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REVIEW OF ESTRUS SYNCHRONIZATION SYSTEMS: MGA

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Introduction

The beef cattle industry has seen rapid gains in economically desirable traits largely due to the selection and expanded use of genetically proven, superior sires made available through artificial insemination (AI). Recent surveys indicate, however less than 5% of the beef cows in the United States are bred by AI, and only half of the cattle producers who practice AI use any form of estrus synchronization to facilitate their AI programs. The inability to predict time of estrus for individual cows or heifers in a group often makes it impractical to use AI because of the labor required for detection of estrus. Available procedures to control the estrous cycle of the cow can improve reproductive rates and speed up genetic progress. These procedures include synchronization of estrus in cycling females, and induction of estrus accompanied by ovulation in heifers that have not yet reached puberty or among cows that have not returned to estrus after calving.

The following protocols and terms will be referred to throughout this manuscript.

<u>*Protocols:*</u>

PG: Prostaglandin $F_{2\alpha}$ (PG; Lutalyse, Estrumate, ProstaMate, InSynch).

MGA-PG: Melengestrol acetate (MGA; .5 mg/hd/day) is fed for a period of 14 days with PG administered 17 to 19 days after MGA withdrawal.

GnRH-PG (Select Synch): Gonadotropin-releasing hormone injection (GnRH; Cystorelin, Factrel, Fertagyl, OvaCyst) followed in 7 days with an injection of PG.

MGA-GnRH-PG (MGA® Select): MGA is fed for 14 days, GnRH is administered 12 days after MGA withdrawal, and PG is administered 7 days after GnRH.

7-11 Synch: MGA is fed for 7 days, PG is administered on the last day MGA is fed, GnRH is administered 4 days after the cessation of MGA, and a second injection of PG is administered 11 days after MGA withdrawal.

<u>*MGA-based protocols for fixed-time AI:*</u>

MGA® Select + fixed-time AI: MGA is fed for 14 days, GnRH is administered 12 days after MGAwithdrawal, and PG is administered 7 days after GnRH. Insemination is performed 72 hours after PG with GnRH administered at AI.

7-11 Synch+ fixed-time AI: MGA is fed for 7 days, PG is administered on the last day MGA is fed, GnRH is administered 4 days after the cessation of MGA, and a second injection of PG is administered 11 days after MGA withdrawal. Insemination is performed 60 hours after PG with GnRH administered at AI.

Terms:
Estrous response: The number of females that exhibit estrus during a synchronized period.
Synchronized period: The period of time during which estrus is expressed after treatment.
Synchronized conception rate: The proportion of females that becomes pregnant of those exhibiting estrus and inseminated during the synchronized period.
Synchronized pregnancy rate: Proportion of females that become pregnant of the total number treated.

There are several advantages to a successful estrus synchronization program. These include 1) cows or heifers are in estrus during a predictable interval, which allows for artificial insemination, embryo transfer or other planned reproductive techniques; 2) the time required to detect estrus is reduced, which in turn decreases labor expense associated with the breeding program; 3) cattle will conceive earlier during the breeding period; and 4) calves will be older and heavier at weaning.

To avoid problems when using estrus synchronization, females should be selected for a program when the following conditions are met 1) adequate time has elapsed from calving and the time synchronization treatments are implemented (a minimum of 40 days postpartum at the beginning of treatment is suggested); 2) cows are in average or above-average body condition (scores of at least 5 on a scale of 1 to 9); 3) cows experience minimal calving problems; 4) replacement heifers are developed to prebreeding target weights that represent at least 65 percent of their projected mature weight; and 5) reproductive tract scores (RTS) are assigned to heifers no more than two weeks before a synchronization treatment begins (scores of 3 or higher on a scale of 1 to 5) and at least 50% of the heifers are assigned a RTS of 4 or 5 (Patterson et al., 2000a).

Development of Methods to Synchronize Estrus

The development of methods to control the estrous cycle of the cow has occurred in six distinct phases. The physiological basis for estrus synchronization followed the discovery that progesterone inhibited ovulation (Ulberg et al., 1951) and preovulatory follicular maturation (Nellor and Cole, 1956; Hansel et al., 1961; Lamond, 1964). Regulation of estrous cycles was believed to be associated with control of the corpus luteum, whose life span and secretory activity are regulated by trophic and lytic mechanisms (Thimonier et al., 1975; Patterson et al., 2003). The Progesterone Phase included efforts to prolong the luteal phase of the estrous cycle or to establish an artificial luteal phase by administering exogenous progesterone. Later, progestational agents were combined with estrogens or gonadotropins in the Progesterone–Estrogen Phase. Prostaglandin $F_{2\alpha}$ and its analogs were reported in 1972 to be luteolytic in the bovine (Lauderdale, 1972; Rowson et al., 1972; Liehr et al., 1972; Lauderdale et al., 1974) and ushered in the PG Phase. Treatments that combined progestational agents with PG characterized the Progestogen-PG Phase. All of these protocols addressed control of the luteal phase of the estrous cycle since folliclular waves were not recognized at the time.

Precise monitoring of ovarian follicles and corpora lutea over time by transrectal ultrasonography expanded our understanding of the bovine estrous cycle and particularly the change that occurs during a follicular wave (Fortune et al., 1988). Growth of follicles in cattle occurs in distinct wave-like patterns, with new follicular waves occurring approximately every 10 days (6-15 day range). We now know precise control of estrous cycles requires the manipulation of both follicular waves and luteal lifespan (GnRH-PG Phase).

A single injection of gonadotropin-releasing hormone (GnRH) to cows at random stages of their estrous cycles causes release of luteinizing hormone leading to synchronized ovulation or luteinization of most large dominant follicles (≥ 10 mm; Garverick et al., 1980; Bao and Garverick, 1998; Sartori et al., 2001). Consequently, a new follicular wave is initiated in all cows within 2 to 3 days of GnRH administration. Luteal tissue that forms after GnRH administration is capable of undergoing PG-induced luteolysis 6 or 7 days later (Twagiramungu et al., 1995). The GnRH-PG protocol increased estrus synchronization rate in beef (Twagiramungu et al., 1992a,b) and dairy (Thatcher et al., 1993) cattle. A drawback of this method, however, is approximately 5 to 15% of the cows are detected in estrus on or before the day of PG injection, thus reducing the proportion of females detected in estrus and inseminated during the synchronized period (Kojima et al., 2000). This information stimulated research in the Progestogen-GnRH-PG Phase.

