ESTRUS SYNCHRONIZATION OF BEEF AND DAIRY COWS

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ABSTRACT

An estrus synchronization trial was conducted to determine the efficacy of adding an injection of gonadotropin releasing hormone (GnRH) at initiation of the controlled intravaginal drug releasing device (CIDR®) progesterone synchronization protocol in heifers. Nulliparous (n=121) beef heifers were randomly assigned to one of two treatment groups. All heifers received a CIDR® implant at the initiation of the breeding season. Half of the heifers (Select Synch) received an injection of GnRH. Heifers in the Select Synch treatment group had a lower numerical response (76.7% versus 88.3%) to treatment (detected in heat) and an overall lower artificial conception rate (46.0% versus 53.3%), but no statistical difference was detected. Days to conception and artificial insemination conception rates for both groups were similar for all heifers inseminated.

Three hundred multiparous Hereford, crossbred and composite beef cows were assigned to one of two breeding groups (Early and Late) based on calving date and randomly assigned to receive an injection of GnRH at the time of CIDR® insertion (Select Synch). The addition of GnRH did not impact the percentage of cows detected in estrus or days to conception. Conception rates were not affected by the addition of GnRH (Select Synch), however cows in the early breeding group were more likely to become pregnant (58% versus 45%) by artificial insemination ($P<0.02$).

An experiment evaluated the efficacy of the CIDR® protocol to synchronize estrus in Arizona Holstein dairy cows (n=696). Cows assigned to the CIDR® protocol (n=337) received a CIDR® insert at the end of the voluntary waiting period (55 days). CIDR® s

were removed and an injection of prostaglandin was administered seven days after insertion. There was no difference due to CIDR® treatment in number of services per conception or first service conception rate. CIDR® treatment reduced days to first service, days open at first service, and days open ($P<0.02$). Warm season had a deleterious effect on number of services, days to first service, first service conception rate and days open ($P<0.0001$). In summary, estrus synchronization improved postpartum reproductive performance; however, thermal stress continues to be a major barrier to reproductive efficiency.

CHAPTER 1

INTRODUCTION

Humans have attempted to improve food producing plants and animals longer than recorded history. Some of the first examples include the development of corn, other grains and the domestication of animals by early people. Over the previous century, there have been many technologies developed that have allowed for the advancement of livestock breeding practices. Some of these technologies include frozen semen, artificial insemination, embryo transfer, estrus synchronization, sexed semen and cloning. While these technologies have allowed for the rapid advancement of increasing the genetic merit of animals, many are not adopted by livestock producers. One notable exception to this is artificial insemination (AI) with frozen semen in cattle. Fortunately, bovine semen is very stable and effective freezing techniques have been developed. Because of the production systems practiced by the majority of dairy producers, AI was quickly adopted and is now practiced by the majority of dairy producers. A 2005 survey of dairy producers indicated that adoption rate of AI in United States dairy herds was 81.4% (Khanal et al., 2010). The majority of beef producers have not been as quick to incorporate AI as a major part of their management systems. In fact, less than 8% of beef cows in the United States are artificially inseminated on an annual basis (USDA, 2009). One of the major barriers to adoption of AI in beef herds is the need to accurately detect estrus with the economic resources and labor available. Methods that successfully synchronize estrus and ovulation have been evaluated as a way to decrease the amount of time needed for estrus detection and to incorporate timed artificial insemination or "breeding by appointment" in both beef and dairy herds.

Controlled intravaginal drug releasing devices (CIDR®) are used in bovine reproduction to deliver progesterone (1.38 g) for estrus synchronization. The standard CIDR® protocol is to apply the CIRD on day 0 of the breeding season. The CIDR® is removed at day 7 and a 5 ml intramuscular injection of dinoprost promethamine, $PGF_{2\alpha}$ (Lutalyse®, Pfizer, 5 mg/ml) is administered to all heifers. Detection of estrus is initiated following CIDR® removal for five days. The objective of the beef heifer and postpartum beef cow experiments are to determine whether a 2 ml intramuscular injection of gonadorelin hydrochloride (Factrel®, Fort Dodge Animal Health, Fort Dodge, Iowa; 50 mg/ml) at the time of CIDR® insertion would improve reproductive performance in subject animals. The objective of the dairy experiment is to test whether the standard CIDR® protocol would improve reproductive performance on an Arizona dairy. A secondary goal of the dairy experiment is to determine the effect of thermal stress on synchronized versus control cows.

CHAPTER 2

LITERATURE REVIEW

Reproductive Cycle

The female bovine reproductive cycle begins with birth. A variable amount of time is needed for the female to reach puberty, or the ability to initiate estrous cycles and become pregnant. Following the initiation of cyclicity, the female will be inseminated by either a bull or through AI. If fertilization of the ovum is successful, the female will initiate pregnancy. In the case that fertilization does not occur, the female returns to ovarian and estrous cyclic activity. Once the female enters the gestational period of her reproductive cycle, a variable percentage of cows can suffer early (days 15-17 of the cycle) or late (up to 42-56 days post-insemination) embryonic loss due to compromised oocytes, infectious agents or nutrition (Santos et al., 2004). Later term abortions may also occur for a variety of reasons, including ingestion of toxic plant materials, disease, inadequate nutrition or other stressors. Following successful parturition, a cow will go through a period of postpartum quiescence before she re-initiates ovarian activity and estrous cyclicity.

Ovarian activity and estrous cyclicity

A major function of the female reproductive system is the production of gametes through ovarian activity and estrous cyclicity. This entire process is regulated by hormonal inputs. The regulation of one hormone by another, or feedback system, is the physiological mechanism that allows for estrous cyclicity in the bovine female. This cyclicity, initiated after puberty, is responsible for the periodic release of the ovum at a time when chances for successful fertilization and pregnancy are optimal. Ova, in the presence of capacitated sperm, have the potential for fertilization. Through sexual receptivity at estrus, the bovine female enhances her chances of successful fertilization by timing the release of the ovum with the presence of viable sperm. If pregnancy is not established, hormonal processes must occur which allow for fertilization at a later date.

The bovine estrous cycle is generally 18-21 days in length. The onset of behavioral estrus is generally accepted as the start of the estrous cycle and is termed day 0 (Senger, 2003). Upon ovulation, which occurs after estrus, the female enters the luteal phase of the cycle. The dominant ovarian structure is the corpus luteum during this period of the estrous cycle. The main function of the corpus luteum is the production of progesterone. As the corpus luteum develops, concentrations of circulating progesterone increase. The luteal phase is generally 15-17 days following ovulation (Senger, 2003). By the end of the luteal phase, progesterone concentrations will decline as a result of a luteolytic signal from the uterus. This signal is in the form of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) and causes the corpus luteum to regress. Once regression of the corpus luteum is initiated, the female enters the follicular phase of the estrous cycle. The dominant ovarian structure during this relatively short phase (3-6 days) is the follicle (Senger, 2003; Hafez, 2000). The reproductive system is now under the influence of estradiol produced by the growing and mature follicles (Senger, 2003; Goodman, 1988). The cow will enter the state of estrus as a result of increased estradiol shortly before the end of the follicular phase. Estrus in the cow will generally last 12-18 hours with ovulation occurring 10-12 hours after the end of estrus (Senger, 2003; Hafez, 2000). The cow now enters the luteal portion of the cycle again. If fertilization occurs, the luteal phase of the cycle will be extended.

Hormones of the estrous cycle

The estrous cycle is a result of the coordinated communication between the brain, pituitary, ovary and uterus (Senger, 2003). Six different hormones are primarily responsible for this communication: gonadotropin releasing hormone (GnRH) from the hypothalamus, leutenizing hormone (LH) and follicle stimulating hormone (FSH) from the anterior pituitary, estradiol and progesterone from the ovary and prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) from the uterus (Senger, 2003). These six hormones are transported in the circulatory system in specific sequences to stimulate, inhibit, or interact with the target organ to elicit a wide range of physiological responses (Senger, 2003).

Progesterone and estradiol are the two most important ovarian steroid hormones (Senger, 2003). The ovarian follicle is the exclusive source for secreted estradiol (Senger, 2003; Goodman, 1988). Following luteolysis, progesterone concentrations begin to decline and estradiol concentrations will increase and peak at the onset of the preovulatory LH surge (Senger, 2003; Goodman, 1988). The major source for estradiol release is the rapidly growing preovulatory follicle (Senger, 2003; Goodman, 1988). Estradiol is responsible for many effects in the female including secondary sex characteristics and behavioral estrus (Senger, 2003; Hafez, 2000). Estradiol is secreted throughout the estrous cycle, however, the highest concentrations are found during the follicular phase, which lasts 3-6 days in cattle (Senger, 2003; Hafez, 2000).

Estrus is characterized as the period of sexual receptivity of the female, with the high secretion of estradiol from the preovulatory follicle. Estrus usually lasts 12-18 hours in the cow with ovulation occurring 10-12 hours following the end of estrus (Senger, 2003; Hafez, 2000). Both estradiol and progesterone are necessary for the initiation of estrus (Senger, 2003; Goodman, 1988). During the estrus period, the production of prostaglandins is increased by estrogens, which facilitates uterine contractility that promotes sperm and ovum transport.

Following ovulation of the follicle, cells within the follicle differentiate to form luteal cells (Senger, 2003; Hafez, 2000). The resulting structure, the corpus luteum (CL), is now capable of synthesizing and releasing progesterone. A primary purpose of progesterone is to prepare the female reproductive tract for pregnancy if fertilization occurs (Senger, 2003; Hafez, 2000). Progesterone secreted by the CL will remain high if a pregnancy is established. Luteal progesterone will prevent cyclicity from occurring until a luteolytic signal is released from the uterus. The luteal phase of the cycle will last 15-17 days if pregnancy does not occur (Hafez, 2000). Progesterone is secreted exclusively by the CL (Senger, 2003; Goodman, 1988).

The hypothalamus is the source for several releasing hormones, including GnRH (Senger, 2003; Hafez, 2000). GnRH is a decapeptide composed of 10 amino acids and is also known as luteinizing hormone releasing hormone (LHRH); (Senger, 2003; Hafez, 2000). The release of GnRH stimulates the release of two gonatropins from the anterior pituitary, LH and FSH (Senger, 2003; Hafez 2000). FSH is responsible for the stimulation and growth of ovarian follicles (Senger, 2003). The release of both FSH and LH is pulsatile, which reflects the pulsatile release of GnRH (Senger, 2003). A preovulatory surge of LH is responsible for the rupture of the ovulatory follicle and subsequent ovulation (Luo et al., 2011). The frequency and amplitude of gonadotropin release is in large part dictated by the gonadal steroids.

There are two distinct patterns of LH release in the cow, the pulsatile release throughout the estrous cycle and the preovulatory LH surge (Crowe, 2008)The preovulatory LH surge is characterized as a rapid release of large amounts of LH from the pituitary (Crowe, 2008; Goodman, 1988). The pattern of tonic LH release is related to different phases of the estrous cycle (Crowe, 2008, Goodman, 19988; Rahe et al., 1980). During the early part of the estrous cycle (day3), LH release is characterized as being of low amplitude(0.3-1.8 ng/ml) and high frequency (20-30 pulses/24 h). During this period, progesterone concentrations are relatively low (Crowe, 2008; Rahe et al., 1980). During the mid-luteal phase of the cycle (day 10), LH pulses are classified as exhibiting a high amplitude (1.2-7.0 ng/ml) and low frequency (6-8 pulses/h); (Rahe et al., 1980). The progesterone negative feedback on GnRH release is thought to be responsible for this altered pattern of LH release (Crowe, 2008; Rahe et al., 1980). This relationship is the basis for using exogenous progesterone to induce changes in follicular development.

There are two primary ways in which steroid hormones can regulate the release, synthesis and storage of gonadotropins, a long loop feedback mechanism and a short loop feedback mechanism (Hafez, 2000). The long loop feedback mechanism involves an interaction between the gonadal steroids and the hypothalamus (Hafez, 2000). In the short loop feedback mechanism, estradiol and progesterone affect the release of gonadotropins from the pituitary gland, independent of GnRH release from the hypothalamus (Hafez, 2000). Steroid hormones may exert a positive (stimulatory) or negative (inhibitory) response on the target organ depending on the steroid and its concentration (Hafez, 2000). A classic example of negative feedback occurs when progesterone slows down release of GnRH from the hypothalamus. Positive feedback during the estrous cycle occurs primarily with estradiol stimulating the release of GnRH and LH at the time of ovulation (Senger, 2003). A large amount of estradiol is being produced by the preovulatory follicle on the ovary at this time. The increase in estradiol stimulates GnRH release, which stimulates the rapid release of LH. This preovulatory LH surge is required for ovulation and luteinization shortly after the end of estrus (Hafez, 2000).

Ovarian steroids can modulate the release of LH. Increasing concentrations of progesterone in the early part of the estrous cycle lead to a decrease in LH concentrations (Crowe, 2008; Goodman, 1988). Conversely, following luteolysis as progesterone concentrations decrease, LH concentrations begin to elevate (Crowe, 2008; Goodman, 1988). Estradiol may complement the inhibitory effects of progesterone or act directly to inhibit the tonic release of LH (Crowe; 2008; Goodman, 1988).

Mechanisms similar to those that control the preovulatory LH surge may also be responsible for the preovulatory FSH surge. The first FSH surge appears coincident with an increase in the concentration of estradiol. There is a secondary FSH surge following approximately 24 hours after the first FSH surge not associated with increased estradiol concentrations. Turzillo and Fortune, 1990, found that suppression of the secondary FSH surge with bovine follicular fluid resulted in delayed follicular growth and is important for initiation of follicular development. The exact mechanism which controls this secondary FSH surge is not clearly understood (Lucy, 2007; Goodman, 1988).

LH and FSH are both essential for normal follicular growth and development. The action of these gonadotropins is regulated at the ovarian level by an increasing or decreasing response. LH may play a role in the recruitment of follicles through an inhibitory effect on FSH, conversely FSH is known to induce recruitment (Lucy, 2007)). Through the follicular phase, estradiol production in recruited follicles is enhanced by LH release (Lucy, 2007). As estradiol production increases, an inhibitory effect on FSH may trigger selection of a follicle in a process described later. As FSH concentrations decease during the follicular phase in cattle, dominant follicles continue to grow (Lucy, 2007). This may be a result of increased numbers of LH receptors on granulosa cells which elevate cyclic adenosine monophosphate (cAMP) levels during the follicular phase (Lucy, 2007).

In summary, progesterone and estradiol act together during the luteal phase of the estrous cycle to suppress GnRH release, and consequently LH release. Following luteolysis, progesterone concentrations fall, which allow the hypothalamus to respond to estradiol and increase GnRH release, hence also increasing LH pulse frequency. Increasing estradiol concentrations initiate estrus behavior and the preovulatory LH surge. Upon ovulation of the ovulatory follicle, estradiol is terminated and corpus luteum formation is initiated. Progesterone from the formed corpus luteum will begin to exert a suppressive effect on gonadotropin release (Senger, 2003).

Follicular Dynamics

In most mammals the primordial follicle reserve is formed during prenatal development or shortly after birth (Lucy, 2007; Greenwald and Terranova, 1988). Primordial follicles are characterized as oocytes surrounded by flattened granulose cells (Lucy, 2007). The pool of primordial follicles is arrested in an extended meiotic prophase (Lucy, 2007; Greenwald and Terranova, 1988). Primordial follicles will begin to acquire cuboidal granulosa cells surrounding the oocyte and progresses from intermediary to primary follicle. Primordial, intermediary, and primary follicles together comprise the reserve of follicles used later in life (Senger, 2003).

Primary follicles result from growth of primordial follicles. They can be subdivided into unilaminar and and multilaminar primary follicles. The unilaminar primary follicle has entered the initial stage of growth due to stimulation by FSH. The unilaminar primary follicle becomes multilaminar through a series of mitotic divisions to become designated as a secondary follicle (Greenwald and Terranova, 1988). In multilaminar follicles, glycoproteins synthesized by the oocyte will begin to form a zona pellucida layer surrounding the oocyte (Senger, 2003; Greenwald and Terranova, 1988). An additional distinguishing characteristic of a secondary follicle is the appearance of theca cells containing LH receptors (Lucy, 2007; Greenwald and Terranova, 1988). Growth of preantral follicles cannot be modulated by gonadotropins because of the absence of LH receptors in theca cells and FSH receptors in granulosa cells (Lucy, 2007; Driancourt et al., 1993). A secondary follicle will be transformed into a tertiary follicle or antral follicle through the formation of an antral cavity. FSH and LH receptors are acquired and the follicle becomes dependent on gonadotropins (Lucy, 2007; Driancourt et al., 1993). Numerous gap junctions exist between theca cells, granulosa cells, and granulosa-cumulus cells in an antral follicle to allow for intercellular communication (Lucy, 2007; Driancourt et al., 1993).

Follicles in the growing pool can either become ovulatory or become atretic and regress (Senger, 2003; Greenwald and Terranova, 1988). More follicles are recruited for growth than are ovulated during an estrous cycle, thus the most common fate for follicles is atresia (Lucy, 2007; Greenwald and Terranova, 1988). Atresia of follicles can occur at variable stages of development and during all stages of the ovarian cycle (Hafez, 2000).

