Proceedings, Applied Reproductive Strategies in Beef Cattle
November 1 and 2, 2005, Lexington, Kentucky

REVIEW OF ESTRUS SYNCHRONIZATION SYSTEMS: MGA®, [1]

D. J. Patterson, D. J. Schafer, and M. F. Smith
Division of Animal Sciences
University of Missouri, Columbia

Introduction

Estrus synchronization and artificial insemination (AI) remain the most important and widely applicable reproductive biotechnologies available for cattle (Seidel, 1995). Although hormonal treatment of heifers and cows to group estrous cycles has been a commercial reality now for over 30 years, beef producers have been slow to adopt this management practice. Perhaps this is because of past failures, which resulted when females that were placed on estrus synchronization treatments failed to reach puberty or to resume normal estrous cycles following calving. In addition, early estrus synchronization programs failed to manage follicular waves, resulting in more days in the synchronized period, which ultimately precluded fixed-time artificial insemination with acceptable pregnancy rates. The development of convenient and economical protocols to synchronize estrus and ovulation to facilitate use of fixed-time AI with resulting high fertility should result in increased adoption of these important management practices (Patterson et al., 2003). Current research has focused on the development of methods that effectively synchronize estrus in postpartum beef cows and replacement beef heifers by decreasing the period of time over which estrus detection is required, thus facilitating the use of fixed timed AI.

Although tools are now available for beef producers to successfully utilize these procedures, transfer of the technology must assume a high priority. Transfer of this technology to beef producers in the U.S. will require an increase in technical support to facilitate successful use and adoption of these procedures, otherwise the products of our research and technology may be used more effectively in foreign countries (i.e., Brazil) whose beef products will ultimately compete with our own (Patterson et al., 2000).

Improving traits of major economic importance in beef cattle can be accomplished most rapidly through selection of genetically superior sires and widespread use of artificial insemination. Procedures that facilitate synchronization of estrus in estrous cycling females and induction of an ovulatory estrus in peripubertal heifers and anestrous postpartum cows will increase reproductive rates and expedite genetic progress. Estrus

[1] Research summarized in this manuscript was supported by National Research Initiative Competitive Grant 00-35203-9175 from the USDA Cooperative State Research, Education, and Extension Service, and Select Sires, Inc., Plain City, OH. The authors gratefully acknowledge Pfizer Animal Health (New York, NY) for providing Lutalyse sterile suspension and EAZI BREED CIDR Cattle inserts; Merial (Athens, GA) for providing Cystorelin; Select Sires, Inc., and ABS Global for providing semen.

synchronization can be an effective means of increasing the proportion of females that become pregnant early in the breeding season resulting in shorter calving seasons and more uniform calf crops (Dziuk and Bellows, 1983). Females that conceived to a synchronized estrus calved earlier in the calving season and weaned calves that were on average 13 days older and 21 pounds heavier than calves from nonsynchronized females (Schafer et al., 1990).

Effective estrus synchronization programs offer the following advantages: 1) cows or heifers are in estrus at a predicted time which facilitates AI, embryo transfer, or other assisted reproductive techniques; 2) the time required for detection of estrus is reduced thus decreasing labor expense associated with estrus detection; 3) cattle will conceive earlier during the breeding period; 4) AI becomes more practical; and 5) calves will be older and heavier at weaning.

WHY BEEF PRODUCERS DO NOT USE EXISTING AND POTENTIAL TECHNOLOGIES. Beef producers cite several reasons for the lack of widespread use of AI to breed heifers and cows. These reasons include: lack of time and labor, available procedures are viewed as being too complicated or costly to implement, inadequate means to detect estrus, or inconvenience (NAHMS, 1998). Continuation of low adoption rates of these technologies in the U.S. will ultimately erode the competitive position of the U.S. cattle industry. Other countries are adopting new technologies for animal production more rapidly than the U.S. For example, growth in the use of AI in Brazil has outpaced that of the U.S. (ASBIA, 2004; NAAB, 2004; Table 1). Beef producers in Brazil artificially inseminate nearly 5 times more cows annually compared with U.S. producers. Given the current scenario, elite seedstock herds in the U.S. will soon provide a sizeable percentage of the germ plasm used worldwide. Unless, however, owners of commercial cowherds aggressively implement reproductive and genetic improvement, the U.S. will lose its competitive advantage in production of high quality beef. International players that are more technically astute and competitively advantaged will position themselves to dominate the production and sale of beef worldwide.

Table 1. Import and domestic beef semen sales in Brazil and the U.S. over 10 years.

	Import and domestic beef semen sales (units sold)		
Country	1993	2003	% change
Brazil[a]	1,874,996	4,896,204	+161
United States[b]	1,025,116	906,923	-8

Export sales in the U.S. rose from 393,365 units in 1993 to 614,904 units in 2003 (+56%, NAAB, 2004). [a]ASBIA, 2004; [b]NAAB, 2004.

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 estrous 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 for AI performed on the basis of detected estrus:*</u>

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

MGA-PG: Melengestrol acetate (MGA; 0.5 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>*Protocols for fixed-time AI:*</u>

*MGA® Select:*MGA is fed for 14 days, GnRH is administered 12 days after MGA withdrawal, and PG is administered 7 days after GnRH. Insemination is performed 72 hours after PG with GnRH administered at AI.

*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. Insemination is performed 60 hours after PG with GnRH administered at AI.

CO-Synch + CIDR: GnRH is administered at CIDR insertion on day 0, followed 7 days later with CIDR removal, and PG. Insemination is performed 66 hours after CIDR removal and PG, with GnRH administered at AI.

<u>*Terms:*</u>

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 became 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.

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 to 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 2 or higher on a scale of 1 to 5) and at least 50 percent 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 follicular 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 that 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 that 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 that are 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 that were 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 controls; 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 that 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 that were anestrus prior to treatment and that 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 that treatment variations of Ovsynch currently being used in postpartum beef cows have not undergone the same validation process that 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 (Figure 1). 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).

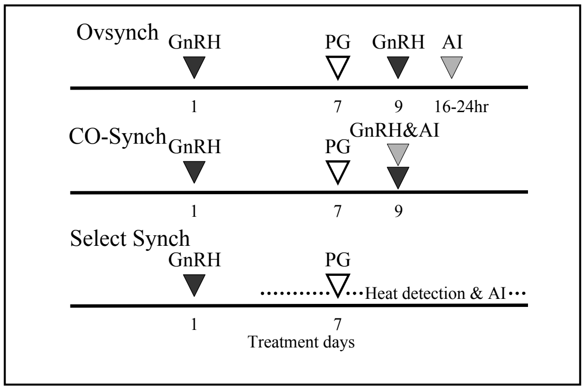

Figure 1. Methods currently being used to synchronize estrus and ovulation in postpartum beef cows using the GnRH-PG protocol: Ovsynch, CO-Synch and Select Synch.

MGA-Based Programs

This manuscript reviews methods to control estrous cycles of beef cows or heifers using MGA in breeding programs involving artificial insemination. Four methods will be outlined for using the MGA 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. Melengestrol acetate 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). Melengestrol acetate 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. Melengestrol acetate is fed at a rate of 0.5 mg/animal/day in a single daily feeding. 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 estrous response during the synchronized period. Therefore, adequate bunk space (60 linear cm/head) must be available so that all animals consume feed simultaneously (Patterson et al., 2003).

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 that 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 that females exhibiting estrus during this period not be inseminated or exposed for natural service because of 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 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).

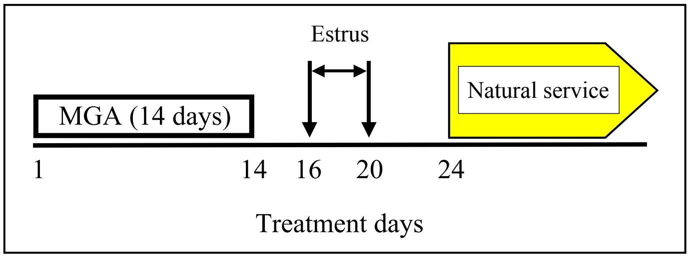

Figure 2. MGA and natural service (adapted from Patterson et al., 2000b).

This system works effectively, however careful consideration of bull to female ratios is advised. 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.

Method 2: MGA + Prostaglandin

This method of estrus synchronization 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. Prostaglandin $F_{2\alpha}$ 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 PG 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). Five available PG products for synchronization of estrus in cattle can be used after the MGA treatment: Lutalyse®, ProstaMate®, InSynch®, Estrumate®, or estroPLAN®. Label-approved dosages differ with each of these products; carefully read and follow directions for proper administration before their use.

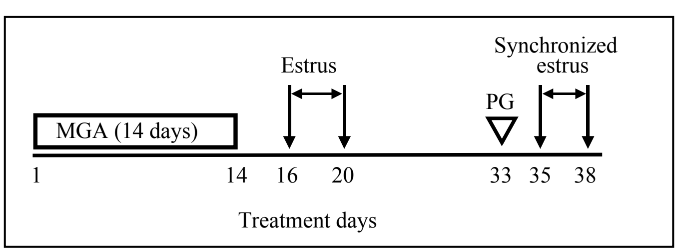

Figure 3. The MGA-PG protocol (adapted from Brown et al., 1988; Deutscher, 2000; Lamb et al., 2000).

