Harnessing basic knowledge of factors controlling puberty to improve synchronization of estrus and fertility in heifers

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Introduction

Puberty in a female has been defined as when ovulation is accompanied by visual signs of estrus and normal luteal function (see review by Moran et al., 1989), and pregnancy success during the breeding season has been correlated with the percentage of heifers that reached puberty before or early in the breeding season (Short and Bellows, 1971). Development of replacement heifers is a major economic investment for all beef and dairy operations, and the costs associated with heifer development cannot be recovered if heifers do not conceive and remain productive in the herd. Therefore, heifers need to conceive early in the breeding season to decrease the risk of being culled.

Age at puberty is an important trait when heifers are inseminated during a restricted breeding season to calve at 2 yr of age (Ferrell, 1982). Previous research has demonstrated up to a 21% increase in fertility from a heifer's pubertal estrus to the third estrus (Byerley et al., 1987; Perry et al., 1991), and age and post-weaning gains across several breeds have been shown to impact age at puberty (Ferrell, 1982; Freetly and Cundiff, 1998). A practical on farm method that has been developed to determine pubertal status is reproductive tract scoring (Andersen et al., 1991). Using this method, previous studies have reported differences in response to estrous synchronization between pubertal and prepubertal heifers (Patterson and Bullock, 1995; Wood-Follis et al., 2004; Leitman et al., 2008). Furthermore, the use of reproductive tract scores to determine pubertal status has demonstrated that heifers with

infantile tracts have decreased conception rates following estrous synchronization compared with peripubertal and pubertal heifers (Patterson et al., 2006).

Previous reviews have focused on factors that control the maturation of the hypothalamic-pituitary-ovarian axis (Day and Anderson, 1998) and management considerations that impact heifer development and puberty (Patterson et al., 1992). This review will focus on how the knowledge that has been gained from basic research has been utilized to improve estrous synchronization rates and pregnancy success in replacement heifers.

Mechanisms controlling puberty

The development of RIA has allowed for accurate measurement of blood hormone concentrations, which are used to characterize the pubertal process and determine when corpora lutea (**CL**) form. The individual functions of the hypothalamus, pituitary, and ovaries are established before puberty occurs. As puberty approaches, the progressive decrease in negative feedback of estradiol on LHRH secretion allows increased secretion of LH to stimulate follicular growth and increased estradiol secretion to eventually reach concentrations sufficient to induce the pubertal LH surge (Day and Anderson, 1998). The period of time over which this change in estradiol feedback on LH secretion occurs is referred to as the peripubertal period and begins approximately 50 d prior to puberty in heifers (Day et al., 1984; 1987).

The Role of Progesterone in Initiation of Normal Estrous Cycles

Across several herds in two multi-state studies, the percentage of heifers that had reached puberty at the start of the breeding season was variable and ranged from 19 to 100% (Lucy et al., 2001; Lamb et al., 2006). Exposure of heifers to a progestin has been reported to hasten the onset of puberty in heifers (Gonzalez-Padilla et al., 1975; Short et al., 1976; Burfening, 1979; Sheffield and Ellicott, 1982). Therefore, many estrous synchronization protocols have included treatment with a progestin (Patterson et al., 1989; Odde, 1990; Lamb et al., 2006) to induce puberty. When peripubertal beef heifers were treated with MGA for 8 d, an increased proportion of heifers initiated estrous cycles following treatment withdrawal

compared with untreated controls (Imwalle et al., 1998). In contrast, when postpartum anestrous beef cows were treated with MGA for 14 d, only 13% ovulated within 7 d of treatment withdrawal (Perry et al., 2002).

Different progestins are known to differ in their chemical structure, potency, pharmacokinetics, metabolism (Stanczyk, 2003), and in binding affinity to the progesterone receptor (Moffatt et al., 1993; Bauer et al., 2000; Perry et al., 2005). The ability of progestins to change LH pulse frequency and amplitude appears necessary to hasten the onset of puberty (Day and Anderson, 1998), and this ability appears to be restricted to the peripubertal period of time. Exposure to a norgestomet (synthetic progestin) implant was able to induce puberty at 12.5 mo of age but not at 9.5 or 11 mo of age (Hall et al., 1997). Following 9 d of low dose exposure to norgestomet, the number of neurons positive for the estrogen receptor in the preoptic area was decreased, and expression of estrogen receptors in the anterior hypothalamus and ventromedial nucleus was negatively correlated with LH pulse frequency (Day and Anderson, 1998).