The continual growth and regression of antral follicles during the normal bovine estrous cycle is commonly known as follicular dynamics (Lucy 2007; Sirois and Fortune, 1988). All follicles will undergo regression at some variable stage of the cycle, with the exception of the follicle destined to ovulate. All ovulatory follicles are subject to periods of recruitment, selection and dominance (Lucy, 2007; Driancourt et al., 1993). Recruitment is the mechanism by which a cohort of follicles enters the gonadotropic-dependent phase of the ovarian cycle (Fortune et al., 2001; Driancourt et al., 1993; Lucy, 1992). Selection is the process which reduces the cohort of recruited follicles to the ovulatory quota (Fortune et al., 2001; Sunderland et al., 1994). The third mechanism, dominance, allows the selected follicle to suppress growth of other recruited follicles and progress to ovulation or atresia (Fortune et al., 2001; Sunderland et al., 1994).

Recruitment is the process by which several primary follicles out of a larger pool of preantral follicles are stimulated, possibly by gonadotropin, to progress toward antral follicles (Fortune eta l, 2001; Driancourt et al., 1993). An increased number of small follicles (2-4 mm) have been shown to appear in response to a release of FSH. There are two peaks in plasma FSH during the preovulatory period (Lucy 2007; Badinga et al., 1992). The first peak has been associated with the preovulatory LH surge with a second peak following approximately 24 hours later. It has been hypothesized that one or both of these FSH peaks are responsible for stimulation of the first follicular wave following ovulation. A mid-luteal rise in plasma FSH may be responsible for a second rise in frequency of small follicles (Lucy 2007; Badinga et al., 1992). Through the previously described process of selection, one of these recruited follicles is destined to continue growing and exert dominance over the other follicles in the cohort. The follicles which regress and eventually become atretic during this process are termed subordinate follicles.

A decline in plasma FSH may trigger the selection process which determines the dominant follicle (Fortune et al., 2001; Adams et al., 1993). Addition of exogenous FSH can delay the onset of selection of a dominant follicle, however the importance of FSH to the development of the dominant follicle is well established (Fortune et al., 2001; Turzillo and Fortune, 1993). Charcoal extracted bovine follicular fluid, which has a high concentration of inhibin, can be used to suppress endogenous FSH. Dominant follicles were exposed to decreased concentrations of FSH by treatment with bovine follicular fluid and luteolysis was induced. The decreased concentration of plasma FSH was coincident with an interruption of the growth of the first wave dominant follicle (Turzillo and Fortune, 1993). These data suggest that FSH plays a critical role in the continued growth of the dominant follicle. Increases in blood FSH concentrations lead to larger diameters and greater estradiol synthesis in follicles greater than 4 mm. These growing follicles are dependent on FSH and are subjected to the selection process (Lucy, 2007).The process of superovulation with exogenous FSH to create a cohort of dominant follicles demonstrates the capability of follicles to establish dominance if blood FSH support is present.

A selected follicle may continue to grow and develop in the presence of basal gonadotropin secretion because of an acquired sensitivity to LH. Other recruited follicles in the cohort have less sensitivity to FSH and their continued growth is inhibited (Fortune et al., 2001; Baird, 1987). FSH receptors are detected on bovine granulosa cells of estrogen-active follicles on day 3 of the estrous cycle. The number of LH receptors on both theca and granulosa cells of estrogen –active follicles is greater on day 7 of the estrous cycle as compared to day 3 (Lucy, 2007; Ireland and Roche, 1983). Thus, there may be an increased responsiveness to LH in these dominant follicles and the dominant follicle becomes LH-dependent, rather than FSH dependent. In this situation, under basal LH stimulation, a greater amount of estradiol is produced by the preovulatory follicle. Fortune and Quirk, (1988), showed that estradiol produced by preovulatory follicles may exert a positive feedback on its own production in addition to inhibiting FSH secretion necessary for maintenance of follicles. The increased concentration of estradiol may also support continued follicular development during periods of low FSH by increasing the sensitivity of granulosa cells to LH. Bodensteiner et al., (1996), hypothesized that the growth termination of the dominant follicle would be associated with changes in the number of gonadotropin receptors on granulosa cells and estradiol in follicular fluid. They detected differences in follicular fluid estradiol, but not numbers of granulosa cell gonadotropin receptors associated with early follicular growth divergence and eventual regression of the dominant follicle. This suggests that the increase in estradiol production from a preovulatory follicle preceeds an increase in the number of gonadotropin receptors.

Two models explaining the development of the dominant follicle have been proposed (Lucy, 2007). The first, the Missouri model, hypothesized that the follicle which acquired LH receptors before other follicles in the cohort could starve the other follicles in the cohort by inhibiting FSH while not inhibiting LH (Xu et al., 1995). This hypothesis is supported by the fact that a low-progesterone environment, and consequently a high-LH pulse frequency, causes the dominant follicle to persist (Lucy et al., 1990; Sirois and Fortune, 1990; Savio et al., 1993). Conversely, removal of LH support causes a dominant follicle to become atretic (Savio et al., 1993). The Missouri model does not explain the increased estradiol synthesis by the selected follicle, as LH has not been shown to increase estradiol synthesis in bovine granulosa cells (Fortune et al., 1991).

Other work has suggested that selection of the dominant follicle occurs prior to initiation of LH receptor expression in granulosa cells (Evans and Fortune, 1997). Both local and systemic IGF-I concentrations have been associated with follicular growth in cattle (Echternkamp et al., 2004; Spicer, 2004; Webb et al., 2004). The Cornell model proposes that the recruitment of a follicular wave is initiated by an increase in FSH. One of the recruited follicles in this wave has a slight developmental advantage over the other follicles. An increase in IGFBP-4/5 protease (pregnancy-associated plasma protein-A) that degrades IGFBP-4 and 5 within the follicular fluid is associated with FSH. As a result of decreased IGFBP there is an increase of free IGF-I within the follicular fluid, which supports estradiol synthesis. The dominant follicle produces more estradiol and grows faster in response to FSH. The resulting increase in estradiol decreases FSH and initiates atresia in the remaining follicles.

A third model suggested by Beg and Ginther (2006) puts both the Missouri and Cornell models together. They hypothesize that the increase in LH receptor expression in granulosa cells and increase in free IGF-I occurs at approximately the same time. In summary, one follicle has a developmental advantage over the others in the recruited wave and is fortunate enough to become the dominant follicle.

Follicular waves

Early work attempting to describe follicular development in the female focused on patterns of circulating hormones and physically visualizing follicles obtained from slaughter animals. This led to a number of theories regarding changes follicles underwent during an estrous cycle. Some groups felt there were two sequential growths of follicles during a cycle (Swanson et al., 1972), whereas others felt there were three (Ireland and Roche, 1987). Others (Donaldson and Hansel, 1968; Dufour et al., 1972) suggested that follicular development was independent of the estrous cycle.

After 2-4 days of recruitment, a cohort of several small follicles will begin to grow. The previously described selection process occurs and a dominant follicle will appear. This dominant follicle will remain active until approximately day 8-11 of the estrous cycle (Lucy 2001; Ginther et al., 1989). If luteolysis is induced through exogenous prostaglandin $F_{2\alpha}$, this dominant follicle can ovulate. In the majority of cases, the first dominant follicle regresses and a second follicular wave emerges. If this second dominant follicle does not ovulate, it will undergo atresia and regress. A third wave dominant follicle will appear and usually will become the ovulatory follicle. Most cattle have either 2 or 3 follicular waves, but estrous cycles consisting of 1 to 4 waves have been detected (Lucy et al., 1992). In addition to the cyclic cow, follicular waves have been documented in prepubertal heifers (Adams et al., 1994; Evans et al., 1994), postpartum anestrous cows (Murphy et al., 1990; Savio et al., 1990) and during pregnancy (Ginther et al., 1989; Taylor and Rajamahendran, 1991).

Length of the luteal phase in normal bovine estrous cycles seems to be related to the number of follicular waves (Wolfenson et al., 2003; Taylor and Rajamahendran, 1994; Ahmad et al., 1997). If plasma progesterone declines during the growth stage of the second wave dominant follicle, this follicle will become the ovulatory follicle.

Conversely, if progesterone concentrations remain elevated following the growth stage of the second wave dominant follicle, the follicle will regress and be replaced by a third wave dominant follicle. Thus, progesterone may play a key role in follicular turnover (Crowe, 2008; Taylor and Rajamahenrdran, 1994). It is theorized that the effect of progesterone may be by feedback on the hypothalamic-pituitary axis, or directly on the follicle. Fortune and Vincent, (1983), demonstrated that progesterone can directly suppress estradiol synthesis by the follicular granulosa cells. Elevated plasma progesterone during the luteal phase may lead to atresia of the dominant follicle through the suppression of estradiol production, which allows recruitment of a new cohort of follicles.

Progesterone may be exerting an influence on follicular turnover through alterations in LH release. Follicular growth during different stages of the estrous cycle is influenced by LH release, as described earlier (Crowe, 2008; Rahe et al., 1980). Changes in circulatory progesterone concentrations can alter the pulsatile release of LH (Crowe, 2008; Roberson et al., 1989). Cows exhibit the high frequency, low amplitude pattern of LH release, characteristic of the follicular phase in normal estrous cycles, under subluteal progesterone concentrations (Crowe, 2008; Rahe et al, 1980). Normal progesterone concentrations result in LH pulses of a lower frequency and higher amplitude, characteristic of the luteal phase in a normal estrous cycle (Fortune et al., 2001; Rahe et al., 1980). It is suggested that subnormal levels of progesterone (1-2 ng/ml) maintain and induce maturation in dominant follicles, simulating the events occurring during the follicular phase of the estrous cycle (Lucy 2007). Normal concentrations of circulatory progesterone support turnover of dominant follicles, characteristic of the luteal phase in a normal estrous cycle (Lucy 2007).

Initiating cyclicity in beef and dairy heifers

Many beef and dairy heifer management programs develop heifers so that they conceive at 14 to 16 months of age and calve at approximately 2 years of age. Beef heifers that calve early in their first breeding season wean more and heavier calves in their lifetime (Lesmeister et al., 1973). Because the fertility of the first estrus is lower than that of subsequent estrous periods, heifers should experience two or three estrous cycles before the onset of the breeding season (Perry et al., 1991; Byerley et al., 1987). Therefore, heifers should attain puberty by 12 months of age to achieve optimal reproductive performance.

The stage of development in which the female first expresses estrus and ovulates is known as the physiological onset of puberty (Short, 1984). The first estrus and ovulation is a sudden event that is a result of a series of complex developmental events that occur within the reproductive axis. While some components of the reproductive endocrine axis may be functional prior to the onset of puberty, the heifer must have developed and functional ovarian and pituitary tissue and neuroendocrine mechanisms that support cyclicity (Perry 2011; MacKinnon et al., 1987; Staigmiller et al., 1979). A prepubertal increase in pulsatile LH secretion is thought to be a key, major endocrine event leading to first ovulation in heifers.

Schams et al., (1981) and Schill et al., (1982) both detected pulses of LH in the peripheral circulation of heifers as early as one month of age. In heifers as young as one month of age exogenous LHRH can elicit the release of LH from the anterior pituitary (Schams et al., 1981). The magnitude of LH release increases as the heifer becomes older, thought to be partially as a result of an increase in pituitary LHRH receptors (Perry, 2011; Amann et al., 1986). Ovarian response to gonadotropins begins before first ovulation and also increases with age (Perry, 2011; Day and Anderson, 1998; Marion and Geir, 1971; Seidel et al., 1971). While this evidence suggests that the hypothalamic-pituitary-ovarian axis is functionally competent before the onset of puberty, the heifer is still not sexually mature.

Ovarian steroids influence the release of gonadotropins in either a facilitative or inhibitory manner through feedback mechanisms. As described earlier, increasing estradiol during the follicular phase of the estrous cycle induces a preovulatory surge of LH. By 3 to 5 months of age this mechanism is functional in heifers (Day and Anderson, 1998; Staigmiller et al., 1979; Schillo et al., 1983). In the prepubertal heifer, estradiol seems to have an inhibitory effect on LH secretion. When the influence of estradiol was removed through ovariectomy, concentrations of circulating LH increased as early as one month of age (Odell et al., 1970). The suppression of LH release diminishes as the heifer ages until the onset of puberty (Day and Anderson, 1998; Day et al., 1984). A decrease in the number of unoccupied estradiol receptors in both the hypothalamus and the pituitary has been associated with a reduction of responsiveness to estradiol negative feedback (Perry, 2011; Kinder et al., 1987). It has been hypothesized that decreased responsiveness to the negative feedback of estradiol allows pulsatile LH to increase to a level that stimulates the development of ovarian follicles to the preovulatory stage (Schillo et al., 1992).

The greatest period of ovarian growth in heifers is from birth to 4 months of age and increases again from 8 months until the onset of puberty (Desjardins and Hafs, 1969). The changes in ovarian weight are associated with changes in folliculogenesis, or the enlargement of follicles. The major source of estradiol in prepubertal animals is the dominant follicles (Perry, 2011; Tortonese et al., 1990). The pattern of circulatory estradiol concentrations may reflect follicular growth and regression in the prepubertal heifer, similar to the estrous cycle. Two distinct increases in progesterone concentrations have been detected prior to first ovulation in heifers (Gonzalez-Padilla et al., 1975). These increases are shorter in duration and lower in magnitude than a normal luteal phase and are termed short luteal phases. Ovulation may not be necessary for the ovary to form the luteal tissue which provides prepubertal progesterone (Berardinelli et al., 1979).

Progestin treatment in heifers can be used to hasten or induce puberty. Anderson et al., 1996, were able to induce puberty in prepubertal heifers by administering norgestomet. Their results indicated that LH secretion was increased following the removal of the progestin. While follicular dynamics were not significantly altered, uterine weights were greater in treated heifers, consistent with increased estradiol. The removal of the progestin acted to remove the negative feedback of estradiol on LH secretion.

Postpartum anestrus in beef cows

Reproduction is the main factor limiting production efficiency of beef and dairy herds. Some recent estimates of the annual costs associated with delays in beef heifers reaching puberty or beef cows not re-initiating ovarian activity and estrous cyclicity indicate that these costs exceed $500,000,000 (Bellows, et al., 2002). Estimates in the dairy industry vary from $2.00 to $5.00 for each additional day open. De Vries, 2006, developed an economic model which showed the average value of a new pregnancy in dairy cows to be $278. The average cost of a pregnancy loss was modeled to be $555 on average. The largest losses occur because cows fail to become pregnant and calve on a regular interval. In order for a beef cow to have a calving interval of 365 days, she must reinitiate estrous cycles and conceive by day 85 postpartum (based on a 280 day gestation period). Delays in resumption of postpartum estrous cycles can be linked to general infertility, lack of uterine involution, short estrous cycles and anestrus. Anestrus can be further divided into lactational (suckling inhibition) or nutritional anestrous. The anestrous postpartum interval is a major factor contributing to reproductive failure and calving intervals that exceed a year. (Short et al., 1990). Endocrine and physiological changes determine when postpartum estrous cycles are initiated and whether conception occurs. The physiological factors that influence the postpartum period are very similar for both beef and dairy cows. The differences observed are due to variation in management and production systems for beef and dairy herds.

General infertility decreases the ability of a cow to become pregnant by 20-30% for each estrus, regardless of stage of the reproductive cycle. While this is a factor that must be accounted for, it is hard to separate all of the components that contribute to this impaired ability of the cow to conceive and become pregnant.

Incomplete uterine involution has long been recognized as a barrier to fertility in the early postpartum period (Short et al., 1990). As early as 1968, the work of Graves et al. showed that fertilization and pregnancy rates were very low for cows that were bred less than 20 days postpartum. Normal fertility concentrations were attained by 20 to 40 days postpartum. Short et al., 1974 further confirmed that an incompletely involuted uterus was a barrier to fertilization and pregnancy by inseminating early postpartum cows either conventionally (uterine body semen placement) or depositing the semen in the tips of the uterine horns. Ova were recovered three days following insemination and fertilization rates were determined. In cows less than 20 days postpartum, cows inseminated in the tip of their uterine horns had a greater fertilization rate compared to cows inseminated in the uterine body. After 20 days postpartum, fertilization rates were similar for both groups. Their conclusions were that the early postpartum uterus presented a barrier to sperm transport. In most beef production systems this is not a concern because producers do not breed these cows as early as 20 days postpartum.

In beef cows, a well-documented transient increase in progesterone usually occurs during the ten days preceding the first postpartum estrus (Crowe, 2008; Rawlings et al., 1980; Wetteman, 1980). A normal luteal phase preceded by estrus often follows this transient increase in progesterone (Crowe, 2008; Perry et al., 1991). Perry et al. (1991) reported that the size of preovulatory follicles was not different at first or second ovulation after calving, but behavioral signs of estrus were less obvious, luteal phases were shorter in duration and less progesterone was produced after the first compared to the second postpartum ovulation in beef cows. Werth et al. (1996) evaluated patterns of change in concentrations of progesterone in circulation compared with dates of estrus and conception when artificial insemination (AI) occurred at first estrus after calving. Their main finding was that conception as a result of AI at the first estrus after calving was less if a transient increase in progesterone did not precede estrus (76 vs. 41%; $P<0.01$). They also confirmed earlier reports that the majority of cows have increases in progesterone before the first postpartum estrus.

