Practical Manipulation of the Estrous Cycle in Beef Cattle

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Introduction

The widespread use of AI in beef cattle is strictly dependent upon development of effective methods to control estrus. Many methods to manipulate the estrous cycle in beef cattle have been developed and are available for use in AI programs within the industry. However, less than 10% of beef females in the USA are bred by AI. Many factors have contributed to the low degree of adoption of AI technology by beef producers. These factors include but are not limited to tradition, the marketing system for the industry, the extensive, low-input nature of many of our beef production systems and the degree of efficacy of existing estrous control methods. The economic advantages of an effective AI program have been well-defined in the past and the movement of the beef industry towards value-based marketing has heightened the importance of the use of AI. The effective use of current methods of estrous cycle manipulation and the development of future systems with improved efficacy are critical to expansion of the use of AI in beef cattle.

Importance of Estrous Cycle Manipulation

The base tools that are necessary to AI beef cattle to sires of superior genetic merit have existed for many years. Using twice-daily heat detection, one can achieve normal conception rates through AI if performed at an appropriate time relative to estrus. The benefits achieved through the use of sires of superior genetic merit are easily defined as increased performance of calves produced by AI and the long-term effects on cow herd productivity. An obvious example of the enhancement of productivity that can be achieved with AI in cattle is the increase in milk production over the past 3 decades in the dairy industry.

However, even with the ready availability of the base technology to perform AI and with the benefits well defined and recognized, AI has not been used extensively in beef production. A major factor that has prevented the widespread use of AI is that the process of twice-daily heat detection, moving and sorting individual or groups of cows and calves to the working facilities, inseminations on a twice daily basis, etc. is not practical for many beef producers. The extensive nature of many cattle operations, lack of adequate facilities and sufficient labor, the distant location of cattle from working facilities during grazing rotations, and other related factors all impede the use of AI. For most beef producers to implement an AI program, it is critical that this process be reduced to a short period of AI during which a majority of the females become pregnant. Simply defined, the importance of estrous cycle manipulation is that it is requisite for the expansion of the use of AI in beef cattle.

Although methods of estrous cycle manipulation have been and are available to beef producers, they are not widely used within the industry. We are continually learning more about how the reproductive system of the cow functions and the impact of these reproductive management tools on this system. This new information is progressively allowing us to recognize the advantages and limitations of the existing commercial products. More importantly, this enhanced understanding has and is leading towards development of systems of estrous control that may be more effective. The increased understanding of current methods and development of new approaches to estrous cycle control are essential to raise producer confidence in these procedures and augment the implementation of AI in beef cattle.

Production Goals for Optimal Estrous Control Systems

The extent to which producers will use a technology to synchronize estrus is dependent upon the efficacy of the treatment. Effectiveness can be defined in several ways and different producers would have different

goals that they wish to achieve. For example, the capacity for timed insemination rather than mating based on estrus detection is of paramount importance to some producers but less critical for others. The following endpoints represent the production goals we have established for our research program in estrous synchrony:

1. The system of synchrony should enhance the reproductive performance of the cow herd as measured by average number of days to conception rather than simply concentrate the breeding period to a shorter interval.

2. The system should be effective in all cows and heifers within the herd. Onset of estrus should be induced in a majority of anestrous females and the synchronized estrus in cyclic females must be of a fertility equal to or greater than a spontaneous estrus.

3. Greater than 50% of the herd should become pregnant to AI over a maximum of 3 days or to a timed insemination protocol.

4. The system should be designed to minimize cattle handling, use treatments that are easy to administer and be of reasonable cost while attaining the above goals.

A hidden requirement that is essential to achieve the above goals is that the herd must be adequately managed from both a reproductive and nutritional standpoint. Cows must be maintained in an adequate body condition, a controlled breeding season is requisite, the first-calf heifers should calve before the cowherd or early in the main calving season and appropriate replacement heifer selection and management are necessary.

Physiological Requirements of Estrous Control Systems

In order to fully achieve the goals indicated above, we believe there are 3 key physiological requirements that must be provided for within the estrous control system:

1. A synchronous decline in progesterone (or exogenous progestin) must occur in all animals as a result of luteal regression or withdrawal of the progestin source.

2. Adequate stimulus must be provided to the reproductive system of anestrous females to induce

ovulation in a majority of females in this reproductive classification.

3. Ovarian follicle growth must be managed to: a) ensure that follicles which ovulate yield oocytes of normal competency and b) that stage of follicular growth is approximately equal at the time of the progesterone/progestin decline to allow a precise timing of estrus and for use of methods to synchronize ovulation.

Using what has been learned about function of the reproductive system in cattle and the impact of various treatments on this system, the development of approaches which meet the stated production goals and physiological requirements is realistic. The intent of the remainder of this paper is to first review the major systems of estrous control that are available and then to discuss new and future systems of estrus control and their potential for use in beef cattle.