Management related considerations to long-term feeding of MGA to heifers. Long-term feeding of MGA to beef heifers and associated effects on fertility may be a concern in specific production systems. It is not uncommon for heifers to be placed on MGA for extended periods of time and subsequently exposed for breeding after placement in backgrounding programs that necessitate long-term MGA administration. Zimbelman et al. (1970) reported no negative effect of either long-term or repeated intervals of feeding MGA to beef cows and heifers, other than the expected reduced conception rate when cattle were bred at the synchronized estrus 3 to 7 days after the last day of MGA feeding. Patterson et al. (1993) designed a study (Figure 4) to compare estrous response and fertility during synchronized estrous periods among beef heifers that were fed MGA for 87 days (long-term, LT) or 14 days (short-term, ST) prior to PG. Heifers were stratified by age and weight to LT- or ST-MGA treatments (Table 2), and received 0.5 mg MGA per head per day for 87 or 14 days, respectively. Heifers in each group were administered PG 17 days after MGA withdrawal. Heifers in both groups that failed to exhibit estrus within 6 days after the first injection of PG, were administered a second injection of PG 11 days later (Figure 4).

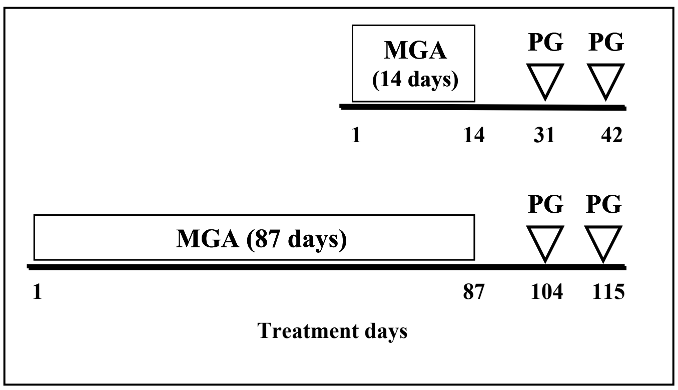

Figure 4. Comparison of short-term and long-term MGA treatments.

Transrectal ultrasonography was used to examine ovaries of all heifers at the end of treatment with MGA and at the time PG was administered. Heifers that failed to exhibit estrus after the first injection of PG were re-examined prior to the second PG injection. All heifers were exposed for natural-service for an additional 45 d after the AI period. More ST-treated heifers exhibited estrus after the first injection of PG than LT-treated heifers (Table 3; $P < 0.05$). Total response after the two injections of PG, however, did not differ between treatments. Furthermore, there were no significant differences between treatments in synchronized conception or pregnancy rates, or pregnancy rates at the end of the breeding period (Table 3). A higher incidence of luteinized follicular cysts (Table 4) was observed among heifers in the LT-treatment compared with heifers in the ST-treatment [LT, 11/30 (37%); ST, 0/31 (0%)]. This observation may explain differences in estrous response between treatments following the first injection of PG. These data indicate that long-term feeding of MGA may result in a higher than normal incidence of luteinized follicular cysts and an associated reduction in estrous response after PG. The data indicate, however, that re-injection with PG resulted in satisfactory breeding performance among heifers that were fed MGA for extended periods of time.

Table 2. Ages and weights of heifers at the time PG was administered.

Treatment	No. of heifers	Age, d	Weight, kg
Short-term, 14 d	31	427	393
Long-term, 87 d	30	423	387

[1]Adapted from Patterson et al., 2003.

Table 3. Estrous response and fertility of heifers treated long-term or short-term with MGA.

Response variable	Short-term MGA, 14 d			Long-term MGA, 87 d		
	1st PG[a]	2nd PG[a]	Total	1st PG[a]	2nd PG[a]	Total
Estrus response	24/31 (77%[b])	4/7 57%)	28/31 (90%)	16/30 (53%[c])	10/14 (71%)	26/30 (87%)
Synchronized conception	15/24 (63%)	3/4 (75%)	18/28 (64%)	12/16 (75%)	6/10 (60%)	18/26 (69%)
Synchronized pregnancy	--------		18/31 (58%)	--------		18/30 (60%)
Final pregnancy	--------		28/31 (90%)	--------		27/30 (90%)

[a]1st PG refers to animals that responded to PG administered 17 days after MGA withdrawal. 2nd PG refers to animals that failed to respond to the first injection of PG that were reinjected 11 days later.
[b, c]Percentages within row and between treatments with unlike superscripts differ ($P < 0.05$; Adapted from Patterson et al., 2003).

Table 4. Ovarian morphology of heifers treated long-term or short-term with MGA.

Treatment	Normal		Abnormal[a]	
Short-term	31/31	(100%)	0/31	(0%)
Long-term	19/30	(63%)	11/30	(37%)

[a]Abnormal = presence of luteinized follicular cysts, 20-45 mm diameter (Adapted from Patterson et al., 2003).

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 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.

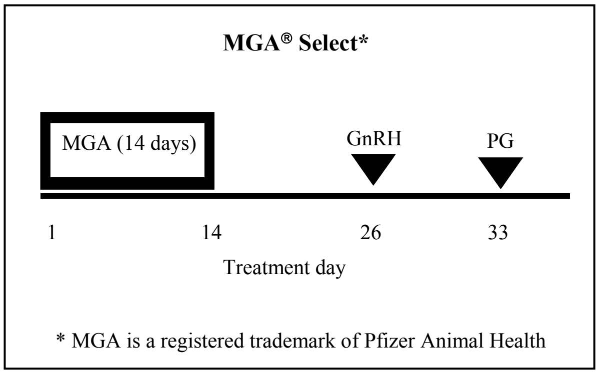

Figure 5. The MGA® Select protocol (Wood et al., 2001). MGA is fed for a period of 14 days followed in 12 days (day 26) by an injection of GnRH, and PG 19 days after MGA withdrawal (day 33).

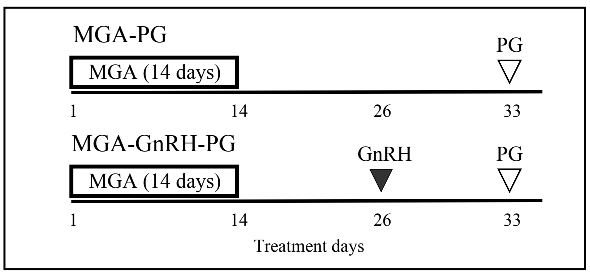

Figure 6. Cows were fed MGA for 14 days; 19 days after MGA withdrawal PG was administered to all cows. GnRH was administered to ½ of the cows 7 days prior to PG (Patterson et al., 2002).

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., 2002; Figure 6).

The following tables provide a summary of the results from the study conducted during the 2001 breeding season. Table 5 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 that were estrous cycling prior to the time treatment with MGA began. Estrous cyclicity status was determined based on two blood samples for progesterone obtained 10 days before and on the first day of MGA.

Table 5. Number of cows within age group per treatment, days postpartum, body condition and estrous 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	Estrous cycling (%)
MGA-PG	2, 3 & 4	52	47	5.2	35
	5+	48	39	5.2	15
	Total	100	44	5.2	40
MGA Select	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. Estrous 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 6 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 6. 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 ($P<0.05$).

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 Select	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 that was designed to: 1) shorten the feeding period of MGA without compromising fertility; and 2) 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).

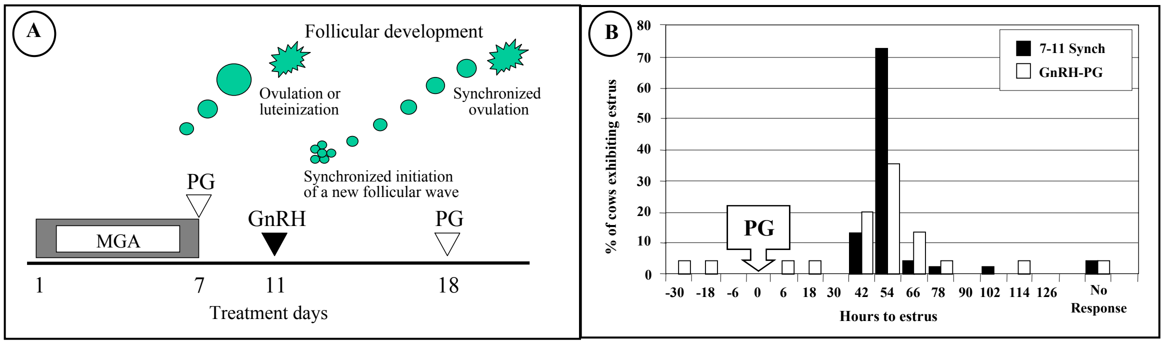

Figure 7A. Illustration of the treatment schedule and events associated with the 7-11 Synch protocol (Kojima et al., 2000). **Figure 7B.** Estrous response of cows treated with the 7-11 Synch or GnRH-PG protocols (Kojima et al., 2000).

Additional considerations. An additional consideration for Methods 2, 3, and 4 (MGA-PG, MGA Select, and 7-11 Synch) 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 that were 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 (Federal Register, 1997; Kojima et al., 2001; Patterson et al., 1989; Wood-Follis et al., 2004; Zimbelman, 1963; Zimbelman and Smith, 1966).

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., 2002; Wood et al., 2001; Stegner et al., 2004b).