Looper et al. (2003) evaluated the effect of postpartum weight changes and body condition on days to first estrus, normal luteal activity and conception in beef cows. In agreement with prior findings, the thinner cows and cows which had lost weight had longer intervals to first estrus, normal luteal activity and conception. However, regardless of body condition, cows that had elevated progesterone concentrations prior to the first detected estrus had a greater percentage of normal luteal life spans (81%) as compared to those cows without prior progesterone exposure (36%). Their conclusions were that an increase in plasma progesterone prior to the first estrus may enhance subsequent luteal function.

Postpartum anestrus in dairy cows

In lactating dairy cows, higher producing individuals are more vulnerable to fertility problems such as lower AI conception rates, weaker expression of estrus and greater embryonic losses (Lucy, 2001). Similar to findings in beef cattle, luteal insufficiency has been associated with reduced fertility in dairy cattle (Fonseca et al., 1983). Additionally, it has been observed that concentrations of progesterone prior to the preovulatory LH surge were increased in cows that conceived as compared to those who failed to conceive (Erb et al., 1976). Based on this evidence one can presume that the magnitude of progesterone concentration may be associated with factors that increase the probability of conception.

Most cows re-establish ovarian follicular development shortly after calving. Reproductive or metabolic challenges coincident with calving will typically delay resumption of ovarian follicular activity. The first postpartum ovulation has been observed around day 15 for most cows (Crowe, 2008). For cows that were challenged in the transition period, first ovulation is delayed until 30-35 days (Crowe, 2008). This is coincident with the second ovulation in normal cows. It has been documented that the more cycles a cow completes prior to insemination, the greater the likelihood of her becoming pregnant (Crowe, 2008). For a dairy producer, this means that the cows without metabolic or calving problems are more likely to become pregnant following the voluntary waiting period. A goal of hormonal management of dairy and beef cows is to initiate postpartum follicular development and ovulation as early as possible to give the cow a chance to become pregnant.

A major reason for not realizing that ovarian activity is commencing so early after calving is that most of the ovulations during the first 55 d are “silent” heats, or not accompanied by estrual behavior (Crowe, 2008). Dairy producers may not see visual indicators of estrus or cyclicity, but the overall fertility of those cows is improved. Initiating cyclicity is important because it allows estrogens produced from the follicles to clear her reproductive tract and establish a normal environment for sperm transport and fertilization.

Progesterone concentration is the major factor that affects LH pulse frequency in cyclic cows (Crowe, 2008). When progesterone concentrations are suppressed, there is a subtle increase in LH pulse frequency which allows for increased follicular growth. These prolonged luteal phases can allow for a fourth follicular wave (Savio et al., 1990).

Heat stress impacts on reproduction

Heat stress has long been recognized as a detriment to reproductive efficiency in cattle, particularly in the Southwestern and Southeastern United States. Documented impacts of heat stress on the cow include altering the duration of estrus (Gangwar et al., 1965, Nebel et al., 1997), colostrum quality (Nardone et al., 1997), conception rate (Ingraham et al., 1976), uterine function (Collier et al, 1982), endocrine status (Collier et al., 1982; Wolfenson et al., 1988b, Wise et al., 1988a; Howell et al., 1994), follicular growth and development (Wilson et al., 1998), luteolytic mechanisms (Wilson et al., 1998), early embryonic development (Biggers et al., 1987), and fetal growth (Wolfenson et al., 1988a). The most accurate indicator of heat stress is detecting changes in rectal temperature, however, from a practical standpoint, heat stress occurs when the temperature humidity index (THI) exceeds 72 (Armstrong, 1994).

THI was originally developed by Thom (1958) for use in humans, later calculated for use in cattle by Berry et al (1964). The Livestock Conservation Institute later categorized THI values into mild, moderate, and severe stress levels. There is some evidence that the supporting data for this categorization may not be clear and may underestimate effects of heat stress on cattle (Collier and Zimbelman, 2007).

Heat stress can reduce the ability of producers to detect estrus and inseminate cows. Nebel et al. (1997) reported that Holsteins in Virginia had less mounts per estrus in summer (4.5) compared to winter (8.6). An additional study by Thatcher and Collier (1986) estimated the percentage of undetected estrous periods in a commercial dairy in Florida. The June through September period resulted in 76-82% of heats being undetected versus 44-65% during October through May. There is contradictory evidence on the role of adrenocorticotropic hormone (ACTH) and estradiol-17β on estrus in heat-stressed cows. ACTH has been associated with a reduction in estradiol-induced sexual behavior (Hein and Allrich, 1992). Reports of circulatory cortisol secretion during heat stress have documented increased (Roman-Ponce et al., 1981; Wise et al., 1988a; Elvinger et al., 1992), transitory (Miller and Aniston, 1974; Elvinger et al., 1992), no increase (Wise et al., 1988b; West et al., 1991) or a depression (Abilay et al., 1975) in secretion. There is also conflicting evidence on the effect of heat stress on estradiol-17β concentrations. Heat stress has been associated with depressed peripheral estradiol concentrations at estrus (Gwazdauskas et al., 1981, Wilson et al, 1988), whereas Rosenberg et al, (1982) was not able to show the same response. Another possible explanation for the depressed estrus behavior may be the physical lethargy produced by heat stress or an adaptive response to decrease heat stress (Hansen and Arechiga, 1999).

Heat stress can also affect embryonic development and survival. The first few days of pregnancy have been shown to be very susceptible to detrimental effects of heat stress. Embryonic survival was reduced in heifers exposed to heat stress one day (Ealy et al., 1993) or day 1 to 3 after insemination (Dunlap and Vincent, 1971). The preimplanted embryo may acquire thermal resistance as it progresses from zygote to blastocyst, implying more heat resistance as the embryo ages (Ealy et al., 1993). The developing embryo is not immune to the deleterious effects of heat stress, Biggers et al. (1987) showed compromised embryonic development 8-16 days after pregnancy was initiated. A hormone that has been implicated in compromising embryonic development and survival is ghrelin (Rhodes et al., 2009). Ghrelin is a known regulator of feed intake and circulatory concentrations increase during heat stress (Rhodes et al., 2009). Rodent studies have shown that increased circulatory ghrelin was associated with elevated secretions in the reproductive tract (Kawamura et al., 2003). Rodent and embryo cultures have both shown increased embryonic loss and decreased embryonic development (Rhodes et al., 2009).

Impacts of heat stress on follicular growth and dynamics can either directly affect the oocyte or alter follicular function. Heat stress has been shown to reduce the volume and diameter of a first wave dominant follicle (Badinga et al., 1993). Other work (Wolfenson et al., 1995) reported that heat stress beginning on day 1 of the estrous cycle caused an increase in the number of follicles $\geq$ 10 mm in diameter, earlier emergence of the second wave dominant follicle and a reduction in plasma concentrations of inhibin. Wilson et al. (1998) initiated heat stress at day 11 of the estrous cycle and reported more estrous cycles with three follicular waves versus two, reduced estradiol-17β concentrations in blood, and longer estrous cycles.

Estrus synchronization options

Estrus synchronization protocols intend to synchronize the growth and maturation of a dominant follicle with the onset of luteal regression. Protocols in cycling cows will generally involve one of three approaches: 1) inhibit ovulation following spontaneous corpus luteum regression (long-term progestin treatment), 2) induction of corpus luteum regression ($PGF_{2\alpha}$ treatment), and 3) a combination of 1 and 2 (Smith et al., 2005). The majority of protocols in use today involve the combination of approaches. Long-term progestin treatment (14 days) has been shown to be very effective at synchronizing estrus; however fertility is reduced due to the ovulation of a persistent follicle. A limitation of the second approach is that animals in the first 5 to 6 days of the estrous cycle will not respond to prostaglandin. Very acceptable fertility rates have been shown with this approach in cows that respond. Combining the first and second approach has been shown to be very effective in synchronizing estrus without compromising fertility. The addition of GnRH at the beginning of progestin treatment to initiate follicular turnover has helped to improve synchronization and fertility rates (Lamb et al., 2001).

Before considering an estrous synchronization system, beef producers should ensure that certain conditions are met. First, there must be an adequate postpartum interval (at least 40 days and preferably 60 days). Secondly, cows must be in adequate or above average body condition (scores of at least 5 on a 1 to 9 scale). Third, cows must not have experienced calving problems. Fourth, replacement heifers should have achieved at least 65% of their mature weight. Heifers should also have reproductive tract scores (RTS) of 2 or higher and at least 50% of the heifers should have a RTS of 4 or 5 (Patterson et al., 2005).

Progestins

Progestins mimic the actions of progesterone produced by the corpus luteum by inhibiting estrus and ovulation. Following the removal of the progestin, progesterone concentrations will be low and the cow will return to estrus and ovulation can occur. There are two commercially available progestins for use in synchronization programs, Melengestrol Acetate (MGA) and the CIDR® (Controlled Internal Drug Release).

MGA is an orally active progestin used in cows and heifers to suppress estrus and prevent ovulation (Imwalle et al., 2002). Melengestrol acetate is a synthetic progestin that is administered in feed at the rate of 0.5 mg/animal/day. When consumed by cows or heifers, MGA suppresses estrus and prevents ovulation. It is generally recommended that cows or heifers are not inseminated or bred at the first estrus after MGA removal because of compromised fertility. MGA can be fed in long term (> 7 days, usually 14) or short term protocols ($\leq$ 7days). Long term MGA protocols result in a high degree of synchrony, however fertility is compromised. Short term MGA treatments do not generally have the fertility associated problems with them; however synchrony is not as consistent.

The CIDR® is an intravaginal nylon insert that is covered by progesterone (1.38 g) impregnated silicone skin and used in conjunction with other hormones to synchronize estrus. Upon insertion, blood progesterone levels rise and are maintained at a constant level until removal in seven days. Retention rates generally exceed 97%. Some vaginal irritation that results in yellow or clear mucus is observed upon CIDR® removal. The inserts are developed to be used one time only and sanitation is a must. $PGF_{2\alpha}$ is given on day six of treatment or upon CIDR® removal on day seven after insertion.

After CIDR® treatment, there will be two populations of females: females without corpora lutea and females with corpora lutea greater than six days old. All females with corpora lutea following treatment are potentially responsive to an injection of $PGF_{2\alpha}$. A documented advantage to the use of a CIDR® is that they have been shown to hasten cyclicity in prepubertal heifers and anestrus cows.

Several modifications to the basic CIDR® treatment are currently being evaluated. One of the most researched is the inclusion of the CIDR® in the CO-Synch protocol. The CIDR® is inserted upon the first GnRH injection and removed when $PGF_{2\alpha}$ is administered. Overall, there appears to be a positive benefit to including the CIDR® in the CO-Synch protocol; however these benefits are minimized when cows are cycling or were in higher body condition (Lamb et al., 2001).

One other area of research is the use of CIDR® s to “prime” the reproductive gonadotropic axis. Because of the well documented benefits of including a CIDR® in synchronization protocols for anestrus cows, thought has been given to using them to hasten the return to cyclicity in postpartum dairy cows. This area warrants further research to substantiate.

CHAPTER 3

HORMONAL MANAGEMENT OF BEEF HEIFERS

Abstract

An estrus synchronization trial was conducted to determine the efficacy of adding an injection of gonadotropin releasing hormone (GnRH) at initiation of the controlled intravaginal drug releasing device (CIDR®) progesterone synchronization protocol in heifers. Improvements to the CIDR® synchronization protocol would be evaluated by increased number of heifers detected in estrus, improved conception rates and reduced days to conception from the initiation of the breeding season. Sixty-one nulliparous beef heifers were randomly assigned to one of two treatment groups. All heifers received a CIDR® implant at the initiation of the breeding season. Half of the heifers (Select Synch) received a 2ml intramuscular injection of gonadorelin hydrochloride (Factrel®, Ft. Dodge Animal Health, Ft. Dodge, Iowa; 50 mg/ml). Age, weight, reproductive tract score and body condition did not differ between the two treatment groups. Heifers in the Select Synch treatment group had a lower numerical response (76.7% versus 88.3%) to treatment (detected in heat) and an overall lower artificial conception rate (46.0% versus 53.3%), but no statistical difference was detected. Days to conception and artificial insemination conception rates for both groups were similar for all heifers inseminated.

Introduction

Beef producers need to be able to successfully synchronize estrus and artificially inseminate heifers in order to maximize genetic progress in their herds. Many synchronization protocols exist for use in heifers. The incorporation of a controlled intravaginal drug-releasing device (CIDR®) in synchronization protocols tends to show an advantage over those not incorporating an exogenous progesterone source. One of the advantages of including a progesterone source in a synchronization protocol can be to initiate puberty in heifers. Heifers that conceive early in the breeding season have a greater amount of time for postpartum recovery and rebreeding in the ensuing calving season. In addition, their calves should be heavier and more valuable than their later born contemporaries. Most of the CIDR® based protocols minimize the number of times that cattle are handled and eliminate the need for extended heat detection.

There are several prerequisites for successful breeding of heifers. Heifers should have reached puberty and be cycling. A weight guideline is that heifers should have reached 65% of their mature body weight and be in adequate condition (score 5 or greater) for breeding. Reproductive tract scores are determined by rectal palpation of the uterus and ovarian structures. Heifers should be at, or near, reproductive tract score of 4.0 (cycling or near cycling) in order to initiate breeding. The reproductive tract scoring system is shown in Table 1.

Table 1. Reproductive tract scoring system (adapted from Odde et al, 1994)

Score	Uterine Horns	Ovaries
1	Immature, <20 mm diameter, no tone	15 mm x 10 mm x 8 mm, no structures
2	20-25 mm diameter, no tone	18 mm x 12 mm x10 mm, 8 mm follicles
3	2020-25 mm diameter, slight tone	22 mm x 15 mm x 10 mm, 8-10 mm follicles
4	30 mm diameter, good tone	30 mm x 16 mm x 12 mm, >10 mm follicles, possible corpus luteum
5	>30 mm diameter, good tone	>32 mm x 20 mm x 15 mm, corpus luteum present

The standard CIDR® protocol is to apply the CIDR® on day 0 of the breeding season. The CIDR® is removed at day 7 and a 5 ml intramuscular injection of dinoprost promethamine, $PGF_{2\alpha}$ (Lutalyse, Pfizer, 5 mg/ml) is administered to all heifers. Detection of estrus is initiated for five days following CIDR® removal. Heifers are determined to be in estrus based on visual observation of mounting and standing. Estrus detection aids may be used. Heifers are usually inseminated 12 hours after detection of standing heat based on the am/pm rule. An alternative protocol adds an injection of GnRH at the time of CIDR® insertion to initiate follicular turnover (Select Synch).

The objectives of this study were to evaluate the efficacy of adding GnRH to the standard CIDR® protocol. Results are evaluated by comparing the percentage of heifers that responded to treatment (detected in heat) and the conception rate of treated heifers.

Material and methods

Nulliparous beef heifers (n=121) from the University of Arizona V-V Ranch were selected at the initiation of the 2003 breeding season to by synchronized using EAZI-BREED CIDR® (Pfizer Animal Health, New York, New York) intravaginal progesterone inserts (1.38 g progesterone/insert). Heifers were randomly assigned to either receive (n=61) a 2 ml intramuscular injection of gonadorelin hydrochloride (Factrel®, Fort Dodge Animal Health, Fort Dodge, Iowa; 50 mg/ml) at the time of CIDR® insertion (Select Synch) or no injection (CIDR®); (n=60). Body condition scores, reproductive tract scores and weights were collected prior to breeding and used to randomize the heifers to treatment. The heifers were predominantly crossbred with a majority having Hereford or Angus influence. The CIDR® insert was removed seven days following insertion and a 5 ml intramuscular injection of dinoprost promethamine (Lutalyse®, Pfizer, 5 mg/ml) was administered to all heifers. Detection of estrus was initiated following CIDR® removal for five days. Heifers were determined to be in estrus by either visual observation of mounting and standing behavior or as indicated by the heat detection patch (Estrotect, Rockway, Inc., Spring Valley, Wisconsin). Heifers were inseminated based on the am/pm rule by one of two inseminators. Pregnancy was detected by ultrasound at 30 days post breeding and confirmed in the fall by rectal palpation. The location of the heifer trial was the University of Arizona Feedlot, West Campus Agricultural Center in Tucson, Arizona. Heifers were kept in an approximately 2 hectare dry lot and fed ad libitum hay. Treatment data were analyzed using SAS 9.3 (2011).

Results

The mean age of heifers assigned to the CIDR® treatment did not differ (*P=0.748*) from the age of heifers assigned to the Select Synch group (406 days vs. 408 days) (Figure 1; Table 2). No difference in weight (*P=0.9943*) was detected for either group (Figure 2; Table 2). Mean body condition score was equal (*P=0.3949*) for both groups (Figure 3; Table 2). Reproductive tract score was not different (*P=0.5779*) for either treatment (Figure 4; Table 2).

Table 2. Number, age, weight, body condition scores and reproductive tract scores of V-V heifers

	Treatment	
Item	CIDR®	Select Synch
Number	60	61
Age, days	406.1 ± 33.5	414.9 ± 34.1
Weight, kg	306.9 ± 33.5	311.9 ± 28.4
Body condition score	5.9 ± 0.3	6.0 ± 0.2
Reproductive tract score	4.2 ± 0.9	4.1 ± 0.8

Response to treatment was evaluated by measuring the percent of heifers that were detected in estrus, artificially inseminated and became pregnant. The heifers in the CIDR® treatment group had a numerical advantage of 11.6% greater detected estrual response over the heifers assigned to the Select Synch group, but no statistical significance was found (Figure 5, Table 3). Percent of heifers that conceived to artificial insemination did not differ between treatments (Figure 6; Table 3); however, more heifers became pregnant by artificial insemination in the CIDR® treatment group because of the greater number of respondents (Figure 7; Table 3). Days to conception were not different for either treatment (Figure 8; Table 3).

