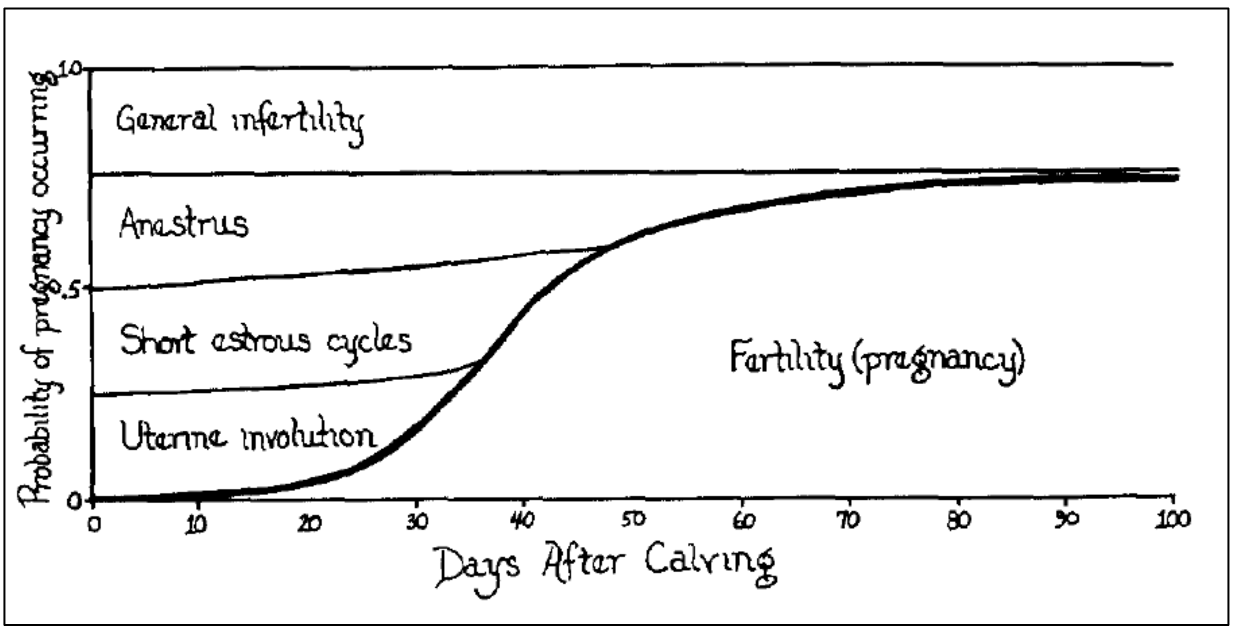


**Figure 7.** Schematic diagram from Short et al. (1990) which depicts the probability of pregnancy of postpartum cows due to uterine involution, short estrous cycles, anestrus and general infertility during the postpartum period.

Illustrated in Figure 7 from Short's 1990 review are the relationships between probability of a pregnancy occurring (infertility vs. fertility) and time after calving. The four main factors that contribute to infertility (general infertility, uterine involution, short estrous cycles and anestrus) all play a role in the probability of pregnancy. Three of these factors are related specifically to the postpartum period. Shown in Figure 7 are the time relationships that these components have to infertility.

*Uterine Involution.* Involutionary processes in the genital tract begin immediately after calving (Moller, 1970). Kiracofe (1980) reviewed the literature on this subject and concluded that there was no relationship between uterine involution and length of the postpartum anestrus period. Involution of the uterus is a barrier to fertility for approximately 30 days post calving. Based on experiments conducted in Miles City, Short et al. (1990) concluded that infertility during the first 20 days after calving is caused by a physical barrier to sperm transport and not to any inherent defect in the ova or other physiological mechanisms. In reality, involution of the uterus – when it proceeds normally – is not a problem to beef cattle fertility because very few cows will return to estrus early enough for it to be a concern.

*Short Estrous Cycles.* Anderson (2006) provides a concise, thoughtful explanation of postpartum reproductive activity and short cycles. That paper explains that the endocrine changes that precede first estrus must be imitated to successfully induce estrus in anestrous cows. Ovarian function begins rapidly after calving. A wave-like pattern of follicle growth begins approximately two weeks postpartum and multiple waves of growth occur prior to the first ovulation (Murphy et al., 1990). Diameter of the dominant follicle increases with each successive follicular wave up to either ovulation (Murphy et al., 1990) or the fourth or fifth wave in cows with longer postpartum intervals (Stagg et al., 1995). The first ovulation postpartum is preceded by an increase in the pulsatile secretion of LH (Walters et al., 1982). The initial postpartum ovulation occurs if the dominant follicle can produce sufficient estradiol to induce the preovulatory gonadotropin surge.