Existing Systems of Estrous Synchronization

Use of Prostaglandin $F_{2\alpha}$ for Estrous Synchronization

The hormone prostaglandin $F_{2\alpha}$ or analogues of this hormone ($PGF_{2\alpha}$) were initially developed in the 1970s to synchronize estrus in cattle. The principle behind this method is to induce synchronous regression of the corpus luteum (CL) in all cows, thereby resulting in a synchronized estrus. Since a CL is required for $PGF_{2\alpha}$ to demonstrate this action, systems based solely on the use of $PGF_{2\alpha}$ are not effective in anestrous cows or pre-pubertal heifers. A single injection of $PGF_{2\alpha}$ does not consistently induce regression of the CL in cows treated before day 5 of the estrous cycle (Lauderdale *et al.*, 1974) but is effective from days 6 to 17 of the estrous cycle (Lauderdale, 1972). After day 17 of the estrous cycle, $PGF_{2\alpha}$ does not appear to influence the process of luteal regression nor does it shorten the estrous cycle of females treated at this stage of the cycle. Since these females will spontaneously show estrus in the next 2 to 6 days, they are synchronized by default when using $PGF_{2\alpha}$. Therefore, a single injection of $PGF_{2\alpha}$ to a group of cyclic females would be anticipated to synchronize estrus in all cows except those in the first 5 days of their estrous cycle.

A variety of approaches to the use of $PGF_{2\alpha}$ have been developed in an effort to ensure that estrus was synchronized in nearly 100% of cyclic females. Most common is a two-injection method of estrous synchrony, in which the injections are spaced at an interval of 10 to 14 days. With this approach, estrus would be synchronized in 75 to 80% of cyclic females following the first

injection, and virtually 100% of females after the second injection. The high response to the second injection with this scheme is the result of no cows being in the first 5 days of their estrous cycle at the time of the second injection. In practice, often the cows in estrus after the first injection are inseminated, and the second injection administered only to those cows that fail to respond to the first injection. Alternatively, heat detection and breeding for 5 days prior to administration of a single dose of $PGF_{2\alpha}$ is another approach to eliminate the classification of cows that will not respond to the treatment.

Theoretically, the schemes described in the previous paragraph should result in a synchronized estrus in nearly 100% of cyclic females. However, it has been demonstrated that the CL of cattle on days 5 to 9 of their estrous cycle are less responsive to $PGF_{2\alpha}$ than CL of cattle in latter stages of the estrous cycle (King et al., 1982; Tanabe and Hahn, 1984; Stevenson et al., 1984; Watts and Fuquay, 1985). In a summary of data regarding the effects of day of the estrous cycle on responsiveness to $PGF_{2\alpha}$ (J. Chenault, unpublished data) it was determined that a majority of females treated between days 5 and 17 of the estrous cycle were responsive to $PGF_{2\alpha}$, but the response was lowest in females treated between days 5 and 9 (67%), intermediate for those treated on days 9 to 12 (77%) and greatest in females treated after day 12 (91%).

In $PGF_{2\alpha}$ synchrony systems, estrus typically occurs 2 to 5 days after treatment. It has been demonstrated that stage of the estrous cycle at which $PGF_{2\alpha}$ was administered will influence the interval to estrus. Estrus was observed between 48 and 59 hours after estrus in females administered $PGF_{2\alpha}$ between days 5 to 8 of the cycle, and between 53 and 72 hours in females treated between days 12 to 15 of the cycle (King et al., 1982; Tanabe and Hahn, 1984; Stevenson et al., 1984; Watts and Fuquay, 1985). Females in varying stages of the estrous cycle would be anticipated to have dominant follicles at varying stages of development at the time of treatment. It has been demonstrated that the time to estrus following $PGF_{2\alpha}$ treatment on different days of the estrous cycle is a function of time required for an ovulatory follicle to develop (Kastelic et al., 1990; Kastelic and Ginther, 1991). As a result of the range in stages of the estrous cycle and thus follicular development that will be represented in a group of cyclic females, the variation in time to estrus following administration of $PGF_{2\alpha}$ is predetermined.

In a majority of reports in which estrus has been synchronized with $PGF_{2\alpha}$ and AI has been performed based upon heat detection, fertility is approximately equal to that of females inseminated following detection of a spontaneous estrus. However, as a result of the inherent variability of time to estrus following synchronization with $PGF_{2\alpha}$, conception rate to a timed insemination is typically reduced (Moody and Lauderdale, 1977; Fogwell et al., 1986).

In summary, $PGF_{2\alpha}$ can be used to synchronize an estrus of normal fertility in a majority of the cyclic females within a herd. The precision of the synchronized estrus is acceptable for an AI program in which heat detection is used to determine the appropriate time to AI. The synchronized estrus is not precise enough to permit timed AI in most instances.

Progestin - Based Systems

Progesterone, or progesterone-like compounds (progestins) have been investigated for use in estrous synchronization for several decades. A relatively low level of progestin in the circulation of female cattle will suppress estrus until the source of progestin is removed. The principle for these methods of synchrony is that an exogenous source of progestin is provided via the animal's feed or implants as a substitute, or in conjunction with, progesterone originating from the CL. Synchronous removal of all progestin sources in all females should result in a synchronized estrus.