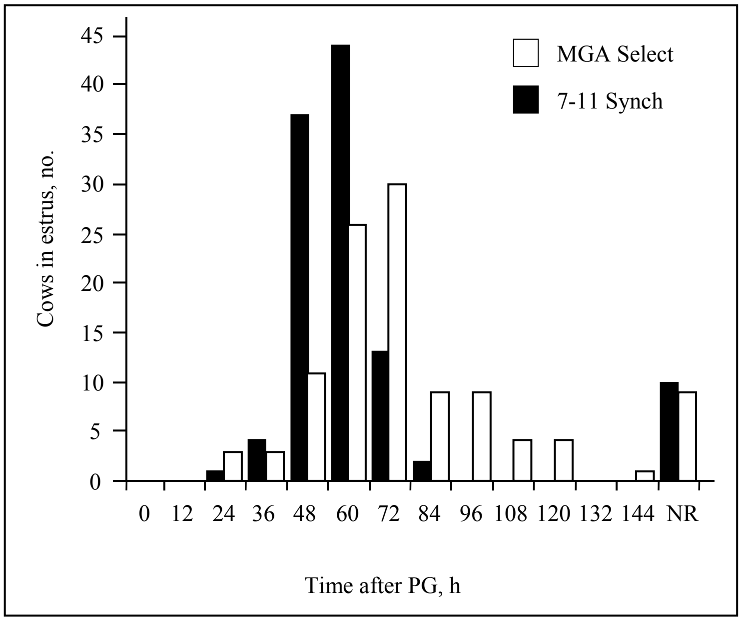

Figure 8. Distribution of estrus for MGA Select and 7-11 Synch treated cows. Non-responders (NR) refer to the number of cows that failed to exhibit estrus during the synchronized period (0 to 144 hous). Adapted from Stegner et al. (2004b).

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., 2005). 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., 2002; Stegner et al., 2004a). 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. (2005) 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 7 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 8 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 8) between cows that were estrous cycling or anestrus prior to initiation of the MGA Select and 7-11 Synch protocols.

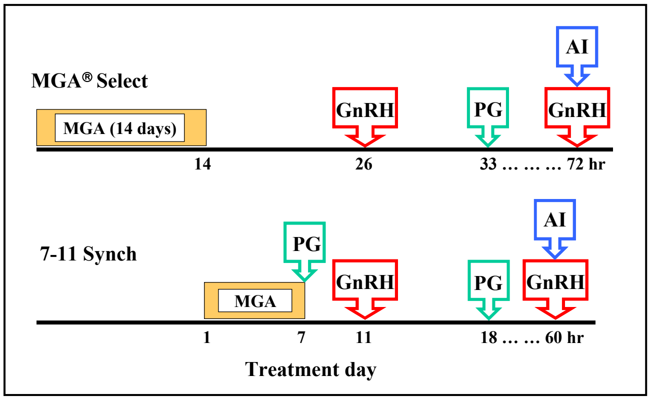

Figure 9. Comparison of the MGA Select and 7-11 Synch protocols in conjunction with fixed-time AI. From Bader et al. (2005).

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).

Table 7. 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., 2005).

Table 8. Pregnancy rates after fixed-time AI based on estrous cyclicity prior to initiation of treatments.

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)

From Bader et al. (2005).

Perry et al. (2005) 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 that were 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 et al., 2005). The authors suggested that oocyte and luteal competence may be more dependent on steroidogenic capacity of the follicles from which they were ovulated than follicle size (Perry et al., 2005). A key observation from the preceding study suggests that follicular competence is important for both the establishment and maintenance of pregnancy. Vasconcelos et al. (2001) observed reduced peak concentrations of circulating estradiol (E_2), 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).

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 or 7-11 Synch) to synchronize estrus prior to fixed-time AI is that 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 et al. (2005) and potentially minimizes problems with late embryonic/fetal mortality described by Perry et al. (2005) 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 E_2 and lower P_4 concentrations similar to the early luteal phase. Pregnancy rates based on pre-treatment estrous cyclicity 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.

How Do MGA- and CIDR-Based Protocols Compare?

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 that were presynchronized with MGA or CIDR inserts prior to GnRH and PG (Kojima et al., 2004; Figure 10). 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 days after GnRH. The CIDR treated heifers (CIDR; n = 177) had CIDRs inserted 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.

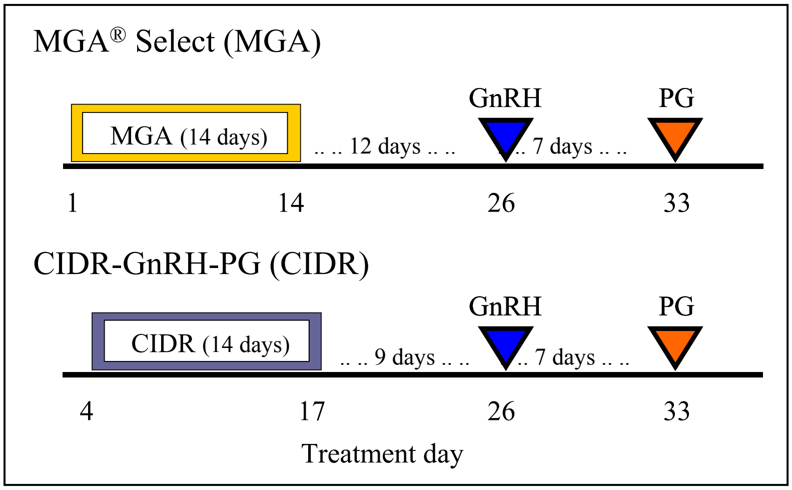

Figure 10. Substituting CIDR inserts for MGA in the MGA Select protocol in beef heifers. From Kojima et al. (2004).

Heifers were monitored for signs of behavioral estrus beginning the day PG was administered. AI was performed approximately 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 9). 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 9. Estrous response, AI pregnancy, and final pregnancy rates.

	Estrous response	AI pregnancy rate	Final pregnancy rate
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 %)
Difference	+ 3 %	[a,b] P = 0.01 + 16 %	+ 2 %

From Kojima et al. (2004).

How Do MGA Select and Co-Synch + CIDR Compare in Synchronizing Ovulation Prior to Fixed-time AI in Postpartum Beef Cows?

Previous research in our laboratory demonstrated the efficacy of using the MGA Select protocol to synchronize estrus and ovulation prior to fixed-time AI that was performed 72 h after PG (Perry et al., 2002; Stegner et al., 2004c; Bader et al., 2005). Other research showed an improvement in pregnancy rates resulting from fixed-time AI after treatment with the Co-Synch + CIDR protocol when insemination was performed 66 h as opposed to 48, or 54 h following CIDR removal and PG administration (Lamb et al., 2001; Bremer et al., 2004; Larson et al., 2004). Schafer (2005) designed a study to compare pregnancy rates resulting from fixed-time AI among cows assigned to the MGA Select and CO-Synch + CIDR protocols (Figure 11).

Crossbred, lactating, beef cows (n = 650) at four locations (n = 210; n = 158; n = 88; n = 194) were assigned within age group by calving date (days postpartum, **DPP)** and body condition score (**BCS**; 1 to 9 scale, 1 = emaciated, and 9 = obese) to one of two treatments (Table 10) during the spring 2004 breeding season (Schafer, 2005). Cows assigned to the MGA Select treatment (MGA Select; n = 327) were fed melengestrol acetate for 14 d, GnRH was injected on d 26, and **PG** was injected on d 33. CO-Synch + CIDR treated cows (CO-Synch + CIDR; n = 323) were fed carrier for 14 d, were injected with GnRH and equipped with an EAZI-BREED™ Controlled Internal Drug Release® insert (**CIDR**) 12 d after carrier removal, and PG was injected and CIDR were removed on d 33. Artificial insemination was performed at 72 h after PG for cows assigned to the MGA Select treatment, and at 66 h after PG administration for cows assigned to the CO-Synch + CIDR treatment (Figure 11). Time of PG administration and AI were recorded for each cow. All cows were injected with GnRH at the time of insemination, and AI was performed by one of three experienced technicians. Three AI sires were used at location 1, and one sire was used at locations 2, 3, and 4. One of the sires used at location 1 was the same sire used at locations 3 and 4. The AI sire and technician were assigned to cows within each treatment by cow age, calving date, and BCS. Cows were exposed to fertile bulls for natural service 14 d after AI for a 60 day natural service period at Locations 1, 3, and 4 and for a 45 day natural service period at Location 2.