Synchronization of Estrus and Ovulation with the GnRH-PG-GnRH Protocol

Administration of PG alone is commonly utilized to synchronize an ovulatory estrus in estrous cycling cows. However, this method is ineffective in anestrous females and variation among animals in the stage of the follicular wave at the time of PG injection directly contributes to the variation in onset of estrus during the synchronized period (Macmillan and Henderson, 1984; Sirois and Fortune, 1988). Consequently, the GnRH-PG-GnRH protocol was developed to synchronize follicular waves and timing of ovulation. The GnRH-PG-GnRH protocol (Figure 1) for fixed-time AI results in development of a preovulatory follicle that ovulates in response to a second GnRH-induced LH surge 48 hours after PG injection (Ovsynch; Pursely et al., 1995). Ovsynch was validated as a reliable means of synchronizing ovulation for fixed-time AI in lactating dairy cows (Pursley et al., 1995; Burke et al., 1996; Pursley et al., 1997a,b; Schmitt et al., 1996). Time of ovulation with Ovsynch occurs between 24 to 32 hours after the second GnRH injection and is synchronized in 87 to 100% of lactating dairy cows (Pursley et al., 1997a). Pregnancy rates among cows inseminated at a fixed time following Ovsynch ranged from 32 to 45% (Pursley et al., 1997b; 1998). The Ovsynch protocol, however, did not effectively synchronize estrus and ovulation in dairy heifers (35% pregnancy rate compared with 74% in PG contols; Pursley et al., 1997b).

Protocols for fixed-time insemination were recently tested in postpartum beef cows. Pregnancy rates for Ovsynch treated beef cows were compared with those of cows synchronized and inseminated at a fixed time following treatment with Syncro-Mate-B (Geary et al., 1998a). Calves in both treatment groups were removed from their dams for a period of 48 hours beginning either at the time of implant removal (Syncro-Mate-B) or at the time PG was administered (Ovsynch). Pregnancy rates following fixed-time AI after Ovsynch (54%) were higher than for Syncro-Mate-B (42%) treated cows. One should note on the day following fixed-time insemination, cows were exposed to fertile bulls of the same breed; no attempt was made to determine progeny paternity. Additionally, we do not know the incidence of short cycles among cows anestrus prior to treatment and perhaps returned to estrus prematurely and became pregnant to natural service.

Recently, variations of the Ovsynch protocol (CO-Synch and Select Synch) were tested in postpartum beef cows (Figure 1). It is important to understand treatment variations of Ovsynch currently being used in postpartum beef cows have not undergone the same validation process Ovsynch underwent in lactating dairy cows. At this point we do not know whether response in postpartum beef cows to the protocols outlined in Figure 1 is the same or different from lactating dairy cows due to potential differences in follicular wave patterns. Differences in specific response variables may include a) the relative length of time to ovulation from the second GnRH injection, b) the anticipated range in timing of ovulation, and c) the degree of ovulation synchrony that occurs.

Two variations from Ovsynch being used most extensively in postpartum beef cows are currently referred to as CO-Synch and Select Synch. CO-Synch (Geary et al., 1998b) is similar to Ovsynch in that timing and sequence of injections are the same and all cows are inseminated at a fixed time. CO-Synch differs from Ovsynch, however, in that cows are inseminated when the second GnRH injection is administered, compared to the recommended 16 hours after GnRH for Ovsynch treated cows. Select Synch (Geary et al., 2000) differs too, in that cows do not receive the second injection of GnRH and are not inseminated at a fixed time. Cows synchronized with this protocol are inseminated 12 hours after detected estrus. It is currently recommended for Select Synch treated cows that detection of estrus begin as early as 4 days after GnRH injection and continue through 6 days after PG (Kojima et al., 2000). Select Synch, similar to Ovsynch, was less effective than the melengestrol acetate (MGA)-PG protocol in synchronizing estrus in beef heifers (Stevenson et al., 1999).

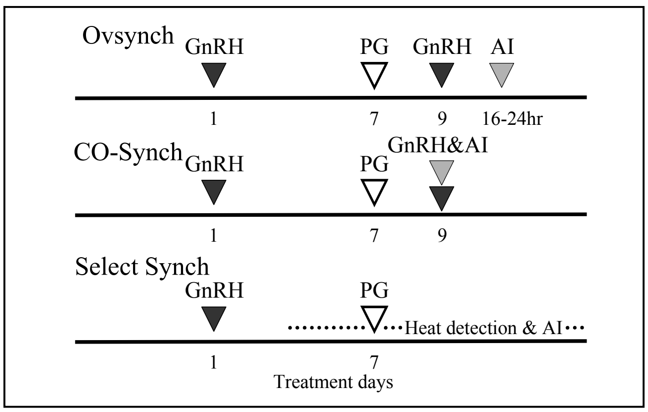

Figure 1. Methods currently being used to synchronize ovulation in postpartum beef cows: Ovsynch, CO-Synch and Select Synch.

The MGA Program

This manuscript reviews methods to control estrous cycles of cows or heifers using MGA in breeding programs involving natural service or artificial insemination. Four methods will be outlined for using the melengestrol acetate (MGA®Premix, Pfizer Animal Health, New York, NY) program to facilitate estrus synchronization in beef heifers or cows. The choice of which system to use depends largely on a producer's goals. Melengestrol acetate is the common denominator in each of the systems presented here. MGA is an orally active progestin. When consumed by cows or heifers on a daily basis, MGA will suppress estrus and prevent ovulation (Imwalle et al., 2002). MGA may be fed with a grain or a protein carrier and either top-dressed onto other feed or batch mixed with larger quantities of feed. MGA is fed at a rate of 0.5 mg/animal/day. The duration of feeding may vary between protocols, but the level of feeding is consistent and critical to success. Animals that fail to consume the required amount of MGA on a daily basis may prematurely return to estrus during the feeding period. This can be expected to reduce the synchronization response. Therefore, adequate bunk space must be available so all animals consume feed simultaneously.

Animals should be observed for behavioral signs of estrus each day of the feeding period. This may be done as animals approach the feeding area and before feed distribution. This practice will ensure all females receive adequate intake. Cows and heifers will exhibit estrus beginning 48 hours after MGA withdrawal, and this will continue for 6 to 7 days. It is generally recommended females exhibiting estrus during this period not be inseminated or exposed for natural service because of the reduced fertility females experience at the first heat after MGA withdrawal.

Method 1: MGA with Natural Service

The simplest method involves using bulls to breed synchronized groups of females. This practice is especially useful in helping producers make a transition from natural service to artificial insemination. In this process, cows or heifers receive the normal 14-day feeding period of MGA and are then exposed to fertile bulls about 10 days after MGA withdrawal (Figure 2).

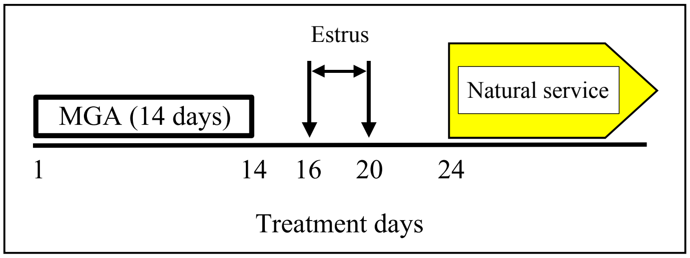

Figure 2. MGA and natural service (adapted from Patterson et al., 2000b).