Early in the investigation of progestin-based systems of estrous control, progestin treatments in excess of 14 days were preferred in order to permit spontaneous regression of the CL during the period of progestin treatment. While this approach was successful in increasing the proportion of cows in which estrus was synchronized, the conception rate declined with increased duration of progestin treatment. The reason for the reduced fertility has since been identified to result from abnormal follicle growth (Lucy et al., 1990, Sirois and Fortune, 1990). Experimental methods to regulate follicular growth in animals treated with progestins for extended periods (Anderson and Day, 1994; McDowell et al., 1998a) and systems of extended progestin treatment which result in normal fertility (Anderson and Day, 1994; Anderson and Day, 1998; McDowell et al., 1998b) have been developed. However, the basis for existing commercially available progestin-based programs has been the utilization of short-term progestin treatments (<10 days). A method to induce regression of the CL either before, or at the time of cessation of progestin exposure, is central to the success of short-term programs.

Two sources of progestin are currently available for use in beef cattle. The synthetic progestin, norgestomet is provided in the SYNCRO-MATE-B® (SMB) program and the feed additive melengestrol acetate (MGA®) is also a commercially available progestin. The SMB program consists of a subcutaneous implant containing norgestomet placed in the ear for 9 days and an injection containing estradiol valerate and

norgestomet which is administered at the time the implant is inserted. The implant provides exposure to the progestin for 9 days and during this interval, the CL of females in the latter stages of the estrous cycle will regress spontaneously. The injection of estradiol valerate and norgestomet was designed to induce premature regression of the CL in females in the early stages of their estrous cycle (Kaltenbach et al., 1964). At the time of removal of the implant, this treatment regimen is intended to ensure that the CL has or is regressing in all females. Therefore, synchronous removal of the implant should result in a simultaneous decline in progestin concentrations and a highly synchronized estrus response.

In cyclic heifers, the incidence of estrus following the SMB treatment was 92.5% across 15 studies (reviewed by Odde, 1990). While the treatment is highly effective in this classification of females, the failure to synchronize estrus in 100% of these females was likely the result of stage of the cycle at the initiation of the treatment. This treatment effectively synchronized estrus in approximately 80% of heifers treated between days 1 to 8 of the estrous cycle (Miksch et al., 1978) and 48% of cows treated on day 3 of the estrous cycle (Pratt et al., 1991).

An important consideration for the use of progestins to synchronize estrus in comparison to $PGF_{2\alpha}$ alone is that it has been demonstrated that short-term progestin exposure will induce onset of estrous cycles in anestrous females. It has been reported that short-term exposure to either norgestomet or MGA in postpartum cows (Smith et al., 1979; Beal and Good, 1986; Anderson and Day, 1998; McDowell et al., 1998b) or prepubertal heifers (Anderson and Day, 1996; Imwalle et al., 1996; Hall et al., 1997) will induce the resumption or onset of estrous cycles in bovine females. The proportion of anestrous females that are induced to ovulate following progestin exposure has been reported to vary widely (from 0 to 66%, see **Induction of Estrous Cycles in Anestrous Females**, below) A clear benefit of progestin-based systems is the capacity induce a proportion of the anestrous females to initiate estrous cycles. This provides an opportunity to inseminate these animals during the synchrony period and reduces the duration of postpartum anestrus in cows and age at puberty in heifers.

The precision of the synchronized estrus with SMB is high, with a majority of animals in estrus 24 to 48 h after implant removal (Miksch et al., 1978; Spitzer et al., 1978). The precise timing of synchrony in cattle treated with SMB permits the use of timed breeding. In three separate experiments, timed insemination in heifers treated with SMB were higher than those of heifers bred based upon estrus detection (Mares et al., 1977; Miksch et al., 1978; Spitzer et al., 1978). The conception rates of cattle treated with SMB

were not significantly different from those of untreated control animals in a review of experiments with this product (Odde, 1990). It has been reported (Beal, 1995) however, that stage of cycle at the initiation of the SMB treatment will influence conception rate at the synchronized estrus. In cows treated in the early (day 1 to 6), middle (day 7 to 12) or late (> day 12) stages of the estrous cycle, conception rates were 71.4, 83.3 and 52.6%, respectively. An obvious explanation for the reduction in conception rates of cyclic cattle treated with SMB in the latter stages of the estrous cycle is not currently evident. In anestrous cows that are induced to ovulate with the SMB treatment, conception rates are lower than contemporaries within the herd that were cyclic a the start of treatment (60 and 44% for cyclic and anestrous cows, respectively). Since precocious initiation of estrous cycles is induced with this treatment, this difference in conception rate should not be surprising.

In summary, SMB can be used to synchronize estrus in a high proportion of cyclic females and induce onset of estrous cycles in varying proportions of anestrous cows or heifers. The precision of estrus is high and is adaptable to timed insemination protocols.