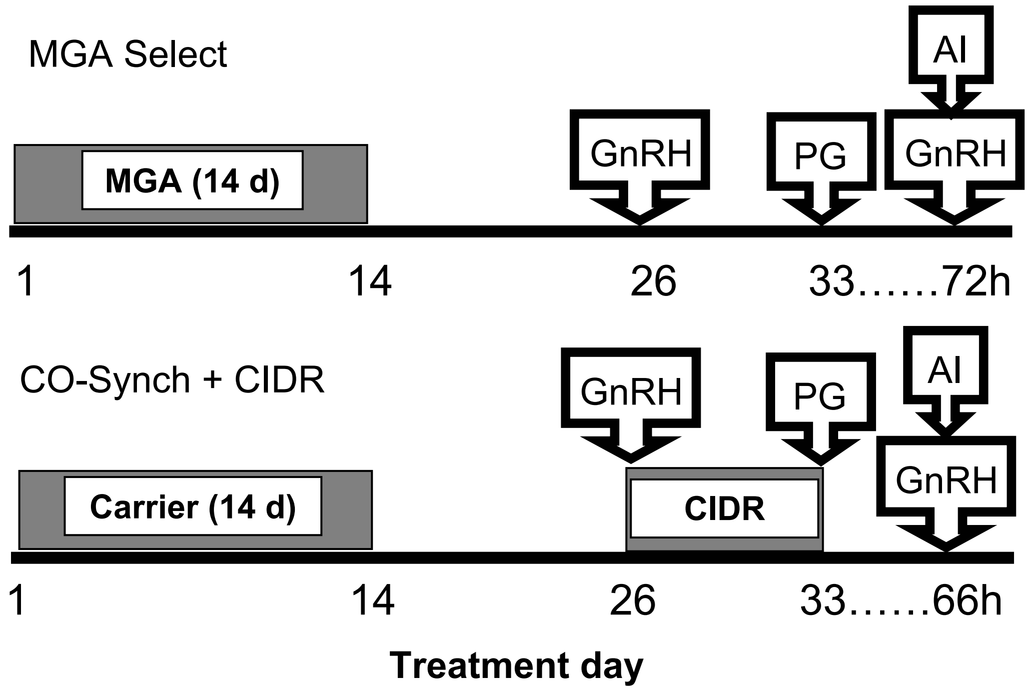

Figure 11. Treatment schedule for cows assigned to the MGA Select and Co-Synch + CIDR protocols. Cows assigned to the MGA Select protocol were fed melengestrol acetate (MGA; 0.5 mg•hd^{-1}•d^{-1}) for 14 d, GnRH was administered 12 d after MGA withdrawal, and PG was administered 7 d after GnRH. Cows were inseminated 72 h after d 33 PG with an injection of GnRH at AI. Cows assigned to the CO-Synch + CIDR protocol were fed carrier for 14 d, on d 26 cows were injected with GnRH and equipped with an EAZI-BREED™ CIDR insert (CIDR), 7 d later CIDRs were removed and PG was administered. Cows were inseminated 66 h after d 33 PG with an injection of GnRH at AI. From Schafer (2005).

The number of cows at each location, age, days postpartum, BCS, and estrous cycling status of cows before the initiation of treatments are shown in Table 10. There were no differences between treatments at the respective locations for age, days postpartum, BCS, or estrous cyclicity status at the initiation of treatment; however, there were differences among locations (Table 10). There was no effect of treatment (P = 0.20), technician (P = 0.63), or sire (P = 0.11) on pregnancy rates resulting from fixed-time AI (Table 11). In addition, pre-treatment estrous cyclicity before the initiation of the MGA Select or CO-Synch + CIDR protocols, did not affect (MGA Select, P = 0.39; CO-Synch + CIDR, P = 0.31; Table 12) pregnancy rates resulting from fixed-time AI. Final pregnancy rates at the end of the breeding season did not differ (P = 0.25) between treatments (Table 11).

Table 10. Number of cows at each location, days postpartum, body condition score, and estrous cycling status for cows before initiation of each treatment (mean ± SE). From Schafer (2005).

Treatment	No.	Age, yr	Time postpartum, d[a]	BCS[b]	Cows with elevated progesterone[c] Proportion	%
Location 1						
MGA Select[d]	106	5.3 ± 0.3	46.4 ± 1.4	5.6 ± 0.06	62/106	58
CO-Synch + CIDR[d]	104	5.4 ± 0.3	45.9 ± 1.4	5.7 ± 0.06	50/104	48
Combined	210	5.3 ± 0.2	46.1 ± 1.0[x]	5.7 ± 0.04[x]	112/210	53[x]
Location 2						
MGA Select[d]	80	5.7 ± 0.3	32.7 ± 1.6	6.1 ± 0.07	29/80	36
CO-Synch + CIDR[d]	78	5.7 ± 0.3	32.4 ± 1.6	6.0 ± 0.07	34/78	44
Combined	158	5.7 ± 0.2	32.5 ± 1.1[y]	6.0 ± 0.05[y]	63/158	40[y]
Location 3						
MGA Select[d]	45	5.5 ± 0.4	44.6 ± 2.1	5.2 ± 0.10	16/45	36
CO-Synch + CIDR[d]	43	5.4 ± 0.4	44.1 ± 2.1	5.3 ± 0.10	15/43	35
Combined	88	5.5 ± 0.3	44.4 ± 1.5[xz]	5.3 ± 0.07[z]	31/88	35[y]
Location 4						
MGA Select[d]	96	5.2 ± 0.3	43.8 ± 1.4	5.3 ± 0.07	78/96	81
CO-Synch + CIDR[d]	98	5.3 ± 0.3	41.7 ± 1.4	5.3 ± 0.07	78/98	80
Combined	194	5.2 ± 0.2	42.8 ± 1.0[z]	5.3 ± 0.05[z]	156/194	80[z]
Combined						
MGA Select	327	5.4 ± 0.2	41.9 ± 0.8	5.5 ± 0.03	185/327	57
Combined						
CO-Synch + CIDR	323	5.4 ± 0.2	41.0 ± 0.8	5.6 ± 0.03	177/323	55

[a]Number of days postpartum at the initiation of melengestrol acetate (MGA) feeding for MGA Select-treated cows and carrier feeding for CO-Synch + CIDR-treated cows.

[b]Body condition scores of cows at the time of the first blood sample before initiation of treatments (1 to 9 scale, where 1 = emaciated, and 9 = obese).

[c]Estrous cyclicity = the percentage of cows with elevated (≥ 0.5 ng/mL) concentrations of progesterone in serum before treatment. Cows were considered to be estrous cycling if progesterone was elevated in either of two blood samples collected 8 and 1 d prior to treatment.

[d]See Figure 11 for description of protocols.

[x,y,z]Means with at least one superscript in common within columns and between locations are not different, $P > 0.05$.

Table 11. Pregnancy rates after fixed-time artificial insemination and at the end of the breeding season. From Schafer (2005).

Item	Pregnancy rate to fixed-time AI[a]		Pregnancy rate at end of breeding season[b]	
	Proportion	%	Proportion	%
Location 1				
MGA Select[c]	70/106	66	99/106	93
CO-Synch + CIDR[c]	67/104	64	99/104	95
Location 2				
MGA Select	53/80	66	77/80	96[d]
CO-Synch + CIDR	56/78	72	76/78	97[d]
Location 3				
MGA Select	26/45	58	42/45	93
CO-Synch + CIDR	29/43	67	42/43	98
Location 4				
MGA Select	52/96	54	87/96	91
CO-Synch + CIDR	62/98	63	91/98	93
Combined				
MGA Select	201/327	61	305/327	93
Combined				
CO-Synch + CIDR	214/323	66	308/323	95

[a]Pregnancy rate to fixed-time AI determined by ultrasound 40 to 45 d after AI.
[b]Pregnancy rate determined 50 to 60 d after the end of the breeding season.
[c]See Figure 11 for a description of protocols.
[d]Pregnancy rate at the after 45 d breeding season.

Table 12. Pregnancy rates after fixed-time artificial insemination based on estrous cyclicity before initiation of treatments. From Schafer (2005).

	MGA Select[a]				CO-Synch + CIDR[a]			
	Estrous cycling[b]		Anestrus[b]		Estrous cycling		Anestrus	
Location	Proportion	%	Proportion	%	Proportion	%	Proportion	%
1	38/62	61	32/44	73	30/50	60	37/54	69
2	20/29	69	33/51	65	25/34	74	31/44	70
3	11/16	69	15/29	52	8/15	53	21/28	75
4	41/78	53	11/18	61	50/78	64	12/20	60
Combined	110/185	59	91/142	64	113/177	64	101/146	69

[a]See Figure 11 for a description of protocols.
[b]See Table 10 for a description of estrous cyclicity.

The MGA Select protocol results in a consistent synchrony of estrus with the peak estrous response typically occurring 72 h after the administration of PG (Patterson et al., 2002; Stegner et al., 2004a). Furthermore, pregnancy rates following administration of the MGA Select protocol and resulting from fixed-time AI have consistently run ≥ 60%, when AI was performed 72 h after PG (Perry et al., 2002; Stegner et al., 2004c; Bader et al., 2005). The pregnancy rates resulting from fixed-time AI reported in this study following treatment with the MGA Select estrus synchronization protocol are consistent with other published data when insemination was performed 72 h after PG (Perry et al., 2002; Stegner et al., 2004c; Bader et al., 2005).

The CO-Synch + CIDR protocol with fixed-time AI performed 60 h after PG resulted in comparable pregnancy rates when compared to CIDR-based protocols that involve estrus detection and AI up to 84 h after PG followed by fixed-time insemination of non-responders at 84 h (Larson et al., 2004). Other studies reported pregnancy rates to the CO-Synch + CIDR estrus synchronization protocol were optimized when insemination was performed at 66 h after PG compared to AI performed at 48 or 54 h (Bremer et al., 2004). Consideration of these various studies led to the decision to inseminate cows at 66 h following administration of the CO-Synch + CIDR protocol in the study by Schafer (2005). The results reported by Schafer (2005) are comparable to the study by Bremer et al. (2004), and support the concept that there is a critical window of time over which insemination should be performed following administration of the CO-Synch + CIDR protocol.