This system works effectively, however, careful attention to bull to female ratios should be observed. It is recommended that 15 to 20 synchronized females be exposed per bull. Age and breeding condition of the bull and results of breeding soundness examinations should be considered carefully.

Method 2: MGA + Prostaglandin

A more precise means of estrous cycle control involves the combination of MGA with prostaglandin $F_{2\alpha}$. Prostaglandin $F_{2\alpha}$ (PG) is a luteolytic compound normally secreted by the uterus of the cow. PG can induce luteal regression but cannot inhibit ovulation. When PG is administered in the presence of a functional corpus luteum (CL) during days 6 to 16 of the estrous cycle, premature regression of the CL begins and the cow returns to estrus.

In this program, prostaglandin should be administered 19 days after the last day of MGA feeding. This treatment places all animals in the late luteal stage of the estrous cycle at the time of injection, which shortens the synchronized period and maximizes conception rate (Figure 3). Although a 19-day interval is optimal, 17- to 19-day intervals produce acceptable results and provide flexibility for extenuating circumstances (Brown et al., 1988; Deutscher, 2000; Lamb et al., 2000). Four available PG products for synchronization of estrus in cattle can be used after the MGA treatment: Lutalyse®, ProstaMate®, InSynch®, or Estrumate®. Label-approved dosages differ with each of these products; carefully read and follow directions for proper administration before their use.

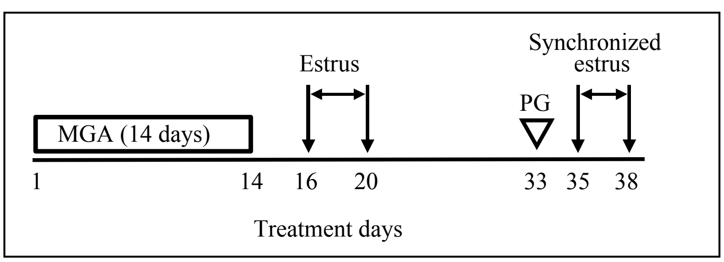

Figure 3. The MGA-PG protocol (adapted from Brown et al., 1988; Deutscher, 2000; Lamb et al., 2000).

Figure 4 (Patterson et al., 2000b) illustrates the distribution of estrus comparing the MGA-PG system to an MGA-only system. The combined MGA-PG system is best suited for use with AI programs because of the high degree of synchrony that can be achieved, which decreases the amount of time required for detection of estrus. Under natural mating conditions there may be an advantage to distribute estrus over several additional days to prevent overworking of bulls used in these programs.

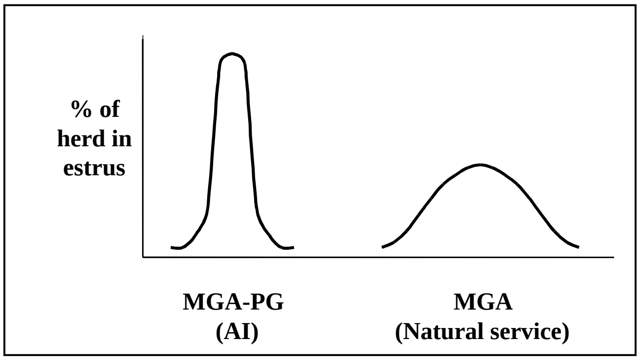

Figure 4. Distribution of estrus comparing the MGA-PG system to an MGA-only system (adapted from Patterson et al., 2000b).

Table 1 provides a summary of field trials involving heifers where MGA was used in conjunction with natural service or MGA-PG was used prior to AI (Patterson et al., 2000b). One of the major advantages in using MGA to control estrous cycles of cattle, as seen from the data presented in Table 1, is the flexibility in matching specific synchronization protocols with the particular management system involved.

Table 1. Summary of estrus synchronization field trials using MGA prior to natural service or MGA-PG prior to AI (Patterson et al., 2000b).

Breeding program	Number of heifers	Estrous response No.	Estrous response %	Synchronized conception rate No.	Synchronized conception rate %	Synchronized pregnancy rate No.	Synchronized pregnancy rate %
Natural service	1749	--------		--------		1151/1749	66
AI	4245	3354/4245	79	2414/3354	72	2414/4245	57

Method 3: MGA® Select

The MGA® Select treatment (Wood et al., 2001; Figure 5) is useful in maximizing estrous response and reproductive performance in postpartum beef cows. The MGA® Select protocol is a simple program that involves feeding MGA for 14 days followed by an injection of GnRH on day 26 and an injection of PG on day 33. The addition of GnRH to the 14-19 day MGA-PG protocol improves synchrony of estrus, while maintaining high fertility in postpartum beef cows.

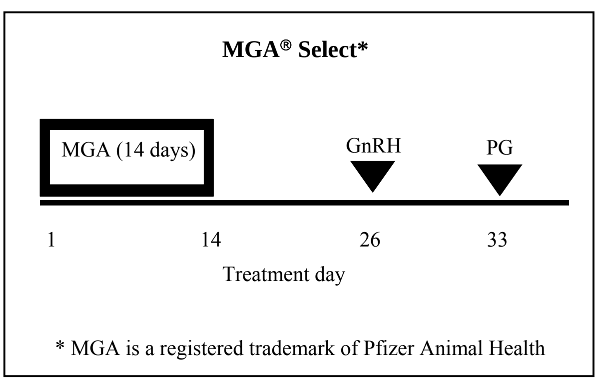

Figure 5. The MGA® Select protocol (Wood et al., 2001). MGA is fed for a period of 14 days followed in 12 days (day 26) by an injection of GnRH, and PG 19 days after MGA withdrawal (day 33).

We conducted experiments during the spring 2000 and 2001 breeding season to compare the 14-19 day MGA-PG protocol with or without the addition of GnRH on day 12 after MGA withdrawal and 7 days prior to PG in postpartum suckled beef cows (Patterson et al., 2001; Figure 6).

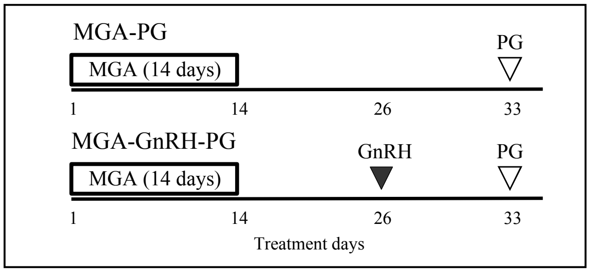

Figure 6. Cows were fed MGA for 14 days; 19 days after MGA withdrawal PG was administered to all cows. GnRH was administered to ½ of the cows 7 days prior to PG (Patterson et al., 2001).