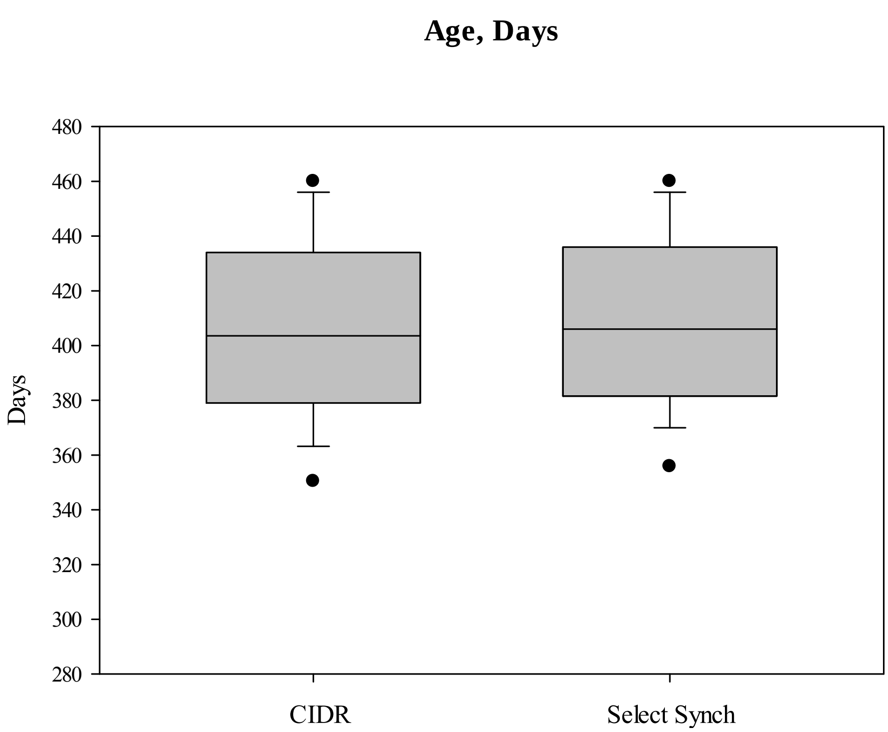

Figure 1. V-V heifer age, days, per treatment

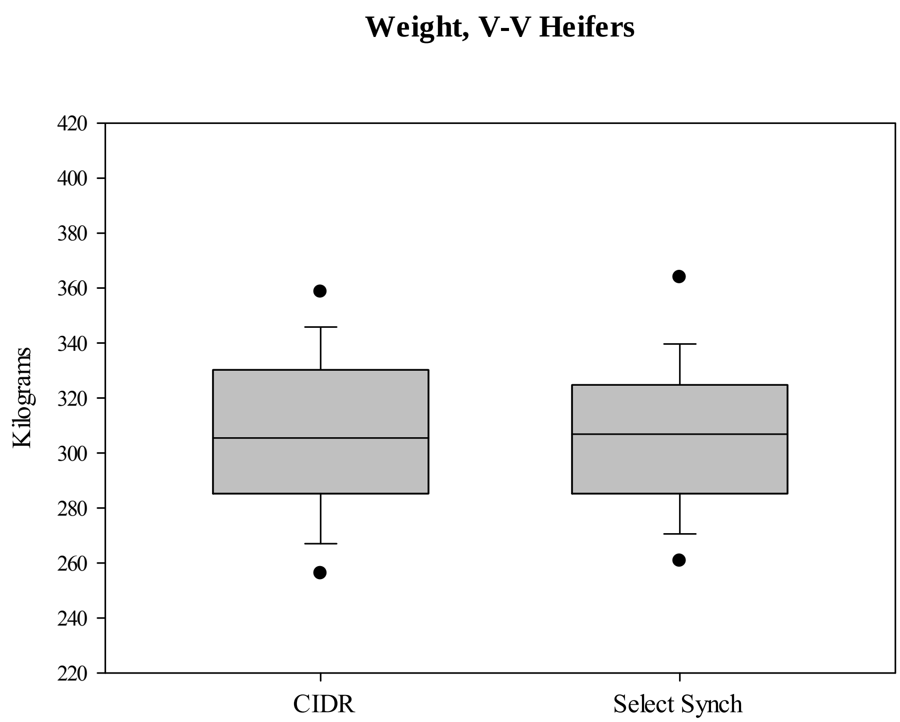

Figure 2. V-V heifer weight, kilograms, per treatment

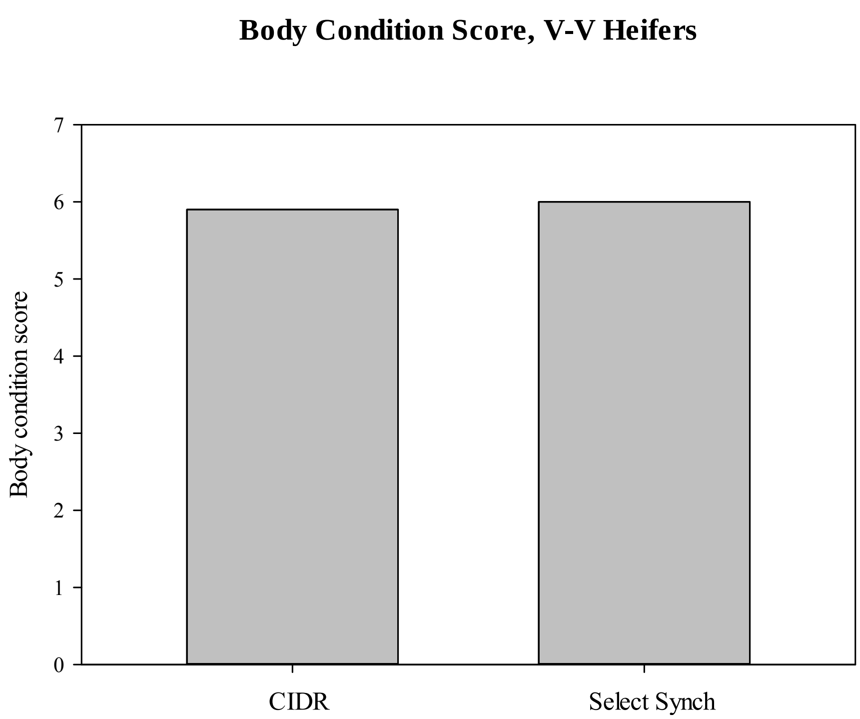

Figure 3. V-V heifer body condition score, per treatment

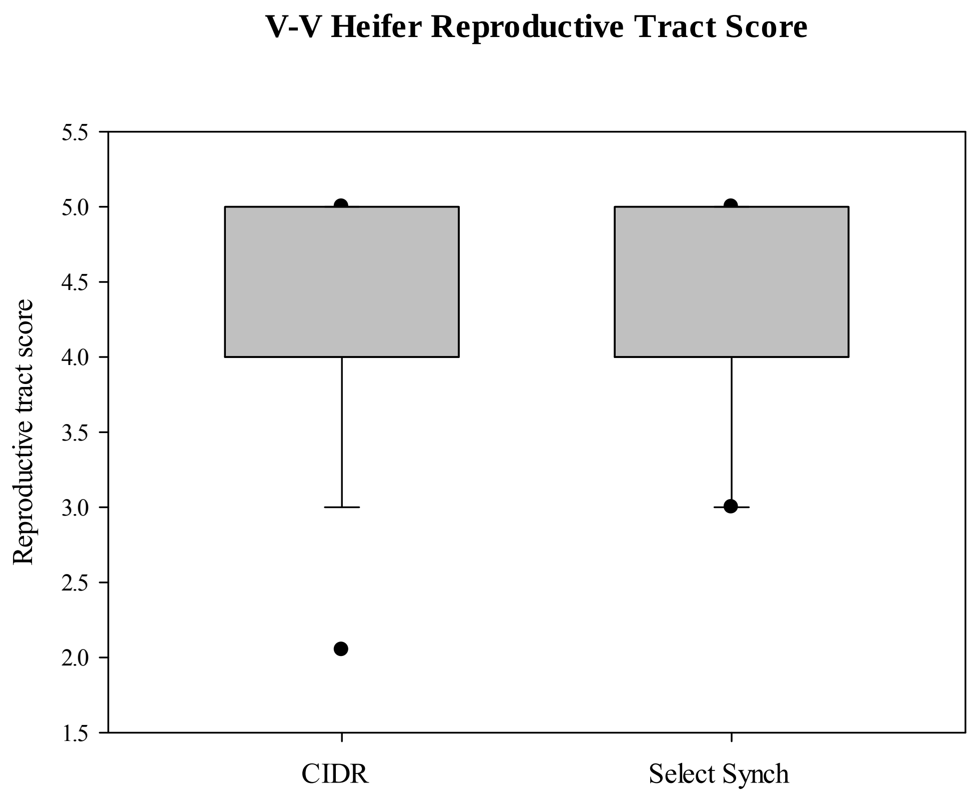

Figure 4. V-V heifer reproductive tract score, per treatment

Table 3. Percent detected in heat, artificial insemination conception rates and days to conception of V-V heifers

	Treatment	
Item	CIDR®	Select Synch
Detected in heat	88.3%	76.7%
AI conception rate (respondents)[1]	60.4%	60.9%
AI Conception rate (overall)	53.3%	46.0%
Days to conception	22.3±27.6	22.0±16.4

[1] Respondents are heifers detected in heat and inseminated within five days of CIDR® removal

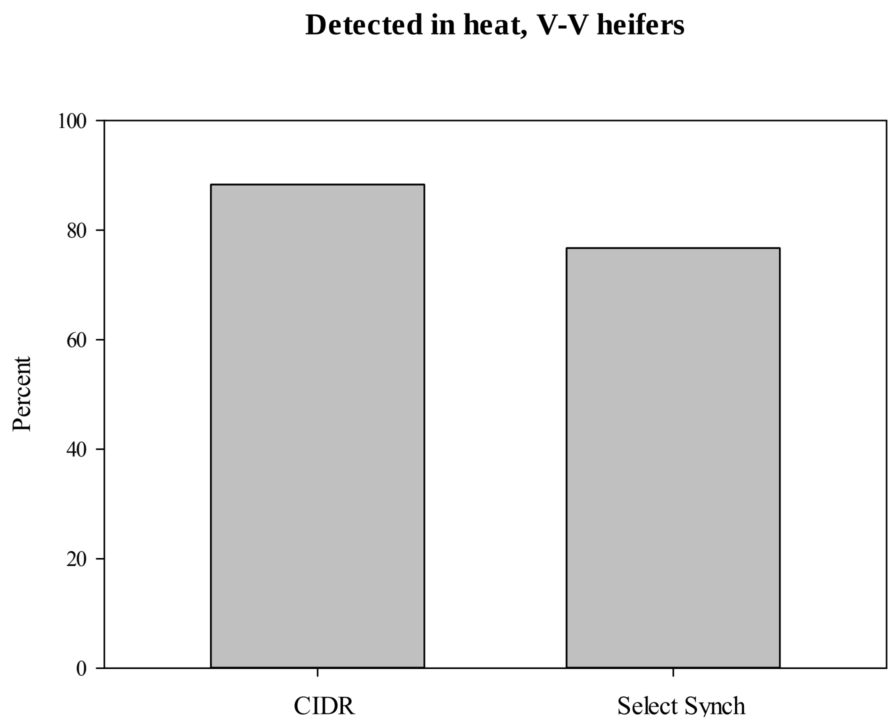

Figure 5. Percent heifers detected in heat, per treatment

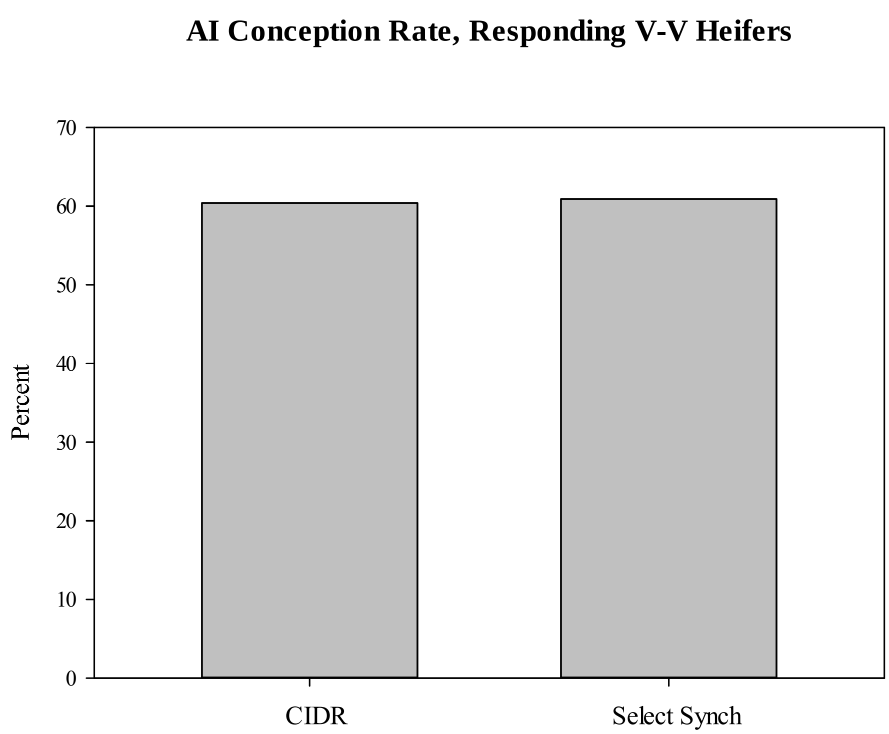

Figure 6. Percent conception rate, responding heifers, per treatment

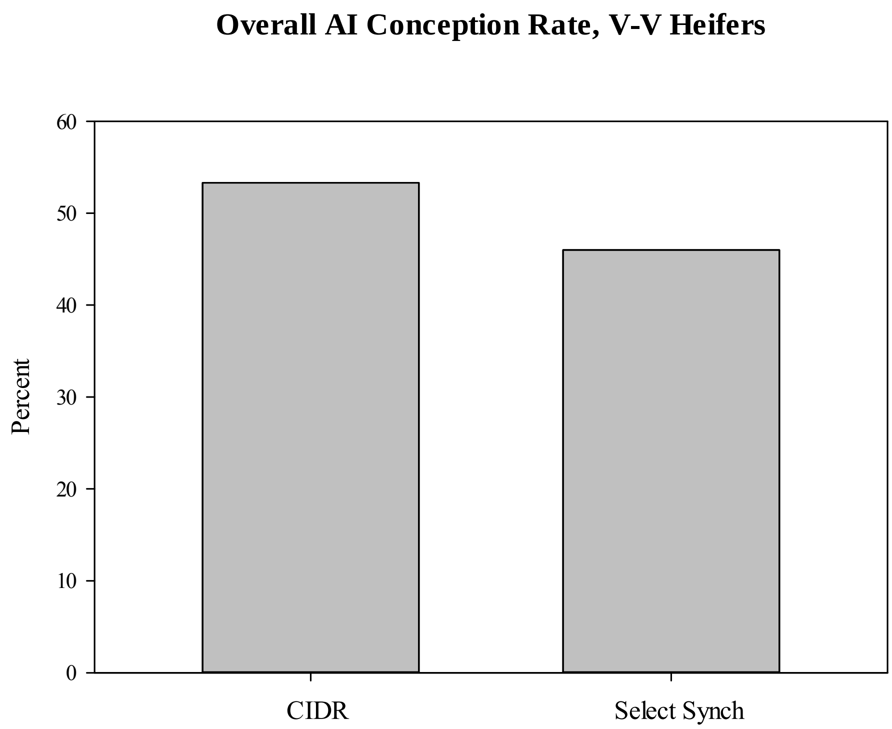

Figure 7. V-V heifer overall conception rate, per treatment

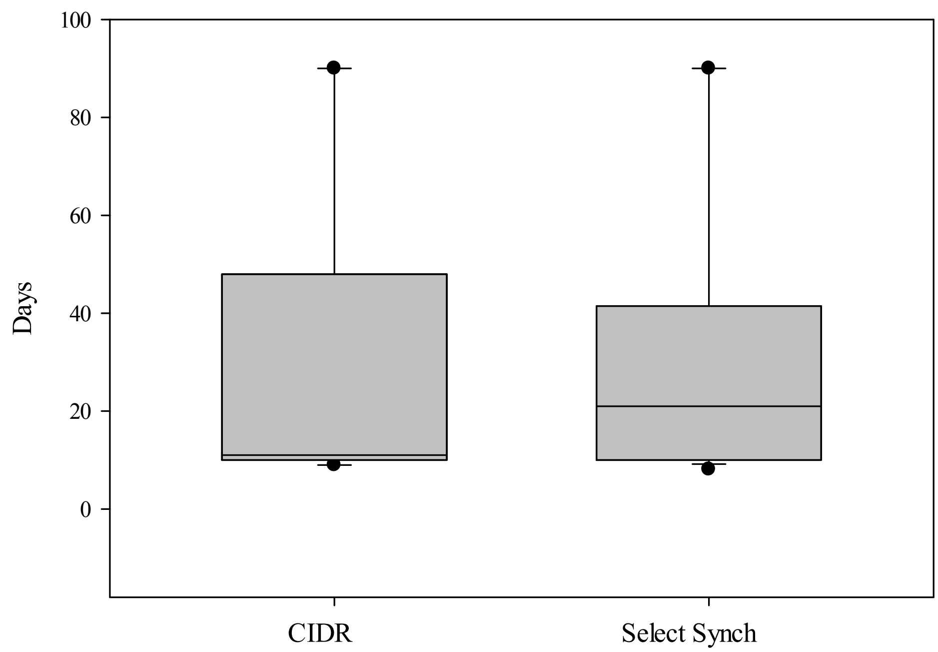

Figure 8. V-V heifer days to conception, per treatment

Discussion

The addition of GnRH to the CIDR® synchronization protocol did not offer any advantage as measured by percent conception or heifers detected in heat. A higher conception rate in the heifers assigned to the Select Synch group was expected. Heifers assigned to the CIDR® group (no GnRH at CIDR® insertion) had a numerically higher estrus detection rate and higher overall conception rate to the artificial insemination; however, no statistical significance was detected.