Successful application of these protocols requires careful consideration of the advantages and disadvantages that accompany their administration. Based on these data both protocols appear to work effectively in mixed-populations of estrous cycling and anestrous cows, despite differences recently reported by Perry et al. (2004). The fertility after treatment was shown to produce pregnancy rates resulting from fixed-time AI consistently ranging from 54 to 72%. The CO-Synch + CIDR protocol may have broader application in comparison to the MGA Select protocol due to shorter treatment duration (< 10 d vs. 36 d), especially in herds with more widespread calving periods. Successful results with either protocol require proper application of each step of the respective treatment. The consistent results that were obtained with the CO-Synch + CIDR protocol may be due to more precise control of progestin treatment among cows that received CIDR inserts compared to more variable MGA intake patterns among cows assigned to the MGA Select protocol.

These results indicate that estrus synchronization with the MGA Select and CO-Synch + CIDR protocols produce comparable pregnancy rates to fixed-time AI when inseminations were performed at 72 and 66 h after PG, respectively. The results reported here present beef producers a choice and means for expediting genetic improvement and reproductive management.

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, that 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 12 for cows that were 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.

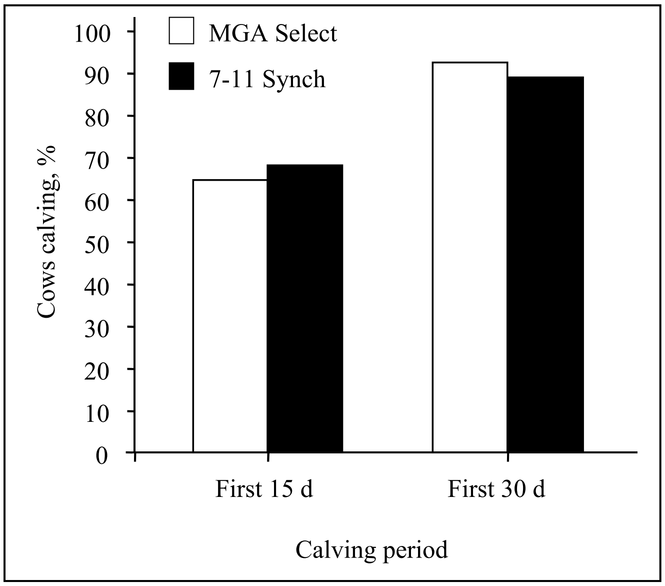

Figure 12. Cumulative calving distribution during the first 15 and 30 days of the calving season for MGA Select and 7-11 Synch- treated cows. [93% of MGA Select and 89% of 7-11 Synch treated cows calved within 30 days from the onset of the calving period]. From Stegner et al. (2004b).

These data 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 result from a more concentrated calving distribution and a resulting increase in the age of calves at weaning.

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., 2005). Calf birth dates were recorded for cows that conceived to fixed-time AI (Figure 13) at each location involved in the study by Bader et al. (2005). The resulting calving distribution for cows that conceived to the respective sires at each of the locations in the two treatments is illustrated in Figure 13. Calving distribution patterns differed among individual sires (Table 13; $P < 0.05$). 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.

Calving distribution patterns for cows involved in the study by Schafer (2005) are illustrated in Figure 14. These data also represent calving profiles among cows that became pregnant on the same day using semen from single sires as indicated by the respective panels. These distributions indicate that successful use of fixed-time AI will not result in an overwhelming number of cows calving on the same day(s). This furthermore suggests that current management practices will not need to be greatly altered to accommodate the early portion of the calving season. Conversely, these data demonstrate that 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 13. Comparison of gestation lengths (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. (2005).

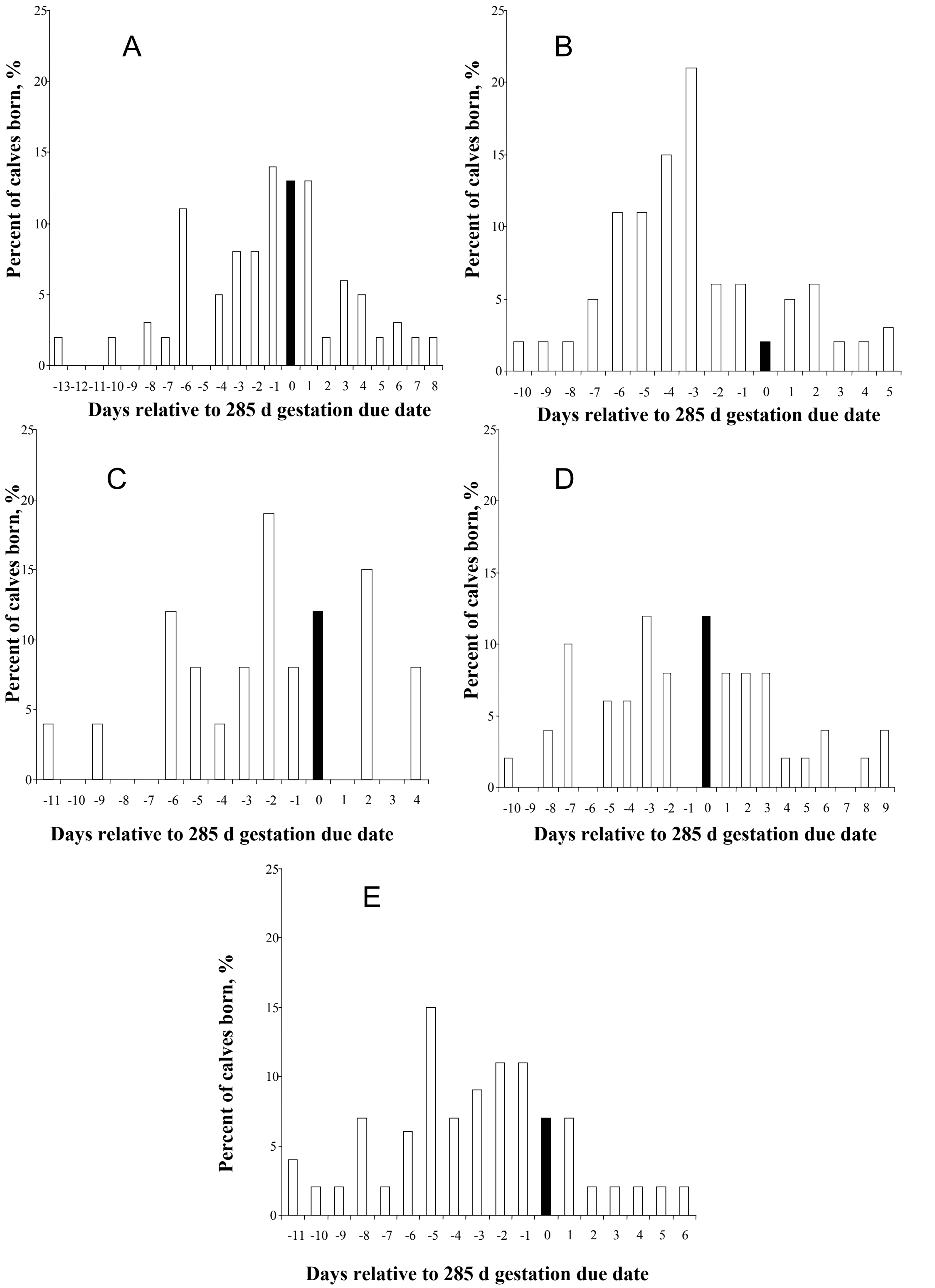

Figure 13. Calving distribution patterns at the respective locations for cows that conceived to fixed-time AI Calving dates among cows that conceived on the same day to the respective sires (A, B, C, D, and E) were 21, 16, 16, 20, and 18 days. Sire B at Location 1 and sire E at Location 3 were the same sire. The shaded bar in each graph represents an anticipated 285 day gestation due date. From Bader et al. (2005).