Combination Treatments of Progestins and $PGF_{2\alpha}$

A system of synchronization that was devised to emphasize the major advantages of both $PGF_{2\alpha}$ and progestins for synchronization of estrus is increasingly being used for estrous control in yearling heifers. This system involves the feeding of MGA for 14 days and injection of a luteolytic dose of $PGF_{2\alpha}$ administered 17 days after the last feeding of MGA (MGA - PGF; Brown et al., 1988). Feeding of the orally active progestin MGA, for 14 days, synchronizes estrus in cyclic females and induces initiation of estrous cycles in some anestrous females. The ensuing estrus occurs during the 7 days following the last day of MGA feeding (Patterson et al., 1989; Odde, 1990; King and Odde, 1993) and is of low fertility as a result of extended progestin treatment; females are not bred at this estrus. The injection of $PGF_{2\alpha}$ is given 17 days after the last feeding of MGA (approximately 10 to 16 days after the infertile estrus) when a majority of females are in the last half of their estrous cycle. As a result, the efficacy of $PGF_{2\alpha}$ for luteal regression is high and the $PGF_{2\alpha}$ - induced estrus is of optimal fertility. With this combination, the capacity of progestins to induce onset of and synchronize estrus is used in order to group females in a stage of the estrous cycle at which $PGF_{2\alpha}$ is of greatest efficacy.

The proportion of yearling heifers that exhibit estrus in response to the MGA-PGF system has been reported to range from 71 to 83% (Brown et al., 1988; Patterson et al., 1990; Beal et al., 1998). Conception rates of females inseminated based upon detection of

heat at an estrus synchronized with the MGA-PGF system are equal to or greater than those achieved with insemination at a spontaneous estrus or following administration of $PGF_{2\alpha}$ alone (Beal, 1995). Since a majority of females are in the second half of their estrous cycle at the time of $PGF_{2\alpha}$ administration with the MGA-PGF system, the precision of estrus is generally higher than that achieved with $PGF_{2\alpha}$ alone. However, results of experiments in which timed insemination has been used with the MGA-PGF system have been variable (Larson et al., 1992; Peters et al., 1993; King et al., 1994) and a single, set-timed insemination protocol that repeatedly results in high conception rates may be difficult to achieve with this program.

The utility of the MGA-PGF system in postpartum cows has been tested with varying degrees of success (Patterson et al., 1990; Yelich et al., 1995a, 1995b; Patterson et al., 1995). The extended duration of this treatment protocol (approximately 34 days from the initiation of MGA feeding to the synchronized estrus) limits the utility of this approach for postpartum cow herds. For example, in order to maintain a consistent start date for the breeding season, only cows that calved in approximately the first 40 days of the preceding calving season would be eligible for this treatment. These females are the least likely to be anestrous at the onset of breeding season and require the range of benefits provided by the MGA-PGF system. One could propose that this may be an excellent system to use on anestrous first-calf heifers that calved early in the season. However, it should be noted that a 15% increase in twinning has been reported with this system in postpartum cows (Patterson et al., 1995).

In summary, the MGA-PGF system is predominantly applicable for synchronized mating of yearling heifers using estrous detection. The MGA-PGF system is effective in both cyclic and many prepubertal heifers and has been demonstrated to yield relatively high estrous responses that are reasonably precise and of normal fertility. Use of this system to synchronize estrus in heifers has increased considerably during the past 5 years. The extended duration of the MGA-PGF treatment requires preplanning and limits its utility for postpartum cows.

Summary of Existing Estrous Control Systems

The systems described above, along with several variations not described, have been available for use in beef cattle for several years. These programs were developed primarily to provide for the requirement that a synchronous decline in progesterone (or exogenous progestin) occurs in all animals as a result of luteal regression and/or withdrawal of the progestin source. The progestin-based systems have also provided some degree of stimulus to the reproductive system of anestrous females to induce initiation of estrous cycles; in part fulfilling this physiological requirement for an estrous control system.

Recent Developments in Estrous Control

New Advances in Estrous Control

With the advent of increased understanding of reproductive physiology in the cow, additional requirements for estrous control systems have been created and our capacity to fulfill existing requirements has increased. First, as a result of the enhanced understanding of how ovarian follicles grow in cattle, the requirement that estrous control systems provide a mechanism to manage ovarian follicular growth has become apparent. The development of various methods to regulate follicles for estrous control has contributed greatly to our capacity to meet this requirement. Secondly, recent advancements in the development and understanding of methods to induce initiation of estrous cycles in anestrous females have allowed the design of systems which provide a more powerful ovulatory stimulus to anestrous cows. These advances have been incorporated into recently developed systems that are currently used in practice and are central components of future systems being investigated.