Heifers in this trial should have been post pubertal, as evidenced by mean reproductive tract scores over 4.0. According to the scoring system developed by Colorado State University, heifers scoring 4.0 or greater should be cycling or very close to cycling (Odde et al., 1994). According to most heifer development programs, heifers should have reached 65% of their mature weight at the initiation of breeding and be in good body condition. Heifers in this trial were over 300 kg and possessed a body condition score of 6.0. Both of these measures are consistent with recommendations from veterinarians and producers for initiation of breeding.

Heat detection is one of the common barriers for producers who want to artificially inseminate heifers. Prior to synchronization protocols being developed, producers had to spend a significant amount of time observing cattle for visual signs of estrual behavior. Many heat detection aids have been adopted in the past and are used today. The development of successful synchronization programs has allowed producers to concentrate labor for heat detection and breeding to a shorter time period. With the CIDR® or Select Synch protocol, heat detection and insemination occur over 5 days.

This has an advantage for beef producers who do not feel that they can invest extended labor in a heifer breeding program.

Conclusions

The Select Synch protocol would not be recommended for use in heifers over the CIDR® protocol based on the response in this trial. Incorporation of GnRH did not increase conception rate or overall pregnancies as expected. This experiment demonstrated that the use of CIDR® s in a synchronization protocol can be an important tool for heifer development programs. Nearly half of all heifers became pregnant by artificial insemination in this trial. Heifers that calve early in the calving season have more valuable progeny. Calves born earlier in the breeding season are older than their contemporaries and should be heavier at the same marketing date. This is further enhanced by the superior genetics that can be incorporated by artificial insemination. Another potential economic advantage could be a smaller number of bulls used for the heifer breeding program following synchronization. Proven calving ease bulls with other attributes that the producer wants to enhance in their herds should be used.

Further research in this area is warranted. Future trials should incorporate the use of timed artificial insemination to further enhance conception rates. A close look at the potential economic advantages of estrus synchronization would also be necessary to be able to convince producers of the practicality and usefulness of this technology.

CHAPTER 4

HORMONAL MANAGEMENT OF POSTPARTUM BEEF COWS

Abstract

An estrus synchronization trial was conducted to determine the efficacy of adding an injection of gonadotropin releasing hormone at initiation of the CIDR® synchronization protocol. Synchronization success would be based on estrual response rate, artificial insemination conception rate and days to conception. Three hundred multiparous Hereford, crossbred and composite beef cows were assigned to one of two breeding groups (Early and Late) based on calving date. Approximately half of the cows in each group were randomly assigned to receive a 2 ml intramuscular injection of gonadorelin hydrochloride (Factrel, Ft. Dodge Animal Health, Fort Dodge, Iowa; 50 mg/ml) at the time of CIDR® insertion (Select Synch). Cows in the Early breeding group were younger (3.3 versus 6.3 years old) than the Late breeding group and approximately a ½ body condition score higher (5.6 versus 6.2). The addition of GnRH did not impact the percentage of cows detected in estrus or days to conception. Conception rates were not affected by the addition of GnRH(Select Synch), however cows in the early breeding group were more likely to become pregnant (58% versus 45%) by artificial insemination ($P<0.02$).

Introduction

Beef producers need to be able to successfully synchronize estrus and artificially inseminate postpartum beef cows in order to maximize genetic progress in their herds. Estrus synchronization can also be used as a way to shorten the postpartum period. Several protocols for estrous synchronization have been evaluated in many different production scenarios. The incorporation of a controlled intravaginal drug-releasing device (CIDR®) in synchronization protocols tends to show an advantage over those not incorporating an exogenous progesterone source. Many of the potential explanations for this can be found in the literature review. Most of the CIDR® based protocols minimize the number of times that cattle are handled and eliminate the need for extended heat detection.

The standard CIDR® protocol is to apply the CIDR® on day 0 of the breeding season. The CIDR® is removed at day 7 and an injection of prostaglandin is administered to all cows. Detection of estrus is initiated for five days following CIDR® removal. Cows are determined to be in estrus based on visual observation of mounting and standing. Also, estrus detection aids may be used. Cows are usually inseminated based on the am/pm rule. An alternative protocol adds an injection of GnRH at the time of CIDR® insertion to initiate follicular turnover.

In order for successful synchronization of estrus in post-partum beef cows, several criteria must be met. Cows should be at least 45-60 days post-partum in order for proper uterine involution and cyclicity to resume. In addition, cows should have adequate energy reserves to meet the demands of lactation and maintenance. Many beef producers use a system of body condition scoring to evaluate energy reserves. Body condition affects the amount of supplement that cows may need during times of nutritional stress and can also be an indicator of potential reproductive success. Cows should be in a body condition score of 5 or greater at calving. Scoring is somewhat subjective and can vary from producer to producer. Scores will range from emaciated (1) to severely obese (9). A description of body condition scores is found in Table 4.

Table 4. Description of body condition scores (adapted from Lowman, 1976)

Condition	BCS	Description
Thin	1	Severely emaciated. All ribs and bone structure easily visible and physically weak.
	2	Emaciated, similar to 1 but not weakened. Little visible muscle tissue.
	3	Very thin, no fat on ribs or brisket, some muscle visible.
Borderline	4	Thin, with ribs easily visible. Muscling evident through shoulders and hindquarters. Backbone visible.
Optimum	5	Moderate to thin. Last two or three ribs can be seen. Little evidence of external fat in brisket, over ribs or around tail head.
	6	Good smooth appearance. Some evidence of fat deposition. Ribs covered.
	7	Very good flesh, brisket full, tail head shows pockets of fat. Ribs very smooth.
Fat	8	Obese, very square over back, brisket distended, heavy fat pockets around tailhead
	9	Very obese, rarely seen. Heavy deposition of fat, even in udder. Can have mobility problems.

Picture 1. Cow in thin body condition (score 2)

Picture 2. Cow in borderline body condition (score 4)

Picture 3. Cow in optimum body condition (score 6)

The objectives of this study were to evaluate the efficacy of adding GnRH to the standard CIDR® protocol in postpartum cows. Results are evaluated by comparing the percentage of cows that responded to treatment (detected in heat) and the artificial insemination conception rate of treated cows.

Materials and methods

The University of Arizona V-V Ranch Beef Cattle

The University of Arizona V-V Ranch is the College of Agriculture and Life Sciences beef cattle and rangeland science research center. This research center addresses environmental, wildlife and domestic livestock issues applicable to Arizona and the Southwest. Vegetation zones, including high desert chaparral, pinon-juniper, and pine, are typical of those on most of the commercial ranches in central and northern Arizona. Transecting the Mogollon Rim, the V Bar V Ranch grazing allotment runs about 48 kilometers east from Camp Verde, Arizona and varies between 6 and 8 kilometers in width. Slightly more than forty acres is private land, with the remainder held under lease from the U.S. Forest Service. Elevations range from 975 to 2,134 meters which has allowed the University of Arizona College of Agriculture and Life Sciences to expand its experiment station network to include higher elevation ecosystems. In addition to 550 cattle, the ranch is also a habitat for a wide variety of wildlife, ranging from mammals, birds and fish to reptiles and amphibians. The ranch is divided into 46 pastures/holding areas and cattle are rotated through them on an annual basis. The majority of cattle are bred to calve in the spring and the breeding season is in the late spring/early summer. During the breeding season, the majority of cattle are in the Cedar Flats area, near the center of the ranch.

Beef Cows

Primiparous (cows having one calf in their lifetime) and multiparous (cows having more than two calves in their lifetime) Hereford, crossbred and composite beef cows (n=300) were selected for inclusion into an early or late breeding group in 2003. Cows selected for the early breeding group were not pregnant or nursing a calf or had calved early in the breeding season. Body condition scores were recorded at the time of CIDR® insertion. Cows in both groups were synchronized for estrus using the EAZI-BREED CIDR® intravaginal progesterone inserts (1.38 g progesterone/insert). Cows were then randomly assigned to either receive (n=150) a 2 ml intramuscular injection of gonadorelin hydrochloride (Factrel®, Ft. Dodge Animal Health, Fort Dodge, Iowa; 50 mg/ml) at the time of CIDR® insertion (Select Synch) or no injection (n=150) (CIDR®). The CIDR® insert was removed seven days after insertion and a 5 ml intramuscular injection of dinoprost promethamine (Lutalyse®, Pfizer, New York, New York; 5 mg/ml) was administered to all cows. Detection of estrus was initiated for five days following CIDR® removal. Cows were determined to be in estrus based on visual observation of mounting and standing behavior or as indicated by a heat detector patch (Estrotect, Rockway, Inc., Spring Valley, Wisconsin) applied at time of CIDR® removal and prostaglandin injection. Cows were inseminated based on the am/pm rule. The am/pm rule basically states that a cow should be inseminated 12 hours after being observed in estrus. Pregnancy was determined by rectal palpation in the fall. The location of the trial was in the Cedar Flats pasture area. Treatment data analyzed using SAS 9.3 (2011).

Results

The age of cows in the Early or Late breeding group did not differ between treatments (Figure 9; Table 5). However, cows in the Early breeding group were significantly younger (*P<0.0001*) than the cows in the Late breeding group. Similarly, body condition score of cows did not differ within groups, but the cows in the Early breeding group were approximately a half score higher (Figure 10; Table 5).

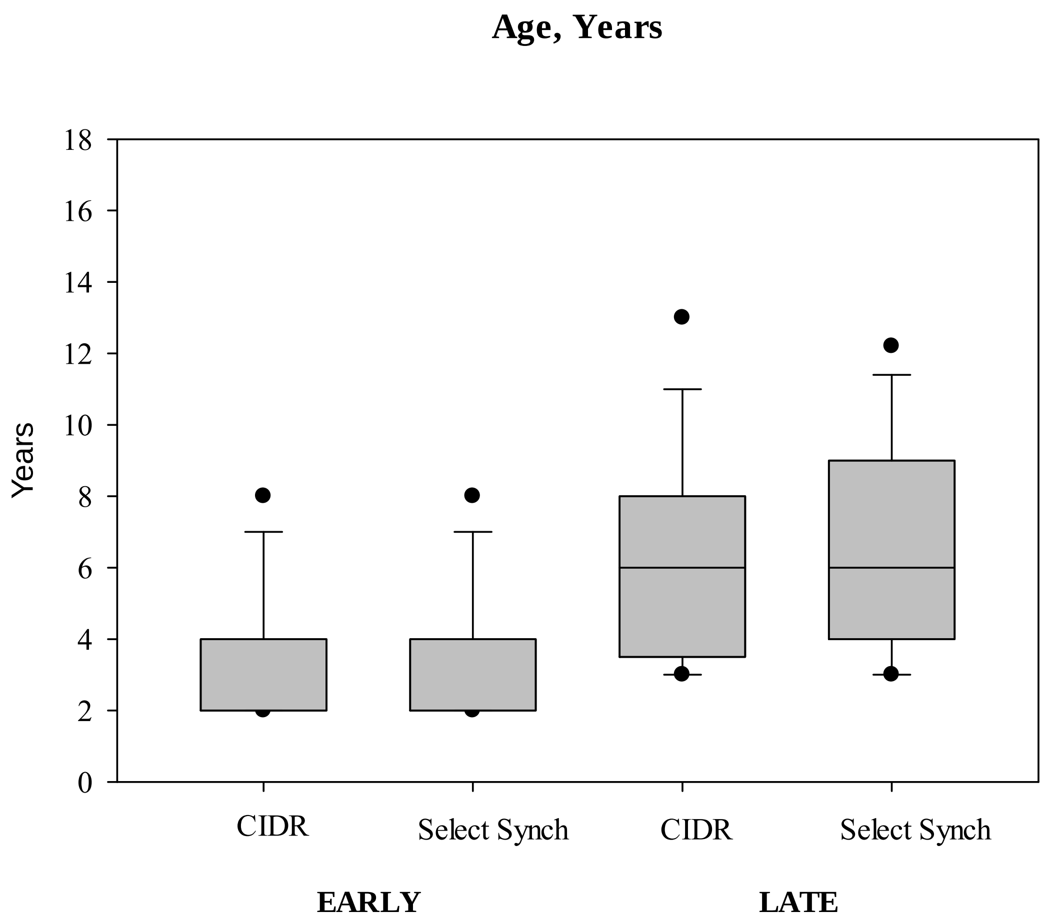

Figure 9. Distribution of V bar V cow age, per group and treatment

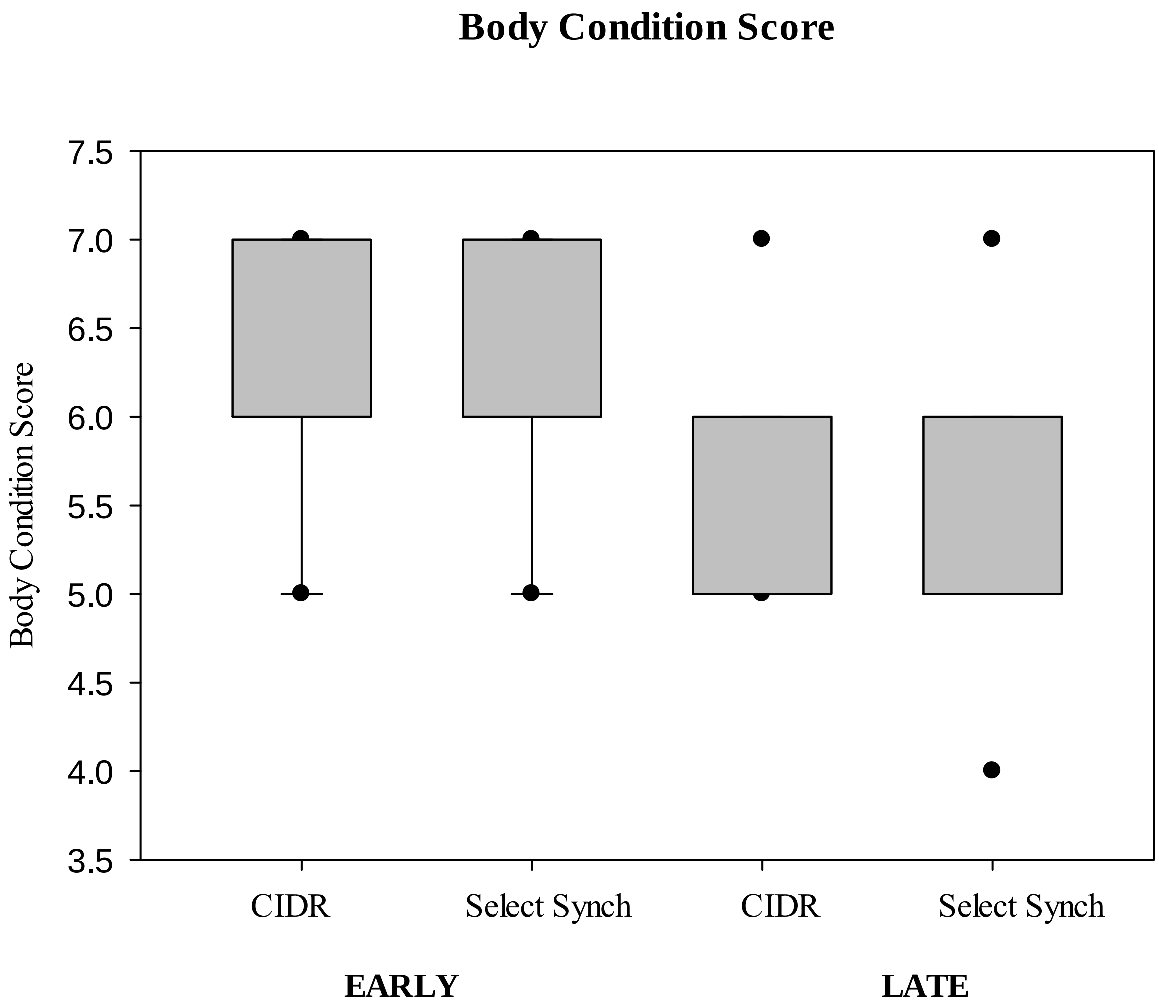

Figure 10. Distribution of V bar V cow body condition score, per group and treatment

Table 5. Age and body condition score of V –V cows

	Treatment			
	Early		Late	
Item	CIDR®	Select Synch	CIDR®	Select Synch
Number	74	73	76	77
Age	3.3 ± 1.9^{a}	3.2 ± 1.9^{a}	6.2 ± 3.0^{b}	6.4 ± 3.1^{b}
Body condition Score	6.2 ± 0.7^{a}	6.2 ± 0.7^{a}	5.6 ± 0.6^{b}	5.7 ± 0.7^{b}

[a,b] Means within a row with different subscripts differ (*P<0.0001*)

Percentage of cows detected in heat did not differ between groups or treatments (Figure 11; Table 6). The addition of GnRH numerically increased the percentage of cows detected in heat in the Early breeding group, but this was not true for the Late breeding group. Cows in the Early breeding group had a greater chance of becoming pregnant ($P<0.02$) by the artificial insemination (Figure 12; Table 6). There was no significant difference between CIDR® or Select Synch treatment groups within either the Early or Late breeding group for percentage of cows becoming pregnant from artificial insemination (Figure 13; Table 6). Days to conception from the start of the breeding season were not different ($P>0.05$) between Early or Late breeding groups. No significant difference in days to conception was detected for either treatment group (Figure 14; Table 2).