The first luteal phase following formation of luteal tissue in prepubertal heifers is usually of short duration. Although the oocyte may become fertilized following the first pubertal LH surge and ovulation, embryo mortality occurs due to the onset of luteolysis before the time of maternal recognition of pregnancy (see reviews by Garverick and Smith, 1986; Garverick et al., 1992). When compared, there were no differences in weight, concentrations of progesterone, LH receptors, adenylate cyclase activity, number of luteal cells, ratio of large to small cells, or $PGF_{2\alpha}$ receptors between CL of short duration and normal duration (see review by Garverick et al., 1992). Therefore the main factor believed to be responsible for the short lived duration of the CL is the premature release of $PGF_{2\alpha}$ from the uterus (Garverick and Smith, 1986; Hunter, 1991; Lishman and Inskeep, 1991; Garverick et al., 1992). Hysterectomy prior to ovulation eliminated the occurrence of short duration CL in postpartum cattle (Copelin et al., 1987) and in prepubertal ewes (Keisler et al., 1983).

Treatment with some progestins, prior to the first ovulation, was able to eliminate the occurrence of short duration CL, but other progestins were not (Ramirez-Godinez et al., 1981; Smith et al., 1987; Zollers et al., 1989). For example, only 46% of anestrous beef cows fed

melengestrol acetate (**MGA**) for 5 d before GnRH-induced ovulation had a normal luteal phase, compared with 100% of cows exposed to progesterone (i.e., in an intravaginal device) for the same 5 d (Smith et al., 1987). When anestrous cows were treated with progesterone (i.e., in a controlled internal drug releasing device [**CIDR**]) or MGA and allowed to spontaneously ovulate more cows treated with progesterone ovulated within 4 d following progestin removal and more progesterone treated cows had a normal length luteal phase compared with cows treated with MGA, or control cows (Perry et al., 2004). Thus, the normal dose of MGA (0.5 $mg \cdot cow^{-1} \cdot d^{-1}$) appears adequate to hasten puberty, but insufficient to prevent the earlier secretion of uterine $PGF_{2\alpha}$ following ovulation.

The Role of Body Composition in Initiation of Normal Estrous Cycles

Several studies have reported that heifers reach puberty at a genetically influenced size (Taylor and Fitzhugh, 1971), and that heifers developed to lighter weights will be older when they reach puberty (Short and Bellows, 1971; Wiltbank et al., 1985). Timing of puberty is dependent on both age and weight and varies among breeds (Wiltbank et al., 1966; Short and Bellows, 1971; Varner et al., 1977). Therefore, the idea of developing heifers to a specific target weight (i.e., usually 65% of mature weight) has become a typical management practice, but specific target weights will vary across breed because the age and weight will differ among breeds (Freetly and Cundiff, 1998). Thus, adequate growth and body condition appears necessary for the initiation of normal estrous cycles.

Leptin is produced by adipose tissue and is regulated by long-term nutritional history (i.e., body condition) and current nutritional status (i.e., feed availability; Chilliard et al., 2005), and it plays a role in regulation of the hypothalamic-pituitary axis (see reviews by Williams et al., 2002; Zieba et al., 2005). Mean serum concentrations of leptin increased as puberty approached (Garcia et al., 2002), and changes in diet did not impact concentrations of leptin when percentage of total carcass fat was similar between treatments (Garcia et al., 2003). Therefore, a minimum amount of body condition (i.e., total body fat) is necessary for puberty and reproductive success to occur.

Some recent studies have proposed that heifers can be developed to only 50 to 55% of mature weight prior to the breeding season. Fewer crossbred heifers that were developed to 53% of mature weight were cycling prior to the start of the breeding season compared with heifers developed to 58% of mature weight, but the percent pregnant in a 45 d breeding season was similar between treatments (Funston and Deutscher, 2004). When heifers were developed to 55% compared with 65% of mature weight, there was no difference between developmental weights in percentage pubertal at 12 mo of age or yearling pregnancy rates after an 80-d breeding season (Patterson et al., 1991). However, more heifers developed to 65% of mature weight were pregnant during the first 45 d of the breeding season compared with heifers developed to 55% of mature weight (Patterson et al., 1989). There also tended to be a difference in postpartum interval with heifers developed to 55% of mature weight taking longer to reinitiate postpartum estrous cycles after calving compared with heifers developed to 65% of mature weight (Patterson et al., 1991). When crossbred heifers were developed to 50% of mature weight 15.7% fewer heifers conceived during the first 30 d of the breeding season compared with heifers developed to 55% of mature weight (Creighton et al., 2005). This is consistent with a recent study that reported that across several breeds, heifers were 55 to 60% of mature BW when puberty was attained (Freetly et al., 2011). Therefore, consideration should be made for heifers to reach 65% mature body weight in order to conceive early in the breeding season.