The following tables provide a summary of the results from the study conducted during the 2001 breeding season. Table 2 provides a summary of the number of cows within age group by treatment, the average number of days postpartum and body condition score on the first day of MGA feeding, and the percentage of cows cycling prior to the treatment with MGA began. Cyclicity status was determined based on two blood samples for progesterone obtained 10 days before and on the first day of MGA.

Table 2. Number of cows within age group per treatment, days postpartum, body condition and cyclicity status at the time treatment with MGA began[1] (Patterson et al., 2002).

Treatment	Age group (yrs)	No.of cows	Days postpartum	Body condition score	Cycling (%)
MGA-PG	2, 3 & 4	52	47	5.2	35
	5+	48	39	5.2	15
	Total	100	44	5.2	40
MGA-GnRH-PG	2, 3 & 4	53	47	5.3	38
	5+	48	40	5.3	13
	Total	101	44	5.3	53

[1]Average number of days postpartum on the day treatment with MGA began. Body condition scores were assigned one day prior to the day treatment with MGA was initiated using a scale 1 = emaciated to 9 = obese. Cyclicity was determined from 2 blood samples for progesterone obtained 10 days and 1 day prior to the day treatment with MGA was initiated.

Table 3 provides a summary of estrous response, synchronized conception and pregnancy, and final pregnancy rates for cows assigned to the two treatments. Estrous response was significantly higher among MGA®Select treated cows compared with the MGA-PG treated cows. Synchronized pregnancy rates were higher among the 5-year-old and older cows assigned to the MGA®Select treatment.

Table 3. Estrous response, synchronized conception and pregnancy rate, and final pregnancy rate at the end of the breeding period (Patterson et al., 2002). [a,b]Percentages within column and category with unlike superscripts are different (P<.05).

Treatment	Age group (yrs)	Estrous response (no.)	Estrous response (%)	Synchronized conception rate (no.)	Synchronized conception rate (%)	Synchronized pregnancy rate (no.)	Synchronized pregnancy rate (%)	Final pregnancy (no.)	Final pregnancy (%)
MGA-PG	2, 3 & 4	44/52	85	36/44	82	36/52	69	49/52	94
	5+	32/48	67	22/32	69	22/48	46 [a]	48/48	100
	Total	76/100	76[a]	58/76	76	58/100	58	97/100	97
MGA-GnRH-PG	2, 3 & 4	46/53	87	33/46	72	33/53	62	51/53	96
	5+	42/48	88	34/42	81	34/48	71 [b]	47/48	98
	Total	88/101	87 [b]	67/88	76	67/101	66	98/101	97

Method 4: 7-11 Synch

We developed an estrus synchronization protocol for beef cattle designed to shorten the feeding period of MGA without compromising fertility, and improve synchrony of estrus by synchronizing development and ovulation of follicles from the first wave of development (Figure 7A; Kojima et al., 2000). This treatment, 7-11 Synch, was compared with the GnRH-PG protocol. Synchrony of estrus during the 24-hour peak response period (42 to 66-hour) was significantly higher among 7-11 Synch treated cows. Furthermore, the distribution of estrus was reduced from 144 hours for GnRH-PG treated cows to 60 hours for cows assigned to the 7-11 Synch treatment (Figure 7B; Kojima et al., 2000). The 7-11 Synch protocol resulted in a higher degree of estrus synchrony (91%) and greater AI pregnancy rate (68%) during a 24-hour peak response period compared to the GnRH-PG protocol (69% and 47%, respectively).

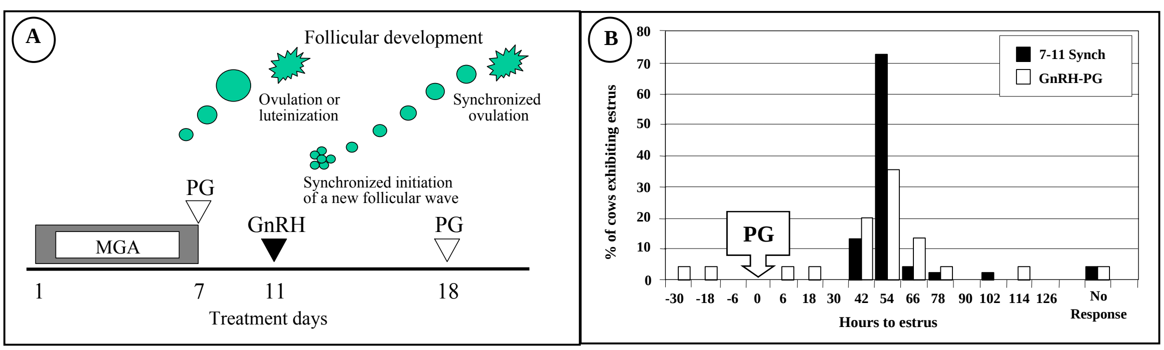

Figure 7A. Illustration of the treatment schedule and events associated with the 7-11 Synch protocol (Kojima et al., 2000). **Figure 7B.** Estrus response of cows treated with the 7-11 Synch or GnRH-PG protocols (Kojima et al., 2000).

Additional considerations

An additional consideration for Methods 2, 3 and 4 pertains to cows or heifers that fail to exhibit estrus after the last PG injection. In this case, cows or heifers would be re-injected with PG 11 to 14 days after the last injection of PG was administered. These females would then be observed for signs of behavioral estrus for an additional 6 to 7 days. This procedure would maximize efforts to inseminate as many females within the first 2 weeks of the breeding period as possible. Cows inseminated during the first synchronized period should not be re-injected with PG. In addition, the decision to use Methods 3 or 4 in heifers should be based on careful consideration of the heifer's age, weight, and pubertal status (Wood-Follis et al., 2004; Kojima et al., 2001).

Using MGA-based Protocols to Synchronize Ovulation Prior to Fixed-time AI

Control of the follicular and luteal phase of the estrous cycle and induction of estrous cyclicity in anestrous cows is essential to the development of estrus synchronization protocols that facilitate fixed-time AI (Perry et al., 2002). Beef producers face uncertainty in knowing the percentage of cows that are anestrus in their herds, and which treatment or combination of treatments can be expected to provide the greatest likelihood of pregnancy following administration. The significance of progestin pre-treatment followed by administration of the GnRH-PG protocol and associated effects related to follicular development and subsequent fertility were demonstrated in previous experiments (Perry et.al., 2002; Kojima et al., 2002; Kojima et al., 2003a,b; Stegner et al., 2004a; Stevenson et. al., 2003). Previous research from our laboratory led to the development of the MGA Select and 7-11 Synch protocols. Both protocols effectively synchronize estrus in mixed populations of estrous cycling and anestrous postpartum beef cows (MGA Select, Wood et al., 2001; 7-11 Synch, Kojima et al., 2000). The two protocols differ in length of treatment (MGA Select - 33 days; 7-11 Synch - 18 days) as well as length of the interval to estrus and resulting synchrony of estrus (Figure 8); however, there were no differences reported in pregnancy rates between these protocols among cows inseminated on the basis of observed estrus (Kojima et al., 2000; Patterson et al., 2001; Wood et al., 2001; Stegner et al., 2004b).