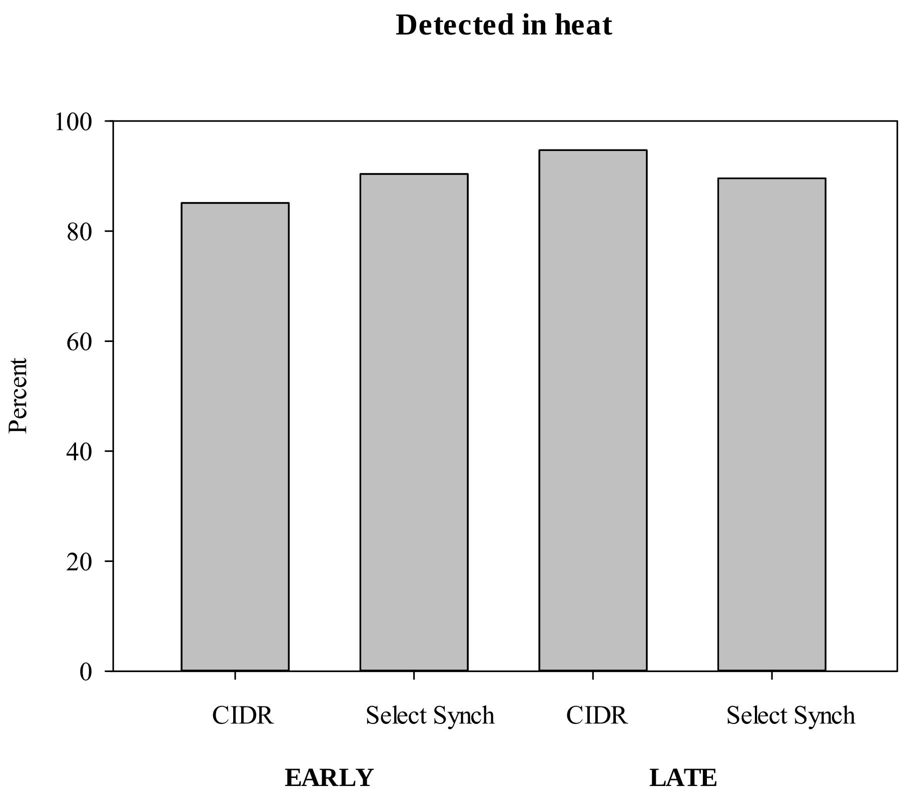

Figure 11. Percent of cows per treatment detected in heat and inseminated within 5 days of CIDR removal

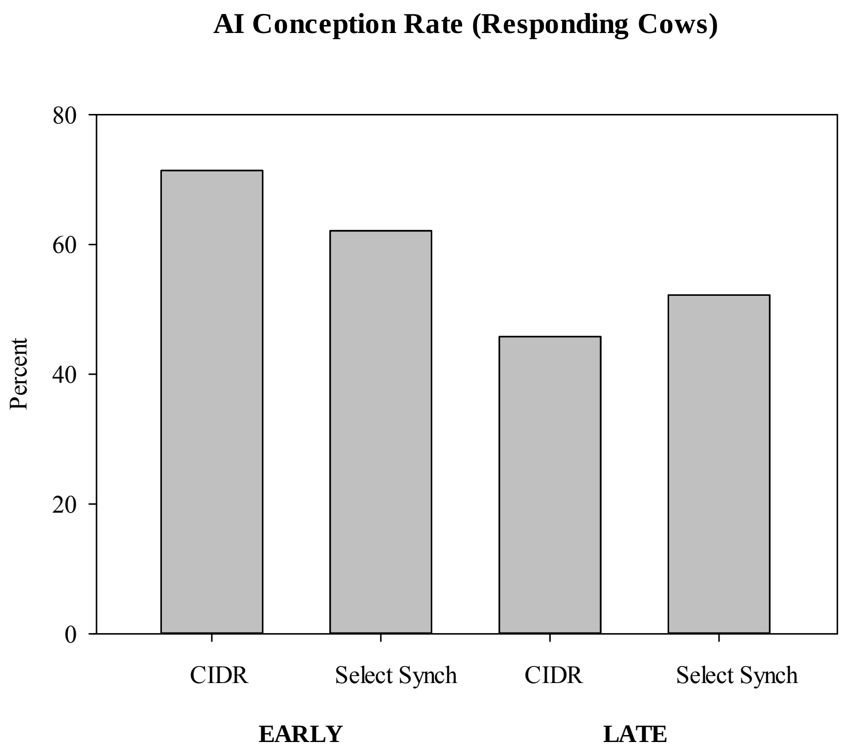

Figure 12. Percent of responding cows per treatment conceiving by artificial insemination

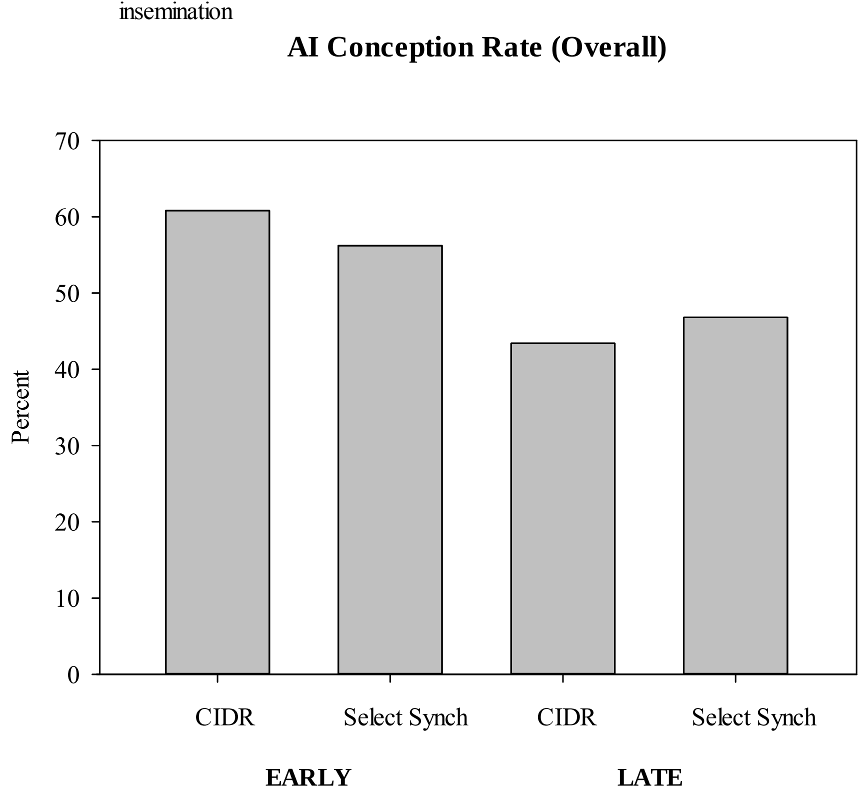

Figure 13. Percent of all cows per treatment conceiving by artificial insemination

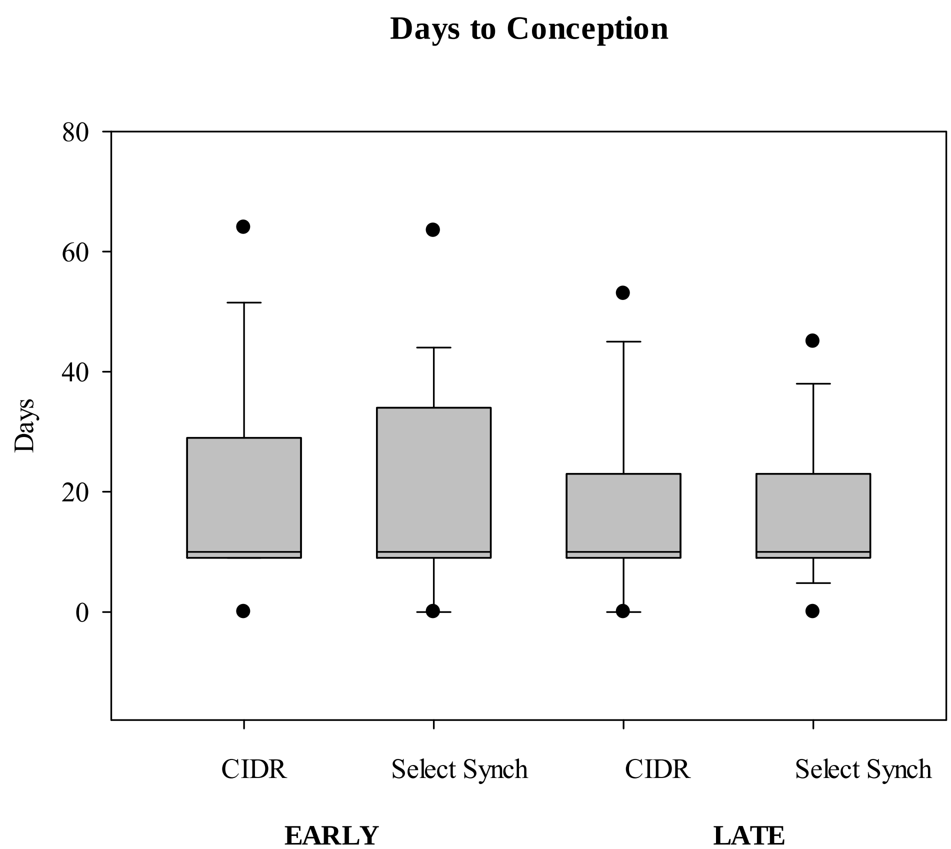

Figure 14. Distribution of days to conception of V-V cows after initiation of breeding season

Table 6. Estrus response, days to conception and conception rate of V-V cows

	Treatment			
	Early		Late	
Item	CIDR®	Select Synch	CIDR®	Select Synch
Detected in heat	85.1%	90.4%	94.7%	89.6%
Days to conception	20.0 ± 18	22.2 ± 19	19.5 ± 16	17.4 ± 13
Pregnancy/estrual insemination	71.4%[a]	62.1%[a]	45.8%[b]	52.2%[b]
Overall AI conception rate	60.8%[a]	56.2%[a]	43.4%[b]	46.8%[b]

[a,b] Means within a row with different subscripts differ (P<0.02)

Discussion

The addition of GnRH did not significantly (*$P>0.05$*) impact synchronization success in postpartum cows in this experiment. Synchronization success was measured by percent of cows detected in heat, pregnancies resulting from artificial insemination and days to conception from the beginning of the breeding season. There was no detectable increase in any of these measures.

The addition of GnRH was expected to increase the number of cows showing estrus and subsequently becoming pregnant by artificial insemination due to follicular turnover at the initiation of treatment. This effect in beef cattle has been suggested by Lamb et al., 2001. While the addition of GnRH numerically increased the number of cows detected in estrus by almost 5% in the Early breeding group, there was no statistical difference between the treatments. Contrary to results in the Early breeding group, Late breeding group cows showed a 5% decrease in cows detected in heat with the addition of GnRH. One of the potential explanations for this observation may be tied to the body condition and postpartum status of the Early versus Late breeding cows. Cows in the Early breeding group were approximately ½ of a body condition score higher. In addition, many of the cows in this group did not have a calf and were not lactating. The combination of greater energy reserves and decreased metabolic demands may have combined to increase the percentage of previously cycling cows in the Early breeding group at initiation of treatment. A more likely explanation may be that the endogenous progesterone concentrations at the onset of treatment were already elevated in cycling cows.

There was a significant difference ($P<0.02$) between the Early and Late breeding groups in percentage of cows that conceived from artificial insemination. Many of the cows in the Early breeding group had not calved and did not have to recover from the effects of parturition or energetic demands of lactation. The addition of GnRH did not produce an advantage for conception rate in the Early breeding group, but there was a slight numerical advantage in the Late breeding group. This is in agreement with Perry and Perry (2009) who found that treatment with GnRH does not stimulate LH release and induce ovulation or extend CL function in all beef cattle.

Conclusions

In conclusion, the addition of GnRH to the CIDR® protocol for beef producers based on this experiment would not be recommended. While the potential advantage of GnRH has been documented in some work, there was not a detected advantage in conception rates that would justify the additional expense. The CIDR® -based protocols are a reasonable synchronization option for beef producers. Very acceptable conception rates were demonstrated in this experiment. Producers that are considering a synchronization and artificial insemination program should make sure that cows are in adequate body condition and at least 45 days postpartum to ensure acceptable conception rates. Further experiments should incorporate the use of transrectal ultrasonography to track follicular development and evaluate follicular turnover in order to more closely evaluate efficacy of GnRH in this protocol. In addition, progesterone concentrations should be quantified at the initiation of the trial to determine percentage of cycling cows.

CHAPTER 5

HORMONAL MANAGEMENT OF DAIRY COWS

Abstract

This experiment evaluated the efficacy of a controlled intravaginal drug release (CIDR®) protocol to synchronize estrus in Arizona Holstein dairy cows. The experiment was run in two phases, Cool season (November through January; n=456) and Warm season (July through September; n=240) to examine the impact of thermal stress on reproductive measures. Cows assigned to the CIDR® protocol (n=337) received a CIDR® insert (1.38 g of progesterone) at the end of the voluntary waiting period (55 days). CIDR® s were removed and an injection of $PGF_{2\alpha}$ (25 mg i.m.) was administered seven days after insertion. CIDR® and control cows were observed for estrus and inseminated approximately 12 hours after standing heat. There was no difference due to CIDR® treatment in number of services per conception (1.8 versus 2.1 in Cool Season and 2.8 versus 2.8 in Warm Season) or first service conception rate (45.8% versus 38.8% in Cool Season and 19.9% versus 17.3% in Warm Season). CIDR® treatment reduced days to first service (7.5 in Cool Season and 6.7 in Warm Season), days open at first service (6.0 in Cool Season and 7.8 in Warm Season), and days open (13.0 in Cool Season and 5.8 in Warm Season) ($P<0.02$). Warm season had a deleterious effect on number of services, days to first service, first service conception rate and days open ($P<0.0001$). In summary, estrus synchronization improved postpartum reproductive performance; however, thermal stress continues to be a major barrier to reproductive efficiency.

Introduction

A major component of profitability in the United States dairy industry is postpartum reproductive success. Other factors, such as increasing input, energy and commodity costs, also play a significant role in profitability. Cows that breed back sooner produce more milk per day of herd life. Anestrus in the postpartum interval is a major factor contributing to failure of cows to conceive and calve at close to a yearly interval. Therefore, research has centered on ways to ensure hastening of postpartum cyclicity. The artificial insemination (AI) industry learned over 50 years ago, that fertility increased as the number of cycles increased within a fixed time (i.e. 60 days) postpartum.

Even if cows ovulate, a short luteal phase subsequent to that ovulation (less than 10 days) can further delay the interval from calving to conception (days open). Short luteal phases usually occur following the first postpartum ovulation. It has been hypothesized that progesterone produced by corpora lutea contributes to increased fertility and maintenance of pregnancy. Therefore an administration of exogenous progesterone might serve as a management tool to improve fertility of cows. Treatment with some progestins before the first postpartum ovulation reduced or eliminated occurrence of short luteal phases. In most synchronization protocols for cattle, prostaglandins are utilized. However, oral and vaginal deliveries of progestins have become valuable components of synchronization programs. In that context, experimental data exists which indicates that variation in biological response depends on the progestin administered.

Heat stress is a major source of production loss in dairy cows. There are direct and indirect effects of heat stress on dairy cows due to ambient temperature, solar radiation and humidity. One of the direct impacts of heat stress on cattle is reduction in reproductive efficiency. The THI index, (THI = t_{db} + .36t_{dp} + 41.5, where t_db = dry-bulb temperature, ^{0}C and t_{dp} = dew point temperature, ^{0}C), was originally developed for use in humans by Thom (1958) and was later used in cattle by Berry et al (1964). THI values are used to estimate cooling requirements and to categorize stress levels for dairy cattle (Armstrong, 1994). There is some concern about whether THI is truly a correct measure of heat stress and an argument is made that the current THI indexes may underestimate the effects of heat stress on cattle (Collier and Zimbleman, 2007). Cattle in an environment where calculated THI is under 72 are categorized as under no environmental stress, 72-79 are under mild stress, 80-89 are under medium stress and 90 or above are under severe stress.