The initial postpartum ovulatory event results in the formation of a corpus luteum (CL) that is short-lived (7-10 days). The short cycle is a normal occurrence at the first spontaneous postpartum ovulation in beef females (Day et al., 1990). The first CL postpartum is short-lived because of the premature release of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) from the uterus (Cooper et al., 1991) due to the low concentrations of progesterone (Zollers et al., 1993) and estradiol (Mann and Lamming, 2000) before ovulation. Low concentrations of progesterone and estradiol before ovulation alter endometrial progesterone and oxytocin receptor concentrations leading to the premature release of $PGF_{2\alpha}$ and the early regression of the CL. Protocols for inducing cyclicity and estrus synchronization that increase progesterone before ovulation and enhance pulsatile LH secretion and follicle growth are important components of any program to successfully induce fertile estrous cycles in anestrous cows.

*Postpartum Anestrus.* Short et al. (1990) lists anestrus as the third, and most important barrier to fertility following parturition. Berardinelli (2007) provides an explanation of the physiological events related to postpartum anestrus. The primary factors that affect the length of the postpartum anestrous interval to the resumption of ovarian cycling activity and breeding are suckling and nutrition. Other factors can affect this interval and include breed, season of calving, environmental stress, disease, multiple births, dystocia, retained placenta, latent effects of pregnancy, and social factors such as presence of bulls (Short et al., 1990). The underlying physiological mechanism(s) for postpartum anestrus and resumption of estrous cycle is analogous to the mechanisms involved with the onset of puberty in the heifer (Figure 1). However, there are other factors that bear upon this system that are not common to those found in the heifer. These include the latent effects pregnancy and parturition, uterine re-modeling, lactation, suckling stimuli, and the cow-calf bond. Again to understand factors that may be manipulated to overcome postpartum anestrus we must understand the underlying physiological bases of the system.

A simplified representation of the basic system with its components and some of the more important factors is given in Figure 8. The mechanisms of the system 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; Williams and Griffith, 1995). The negative effects of pregnancy and parturition are carried over into the puerperium period (2-3 wk) after calving. During this period the pituitary stores or LH and FSH are replenished and the hypothalamus regains its ability to secrete GnRH. The pituitary begins to respond to the hypothalamic "pulse" generator release of GnRH during this time, releasing LH in a low frequency pattern (~4 to 5 pulses/day). This is thought to be caused by increased sensitivity of the hypothalamus to the negative feedback effects of estradiol. Even though dominant follicles develop within 5 to 15 days after parturition they do not attain full maturation and do not ovulate. The reason for this is inappropriate LH signaling from the pituitary caused by the negative feedback effect of estradiol interacting with lactational and suckling factors, and the development of the social bond between the cow and calf. These interactions are powerful negative controls on the resumption of estrous cycles during the postpartum period and are extremely difficult to overcome by management.

Furthermore, the negative effect of these stimuli is compounded if cows are in poor body condition at parturition or on a low plane of nutrition during the first 30 to 45 days after parturition. This situation is exacerbated in first-calf cows because energy must also be used for growth rather than for reproduction which further extends the anestrous period. Factors that extend postpartum anestrus are thought to act or interact at the hypothalamic level delaying changes in the frequency of GnRH and LH release, thus delaying final follicular maturation and ovulation (right side of Figure 8). As time after parturition increases the sensitivity to the negative feedback effect of estradiol begins to decrease, lactational and suckling stimuli begin to wane, and calf begin to become more dependent on solid food instead of milk; diminishing the negative effect of the cow-calf bond. These changes are interpreted at the hypothalamic level to increase the frequency of GnRH which in turn increases the frequency of pituitary LH release appropriate for final maturation of dominant follicles and ovulation; ending postpartum anestrus (left side of Figure 8).