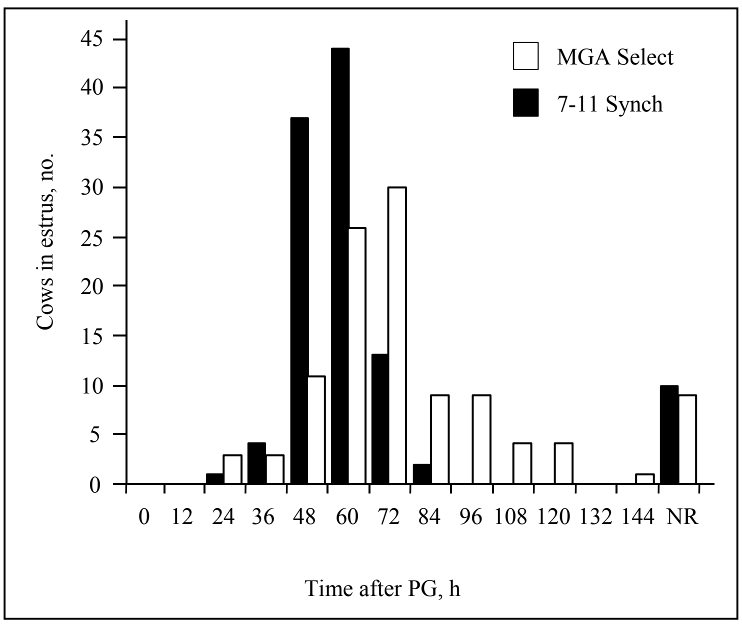

Figure 8. Distribution of cows in estrus for MGA Select and 7-11 Synch treated cows. Non-responders (NR) refers to the number of cows that failed to exhibit estrus during the synchronized period (0 to 144 h). Adapted from Stegner et al. (2004b).

The optimum and/or appropriate time to perform artificial insemination at fixed times following administration of these two protocols was reported (Kojima et al., 2003a; Perry et al., 2002; Stegner et al., 2004b); however, a direct comparison of the protocols to evaluate their efficacy for fixed-time AI was not made until recently (Bader et al., 2004). The MGA Select protocol provides an established synchrony of estrus and improves total herd estrous response, particularly among herds with high rates of anestrus (Patterson et al., 2002). Peak estrous response among cows assigned to the MGA Select protocol typically occurs 72 hours after PG (Figure 8; Patterson et al., 2001; Stegner et al., 2004a; Patterson et al., 2002). Pregnancy rates were optimized for cows assigned to the MGA Select protocol when fixed-time AI was performed at 72 hours after PG (Perry et al., 2002; Stegner et al., 2004c), but were reduced when AI was performed at 48 or 80 hours after PG (Stevenson et al., 2003; Stegner et al., 2004c). The 7-11 Synch protocol (Kojima et al., 2000) improves synchrony of estrus over other protocols (Select-Synch, MGA Select) and peak estrous response typically occurs 56 hours after PG (Figure 8; Kojima et al., 2000; Stegner et al., 2004b). Pregnancy rates resulting from fixed-time AI after administration of the 7-11 Synch protocol were optimized when AI was performed 60 hours after PG (Kojima et al., 2003a).

Bader et al. (2004) compared the MGA Select and 7-11 Synch protocols used in conjunction with fixed-timed artificial insemination (Figure 9). The study was conducted at three locations with cows from the University of Missouri Experiment Station. Table 4 summarizes pregnancy rates resulting from fixed-time AI. There was no effect of treatment (P = 0.25), technician (P = 0.81), or sire (P = 0.94) on pregnancy rates resulting from fixed-time AI. Table 5 summarizes pregnancy rates resulting from fixed-time AI on the basis of estrous cyclicity of cows prior to the initiation of treatment. Pretreatment estrous cyclicity did not influence (P = 0.12) pregnancy rates resulting from fixed-time AI. Furthermore, pregnancy rates resulting from fixed-time AI did not differ (7-11 Synch, P = 0.12; MGA Select, P = 0.50; Table 5) between cows that were estrous cycling or anestrus prior to initiation of the MGA Select and 7-11 Synch protocols.

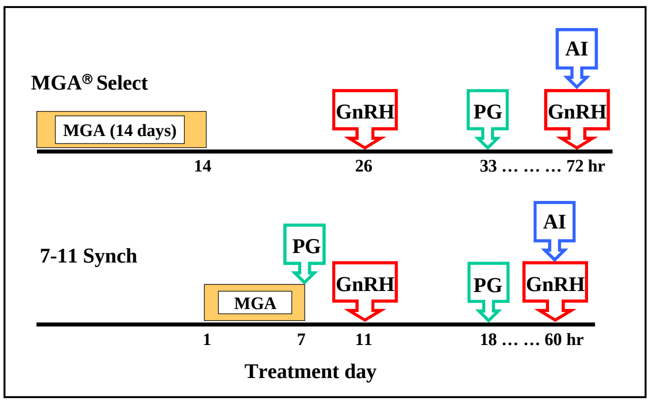

Figure 9. Comparison of the MGA Select and 7-11 Synch protocols in conjunction with fixed-time AI. From Bader et al. (2004).

Pregnancy rates resulting from fixed-time AI utilizing the MGA Select and 7-11 Synch protocols involved in this study are consistent with previously published reports [(MGA Select; Perry et al., 2002; Stegner et al., 2004c); (7-11 Synch; Kojima et al., 2002; Kojima et al., 2003a; Kojima et al., 2003b)]. Furthermore, pregnancy rates resulting from fixed-time AI in this study compare favorably with pregnancy rates after cows were inseminated on the basis of detected estrus using the same protocols to synchronize estrus (Kojima et al., 2000; Patterson et al., 2002; Stegner et al., 2004b).

Perry (2003) reported differences in late embryonic/fetal mortality following fixed-time AI among cows assigned to a CO-Synch protocol. Late embryonic/fetal mortality occurred at higher rates among cows induced to ovulate follicles ≤ 11 mm in diameter. Follicles induced to ovulate in this smaller range (≤ 11 mm) were characterized as being less physiologically mature at the time of ovulation, which may subsequently result in reduced oocyte and/or luteal competence. When cows were detected in standing estrus however, follicle size did not affect pregnancy rates or late embryonic mortality (Perry 2003). The author suggested oocyte and luteal competence may be more dependent on steroidogenic capacity of the follicles from which they were ovulated than follicle size (Perry 2003). A key observation from the preceding study suggests follicular competence is important for both the establishment and maintenance of pregnancy. Vasconcelos et al. (2001) observed reduced peak concentrations of circulating estradiol, decreased size of the corpus luteum, decreased circulating concentrations of progesterone, and lower pregnancy rates to AI when dairy cows were induced to ovulate smaller sized follicles (≤ 14 mm).