Management of Follicular Growth

Management of follicular growth, or follicle programming, is a critical component of estrous control systems. In the absence of follicle programming, wide variation in stage of follicular growth at the time of induced luteal regression or withdrawal of a progestin is responsible for much of the variation observed in interval to estrus. Use of methods to program follicular growth will standardize the stage of follicular growth among cows and can potentially increase the precision of a synchronized estrus (Thatcher et al., 1989; Twagiramungu et al., 1992a, 1992b). Of even greater importance, if follicle growth is programmed and a uniform population of dominant follicles is obtained within a group of females, tools exist to induce the pre-ovulatory surge of LH, estrus and/or ovulation within a narrow window of time (Pursley et al., 1995; Day et al., 1997) and augment the development of timed breeding programs. Finally, the benefits of short-term progestin administration to induce onset of estrous cycles in anestrous females have not been fully utilized due to reduced fertility associated with their use. The reduced fertility associated with progestin use has been traced in most cases to abnormal follicular growth which results in formation of persistent follicles (Sanchez et al., 1993; Mihm et al., 1994; Anderson et al., 1995).

Follicle programming prevents ovulation of persistent follicles and permit capture of the advantages that short-term progestin administration provides to both anestrous and cyclic females (Anderson and Day, 1994; Stevenson *et al.*, 1997; McDowell *et al.*, 1998b; Anderson and Day, 1998).

The key goal of follicle programming is to develop a means to coordinate the emergence and growth of a new wave of follicles in all females. This can be achieved through a variety of approaches. A method we have used is to promote the development of persistent follicles in all cows and induce synchronous atresia of this structure with administration of a progesterone bolus (Anderson and Day, 1994; Anderson and Day, 1998; McDowell *et al.*, 1998a; 1998b). This approach leads to synchronous emergence of a new wave of follicles and is an effective means to program follicles, synchronize estrus and utilize the advantages of progestin administration. The minimum duration of treatment with a progestin necessary to structure an estrous control system of this nature is approximately 14 days.

An alternative to using synchronous atresia of persistent follicles to program emergence and growth of the subsequent wave of follicles is to administer a treatment that induces regression and/or ovulation of antral follicles in the ovary. Through removal of the existing follicle population, the emergence of a new wave of follicles 2 to 4 days later is achieved. The primary agents that have been used for this purpose are GnRH (Thatcher *et al.*, 1993; Pursley *et al.*, 1995) and estradiol or estradiol/progestin combinations (Bo *et al.*, 1995; Bo *et al.*, 1996; Burke *et al.*, 1997a; 1997b, Caccia and Bo, 1998). This approach has been incorporated into systems that are discussed below.

Induction of Estrous Cycles in Anestrous Cows

In beef cattle, the single factor that most dramatically influences the success of an estrous control system is often the relative proportions of cyclic and anestrous cows present at the time of treatment. In most herds, it is not practical to make this determination before the onset of treatments, therefore the relative success or failure of a given approach is often determined after the fact.

Short - term progestin exposure has been reported to induce the onset of estrous cycles in 0 to 66% of anestrous cows (Miksch *et al.*, 1978; Smith *et al.*, 1979; Beal and Good, 1986; Macmillan and Day, 1987; Jubb *et al.*, 1989; Kyle *et al.*, 1992; Macmillan *et al.*, 1994; Anderson and Day, 1994; Stevenson and Pursley, 1994; Macmillan *et al.*, 1995; McMillan *et al.*, 1995; Yelich *et al.*, 1995a and 1995b; Fike *et al.*, 1997; Anderson and Day, 1998; McDowell *et al.*, 1998b). In herds with large numbers of anestrous females, the response to short - term progestin exposure could have a major impact upon the overall success of the synchronization program.

Many factors such as duration of progestin exposure, type of progestin and production system may impact the proportion of cows induced to initiate estrous cycles. However, it is likely that the primary variable that controls the degree of response is the time interval in relation to spontaneous onset of estrous cycles at which the progestin treatment is administered. In other words, progestin exposure will be more effective in cows that are nearing the time of spontaneous onset of estrous cycles whereas in cows not expected to spontaneously ovulate for several weeks, the response will be less. This relationship can be more clearly demonstrated in considering reports regarding the induction of puberty in heifers with short-term progestin exposure. As prepubertal heifers age, or, in other words, the time of spontaneous puberty nears, the efficacy of short-term progestin exposure to induce precocious puberty is increased substantially (Hall *et al.*, 1997). Consideration of many of the reports on this topic suggests that at 9-11 months of age, responses to progestin exposure are variable, ranging from 12 to 89% whereas after 12 months of age, puberty is induced in a majority of heifers (Gonzalez-Padilla *et al.*, 1975; Short *et al.*, 1976; Burfening, 1979; Beal *et al.*, 1984; Patterson *et al.*, 1992; Tanaka *et al.*, 1995; Anderson *et al.*, 1996; Hall *et al.*, 1997).

It has been demonstrated that the proportion of cows that initiate estrous cycles after progestin exposure can be increased with separation of the calf from the cow for 24 to 72 hours (short - term calf removal; Smith and Vincent, 1972; Smith *et al.*, 1979; Kiser *et al.*, 1980). Thus, the addition of a second stimulus, after a period of progestin exposure is an approach to increase the efficacy of short - term progestin treatment. This method is used in the field by some producers.