Controlling follicular development and luteal regression to improve synchrony of estrus and fertility

During the prepubertal period, estradiol, through negative feedback, inhibits secretion of LH but as puberty approaches, decreased negative feedback by estradiol allows increased secretion of LH to stimulate follicular growth and increase estradiol secretion to eventually reach concentrations sufficient to induce the pubertal LH surge (Day and Anderson, 1998). The development of transrectal ultrasonography has allowed for the repeated monitoring of follicular growth and atresia, and it has confirmed the idea that follicles grow in wave-like patterns (Pierson and Ginther, 1984; 1988). This ability to monitor follicular growth and atresia

led to 1) studies designed to increase understanding of the endocrine regulation and steroidogenic function of follicular waves and 2) to the necessity for the development of methods to synchronize both follicular waves and luteal regression for purposes of achieving acceptable pregnancy success to fixed-time AI.

Follicular Waves

In cattle, dominant ovulatory sized follicles develop in sequential waves during both the follicular and luteal phases of the estrous cycle (Fortune, 1994). The bovine estrous cycle usually consists of two or three follicular waves, and each wave begins with the recruitment of a cohort of small antral follicles from the pool of growing small antral follicles. One follicle is subsequently selected from this cohort for continued growth and becomes dominant. The remaining follicles in the cohort become atretic. During a nonovulatory follicular wave, the dominant follicle eventually becomes atretic and a new follicular wave is initiated. A viable dominant follicle present at luteolysis generally becomes the ovulatory follicle (Adams, 1999).

Recruitment.

Recruitment of a cohort of follicles, approximately 3 mm in diameter, is stimulated on each ovary by a transient rise in FSH (Adams, 1999). Peak concentrations of endogenous FSH occurred when the future dominant follicle attained a mean diameter of approximately 4 mm, after which concentrations of FSH declined (Ginther et al., 1996), and were at basal concentrations by the time follicular selection occurred (Ginther et al., 2000b). Inhibition of both FSH and LH arrested follicular growth at 2 to 4 mm in diameter; however, when physiological concentrations of FSH were infused for 48 h follicular growth from 5 to 8 mm was stimulated (Gong et al., 1996).

Abundance of FSH receptor mRNA increased during the early stages (3 to 5 mm) of follicular recruitment and remained constant for 96 h (Bao et al., 1997a). Expression of the steroidogenic enzymes, P450 side chain cleavage (**P450-scc**) and cytochrome P450 aromatase, were detected in the granulosa cells of follicles $\geq$ 4 mm in diameter as early as 12 h after the initiation of a follicular wave (Bao et al., 1997a), and expression appeared to be limited to only the follicles that were recruited to grow from 6 to 9 mm (Bao and Garverick, 1998). The

presence of cytochrome P450 17α-hydroxylase (**P450-17α**) mRNA was detected in the thecal layer beginning 12 to 24 h after the initiation of a follicular wave (Bao et al., 1997a). In addition, mRNA for steroidogenic acute regulatory protein (**StAR**), which facilitates transfer of cholesterol from the outer mitochondrial membrane to the inner membrane (Stocco, 2001), was localized to the thecal cells of healthy 4 mm follicles (Bao et al., 1998).

Selection.

Selection is the process by which a single follicle from the recruited cohort is selected to continue to grow and become dominant, while the remaining follicles of the cohort undergo atresia. With the decline in circulating FSH concentrations, small follicles are presumably unable to continue growth and the selected follicle (i.e., dominant follicle) shifts its dependency from FSH to LH (Ginther et al., 1996). Therefore, the acquisition of LH receptors in the granulosa cells of the selected follicle has been hypothesized to be important for the continued growth of the selected follicle (Bao et al., 1997a), and growth of the selected follicle may be regulated by LH pulse frequency (Kinder et al., 1996). The presence of LH receptor mRNA was observed in granulosa cells of follicles ≥ 8 mm in diameter 36 h after the initiation of a follicular wave, and was usually only observed in the granulosa cells of a single follicle (≥ 8 mm) per follicular wave. Furthermore, expression increased with advanced stages of follicular growth (Bao et al., 1997a).