Table 4. Pregnancy rates after fixed-time artificial insemination and at the end of the breeding season.

Location	Treatment	Pregnancy rate to fixed-time AI[a] No.	(%)	Pregnancy rate at the end of breeding season[b] No.	(%)
1	7-11 Synch[c]	64/104	(62)	98/104	(94)
	MGA Select[c]	68/104	(65)	102/104	(98)
2	7-11 Synch	34/60	(57)	57/59	(97)
	MGA Select	43/62	(69)	60/62	(97)
3	7-11 Synch	30/45	(67)	43/45	(96)
	MGA Select	31/47	(66)	42/47	(89)
Combined	7-11 Synch	128/209	(61)	198/208	(95)
Combined	MGA Select	142/213	(67)	204/213	(96)

[a,b]Fixed-time AI pregnancy rate determined by transrectal ultrasonography 40 to 50 d after AI and final pregnancy rate determined by ultrasonography 45 d after the end of breeding season (From Bader et al., 2004).

Table 5. Pregnancy rates after fixed-time AI based on estrous cyclicity prior to initiation of treatments.[a]

Location	7-11 Synch Estrous cycling No.	(%)	7-11 Synch Anestrus No.	(%)	MGA Select Estrous cycling No.	(%)	MGA Select Anestrus No.	(%)
1	24/34	(71)	40/70	(57)	20/30	(67)	48/74	(65)
2	9/15	(60)	25/45	(56)	12/16	(75)	31/46	(67)
3	8/10	(80)	22/35	(63)	6/8	(75)	25/39	(64)
Combined	41/59	(69)	87/150	(58)	38/54	(70)	104/159	(65)

[a] From Bader et al. (2004).

Premature ovulation of a dominant follicle results in decreased ovulatory size, reduced luteal function, and compromised pregnancy rates compared to animals induced to ovulate larger, more mature dominant follicles (Mussard et al., 2003). The potential advantage in using either of these protocols (MGA Select, 7-11 Synch) to synchronize estrus prior to fixed-time AI is mean follicle diameter at the time ovulation is induced (Kojima et al., 2002; Perry et al., 2002; Kojima et al., 2003a,b; Stegner et al., 2004a) exceeds the range described by Perry (2003) and potentially minimizes problems with late embryonic/fetal mortality described by Perry (2003) and Mussard et al. (2003).

Although presence of luteal tissue at PG affected subsequent pregnancy rate to fixed-time AI, the actual concentration of progesterone (P_4) at PG was not important in determining subsequent pregnancy. The difference between treatments in serum concentrations of P_4 at PG stems from the difference in hormonal environments between the two treatments under which the dominant follicle develops (Stegner et al., 2004a.). MGA Select treated cows have higher concentrations of serum P_4 and lower E_2 during the growth phase of the dominant follicle, than cows treated with 7-11 Synch (Stegner et al., 2004a). This hormonal milieu is similar to the mid-luteal phase of the estrous cycle while, 7-11 Synch cows develop a dominant follicle under higher estradiol (E_2) and lower P_4 concentrations similar to the early luteal phase. Pregnancy rates based on pre-treatment status (estrous cycling versus anestrus) did not differ between treatments or among locations, which points to the efficacy of both protocols in successfully synchronizing estrus prior to fixed-time AI in mixed populations of estrous cycling and anestrous cows.

Management Considerations Related to Estrus Synchronization and Fixed-Time AI

Stegner et al. (2004b) discussed the advantages and disadvantages related to practical application and successful administration of the MGA Select and 7-11 Synch protocols. The advantages shown here and reported in other studies include the following: 1) MGA is economical to use (approximately $0.02 per animal daily to feed), 2) each protocol works effectively in mixed populations of beef cows that were estrous cycling or anestrus at the time treatments are imposed, and 3) pregnancy rates resulting from insemination performed on the basis of detected estrus or at predetermined fixed times are comparable and highly acceptable.

Stegner et al. (2004b) noted, however, the feasibility of feeding MGA to cattle on pasture is limiting in some production systems and is viewed as a disadvantage. Furthermore, the MGA Select protocol requires feeding and management of cows for 33 d, whereas the 7-11 Synch protocol involves an 18 d period. Conversely, the 7-11 Synch protocol requires that animals be handled four times, including AI, compared to the MGA Select protocol, which requires three handlings.

The calving distribution is illustrated in Figure 10 for cows assigned to the MGA Select and 7-11 Synch protocols and inseminated on the basis of detected estrus from the study by Stegner et al. (2004b). A high proportion of calves were delivered within the first 15 and cumulative 30 days of the calving season for each protocol, with no differences between treatments. The cumulative number of cows that calved within the first 30 days of the calving period was 93% and 89% for the MGA Select and 7-11 Synch groups, respectively. The calving distribution of cows assigned to each of these protocols must be carefully considered. One of the obvious benefits of estrus synchronization is a shortened calving season that results in more uniform calves at weaning (Dziuk and Bellows, 1983). Reduced length of the calving season translates into a greater number of days for postpartum recovery of the cow to occur prior to the subsequent breeding season. Herd owners must be aware of the risks associated with a concentrated calving period, including inclement weather or disease outbreaks, which separately or together may result in a decrease in the number of calves weaned.

These data, however, support the use of estrus synchronization not only as a means of facilitating more rapid genetic improvement of beef herds, but perhaps, more importantly, as a powerful reproductive management tool. Profitability may be increased by reducing the extent to which labor is required during the calving period, and increasing the pounds of calf weaned that results from a more concentrated calving distribution and a resulting increase in the age of calves at weaning.

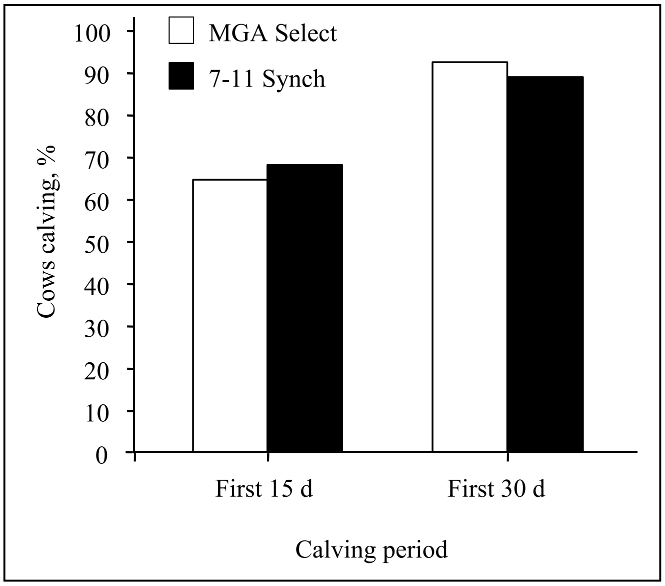

Figure 10. Cumulative calving distribution during the first 15 and 30 days of the calving season for MGA Select and 7-11 Synch- treated cows. [93% of MGA Select and 89% of 7-11 Synch treated cows calved within 30 days from the onset of the calving period]. From Stegner et al. (2004b).