Alternative methods to the use of short - term calf removal have been or are being developed to provide a stimulus following progestin exposure which both increases the proportion of anestrous females that initiate estrous cycles and the precision of the synchronized estrus and/or ovulation. Development of these methods has been possible as a result of the ability to program follicular growth, ensuring that follicles capable of responding to an exogenous ovulatory stimulus are present at the time it is delivered. The two primary factors that have been investigated for synchronization of ovulation are GnRH and estradiol. It has been demonstrated that treatment with estradiol after short - term progestin exposure increases the incidence of induced ovulation and estrus in anestrous postpartum cows (McDougall *et al.*, 1992; Macmillan *et al.*, 1995; Fike *et al.*, 1997). The combination of GnRH following short - term progestin exposure increased pregnancy rates of postpartum cows (Stevenson *et al.*, 1997) as compared to cows receiving two injections of $PGF_{2\alpha}$.

GnRH - Based Systems

As a result of the ability to program growth of ovarian follicles with GnRH (for review, see Twagiramungu *et al.*, 1995) several programs of estrous control have recently been developed for beef cattle using GnRH. The central components of essentially all GnRH - based systems of estrous control include administration of GnRH (or an analogue) followed 6 or 7 days later with $PGF_{2\alpha}$ (GnRH-PGF). Administration of GnRH results in synchronous emergence of a new wave of follicular growth 2 to 4 days later and regression of corpora lutea on days 6 or 7 permits initiation of the follicular phase. Since a majority of follicles are in a standard stage of development at the time of luteal regression, the precision of the synchronized estrus is increased (Thatcher *et al.*, 1989; Twagiramungu *et al.*, 1992a, 1992b).

The base GnRH-PGF system and several modifications of this system are currently being used and/or investigated for synchronization of estrus in beef cattle. The GnRH-PGF system enhanced synchronization rate by approximately 13% as compared to females receiving only $PGF_{2\alpha}$ (Forbes *et al.*, 1997a) while others have reported no difference between these treatments (Geary *et al.*, 1997). We have detected a non-significant increase (P = .16) of 27% in synchronization rate with the GnRH - PGF system (Anderson and Day, unpublished). Conception rates of cows in which estrus was synchronized with a GnRH - PGF system have been similar to a spontaneous estrus or to an estrus synchronized with $PGF_{2\alpha}$ alone (Twagiramungu *et al.*, 1992a, 1992b; Anderson and Day, unpublished; Forbes *et al.*, 1997a; Geary *et al.*, 1997). Increased precision of estrus often accompanies the use of the GnRH - PGF system as compared to $PGF_{2\alpha}$ - based systems (Twagiramungu *et al.*, 1992b; Anderson and Day, unpublished observations; Forbes *et al.*, 1997b). Pregnancy rates for the GnRH - PGF system as compared to $PGF_{2\alpha}$ - based systems during the synchrony period have been reported to not differ (76 vs. 70%, respectively, Twagiramungu, 1992b; 51 vs. 42%, respectively, Geary *et al.*, 1997; 53 vs. 38%, respectively, Anderson and Day, unpublished) or to be significantly enhanced (39 vs. 28.5%, respectively, P< .05; Forbes *et al.*, 1997a). Generally, the GnRH - PGF system may increase synchronization rate, the synchronized estrus is of normal fertility and pregnancy rates during the synchrony period may be enhanced as compared to $PGF_{2\alpha}$ - based systems.

One mechanism by which the GnRH - PGF system may increase synchronization rate as compared to $PGF_{2\alpha}$ - based systems is through induction of reinitiation of estrous cycles in some anestrous cows. We have demonstrated that the GnRH - PGF system induced precocious reinitiation of estrous cycles in approximately 25% of anestrous postpartum cows

(Anderson and Day, unpublished) and others (Forbes *et al.*, 1997a) reported an increased incidence of estrus in 14.5% of anestrous cows receiving the GnRH-PGF treatment. The increased synchronization rate that often accompanies the use of the GnRH-PGF treatment is likely the result of the increased incidence of synchronized estrus that occurs in anestrous females (Forbes *et al.*, 1997b; Anderson and Day, unpublished).

In order to increase the effectiveness of this approach in anestrous cows, one modification that has been evaluated is the addition of a progestin during the interval between the GnRH and $PGF_{2\alpha}$ injection (GnRH-P-PGF). Use of a norgestomet implant as the source of progestin in this modified system increased the synchronization rate by approximately 11% and the incidence of synchronized estrus in anestrous cows by approximately 21% as compared to the GnRH-PGF system (Forbes *et al.*, 1997a, 1997b). In the same experiment however, pregnancy rates were not significantly different between the GnRH-PGF system and the GnRH-P-PGF system (41.6 vs. 39%, respectively; Forbes *et al.*, 1997a). Inclusion of a norgestomet implant in the GnRH-P-GnRH system increased synchronization rate and induction of estrus in anestrous cows but only marginally affected pregnancy rates during the synchrony period as compared to the GnRH-PGF system.