The presence of 3β-hydroxysteroid dehydrogenase mRNA was usually only detected in the granulosa layer of the same healthy follicle (≥ 8 mm in diameter) as LH receptors (Bao et al., 1997b). Abundance of P450-scc, P450-7α mRNA (Bao et al., 1997a), and StAR (Bao et al., 1998) also increased in the selected follicle as it continued to develop. This increase in steroidogenic enzymes and StAR expression in the selected follicle may be necessary for the high concentrations of estradiol produced by the dominant follicle (Bao and Garverick, 1998).

At selection, a deviation in the growth rates of the selected and subordinate follicles occurs. Follicular deviation is defined as the initial difference in growth rates between the largest and second largest follicles. At follicular deviation, the selected follicle continues to grow while the subordinate follicles enter atresia (Ginther et al., 1996). In cattle, deviation usually occurs when the largest follicle reaches a diameter of approximately 8 mm approximately 2.7 d

after the initiation of a follicular wave (Ginther et al., 1997; 1999) or 61 h after the LH surge (Kulick et al., 1999).

Dominanc.

Dominance occurs when a follicle has been selected and inhibits the emergence of a new follicular wave (Ginther et al., 1996). Following selection and establishment of a dominant follicle, follicular recruitment is inhibited until dominance is lost or ovulation occurs. Inhibition of follicular recruitment may be mediated by inhibiting the transient rise in circulating concentrations of FSH (Adams, 1999). Injections of bovine follicular fluid (Adams et al., 1992) or estradiol (Ginther et al., 2000a) inhibited the transient rise in FSH and delayed follicular recruitment. An alternative hypothesis is that the dominant follicle directly inhibits growth of small follicles through the secretion of a factor(s) that acts directly on other follicles in the ovary. Mizunuma et al. (1999) reported that the addition of activin A to cultured preantral mice follicles inhibited follicular growth and secretion of estrogen and inhibin in response to FSH. In addition, the culture of small preantral follicles in the presence of secondary mice follicles inhibited small preantral follicle growth in response to FSH treatment (Mizunuma et al., 1999). Regardless of the mechanism, destruction of a dominant follicle results in a transient rise in circulating concentrations of FSH and subsequent initiation of a new follicular wave (Adams et al., 1992). Therefore, it is unclear at this time whether a dominant follicle inhibits follicular recruitment by inhibition of FSH and(or) a direct effect on subordinate follicles.

Time Course of Follicular Development. Many changes occur during the growth and development of a follicle including: proliferation and differentiation of follicular cells, antrum formation, oocyte growth, and oocyte maturation (nuclear and cytoplasmic). The preceding changes prepare a follicle for ovulation and the oocyte for fertilization (Gosden et al., 1997). Bovine follicles require 27 d to grow from 0.13 mm to 0.67 mm (i.e., preantral to early antral), 6.8 d to grow from 0.68 mm to 3.67 mm, and 7.8 d to grow from 3.68 mm to 8.56 mm. Thus it takes about two estrous cycles for follicles to grow from 0.13 mm to follicular deviation (Lussier et al., 1987).

Control of Luteal Function and Follicular Waves to Improve Pregnancy Success

Regression of the CL and synchronization of follicular waves, culminating in a fertile ovulation at a predetermined time, has been the focus of several investigators. Two approaches to synchronizing bovine follicular waves include: 1) prolonging the lifespan of a dominant follicle and 2) ovulating or initiating atresia in the dominant follicle to thereby initiate a new follicular wave. These two methods are described subsequently in detail.

Persistent follicles. Treatment of estrous cycling heifers or cows with low doses of a progestin, following luteolysis, resulted in the formation of persistent follicles (Zimbelman and Smith, 1966; Sirois and Fortune, 1990; Fortune et al., 2001). Persistent follicles are characterized by an extended dominant life span and increased estradiol production (Zimbelman and Smith, 1966b; Siriois and Fortune, 1990; Fortune and Rivera, 1999). Administration of low (i.e., subluteal) concentrations of progestins to cattle, in the absence of luteal tissue, increased LH pulse frequency (Savio et al., 1993; Kojima et al., 1995; Kinder et al., 1996); however, midluteal phase concentrations of progesterone decreased LH pulse frequency and persistent follicles did not form (Sirois and Fortune, 1990; Savio et al., 1993). Thus, the formation of persistent follicles has been associated with increased LH pulse frequency, and infusion of exogenous LH induced persistent follicle formation (Duffy et al., 2000).