More recently, calving dates for cows that conceived on the same day to fixed-time AI were recorded to address concerns that pertain to the subsequent calving period (Bader et al., 2004). Calf birth dates were recorded for cows that conceived to fixed-time AI (Figure 11) at each location. The resulting calving distribution for cows that conceived to the respective sires at each of the three locations in the study is shown in Figure 11. Analysis of calving distribution for individual sires differed (Table 6; $P < 0.05$). Calving distribution among cows that conceived to fixed-time AI for Location 1 (sires A and B) was 21 and 16 days, respectively. Distributions for Location 2 (sires C and D) were 16 and 20 days, respectively. The calving distribution among cows at location 3 (sire E), was 18 days. Sire B at Location 1 and sire E at Location 3 was the same sire. Cows that conceived on the same day gave birth to calves over a 16 to 21 day period, dependent upon the respective sire. This distribution suggests successful use of fixed-time AI will not result in an overwhelming number of cows calving on the same day(s). This furthermore suggests current management practices will not need to be greatly altered to accommodate the early portion of the calving season. Conversely, these data suggest successful application of estrus synchronization protocols that facilitate fixed-time AI support improvements in whole-herd reproductive management and expanded use of improved genetics.

Table 6. Comparison of gestation length (Mean ± SE) among AI sires and locations.

Location	Sire	Gestation length, days	Range, days
1	A	283.5 ± 0.5	272 - 292
	B[a]	282.1 ± 0.5	275 - 290
2	C	282.9± 0.8	274 - 289
	D	284.1 ± 0.6	275 - 294
3	E[a]	282.0 ± 0.5	274 - 291

[a]Sire B at location 1 and sire E at location 3 are the same sire.
From Bader et al. (2004).

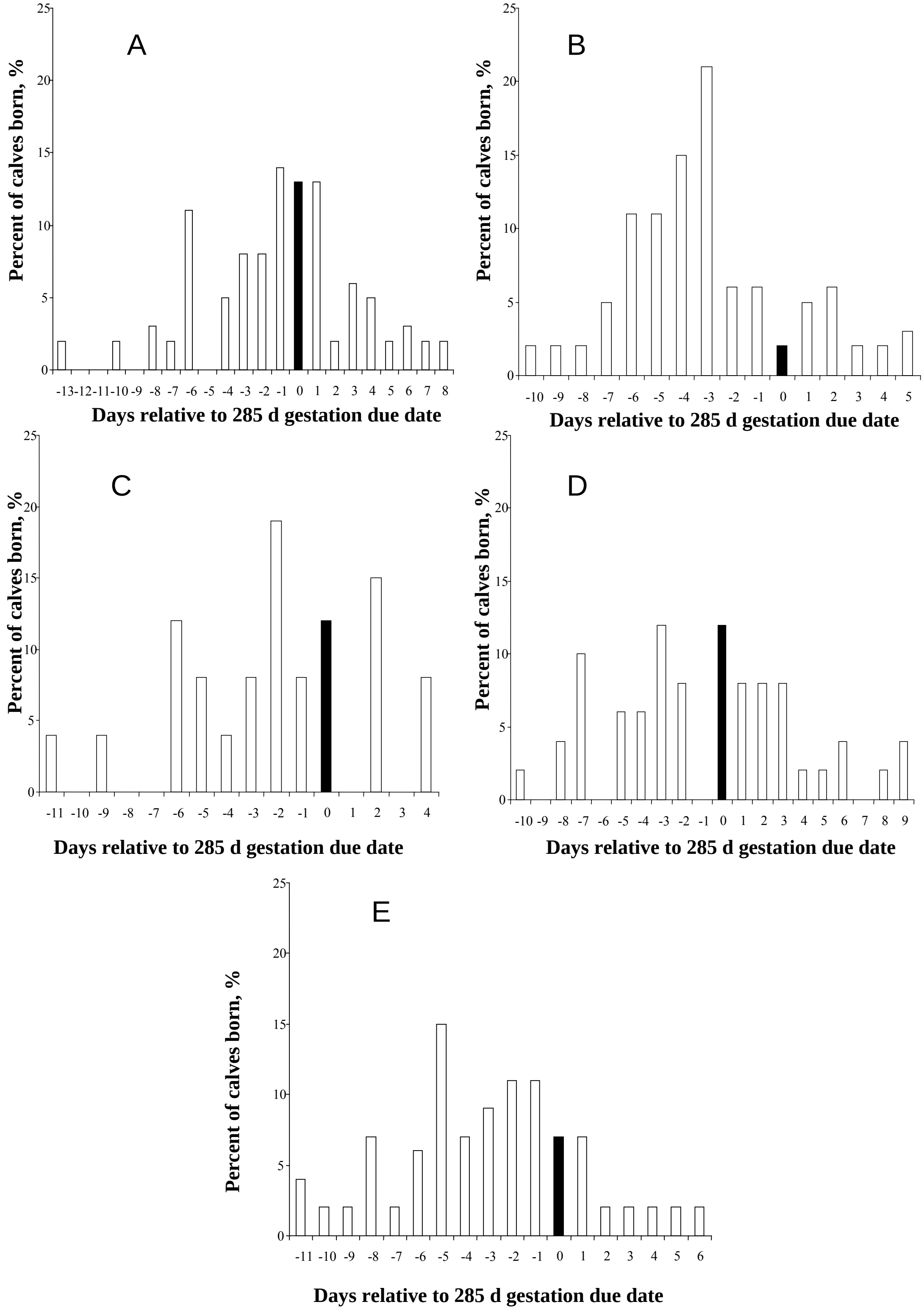

Figure 11. Calving distribution for cows that conceived to fixed-time AI at each location. Calving dates among cows that conceived on the same day to the respective sires (A, B, C, D, and E) were 21, 16, 16, 20, and 18 days. Sire B at Location 1 and sire E at Location 3 was the same sire. The shaded bar in each graph represents an anticipated 285 day gestation due date. From Bader et al. (2004).

Can EAZI-BREED CIDR Inserts Be Substituted For MGA?

Substituting EAZI-BREED CIDR inserts for MGA in the MGA Select protocol in beef heifers. We recently designed a study to compare estrous response, timing of AI and pregnancy rate resulting from AI among beef heifers presynchronized with MGA or CIDR inserts prior to GnRH and PG (Kojima et al., 2004; Figure 12). Heifers (n = 353) at three locations (location 1, n = 154; 2, n = 113; and 3, n = 85) were randomly assigned to one of two treatments by age and weight. The MGA Select-treated heifers (MGA; n = 175) were fed MGA (0.5 mg/head/day) for 14 days, GnRH (100 µg i.m. Cystorelin) was injected 12 days after MGA withdrawal, and PG (25 mg i.m. Lutalyse) was administered 7 d after GnRH. CIDRs (CIDR; n = 177) were inserted in heifers for 14 days, GnRH was injected 9 days after CIDR removal, and PG was administered 7 days after GnRH. CIDR-treated heifers received carrier without MGA on days that coincided with MGA feeding.