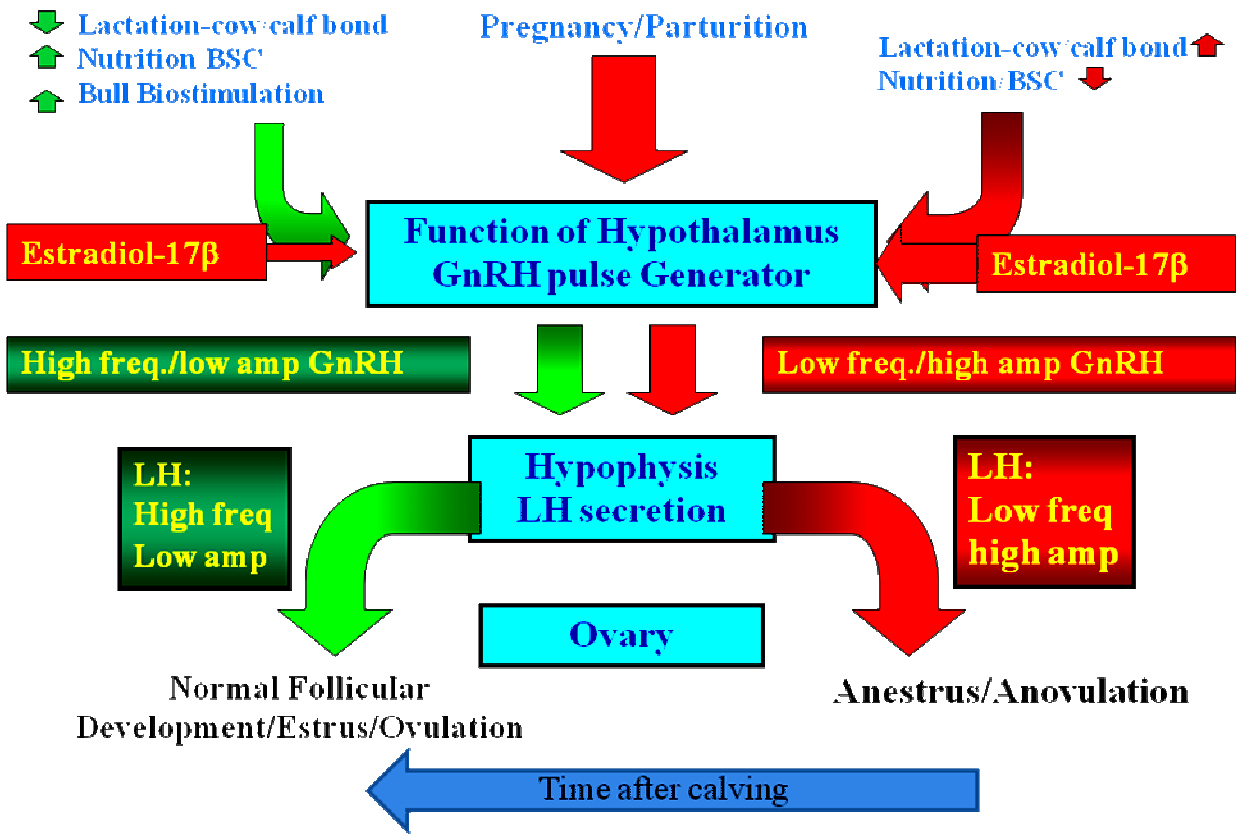


**Figure 8.** Simplified model for the mechanism whereby factors associated with influencing the postpartum anestrus to resumption of estrous cycles affect the hypothalamic-pituitary-ovarian axis in the suckled beef cow. Arrows and text boxes to the right in the figure represent inhibitory stimuli and increase the anestrous interval, while arrows and text boxes to the left represent stimulatory stimuli and decrease the anestrous interval. Up and down arrows next to factors along the top portion of figure represent stimulatory and inhibitory effects of various factors.

**Reducing Length of Postpartum Anestrus**

Numerous reviews and symposium papers are available that address causes and strategies for reducing postpartum anestrus. Suckling/lactation has been reviewed by Williams (1990) and Stevenson et al. (1997 and 2003). Nutritional factors play a large role in regulation of anestrus and have been reviewed by Dunn and Kaltenbach (1980), Short and Adams (1988) and Randel (1990). During this symposium, Funston (2008) will also provide current concepts of the interaction of nutrition and reproduction in the bovine.

Berardinelli (2007) provides a timely review and description of the impact and use of biostimulation (bull exposure) as a tool for reducing the length of the postpartum anestrus period. Readers are referred to that paper for a more in-depth discussion of this topic.