The objectives of this experiment were to evaluate the efficacy of using exogenous progesterone in the form of a controlled intravaginal drug releasing device (CIDR®) in postpartum dairy cows after the voluntary waiting period, during periods of thermal stress and no thermal stress. Reproductive measures evaluated would include days to first service, number of services, first service conception rate, overall conception rate and days open.

Materials and methods

Holstein dairy cows on a cooperating dairy in Coolidge, Arizona (Goldman Dairy) were randomly assigned to either receive an EAZI-BREED CIDR® intravaginal progesterone insert and a luteolytic injection (n=474) or no insert (n=487). The cooperating dairy had approximately 2,000 cows. Cows were milked four times per day for 60 days postpartum and then twice per day until dry-off. This trial was implemented twice, once during the Cool (November, 2004 through January 2005) Season (n=582) and once during the Warm (July, 2005 through September 2005) Season (n=379) to evaluate the effects of heat stress on synchronization and conception. The design of the study was to have each cow in the trial have an opportunity to become inseminated following the 55 day voluntary waiting period. Farm management provided calving dates for cows and as they approached the end of the voluntary waiting period, they were randomly assigned to the CIDR® group or Control group. The farm reproductive team was provided weekly with a list of cows that were to receive the CIDR® insert and they administered the insert and luteolytic injection. Seven days following CIDR® insertion, the CIDR® was removed and a 5 ml intramuscular injection of dinoprost promethamine (Lutalyse®, Pfizer, New York, New York; 5 mg/ml) was administered to cows assigned to the CIDR® group. Cows were observed for estrus by the farm employees and inseminated, based on the am/pm rule. Five artificial insemination sires were randomly assigned by the farm genetic consultant over both groups. Cows were determined to respond to CIDR® treatment if they were inseminated within 5 days following CIDR® removal. Farm management did not want to inseminate any cows that were not exhibiting signs of estrus behavior (no timed artificial insemination). Cows were rectally palpated for pregnancy by the consulting farm veterinarian and recorded in the farm dairy management software, DHI-Plus (DHIA, Provo, UT). Data were collected to evaluate days open, average number of services, average days to first service, average days open to first service, first service conception rate, and whether cows were inseminated within the first 21 days of the breeding period.

Maximum air temperature, average maximum daily air temperature, average temperature and dew point temperature were obtained from the AZMET (Arizona Meteorological Network, University of Arizona) weather station nearest to the cooperating dairy in Coolidge, Arizona. The weather station is approximately 5 miles from the dairy.

Data were analyzed using the PROC-mixed procedure of SAS (SAS Institute, Cary, NC).

Results

Cows were assigned to either receive a CIDR® at the end of the 55 day voluntary waiting period or to serve as controls in both Cool and Warm Season groups. Initially, 474 cows were assigned to receive a CIDR® and 487 assigned to the Control group based on calving dates provided by farm management. Because of incomplete data entry, early breeding, culling and other losses, 337 cows had complete data in the CIDR® group and 359 in the Control group. There were more cows evaluated in the cool season (Table 7).

Table 7. Profile of dairy cows analyzed

	Treatment			
	Cool Season		Warm Season	
Item	CIDR®	Control	CIDR®	Control
Number assigned	266	316	208	171
Number analyzed	201	255	136	104
Days fresh	58.2 ± 5.0	56.7 ± 5.9	56.3 ±4 .7	57.4 ± 5.4

Temperature Humidity Indices were calculated based on AZMET data for the months of the trial (Table 8). Cows in the Cool Season treatment group had lower calculated THI values based on maximum daily temperature, maximum average daily temperature and average temperature compared to the Warm Season treatment group.

Table 8. Air temperature (^{0}C), dew point temperature (^{0}C) and calculated temperature humidity index (THI), Coolidge, Arizona

Month	November[1]	December[1]	January[1]	July[2]	August[2]	September[2]
Maximum temperature	30	26.1	25.6	46.1	43.9	41.1
Average maximum temperature	21.1	18.3	18.9	42.2	38.3	38.3
Average temperature	12.8	10.0	11.1	32.2	29.4	28.3
Dew point temperature	3.3	1.1	6.7	11.7	17.2	8.9
Maximum THI	72.4	67.7	69.2	91.5	91.3	85.5
Average maximum THI	63.5	59.9	62.5	87.6	85.7	82.7
Average THI	55.2	51.6	54.7	77.6	76.8	72.7

[1]Cool Season treatment
[2]Warm Season treatment

Cows did not differ (*P=0.2033*) in days fresh at initiation of treatment in either Cool or Warm season breeding groups (Figure 15; Table 5). Percent of cows responding was measured as cows that had been inseminated within 5 days of CIDR® removal. There was almost a two-fold response advantage in the Cool Season group (Figure 16; Table 6).

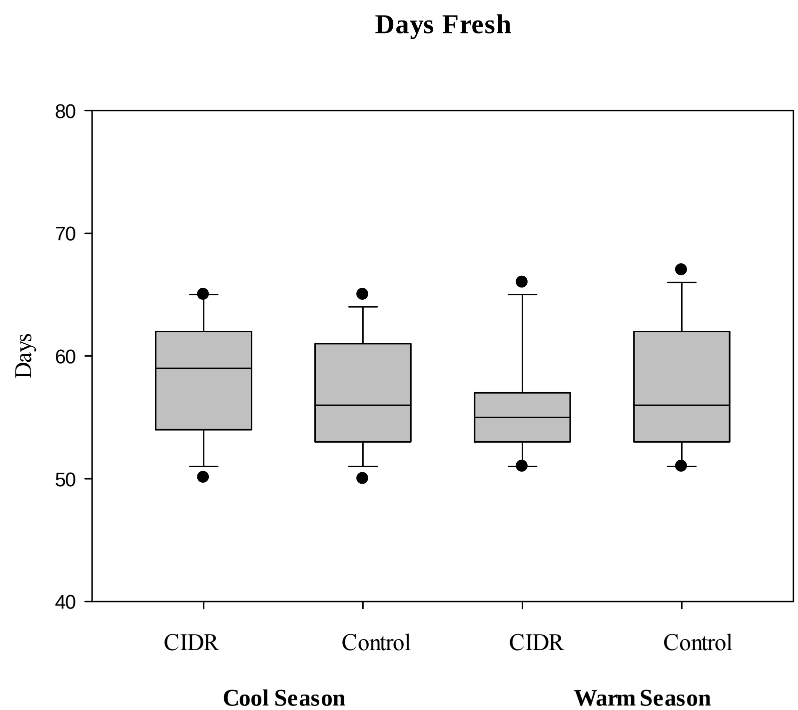

Figure 15. Days fresh at initiation of breeding season

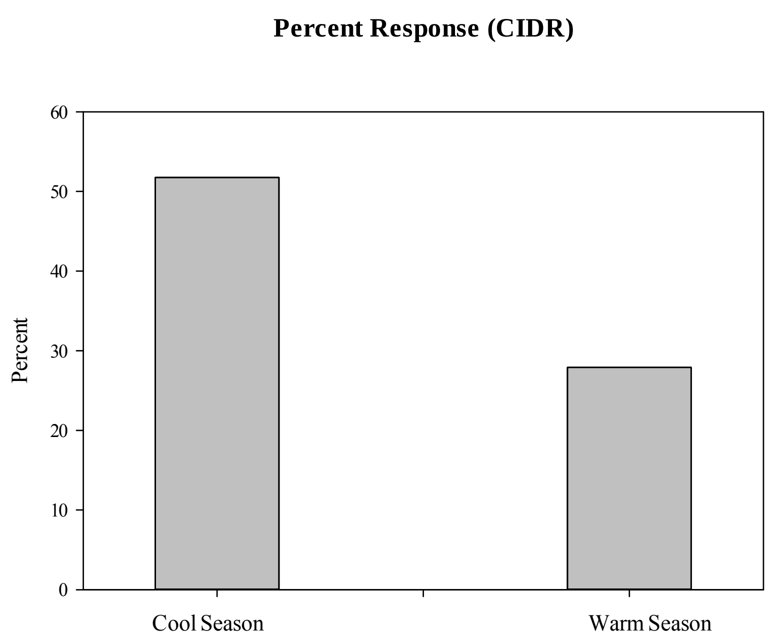

Figure 16. Percent response to CIDR® treatment

Table 9. Mean reproductive measures of dairy cows

Item	Treatment			
	Cool Season		Warm Season	
	CIDR®	Control	CIDR®	Control
Number of services	1.8 ± 1.0 [a]	2.1 ± 1.2 [a]	2.8 ± 1.4 [b]	2.8 ± 1.3 [b]
Days to first service	20.5 ± 17.4 [a]	28.0 ± 29 [b]	33.3 ± 23.4 [c]	40.0 ± 25.5 [d]
Days open at first service	78.6 ± 18.0 [a]	84.6 ± 29.7 [b]	89.6 ± 23.4 [c]	97.4 ± 26.7 [d]
First service conception rate	45.8% [a]	38.8% [a]	19.9% [b]	17.3% [b]
Inseminated first 21 days	59.2% [a]	50.2% [b]	38.2% [c]	28.8% [d]
Days open	105.9 ± 43.0 [a]	118.9 ± 52.7 [b]	149.4 ± 55.0 [c]	155.2 ± 53.0 d

[a-d] Means within a row with different subscripts differ (P<0.02)

CIDR® treatment did not (*P=0.1299*)have an impact on number of services, but there was a negative impact (more services per conception) due to season (*P<0.0001*) (Figure 17; Table 9). This same seasonal advantage (*P<0.0001*) was noted in days to first service (Figure 18; Table 9). There was an improvement (reduction in number of days to first service) in the CIDR® groups (*P=0.0004*), regardless of season (Figure 18; Table 9).

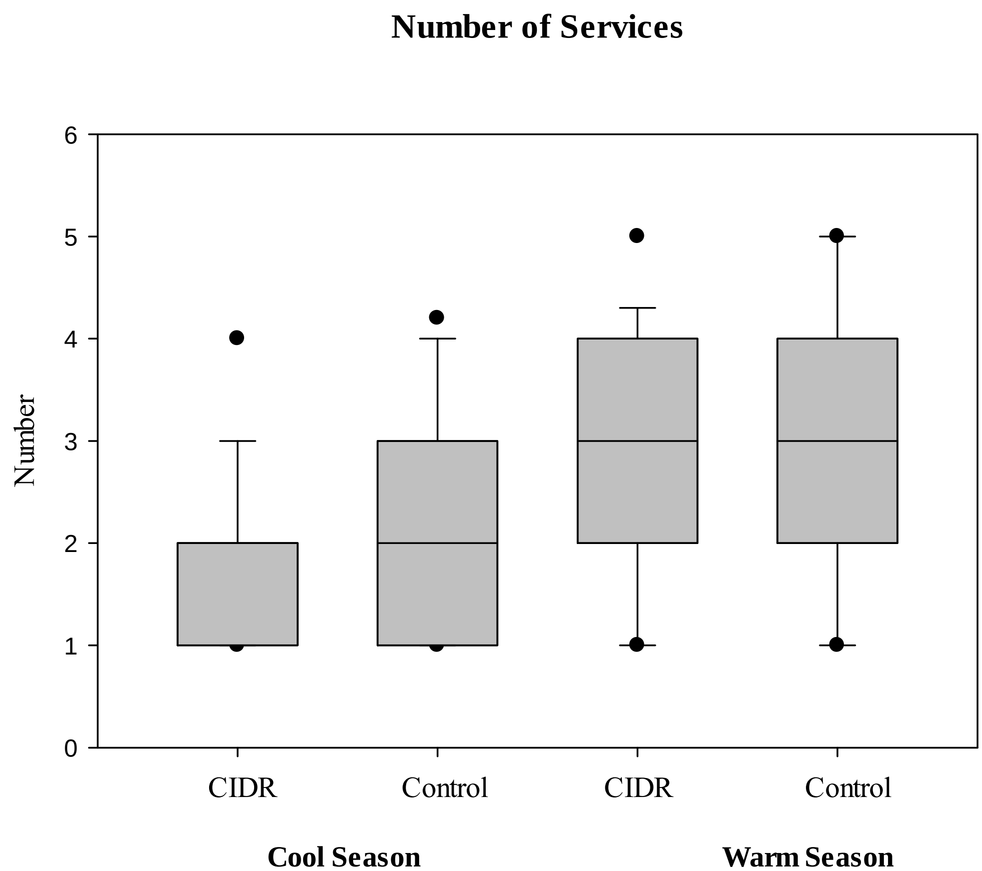

Figure 17. Number of services per conception

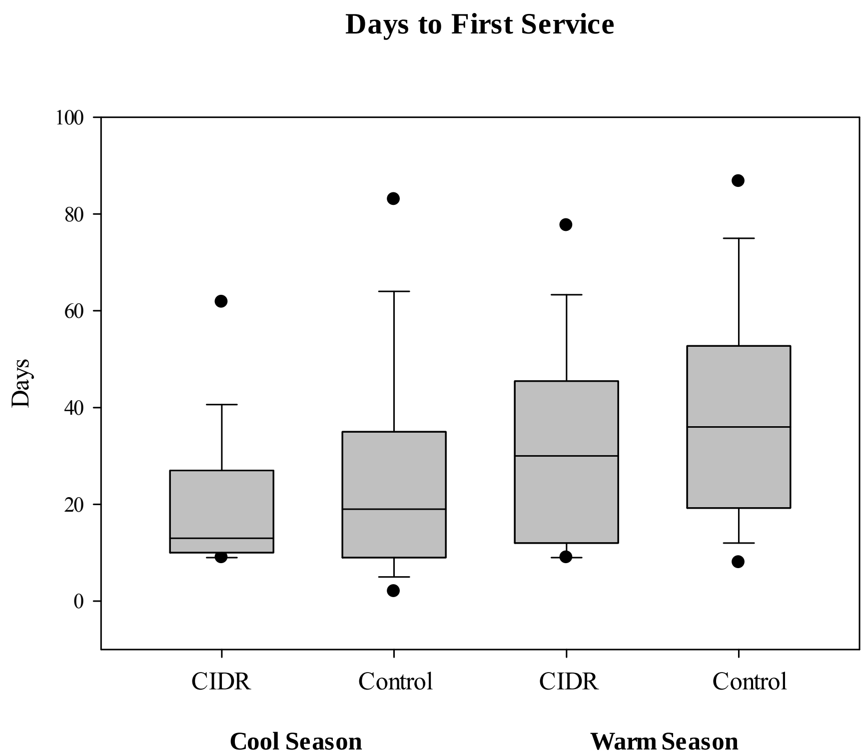

Figure 18. Days to first service from initiation of breeding season

First service conception rate was not improved by CIDR® synchronization (*P<0.0001*). As expected, cows subject to heat stress (Warm Season group) were negatively impacted and exhibited more than a 50% reduction in conception rate to the first insemination (*P<0.0001*) (Figure 19; Table 9). Days open at first service, or the first opportunity that a cow had to become pregnant, was affected by treatment (*P=0.0007*) and season (*P<0.0001*) (Figure 20; Table 9). Cows in the Cool Season group as well as cows that were treated with the CIDR® had a greater chance (*P<0.0001*) of becoming inseminated within the first 21 days of the breeding season (Figure 21; Table 9). Days open was reduced in the cool season by 13 days with the CIDR® treatment and almost 6 days during the warm season (Figure 22; Table 9) (*P<0.0001*).