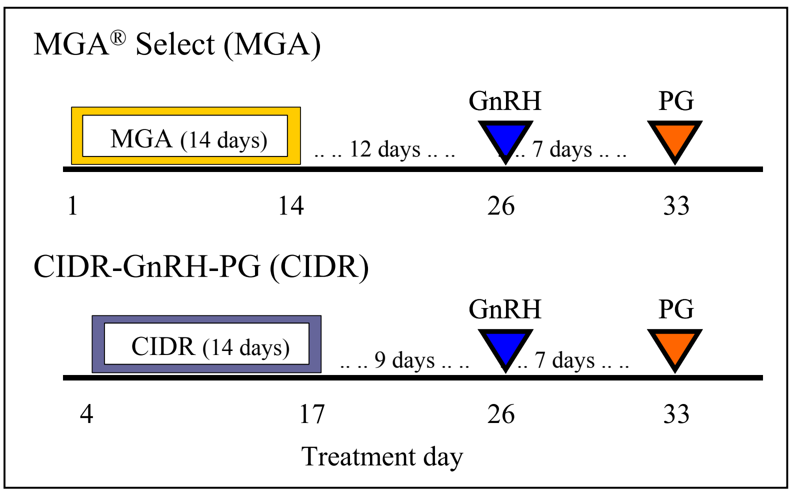

Figure 12. Substituting EAZI-BREED CIDR inserts for MGA in the MGA Select protocol in beef heifers. From Kojima et al. (2004).

Heifers were monitored for signs of behavioral estrus beginning the day PG was administered. AI was performed 12 hours after onset of estrus and recorded as day of AI (Day 0 = PG). Pregnancy rate to AI was determined by ultrasonography 40 days after AI. Estrous response did not differ ($P > 0.10$) between treatments. Peak AI occurred on day 3 for heifers in both treatments (CIDR 122/177, 69%; MGA 93/175, 53%), and distribution of AI was more highly synchronized ($P < 0.05$) among CIDR- than MGA-treated heifers. Pregnancy rate to AI was greater ($P < 0.01$) in CIDR- (112/177, 63%) than MGA-treated heifers (83/175, 47%), however, final pregnancy rate did not differ ($P > 0.10$) between treatments (Table 7). In summary, replacing feeding of MGA with CIDR inserts improved synchrony of estrus and pregnancy rate resulting from AI in replacement beef heifers (Kojima et al., 2004).

Table 7. Estrous response, AI pregnancy, and final pregnancy rates.

	Estrous response	AI pregnancy	Final pregnancy
CIDR	154/177 (87 %)	112/177 (63 %)[a]	164/177 (93 %)
MGA	147/175 (84 %)	83/175 (47 %)[b]	159/175 (91 %)
Total	301/352 (86 %)	195/352 (55 %)	323/352 (92 %)
Diff.	+ 3 %	[a,b] P = 0.01 + 16 %	+ 2 %

From Kojima et al. (2004).

Summary and Conclusions

Expanded use of AI and/or adoption of emerging reproductive technologies for beef cows and heifers requires precise methods of estrous cycle control. Effective control of the estrous cycle requires the synchronization of both luteal and follicular functions. Efforts to develop a more effective estrus synchronization protocol have focused on synchronizing follicular waves by injecting GnRH followed 7 days later by injection of PG (Ovsynch, CO-Synch, Select Synch). A factor contributing to reduced synchronized pregnancy rates in cows treated with the preceding protocols is 5 to 15% of cycling cows show estrus on or before PG injection. We developed new protocols for inducing and synchronizing a fertile estrus in postpartum beef cows and beef heifers in which the GnRH-PG protocol is preceded by either short- or long-term progestin treatment.

Although other types of progestin treatments (CIDR, PRID, or norgestomet) can be substituted in these estrus synchronization protocols, this review focused on use of MGA for the following reasons: a) MGA is economical to use (≈ 2 cents per animal per day to feed), b) MGA was recently cleared for use in reproductive classes of beef and dairy cattle (Federal Register, 1997), c) methodology and understanding of the use of MGA is documented in the literature (Zimbelman, 1963; Zimbelman and Smith, 1966; Patterson et al., 1989), dating back as early as the 1960's, and d) MGA is easily administered in feed and does not require that animals be handled or restrained during administration.

Table 8 provides a summary of various estrus synchronization protocols for use in postpartum beef cows. The table includes estrous response for the respective treatments and the synchronized pregnancy rate that resulted. These data represent results from our own published work, in addition to unpublished data from DeJarnette and Wallace, Select Sires, Inc. The results shown in Table 8 provide evidence to support the sequential approach to estrus synchronization in postpartum beef cows we describe.

Our preliminary studies identified significant improvements in specific reproductive endpoints among cows that received MGA prior to the administration of PG compared with cows that received PG only, including increased estrous response and improved synchronized conception and pregnancy rates. More recently we observed a significant improvement in synchrony of estrus without compromising fertility in postpartum beef cows and beef heifers that were pretreated, either short- or long-term, with MGA prior to GnRH and PG. We proposed the general hypothesis that progestin (MGA) treatment prior to the GnRH-PG estrus synchronization protocol will successfully: 1) induce ovulation in anestrous postpartum beef cows and peripubertal beef heifers; 2) reduce the incidence of a short luteal phase among anestrous cows induced to ovulate; 3) increase estrous response, synchronized conception and pregnancy rate; and 4) increase the likelihood of successful fixed-time insemination. Our data suggest that methods of inducing and synchronizing estrus for postpartum beef cows and replacement beef heifers in which the GnRH-PG protocol is preceded by a progestin offer significant potential to effectively synchronize estrus with resulting high fertility.

Table 8. Comparison of estrous response and fertility in postpartum beef cows after treatment with various estrus synchronization protocols.

Treatment	Estrous response		Synchronized pregnancy rate	
AI based on detected estrus				
2 shot PG	241/422	57%	147/422	35%
Select Synch	353/528	67%	237/528	45%
MGA-PG 14-17 d	305/408	75%	220/408	54%
MGA-2 shot PG	327/348	93%	243/348	70%
MGA-PG 14-19 d	161/206	78%	130/206	63%
MGA® Select	275/313	88%	195/313	62%
7-11 Synch	142/155	92%	101/155	65%
AI performed at predetermined fixed times with no estrus detection				
MGA® Select	Fixed-time AI		281/436	64%
7-11 Synch	Fixed-time AI		446/728	61%

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