## Summary

The process known as anestrus poses challenges in beef cattle management since cows and heifers must have normal estrous cycles in order to successfully conceive on a regular basis. Understanding the physiological processes associated with anestrus – both puberal anestrus and postpartum anestrus – allow the manager to use tools and practices to minimize the impact of anestrus in their herds. Recent data indicates that maturation of the reproductive system in heifers appears to be more dependent on nutrient intake between 4 and 6.5 months of age than previously understood. Management practices such as progesterone therapy, biostimulation by the male, genetic selection tools, and fetal programming all show promise as tools to hasten puberty in heifers. Incidence of postpartum anestrus in cows is heavily impacted by body condition, parity, presence of the calf and days since calving. The transition from anestrus to normal estrous cycles involves progression through uterine involution and a period of short estrous cycles. The physiological events that control postpartum anestrus are very similar to the control of puberal anestrus and responses in the postpartum cow to management practices employed in heifer development generally show similar response.

## Literature Cited

Anderson, L. 2006. Puberty and Anestrus: Dealing with Non-Cycling Females. Proceedings, Applied Reproductive Strategies in Beef Cattle. August 30-31, 2006, St. Joseph, Missouri.

Bazer, F.W., T. L. Ott, T. E. Spencer. 1998. Maternal recognition of pregnancy: Comparative aspects: A review. Placenta 19:375-386.

Berardinelli, J. 2007. Management Practices to Overcome Problems with Puberty and Anestrus. Proceedings, Applied Reproductive Strategies in Beef Cattle September 11 and 12, 2007, Billings, Montana. pp 149-162.

Berardinelli, J. G., R. L. Fogwell and E. K. Inskeep. 1978. Effect of electrical stimulation or presence of a bull on puberty in beef heifers. Theriogenology 9:133-141

BIF. 2002. Guidelines for Uniform Beef Improvement Programs, Eighth Edition. *Guidelines* is a publication of the Beef Improvement Federation, Ronnie Silcox, Executive Director, Animal & Dairy Science Department, The University of Georgia, Athens, GA 30602. Accessed at www.beefimprovement.org 5 November 2008.

Burns, D. S., F. Jimenez-Krassel, J. L. Ireland, P. G. Knight, and J. J. Ireland. 2005. Numbers of antral follicles during follicular waves in cattle: evidence for high variation among animals, very high repeatability in individuals, and an inverse association with serum follicle-stimulating hormone concentrations. Biol Reprod. 73:54-62.

Byerley, D. J., R. B. Staigmiller, J. G. Berardinelli, and R. E. Short. 1987. Pregnancy rates of beef heifers bred either at puberty or third estrus. J. Anim. Sci. 65:645-650.

Casida, L. E., R. K. Meyer, W. H. McShan and W. Wisnicky. 1943. Effects of pituitary gonadotropins on the ovaries and the induction of superfecundity in cattle. Amer. J. Vet. Res. 4:76.

Day, M. L., K. Imakawa, M. Garcia-Winder, D. D. Zalesky, B. D. Schanbacher, R. J. Kittok, and J. E. Kinder. 1984. Endocrine mechanisms of puberty in heifers: Estradiol negative feedback regulation of luteinizing hormone secretion. Biol. Reprod. 31:332–341.

Day, M.L., R. M. Dyer, G. W. Wilson, and W. F. Pope. 1990. Influence of estradiol on duration of anestrus and incidence of short estrous cycles in postpartum cows. Domest. Anim. Endocrinol. 7, 19-25.

Dunn, T.G. and C.C. Kaltenbach. 1980. Nutrition and the postpartum interval of the ewe, sow and cow. J. Anim. Sci. 51(Suppl 2): 29.

Ferrell, C. L. 1982. Effects of postweaning rate of gain on onset of puberty and productive performance of heifers of different breeds. J. Anim. Sci. 55:1272–1283.

Gasser, C. L., D. E. Grum, M. L. Mussard, F. L. Fluharty, J. E. Kinder, and M. L. Day. 2006a. Induction of precocious puberty in heifers I: Enhanced secretion of luteinizing hormone. J. Anim. Sci. 84:2035–2041.

Gasser, C. L., C. R. Burke, M. L. Mussard, E. J. Behlke, D. E. Grum, J. E. Kinder, and M. L. Day. 2006b. Induction of precocious puberty in heifers II: Advanced ovarian follicular development. J. Anim. Sci. 84:2042–2049.

Gasser, C. L., G. A. Bridges, M. L. Mussard, D. M. Dauch, D. E. Grum, J. E. Kinder, and M. L. Day. 2006c. Induction of precocious puberty in heifers III: Hastened reduction of estradiol negative feedback on secretion of luteinizing hormone. J. Anim. Sci. 84:2050–2056.