Insemination immediately following long-term progestin treatment and ovulation of a persistent follicle has been associated with decreased fertility (Zimbelman et al., 1970, Mihm et al., 1994). This decreased fertility following formation and ovulation of persistent follicles may result from alterations in the uterine environment due to increased estradiol secretion (Butcher and Pope, 1979) and(or) premature resumption of meiosis due to prolonged exposure to increased LH pulse frequency (Mattheij et al., 1994). No difference was reported in fertilization rate following ovulation of persistent follicles, but fewer zygotes developed into embryos containing 16 or more cells compared with ovulation of oocytes from control follicles (Ahmad et al., 1995).

Turnover (i.e., in atresia) of persistent follicles can be accomplished through the administration of progesterone. Progesterone as a single injection (Anderson and Day, 1994) or

administered over a 24-h period (McDowell et al., 1998) effectively regressed persistent follicles and initiated new follicular waves, presumably through the reduction of LH pulse frequency and amplitude (McDowell et al., 1998).

Hormonal Induction of a New Follicular Wave. Previous research has attributed the decreased pregnancy rates to fixed-time AI among heifers to the inability to synchronize follicular waves at the initiation of the synchronization protocol (Lamb et al., 2006). Initiation of a new follicular wave occurs following ovulation or turnover (i.e., atresia) of the dominant follicle. Administration of exogenous progesterone, estradiol, or GnRH has been utilized to turnover (i.e., progesterone and estradiol) or ovulate (i.e., GnRH) dominant follicles and to synchronize follicular waves in heifers and cows (Bo et al., 1995; Diskin et al., 2002). When a new follicular wave was initiated at the start of a fixed-time AI protocol the percentage of grade 1 and 2 embryos, total number of blastomeres, and proportion of live blastomeres were increased compared with cows that did not initiate a new follicular wave (Cerri et al., 2005).

Estradiol benzoate has been used to induce atresia of dominant follicles and to initiate a new follicular wave approximately 4.5 d after injection (Burke et al., 2000). When treatment with progesterone and estradiol were combined the dominant follicle stopped growing within 24 h and became atretic, resulting in the initiation of a new follicular wave 4 to 5 d after treatment (Bo et al., 1994; Burke et al., 1999).

A single injection of a GnRH agonist is capable of ovulating dominant ($\geq$ 10 mm) but not subordinate follicles (Ryan et al., 1998). However, only 45 to 50% of heifers at various stages of the estrous cycle ovulated in response to an injection of GnRH (Pursley et al., 1995; Atkins et al., 2008). Following GnRH-induced ovulation, a new follicular wave was initiated approximately 1.6 d later (Roche et al., 1999), and selection occurred in 3 to 4 d (Twagiramungu et al., 1995). The ability of GnRH to induce ovulation and initiate a new follicular wave is dependent on the stage of the estrous cycle (Atkins et al., 2008). Heifers on d 18 of the estrous cycle had increased concentrations of estradiol and a greater release of LH in response to an injection of GnRH compared with heifers that received GnRH on d 15, 10, or 2 of the estrous cycle and the ovulatory response was related to LH release (Atkins et al., 2008).

Progesterone is capable of inhibiting ovulation through the suppression of LH release (for review, see Stormshak and Bishop, 2008), and in vitro studies have indicated that progesterone negatively influences LH release from pituitary cells (Baratta et al., 1994; Janovick and Conn, 1996). Similarly, heifers that had a CIDR inserted 48 h before an injection of GnRH had greater concentrations of progesterone at GnRH administration and a reduced LH surge and reduced ovulation rates compared with heifers that had a CIDR inserted at time of GnRH or 6 h after GnRH administration (Perry and Perry, 2009). Furthermore, cattle treated to have high concentrations of progesterone at GnRH administration had a decreased release of LH in response to the injection of GnRH on d 6 of the estrous cycle compared with cattle treated to have low concentrations of progesterone (Colazo et al., 2008). Progesterone suppressed expression of the GnRH receptor; however, removal of progesterone alone was insufficient to increase expression of GnRH receptors (Nett et al., 2002). The increased sensitivity of gonadotropes to GnRH and increased expression of GnRH receptors occurred prior to an increase in concentrations of estradiol (Turzillo et al., 1994). Therefore, a decrease in progesterone and an increase in estradiol may be important in initiating an increase in LH release.