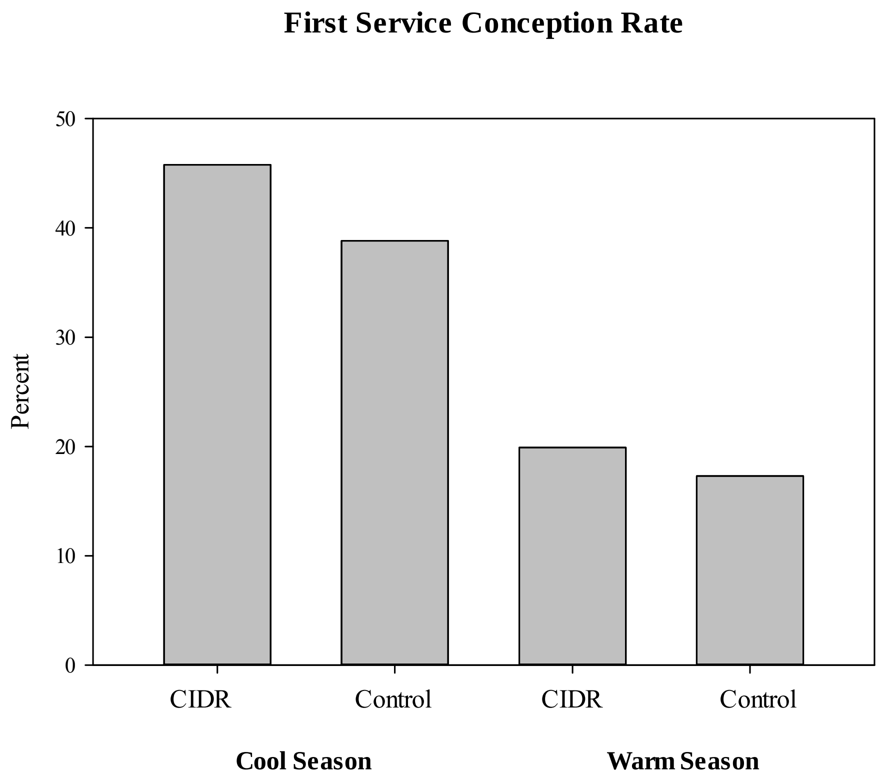

Figure 19. First service conception rate

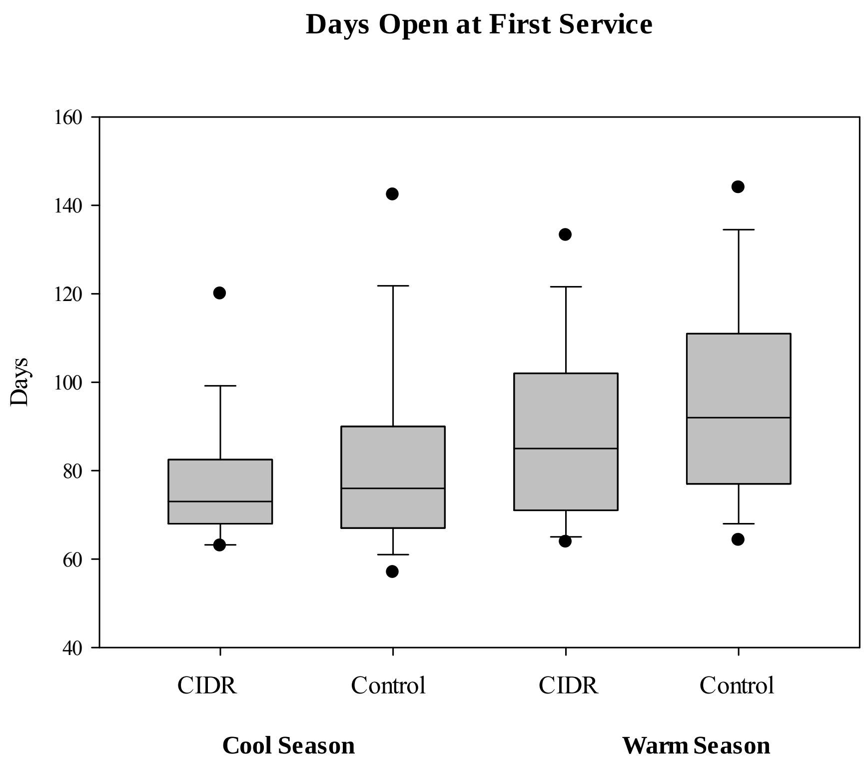

Figure 20. Days open at first service

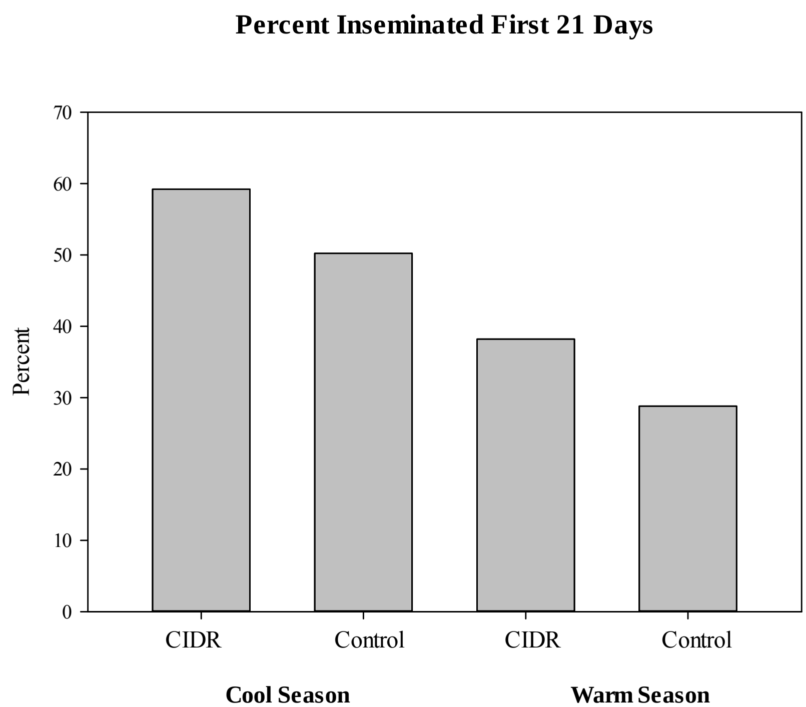

Figure 21. Percent of cows inseminated within the first 21 days of the breeding season

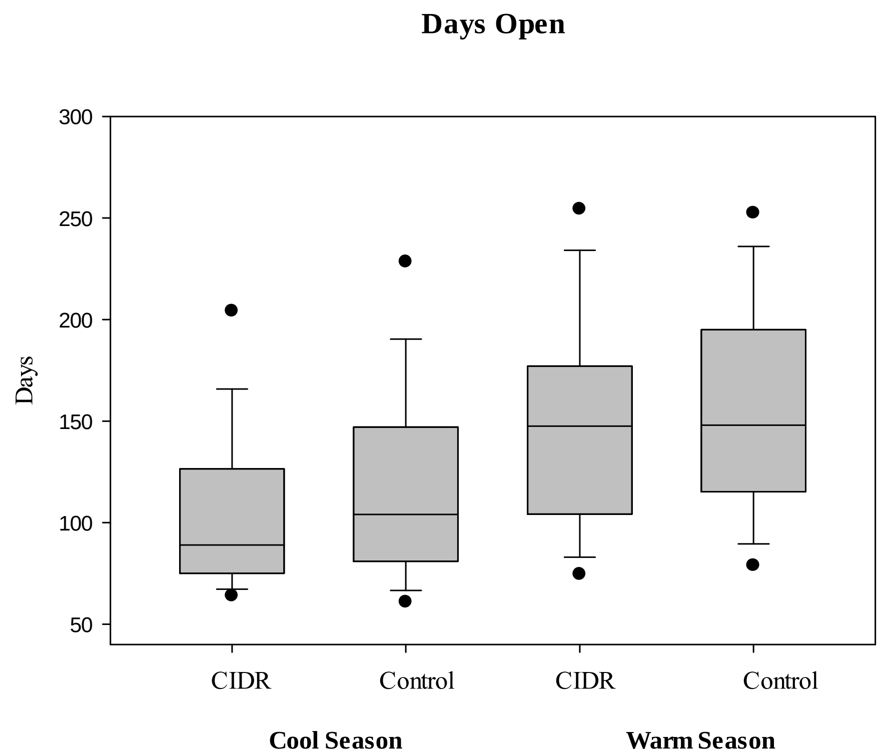

Figure 22. Days open

CIDR® ed cows in the Cool Season group were inseminated at a higher rate (*P<0.0001*) than cows experiencing heat stress (Table 10). In addition, cows in the Cool Season group were inseminated in fewer days (*P<0.0001*) than cows in the Warm Season group (Figure 23; Table 10).

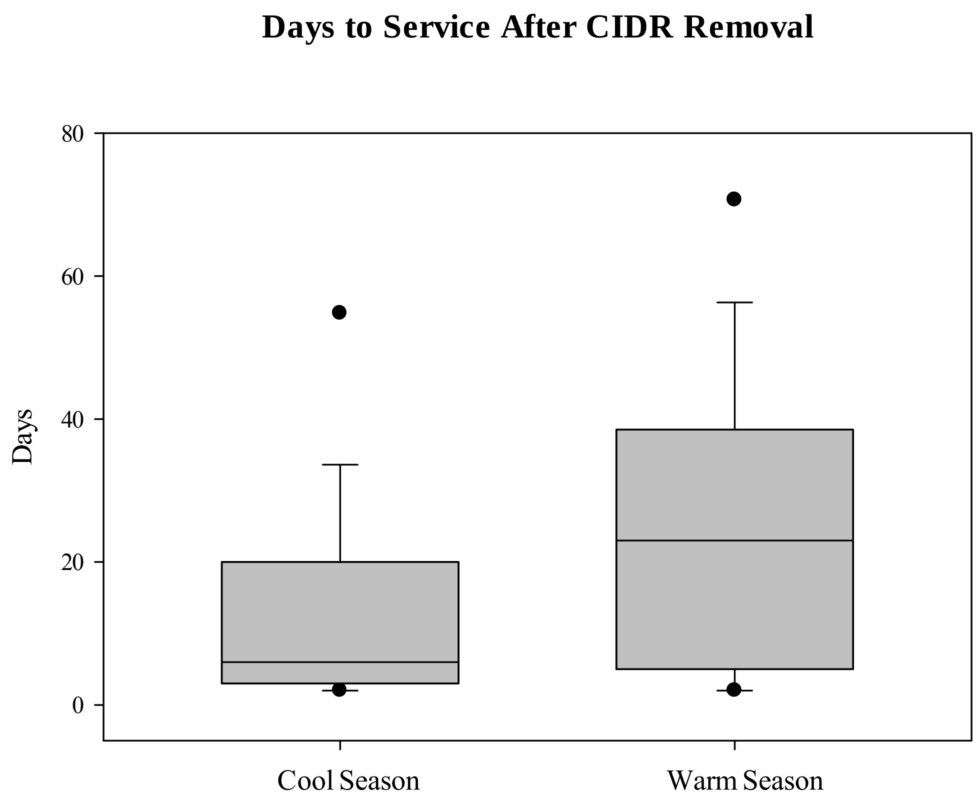

Figure 23. Days to service after removal of the CIDR®

Table 10. Dairy cow response to CIDR® treatment

	Treatment	
	Cool Season	Warm Season
Item	CIDR®	CIDR®
Inseminated within 5 days after CIDR® removal	51.7%[a]	27.9%[b]
Days to insemination after CIDR® removal	13.5 ±17.4[a]	26.3 ± 23.4[b]

[a,b] Means within a row with different subscripts differ (P<0.0001)

Cows in the CIDR® treatment group also became pregnant earlier (*P<0.0001*) in the breeding season (Figure; Table 8).

Table 11. Cumulative 21 day pregnancy rate

	Treatment			
	Cool Season		Warm Season	
21 day breeding period	CIDR®	Control	CIDR®	Control
First	28.9%	22.0%	5.8%	3.8%
Second	59.7%	45.1%	22.1%	16.3%
Third	74.1%	61.2%	32.3%	29.8%
Fourth	80.6%	72.5%	47.8%	43.3%
Fifth	89.6%	82.7%	66.2%	61.5%

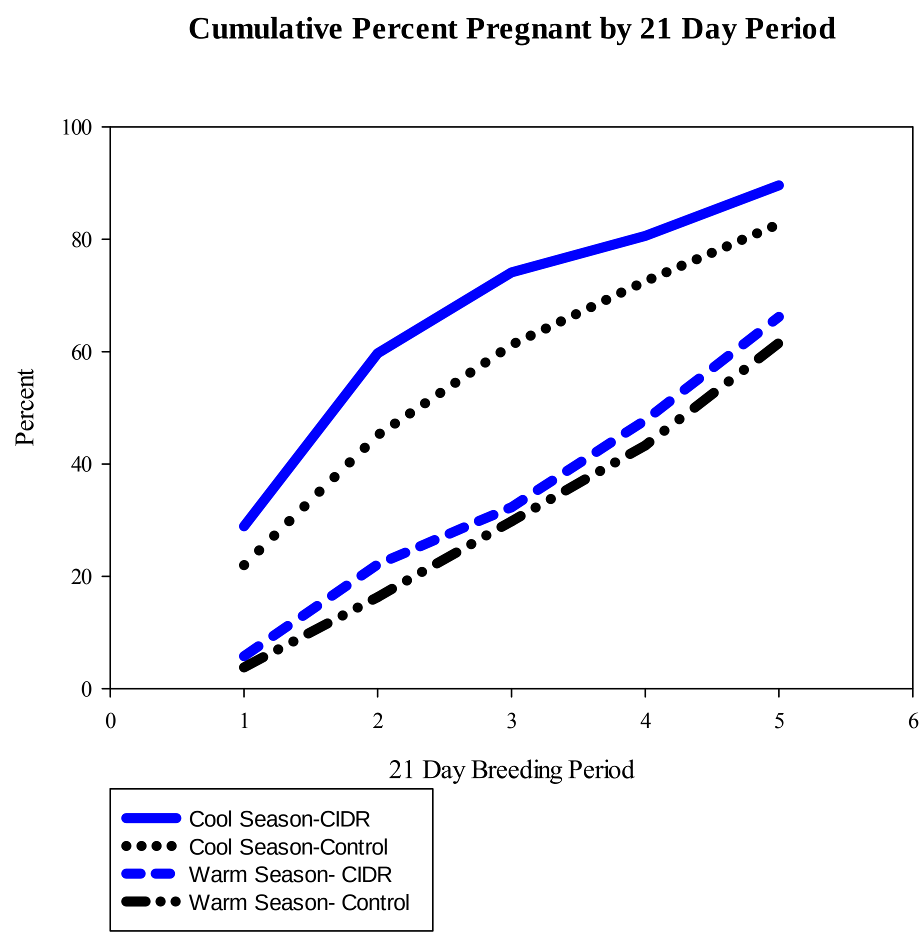

Figure 24. Cumulative percent pregnant by 21 day period following voluntary waiting period

Discussion

The use of CIDR® progesterone inserts improved most of the economically valuable measures of reproductive efficiency, regardless of whether cows were under heat stress or not. Postpartum anestrus in dairy cows is a factor contributing to failure of cows to calve on a yearly interval and remain in the herd. Most herd management programs include a voluntary waiting period. The sooner a cow can be inseminated and become pregnant following this period, the more economically efficient a herd will be. The dairy industry has learned that fertility increases as the number of cycles increase in the postpartum period. Hormonal intervention is usually practiced to enhance this postpartum cyclicity.

In this trial, number of days to first service was a measure of resumption of postpartum cyclicity. There was a detectable difference between the Cool and Warm Season groups ($P<0.0001$). In both seasons, the use of CIDR® s allowed cows to be inseminated a week earlier than their control counterparts ($P<0.02$). Another measure of resumption of postpartum cyclicity is whether cows were inseminated within the first 21 days of the breeding season. As expected, there was a reduction in percent of cows inseminated within the first 21 days during the Warm Season as compared to Cool Season ($P<0.0001$). Again, further validating the value of hormonal intervention, cows in the CIDR® group had a detectable increase in number of cows bred in the first heat period of the breeding season ($P<0.02$).

Season also had a deleterious effect on conception rates. Warm season first service conception rates were reduced by 50% in this trial as compared to cool season

($P<0.0001$). In both seasons, the CIDR® group showed an improvement over the Control group in first service conception rate ($P<0.02$). An additional measure of reproductive success is number of services per conception. There was not a significant advantage in the CIDR® group as compared to controls; however, Warm Season cows had a significantly greater number of services per conception ($P<0.0001$).

The response to CIDR® treatment revealed the same trends discussed earlier between the Cool and Warm Season groups. In the Cool Season, cows had an almost two-fold increase in percentage of cows detected in heat and inseminated as compared to warm season ($P<0.0001$). Cool Season CIDR® treated cows also averaged half as many days to insemination as compared to Warm Season CIDR® treated cows. A look at the cumulative 21 day pregnancy rates through five heat periods reveals both the season and treatment effect. Cows in the Cool Season group and CIDR® treated cows had an advantage in conception rate in both of these experiments ($P<0.0001$).

These experiments further confirm the deleterious effects of thermal stress on reproductive productivity in high producing dairy cows. In addition, they show that some advantage can be realized with hormonal intervention, particularly with the use of exogenous progesterone and prostaglandin.

The economics of improved reproductive performance are not simple to quantify. There are many variables to be taken into account, including input costs, culling costs, replacement costs, milk price and production level. Many times the cost is expressed as cost per day open per cow. Plaizier et al (1997) estimated a cost of $3.36 per day (1997

US dollars) and their review of the literature showed values ranging from \$0.29 to \$2.60. Using 2011 US prices for the CIDR® insert (\$10.00) and prostaglandin (\$2.50), days open would need to be reduced by four days (using the higher value) solely to recoup the cost of synchronization products. If the cost per day open were reduced to \$2.00, then a six day reduction in days open would be needed to justify the additional expense. Another way to evaluate the economic return or value of reducing days open is to consider the value of a pregnancy. Devries (2006) developed a bioeconomic model for a general Holstein herd in the United States. The model showed an average value of \$278 for a new pregnancy. The value was increased early in lactation. Stevenson (2001) estimated the value of a new pregnancy was between \$253 and \$274 in programmed AI breeding protocols. He also showed that the value of pregnancy increased in situations that had lower estrus detection efficiency.

Conclusions

The use of CIDR® s in an Arizona dairy herd can improve many of the economically important reproductive measures. In this experiment, number of days open and time to insemination were reduced in CIDR® treated cows as compared to controls ($P<0.02$). Conception rates were also improved. Heat stress continues to be a barrier to successful reproduction in dairy cows. A producer must be able to balance the cost of increased performance with the economic or biological return that they get from implementing technology, whether that is synchronization and artificial insemination or increasing cow comfort.

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