Gasser, C. L., E. J. Behlke, D. E. Grum, and M. L. Day. 2006d. Effect of timing of feeding a high concentrate diet on growth and attainment of puberty in early-weaned heifers. J. Anim. Sci. 84:3118-3122.

Ireland, J. J., F. Ward, F. Jimenez-Krassel, J. L. Ireland, G. W. Smith, P. Lonergan, A. C. Evans. 2007. Follicle numbers are highly repeatable within individual animals but are inversely correlated with FSH concentrations and the proportion of good-quality embryos after ovarian stimulation in cattle. Human Reprod. 22:1687-95.

Izard, M. K., and J. G. Vandenbergh. 1982. The effects of bull urine on puberty and calving date in crossbred beef heifers. J. Anim. Sci. 55:1160-1164.

Jainudeen, M. R., E. S. E. Hafez and J. A. Lineweaver. 1966. Superovulation in the calf. J. Reprod. Fertil. 12 : 149.

Kinder, J. E., M.S. Roberson, M. W. Wolfe, and T. T. Stumpf. 1994. Management factors affecting puberty in the heifer. Page 69 in Factors Affecting Calf Crop. M. J. Fields, and R. S. Sand, eds., CRC Press, Boca Raton, FL.

Kinder, J. E., E. G. Bergfeld, M. E. Wehrman, K. E. Peters, and F. N. Kojima. 1995. Endocrine basis for puberty in heifers and ewes. J. Reprod. Fertil. Suppl. 49:393-407.

Kiracofe, G.H. 1980. Uterine involution: Its role in regulating postpartum intervals. J. Anim. Sci. 51(Suppl II):16.

Kruz, S. G., R. M. Dyer, Y. Hu, M. D. Wright, and M. L. Day. 1990. Regulation of luteinizing hormone secretion in prepubertal heifers fed an energy-deficient diet. Biol. Reprod. 43:450-456.

Lesmeister, J. L., P. J. Burfening, and R. L. Blackwell. 1973. Date of first calving in beef cows and subsequent calf production. J. Anim. Sci. 36:1–6.

Lucy, M. C., H. J. Billings, W. R. Butler, L. R. Ehnis, M. J. Fields, D. J. Kesler, J. E. Kinder, R. C. Mattos, R. E. Short, W. W. Thatcher, R. P. Wettemann, J. V. Yelich and H. D. Hafs. 2001. Efficacy of an intravaginal progesterone insert and an injection of PGF2alpha for synchronizing estrus and shortening the interval to pregnancy in postpartum beef cows, peripuberal beef heifers, and dairy heifers. J Anim Sci 79:982-995.

Mann, G.E. and G. E. Lamming. 2000. The role of sub-optimal preovulatory oestradiol secretion in the aetiology of premature luteolysis during the short oestrous cycle in the cow. Anim. Reprod. Sci. 64:171-180.

Marden, W. G. R. 1953. The hormone control of ovulation in the calf. Agr. Sci. 43:381.

Martin, L.C., J. S. Brinks, R. M. Bourdon and L. V. Cundiff. 1992. Genetic effects on beef heifer puberty and subsequent reproduction. J Anim Sci 1992. 70:4006-4017.

Martin, J.L., K.A. Vonnahme, D.C. Adams, G.P. Lardy, and R.N. Funston**.** 2007. Effects of dam nutrition on growth and reproductive performance of heifer calves. *J. Anim. Sci.* 85:841.

Moller. K. 1970. A review of uterine involution and ovarian activity during the postparturient period in the cow. New Zealand Veterinary Journal 18:83-90.

Murphy, M.G., M. P. Boland, and J. F. Roche. 1990. Pattern of follicular growth and resumption of ovarian activity in postpartum beef suckler cows. J. Reprod. Fertil. 90:523-533.

Núňez-Dominquez, R., L. V. Cundiff, G. E. Dickerson, K. E. Gregory, and R. M. Koch. 1991. Lifetime production of beef heifers calving first at two vs. three years age. J. Anim. Sci. 69:3467.

Randel, R.D. 1990. Nutrition and postpartum breeding in cattle. J. Anim. Sci. 68:853.

Rhodes, F. M., S. McDougall, C. R. Burke, G. A. Verkerk, and K. L. Macmillan. 2003. Treatment of cows with an extended postpartum anestrous interval. J. Dairy Sci. 86:1876-1894.

Roberson, M. S., R. P. Ansotegui, J. G. Berardinelli, R. W. Whitman, and M. J. McInnerney. 1987. Influence of biostimulation by mature bulls on the occurrence of puberty in beef heifers. J. Anim. Sci. 64:1601-1605.