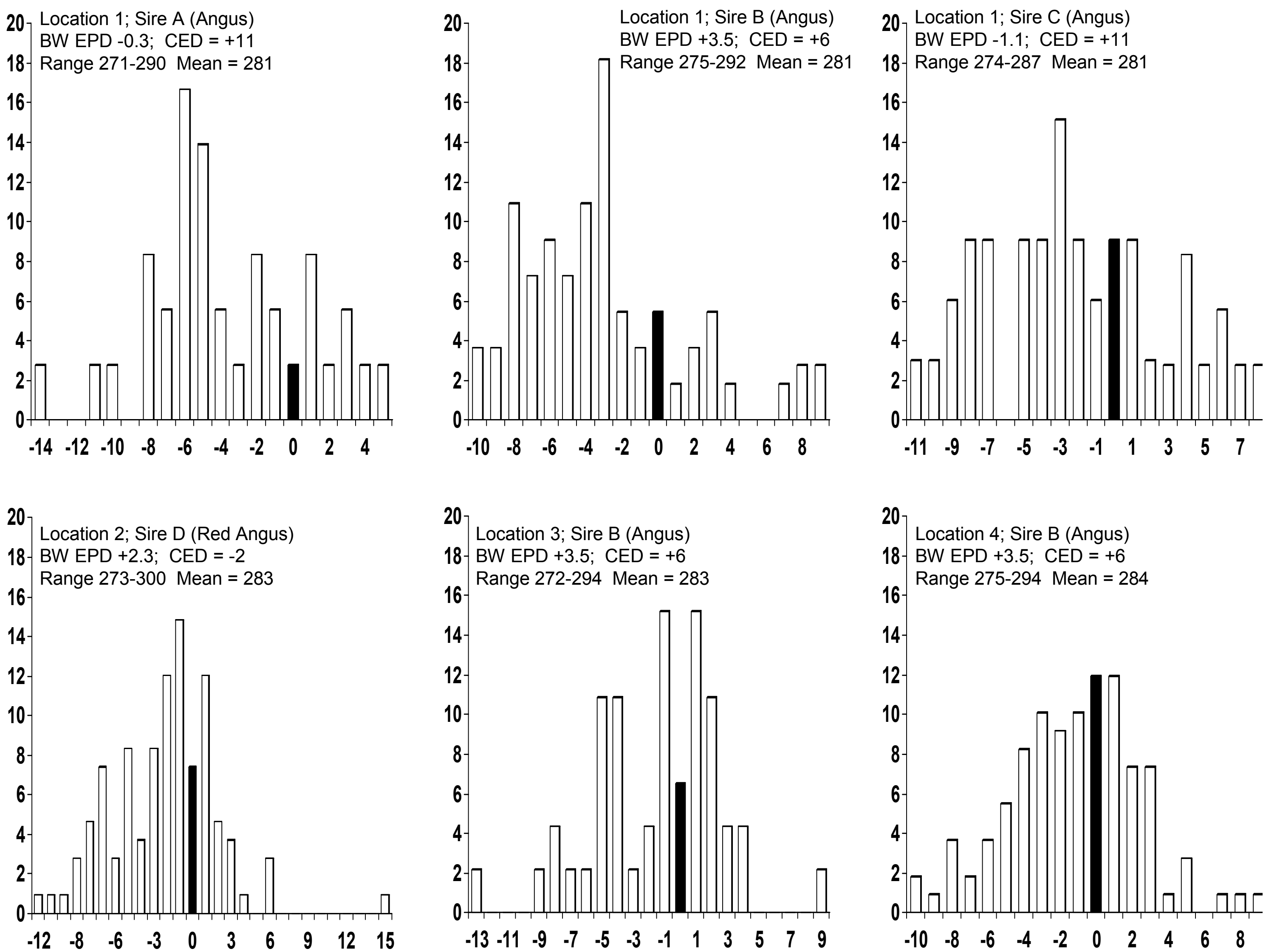

Figure 14. Calving distributions recorded for cows that conceived to fixed-time AI (Schafer, 2005). The shaded bar in each graph represents an anticipated 285 day gestation due date.

Consider the Impact of Estrus Synchronization on Calving Distribution

Economic considerations related to use of estrus synchronization and choice of the various protocols to use in beef heifers and cows was reviewed by Johnson and Jones (2004). Hughes (2005) reported that opportunities to increase profits for cow-calf operations lie in managing females from the later calving intervals forward toward the first and second 21-day calving intervals. Hughes (2005) reports that added pounds are the economic reward to tightening up the calving interval. The CHAPS benchmark values utilize IRM-SPA guidelines for operating high production herds. These guidelines suggest that 61% of the calves within a herd should be born by day 21 of the calving period, 85% by day 42, and 94% by day 63. Hughes (2005) goes on to say that today's high market prices are generating big economic rewards to intensified management, but more specifically "management as usual" may be what is amiss for many cow calf producers.

Figure 15 illustrates the cumulative calving percentages for the University of Missouri Thompson farm over a 10-year period. The graph compares the percentages of calves born during years when only natural service was used, followed by estrus synchronization and AI performed on the basis of observed heat, and finally fixed-time AI. The graph illustrates the respective distributions on the basis of days in the calving season. Notice the increased percentage of calves born early in the calving period during years when AI was performed on the basis of observed heat or at predetermined fixed times in comparison to years in which only natural service was practiced.

Figure 16 illustrates the combined calving data for 3 of the 4 locations in the study by Schafer (2005). Data from the fourth location was not included in the summary since cows that failed to conceive to AI were sold prior to the calving period. It is interesting to note that in comparison to the recommendation by Hughes (2005), 64% of the cows in this study had calved by day 15, 70% by day 21, 77% by day 30, and 91% by day 42. The economic reward from improvements in calf weaning weight that result from an increase in calf age at weaning, in many cases may offset the cost of implementing estrus synchronization in beef herds.

Finally, Figure 17 illustrates the calving profile for cows at the University of Missouri Forage Systems Research Center in Linnueus, MO, over a two year period. This herd maintains a 45-day breeding season, and until the spring of 2004, estrus synchronization and AI were not utilized. Figure 17 illustrates the calving profile of cows that calved during the spring of 2004 as a result of natural service during the 2003 breeding season. Figure 17 also illustrates the calving profile for cows that calved during the spring of 2005 as a result of fixed time AI performed during the 2004 breeding season (Schafer, 2005). This herd has been intensively managed over the years to breed successfully in a 45 day period with natural service. Notice, however, the increased percentage of cows that calved early in the calving period as a result of fixed-time AI performed during the previous year's breeding season. Estrus synchronization at this location in one year resulted in an increase of 7 days postpartum among cows at the start of the breeding period, which translates into an increase in calf age at weaning of seven calf days.

These figures (Figures 15, 16, 17) collectively demonstrate that estrus synchronization can be used effectively to influence calving distribution patterns during the subsequent calving period, which in turn impacts the economics of herds at weaning time.

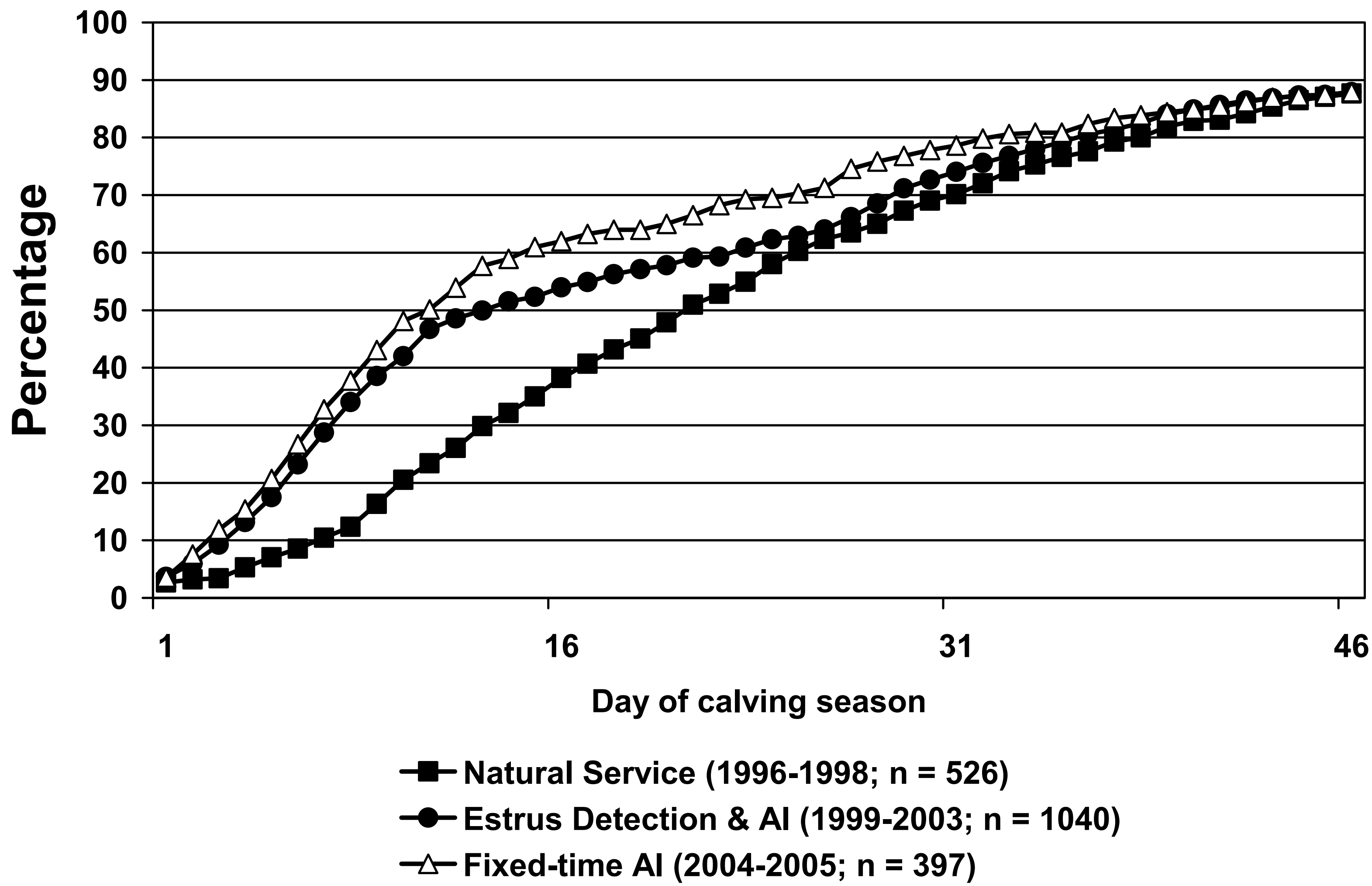

Figure 15. Cumulative calf crop for cows at the University of Missouri Thompson Farm combining years involving natural service, estrus synchronization and AI performed on the basis of observed heat, and fixed-time AI (Schafer and Patterson,unpublished data).