Presynchronization allows more heifers to be at a stage of the estrous cycle that is more likely to respond to an injection of GnRH and result in initiation of a new follicular wave. When heifers were presynchronized with a progestin prior to an injection of GnRH, more heifers ovulated in response to an injection of GnRH compared with heifers that were not presynchronized (Leitman et al., 2008), and presynchronization increased pregnancy success to fixed-time AI in beef heifers (Busch et al., 2007). Injecting $PGF_{2\alpha}$ 3 d before an injection of GnRH decreased progesterone, increased estradiol, increased the percentage of heifers that responded to the injection of GnRH, and decreased the variation in follicle size following CIDR removal (Grant et al., 2011).

Luteal Regression

Upregulation of endometrial oxytocin receptors is reported to have a role in initiation of luteal regression (McCracken et al., 1999). During a normal estrous cycle, expression of oxytocin receptor mRNA (Robinson et al., 2001) and staining for the oxytocin receptor (Kimmins and MacLaren, 2001) was not detectable or was very low during the diestrus period (d 6 to 16) in cattle. However, mRNA abundance (Robinson et al., 2001), staining (Kimmins and MacLaren, 2001), and functional response of oxytocin receptors (Mirando et al., 1993) increased during late diestrus of the estrous cycle. During diestrus, progesterone down-regulates expression of estradiol and oxytocin receptors; however, at the end of the luteal phase, through down-regulation of the progesterone receptor, progesterone loses its ability to down-regulate the estradiol receptor (McCracken et al., 1999). Estradiol can then stimulate oxytocin receptor expression and up-regulate the estradiol receptor. Oxytocin, through binding to the endometrial oxytocin receptor, stimulates release of $PGF_{2\alpha}$ from the uterus (McCracken et al., 1999).

The discovery and production of $PGF_{2\alpha}$ allows for controlled regression of the CL between d 5 and 15 of the estrous cycle (see review by Lauderdale, 2009). However, following $PGF_{2\alpha}$-induced luteal regression, stage of follicular development can affect the timing of estrus. The interval from $PGF_{2\alpha}$ administration to ovulation was shorter among heifers in which luteolysis was induced during the growing and static/plateau phase of follicular growth compared with heifer that had luteal regression induced at the initiation of a new follicular wave (Kastelic et al., 1990; Kastelic and Ginther, 1991). Furthermore, when luteal regression was induced during the static/plateau phase, follicle diameter increased after luteolysis and ovulatory follicle size was larger compared with animals in which luteolysis occurred during the beginning of a follicular wave (Kastelic et al., 1990; Kastelic and Ginther, 1991) or when a growing dominant follicle was present (Kastelic et al., 1990).

Variation in interval to estrus following luteal regression is likely a main factor in reduced pregnancy success to fixed-time AI in heifers, and for fixed-time AI to be successful, estrus in the majority of animals needs to occur in as short of a period of time as possible (Busch et al., 2007). The ability to induce ovulation with GnRH at time of fixed-time AI increases ovulatory response,

but in a recent study, the predicted maximum pregnancy rate of beef heifers occurred at a follicle diameter of 12.5 mm at time of AI, and follicles < 10.7 mm or > 14.9 mm were less likely to support pregnancy than follicles that were 12.5 mm (Perry et al., 2007). Furthermore, pregnancy success was greater among heifers that exhibited estrus within 24 h of fixed time AI compared with heifers that did not exhibit estrus (Perry et al., 2007). Therefore, control of follicular development can impact fixed-time AI pregnancy success (Lamb et al., 2006), and the increased variation in interval to estrus following luteolysis based on stage of follicular develop likely contributes to this impact on pregnancy success.

Summary and conclusions

The basic knowledge gained through research in the areas of endocrine control of puberty, the regulation of follicular growth, and control of short duration CL has improved the ability to hasten the onset of puberty in heifers, eliminate short duration corpra lutea, and improve control of follicular development and luteal regression. The continued research in factors that impact fertility will continue to improve heifer development and pregnancy success by increasing our knowledge of how management can impact the future fertility of heifers. In addition, advancing technologies will likely allow for the selection of heifers that will have greater pregnancy success early in the breeding season if managed correctly.

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