Roberson, M. S., M. W. Wolfe, T. T. Stumpf, L. A. Werth, A. S. Cupp, N. Kojima, P. L. Wolfe, R. J. Kittok, and J. E. Kinder. 1991. Influence of growth rate and exposure to bulls on age at puberty in beef heifers. J. Anim. Sci. 69: 2092-2098.

Seidel, G. E., L. L. Larson and R. H. Foote. 1971. Effects of Age and Gonadotropin Treatment on Superovulation in the Calf. J. Anim. Sci. 33:617-622.

Senger, P. L. 2003. Puberty. Page 128 in Pathways to Pregnancy and Parturition, 2nd ed. P. L. Senger, ed. Current Concept, Inc., Pullman, WA.

Shillo, K. K., P. J. Hansen, L. A. Kamwanja, D. J. Dierschke, and E. R. Hauser. 1983. Influence of season on sexual development in heifers: Age at puberty as related to growth and serum concentrations of gonadotropins, prolactin, thyronine, and progesterone. Biol. Reprod. 28:329-341.

Short, R. E., R. A. Bellows, R. B. Staigmiller, J. G. Berardinelli, and E.E. Custer. 1990. Physiological mechanisms controlling anestrus and infertility in postpartum beef cattle. J. Anim. Sci. 68:799-816.

Short, R.E., R. B. Staigmiller, R. A. Bellows, and R. C. Greer. 1994. Breeding heifers at one year of age: biological and economical considerations. Page 55 in Factors Affecting Calf Crop. M. J. Fields, and R. S. Sand, eds., CRC Press, Boca Raton, FL.

Short, R.E. and D.C. Adams. 1998. Nutritional and hormonal interrelationship in beef cattle reproduction. Can. J Anim. Sci. 68:29.

Smith, B. A., J. S. Brinks, and G. V. Richardson. 1989. Relationships of Sire Scrotal Circumference to Offspring Reproduction and Growth. J Anim Sci 1989 67: 2881-2885.

Stagg, K., L. J. Spicer, J. M. Sreenan, J. F. Roche, and M. G. Diskin. 1995. Follicular development in long-term anestrous suckler beef cows fed two levels of energy postpartum. Anim. Reprod. Sci. 38:49-61.

Stevenson, J.S., G.C. Lamb, D.P. Hoffman, and J.E. Minton. 1997. Review of interrelationships of lactation and postpartum anovulation in suckled and milked cows. Livest. Prod. Sci. 50:57.

Stevenson, J. S., S. K. Johnson, and G. A. Milliken. 2003. Incidence of postpartum in suckled beef cattle: Treatments to induce estrus, ovulation, and conception. The Prof. Anim. Sci. 19:124-134.

Walters, D.L., R. E. Short, E. M. Convey, R. B. Staigmiller, T. G. Dunn, and C. C. Kaltenbach. 1982. Pituitary and ovarian function in postpartum beef cows. II. Endocrine changes prior to ovulation in suckled and nonsuckled cows compared to cycling cows. Biol. Reprod. 26:647-654.

Werth, L. A., S. M. Pritchard, S. M. Azzam, D. A. Fiske, G. H. Pfeiffer, M. K. Neilsen, J. E Kinder. 1991. Evaluating net income from different durations of breeding seasons in beef production using a deterministic simulation model. Agricultural System 37:275-281.

Williams, G. L. 1990. Suckling as a regulator of postpartum rebreeding in cattle: A review. J. Anim. Sci. 68:831.

Williams, G.L., and M. K. Griffith. 1995. Sensory and behavioral control of gonadotrophin secretion during suckling-mediated anovulation in cows. J. Reprod. Fertil. (Suppl.) 49:463-475.

Yavas, Y., and J. S. Walton. 2000. Postpartum acyclicity in suckled beef cows: A review. Theriogenology 54:25-55.

Yelich, J. V., R. P. Wetteman, T. T. Marston, and L. J. Spicer. 1996. Luteinizing hormone, growth hormone, insulin-like growth factor-I, insulin and metabolites before puberty in heifers fed to gain at two rates. Domest. Anim. Endocrinol. 13:325–338.

Zollers, W.G., H. A. Garverick, M. F. Smith, R. J. Moffatt, B. E. Salfen, and R. S. Youngquist. 1993. Concentrations of progesterone and oxytocin receptors in endometrium of post partum cows expected to have a short or normal oestrous cycle. J. Reprod. Fertil. 97:329-337.