Another modification to the GnRH-PGF and GnRH-P-PGF system has been the addition of a second GnRH injection at 48 h after the $PGF_{2\alpha}$ injection (+GnRH). The purpose of the +GnRH treatment is to induce an LH surge and ovulation of follicles that have been programmed by the preceding treatments. This approach can result in a highly synchronous time of ovulation within an 8 hour window (Pursley *et al.*, 1995). The addition of the +GnRH treatment is attractive from the standpoint that it may permit timed AI in postpartum beef cows. The GnRH-P-PGF+GnRH treatment increased pregnancy rates by 12.1% as compared to a $PGF_{2\alpha}$ - based system (Stevenson *et al.*, 1997).

The efficacy of GnRH-P-PGF and the GnRH-P-PGF+GnRH have been directly compared. (Thompson *et al.*, 1997). Cows in GnRH-P-PGF treatment were inseminated on detection of estrus while cows in the +GnRH treatment were inseminated if estrus was detected within 48 hours of PGF and the majority (81%) inseminated on a timed basis at 16 hours after the +GnRH treatment. Pregnancy rates during the synchrony period did not differ among treatments (54 vs. 59%, respectively) indicating that the +GnRH modification is an effective approach to permit timed insemination in most cows which have been pretreated with GnRH-P-PGF treatment.

The interval from the +GnRH treatment to insemination has been investigated. While the current recommendation in dairy cattle is to breed 16 hours af-

ter the +GnRH treatment, in beef herds this necessitates another pass through the chute at an interval that is inconvenient for most producers. The effects of timed insemination coincident with the +GnRH treatment or 24 hours later on conception rate for a GnRH-PGF+GnRH system has been reported (Geary et al., 1997). Pregnancy rates to timed insemination averaged 48% and did not differ among cows bred coincident with the +GnRH treatment or 24 hours later.

In summary, the use of the GnRH-PGF - based systems of estrous control present some promising options for improved methods of estrous synchronization and timed insemination systems in beef cattle. Increased synchronization rates and pregnancy rates and normal fertility at the synchronized estrus are clearly evident in some studies. Furthermore, many of the systems developed provide some convenience benefits in cattle handling and heat detection. Most of the GnRH-PGF systems have the capacity to induce reinitiation of estrous cycles in some anestrous females and the addition of a progestin enhances this effect. Although the range of efficacy has not been clearly defined, it appears that the GnRH-PGF treatment is capable of inducing estrus in approximately 20% of anestrous beef cows, and the inclusion of a progestin may increase this figure to approximately 40%. Fertility of the induced estrus in anestrous females appears to be approximately equal to that of a spontaneous estrus.

Estradiol + Progesterone - Based Systems

Systems of estrous control that include estradiol administered by injection, progesterone delivered intravaginally for 7 to 8 days with a Controlled Internal Drug Release-device for cattle (CIDR-B®, DEC - InterAg, Hamilton, NZ) and $PGF_{2\alpha}$ for luteal regression have been developed and are being investigated. The central components of this approach include: 1) Insertion of a CIDR device for 7 to 8 days which will aid in induction of estrous cycles in anestrous females upon removal (Fike et al., 1997) and provides sufficient progesterone to prevent occurrence of estrus; 2) an initial i.m. injection of estradiol (E, or an estradiol and progesterone combination) given with CIDR insertion which induces atresia of follicles in the ovaries at that time and results in programmed emergence of a new wave of follicular growth approximately 4 days later (Bo et al., 1995; Bo et al., 1996; Burke et al., 1997a; 1997b; Caccia and Bo, 1998); 3) An injection of $PGF_{2\alpha}$ (PGF) at the time the CIDR is removed to regress CL that are present; and 4) A second injection of estradiol (+E) given 24 to 48 hours after CIDR withdrawal to induce estrus and ovulation in anestrous cows (McDougall et al., 1992; Macmillan et al., 1995; Fike et al., 1997; Day et al., 1997) and to synchronize a precise estrus in both cyclic and

anestrous cows (Day et al., 1997; Martinez et al., 1998). This treatment sequence is represented as E-CIDR-PGF+E hereafter.