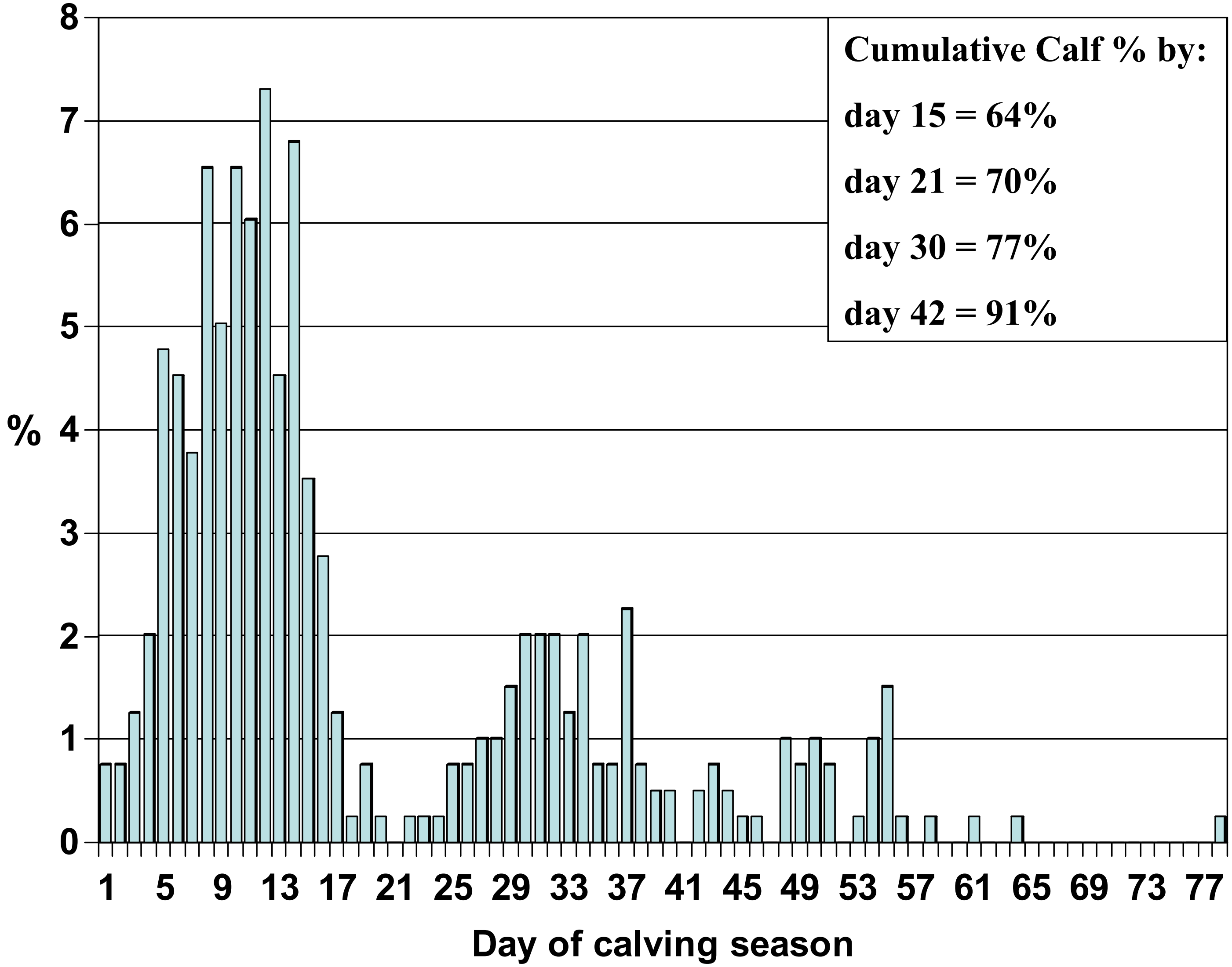

Figure 16. Calving distributions combined for 3 of the 4 locations in the study by Schafer (2005).

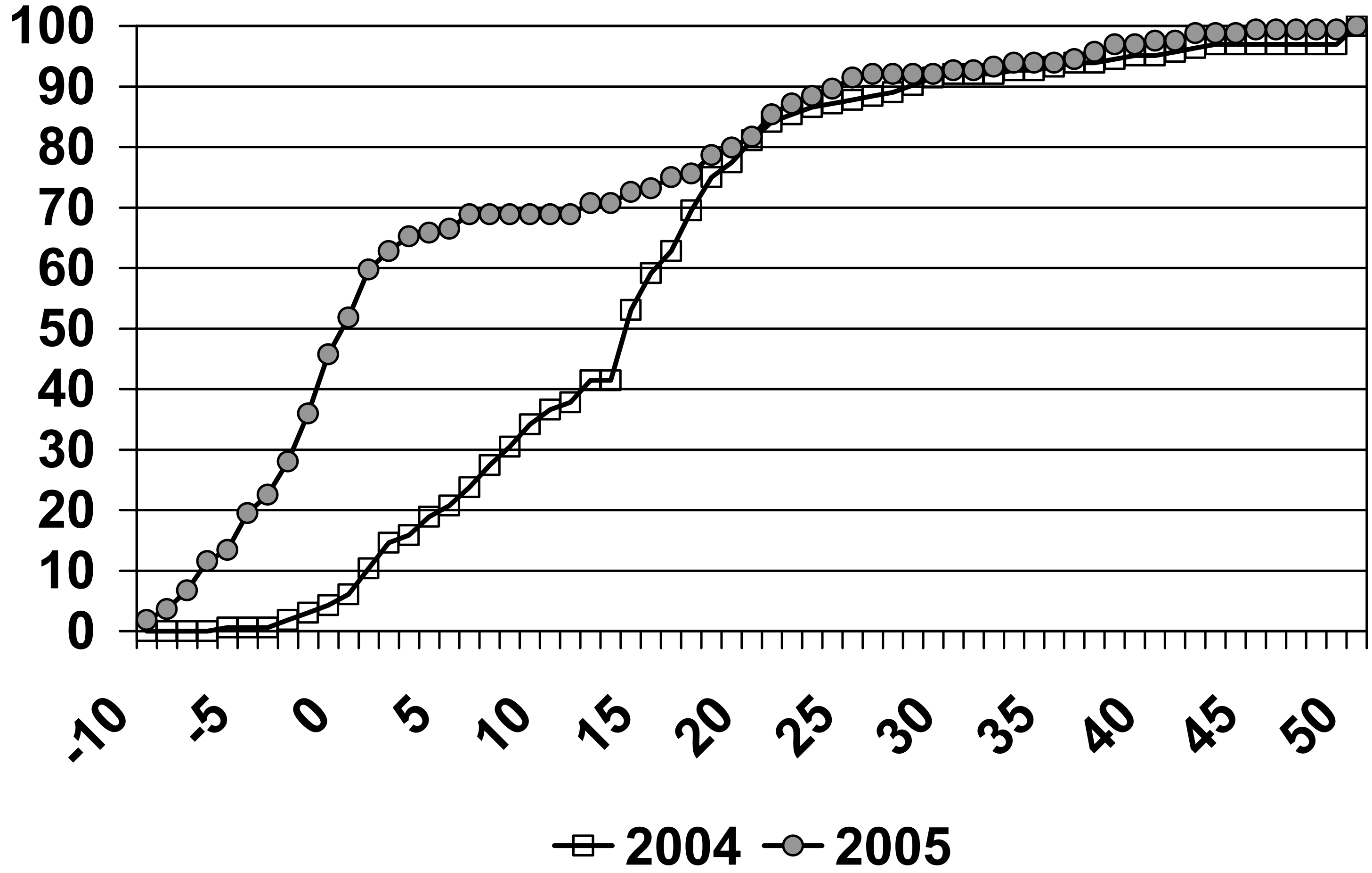

Figure 17. Calving profiles for cows at the University of Missouri Forage Systems Research Center in Linnueus, MO, over a two year period. This herd maintains a 45 day breeding season and until the spring of 2004 estrus synchronization and AI had not been utilized. The figure illustrates the calving profiles of cows that calved during the spring of 2004 as a result of natural service during the 2003 breeding season, and calving profiles for cows that calved during the spring of 2005 as a result of fixed time AI performed during the 2004 breeding season (Schafer, 2005).

Summary and Conclusions

Expanded use of AI and/or adoption of emerging reproductive technologies for beef cows and heifers require precise methods of estrous cycle control. Effective control of the estrous cycle requires the synchronization of both luteal and follicular functions. Efforts to develop more effective estrus synchronization protocols 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 that 5 to 15% of estrous cycling cows show estrus on or before PG injection. New protocols for inducing and synchronizing a fertile estrus in postpartum beef cows and replacement beef heifers in which progestins are used sequentially with the GnRH-PG protocol provide new opportunities for beef producers to synchronize estrus and ovulation and facilitate fixed-time AI.

Table 14 provides a summary of the 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 14 provide evidence to support the sequential approach to estrus synchronization in postpartum beef cows we describe.

These data suggest that new methods of inducing and synchronizing estrus for postpartum beef cows and replacement beef heifers now create the opportunity to significantly expand the use of AI in the U.S. cowherd.

Table 14. 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 @ 72 hr		482/763	63%
7-11 Synch	Fixed-time AI @ 60 hr		446/728	61%
CO-Synch + CIDR	Fixed-time AI @ 66 hr		591/912	65%

References

ASBIA. 1998, 2003. Report of semen sales. Brazilian Association of Artificial Insemination. São Paulo, Brazil.