Only limited published information regarding this approach to estrous control is currently available in beef cattle. We (Day et al., 1997) have evaluated this approach to estrous control in seasonal dairy herds in New Zealand. The optimal E-CIDR-PGF+E system that was evaluated in cyclic cows included 2 mg of estradiol benzoate for the initial dose of estradiol a CIDR administered intravaginally for 7 days, $PGF_{2\alpha}$ at CIDR withdrawal and 1 mg of estradiol benzoate injected 48 hours after $PGF_{2\alpha}$. In one experiment (Day et al., 1997), cyclic cows received no treatment (Control, n=214) or the optimal E-CIDR-PGF+E treatment (n = 94). All anestrous cows (n=143) were identified prior to treatment and received a CIDR for 7 days with 1 mg of estradiol benzoate administered at 48 hours after CIDR withdrawal. In the Control treatment, 92% of the cyclic cows were in estrus during the first 21 days of the breeding season. In the E-CIDR-PGF+E treatment (cyclic cows) and anestrous cows, 98 and 92%, respectively, were in estrus during the first 4 days of the breeding season with greater that 85% of both anestrus and cyclic cows in heat within a 2 day period. Conception rates to first service did not differ among the Control and E-CIDR-PGF+E treatments (57 and 62% respectively) but were lower (P < .05) in the treated anestrous cows (40%). The mean number of days to conception was reduced (P < .05) from 23 days in the Control treatment to 13 days in the cyclic cows receiving the E-CIDR-PGF+E treatment. In the anestrous cows, the mean interval to conception was 22 days and not different from the cows in the Control treatment. Final pregnancy rates at the end of the breeding season were 92.5, 98.1 and 97.4 for the Control, E-CIDR-PGF+E and treated anestrous cows, respectively. Final pregnancy rate tended (P = .09) to be greater in the E-CIDR-PGF+E than in the Control treatment. These data indicate that systems of this nature can induce a highly precise and synchronous estrus in a high proportion of both cyclic and anestrous postpartum dairy cows. Fertility of the synchronized estrus in cyclic cows is equivalent to that at a spontaneous estrus in untreated cyclic cows. While the conception rate is reduced at the synchronized estrus in anestrous females treated with a CIDR and estradiol, the high incidence of induced estrus permitted these females to perform at a level equivalent to cyclic cows in terms of interval to conception and pregnancy rates.

Reproductive performance at a timed insemination in beef heifers treated with a E-CIDR-PGF+E system (n=41) was compared to that in heifers (n=42) which received a GnRH-P-PGF+GnRH treatment (Martinez et al., 1998). Synchronization rate (100 vs. 55%) and pregnancy rate during the synchrony period (76 vs. 48%)

were greater (P < .05) in the heifers receiving the E-CIDR-PGF+E than the GnRH-P-PGF+GnRH treatment, respectively. From this initial report, it appears that the E-CIDR-PGF+E may provide a valuable system for either timed insemination or insemination based upon estrus detection in beef cattle.

The technology used to structure the E-CIDR-PGF+E systems has existed for several years in many parts of the world, however the sequence of treatments being investigated are relatively new. While only limited published information is currently available to describe the potential of this system for estrous control in beef cattle, the available results from both beef and dairy cows are encouraging. The initial reports suggest that this approach will provide a highly synchronous estrus and ovulation in both cyclic and anestrous cows, it is adaptable to a timed insemination program, fertility of cyclic cows is not compromised by this treatment regimen and most anestrous females will be induced to ovulate and show estrus. Additional information will soon become available as systems of this nature are being investigated at present in both beef and dairy cattle.

In conclusion, a variety estrous control systems are currently available for use with beef cattle and the number of options will certainly increase in the next few years. It is as certain that no single approach to estrous control will be the appropriate choice for all production situations. Successful management of estrus for a given situation will depend upon choosing the appropriate approach for the specific circumstances. A continued increase in the understanding of the strengths and weaknesses of the available options and the manner in which they influence the reproductive system of female cattle will aid in this decision process. While no systems reviewed have yet been proven to meet the production goals established at the beginning of this paper, it is encouraging that attainment of these goals appears to be a distinct possibility in the near future.

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Abstract

Comparison of three treatments for bovine endometritis

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Veterinary Record (1998) **142**, 575-579

Three commercial preparations for the treatment of bovine endometritis were compared: an intrauterine infusion of 1500 mg oxytetracycline hydrochloride solution, an intramuscular injection of 500 µg cloprostenol (a synthetic analogue of prostaglandin $F_2\alpha$), and an intramuscular injection of 3 mg oestradiol benzoate/500 kg estimated bodyweight. A total of 300 cases of endometritis were treated, of which 225 involved first, 67 involved second, and eight involved third or subsequent treatments. The overall success rate of treatment was 68 per cent. Oxytetracycline was successful in 73 per cent of cases, cloprostenol in 67 per cent and oestradiol in 63 per cent of cases. There was no significant difference between the success rates of the treatments, except for cows with mild endometritis in which oxytetracycline was more successful than oestradol (86 v 66 per cent, P<0.05). Mild cases were treated more successfully than moderate cases (78 v 61 per cent, P<0.01), and more successfully than severe cases (78 v 44 per cent, P<0.001). Prostaglandin $F_2\alpha$ was more successful if the milk progesterone concentration was >7 ng/ml at the time of treatment (P<0.05). The presence of a smelly discharge at the time of treatment reduced the success rate by 17 per cent (P<0.02). The treatment to conception interval for all successful treatments of endometritis by prostaglandin $F_2\alpha$ was 18.1 days shorter than for oestradiol (68.3 v 86.4 days, P<0.02), and the interval for oxytetracycline was 16.2 days shorter than for oestradiol (70.2 v 86.4 days, P<0.05).