Bader, J.F., F.N. Kojima, D.J. Schafer, J.E. Stegner, M.R. Ellersieck, M.F. Smith, and D.J. Patterson. 2005. A comparison of two progestin-based protocols to synchronize ovulation and facilitate fixed-time artificial insemination in postpartum beef cows. J. Anim. Sci. 83:136-143.

Bao, B., and H.A. Garverick. 1998. Expression of steroidogenic enzyme and gonadotropin receptor genes in bovine follicles during ovarian follicular waves: A review. J. Anim. Sci. 76:1903-1921.

Bremer, V.R., S.M. Damiana, F.A. Ireland, D.B. Faulkner, and D.J. Kesler. 2004. Optimizing the interval from PGF to timed AI in the CoSynch+CIDR and 7-11 Synch estrus synchronization protocols for postpartum beef cows. J. Anim. Sci. 82(Suppl. 2):106.

Brown, L.N., K.G. Odde, D.G. LeFever, M.E. King, and C.J. Neubauer. 1988. Comparison of MGA-$PGF_{2\alpha}$ to Syncro-Mate B for estrous synchronization in beef heifers. Theriogenology 30:1.

Burke, J.M., R.L. d la Sota, C.A. Risco, C.R. Staples, E.J.P. Schmitt, and W.W. Thatcher. Evaluation of timed insemination using a gonadotropin-releasing agonist in lactating dairy cows. J. Dairy Sci. 79:1385-1393.

Deutscher, G.H. 2000. Extending interval from seventeen to nineteen days in the melengestrol acetate-prostaglandin estrous synchronization program for heifers. Prof. Anim. Sci. 16:164-168.

Dziuk, P.J., and R.A. Bellows. 1983. Management of reproduction in beef cattle, sheep and pigs. J. Anim. Sci. 57(Suppl.2), 355.

Federal Register. March 26, 1997. New animal drugs for use in animal feeds; Melengestrol Acetate. Vol. 62. No.58. pp.14304-14305.

Fortune, J.E., J. Sirois, and S.M. Quirk. 1988. The growth and differentiation of ovarian follicles during the bovine estrous cycle. Theriogenology 29:95-109.

Garverick, H.A., R.G. Elmore, D.H. Vaillancourt, and A.J. Sharp. 1980. Ovarian response to gonadotropin-releasing hormone in postpartum dairy cows. Amer. J. Vet. Res. 41:1582-1585.

Geary, T.W., J.C. Whittier, E.R. Downing, D.G. LeFever, R.W. Silcox, M.D. Holland, T.M. Nett, and G.D. Niswender. 1998a. Pregnancy rates of postpartum beef cows that were synchronized using Syncro-Mate B or the Ovsynch protocol. J. Anim. Sci. 76:1523-1527.

Geary, T.W., J.C. Whittier, and D.G. LeFever. 1998b. Effect of calf removal on pregnancy rates of cows synchronized with the Ovsynch or CO-Synch protocol. J. Anim. Sci. 81(Suppl.1)278.

Geary, T.W., E.R. Downing, J.E. Bruemmer, and J.C. Whittier. 2000. Ovarian and estrous response of suckled beef cows to the Select Sych estrous synchronization protocol. Prof. Anim.Sci. 16:1-5

Hansel, W., P.V. Malven, and D.L. Black. 1961. Estrous cycle regulation in the bovine. J. Anim. Sci. 20:621-625.

Hughes, H. Something's amiss with profit part 1. BEEF. February 1, 2005.

Imwalle, D.B., D.L. Fernandez, and K.K. Schillo. 2002. Melengestrol acetate blocks the preovulatory surge of luteinizing hormone, the expression of behavioral estrus and ovulation in beef heifers. J. Anim. Sci. 80:1280-1284.

Johnson, S.K., and R. Jones. 2004. Cost and comparisons of estrous synchronization systems. In proceedings Applied Reproductive Strategies in Beef Cattle. North Platte, NE. pp. 103-115.

Kojima, F.N., B.E. Salfen, J.F. Bader, W.A. Ricke, M.C. Lucy, M.F. Smith, and D.J. Patterson. 2000. Development of an estrus synchronization protocol for beef cattle with short-term feeding of melengestrol acetate: 7-11 Synch. J. Anim. Sci. 78:2186-2191.

Kojima, F.N., J.F. Bader, J.E. Stegner, B.E. Salfen, S.L. Wood, M.F. Smith, and D.J. Patterson. 2001. Comparison of melengestrol acetate (MGA)-based estrus synchronization protocols in yearling beef heifers. J. Anim. Sci. 84(Suppl. 1):250.

Kojima, F.N., J.E. Stegner, B.E. Salfen, R.L. Eakins, M.F. Smith, and D.J. Patterson. 2002. A fixed-time AI program for beef cows with 7-11 Synch. Proc. West. Sec. Am. Soc. Anim. Sci. 53:411-413.

Kojima, F.N., J.E. Stegner, J.F. Bader, D.J. Schafer, R.L. Eakins, M.F. Smith, and D.J. Patterson. 2003a. A fixed-time AI program with 7-11 Synch. Proc. West. Sec. Am. Soc. Anim. Sci. 54:265-267.

Kojima, F.N., J.F. Bader, J.E. Stegner, M.F. Smith, and D.J. Patterson. 2003b. A comparison of two fixed-time AI programs for postpartum beef cows. J. Anim. Sci. 81 (Suppl. 1):50.

Kojima, F.N., J.F. Bader, J.E. Stegner, D.J. Schafer, J.C. Clement, R.L. Eakins, M.F. Smith, and D.J. Patterson. 2004. Substituting EAZI-BREED CIDR inserts (CIDR) for melengestrol acetate (MGA) in the MGA Select protocol in beef heifers. J. Anim. Sci. 82(Suppl. 1):255.

Lamb, G.C., D.W. Nix, J.S. Stevenson, and L.R. Corah. 2000. Prolonging the MGA-prostaglandin $F_{2\alpha}$ interval from 17 to 19 days in an estrus synchronization system for heifers. Theriogenology 53:691-698.

Lamb, G.C., J.S. Stevenson, D.J. Kesler, H.A. Garverick, D.R. Brown, and B.E. Salfen. 2001. Inclusion of an intravaginal progesterone insert plus GnRH and prostaglandin $F_{2\alpha}$ for ovulation control in postpartum suckled beef cows. J. Anim. Sci. 79:2253-2259.

Lamond, D.R. 1964. Synchronization of ovarian cycles in sheep and cattle. Anim. Breed. Abstr. 32:269-285.

Larson, J.E., G.C. Lamb, J.S. Stevenson, S.K. Johnson, M.L. Day, T.W. Geary, D.J. Kesler, J.M. DeJarnette, F.N. Schrick, and J.D. Arsenau. 2004. Synchronization of estrus in suckled beef cows using GnRH, prostaglandin $F_{2\alpha}$ (PG), and progesterone (CIDR): a multi location study. J. Anim. Sci. 87(Suppl.1):368.

Lauderdale, J.W. 1972. Effects of prostaglandin $F_{2\alpha}$ Tham on pregnancy and estrous cycle of cattle. J. Anim. Sci. 35(Suppl. 1):246.

Lauderdale, J.W., B.E. Seguin, J.N. Stellflug, J.R. Chenault, W.W. Thatcher, C.K. Vincent, and A.F. Loyancano. 1974. Fertility of cattle following $PGF_{2\alpha}$ injection. J. Anim. Sci. 38:964-967.

Liehr, R.A., G.B. Marion, and H.H. Olson. 1972. Effects of progstaglandin on cattle estrous cycles. J. Anim. Sci. 35(Suppl. 1):247.

Macmillan, K.L., and H.V. Henderson. 1984. Analyses of the variation in the interval of prostaglandin $F_{2\alpha}$ to oestrus as a method of studying patterns of follicle development during diestrus in dairy cows. Anim. Reprod. Sci. 6:245-254.

Mussard, M.L., C.R. Burke, C.L. Gasser, E.J. Behlke, K.A. Colliflower, D.E. Grum, and M.L. Day. 2003. Ovulatory response, luteal function and fertility in cattle induced to ovulate dominant follicles of early or late maturity. Biol. Reprod. 68(Suppl. 1):332.

NAAB. 1998, 2003. Report of semen sales and custom freezing. National Association of Animal Breeders, Columbia, MO

Nellor, J.E., and H.H. Cole. 1956. The hormonal control of estrus and ovulation in the beef heifer. J. Anim. Sci. 15:650-661.

NAHMS. 1998. Part IV. Changes in the U.S. Beef Cow-Calf Industry. 1993-1997. pp. 1. USDA-APHIS Center for Epidemiology and Animal Heath, Fort Collins, CO.

Patterson, D.J., G.H. Kiracofe, J.S. Stevenson, and L.R. Corah. 1989. Control of the bovine estrous cycle with melengesrol acetate (MGA): A review. J. Anim. Sci. 67:1895-1906.

Patterson, D.J., J.M. Kearnan, N.W. Bradley, K.K. Schillo, and B.L. Woods. 1993. Estrus response and fertility in yearling beef heifers after chronic treatment with an oral progestogen followed by prostaglandin $F_{2\alpha}$. University of Kentucky Beef Cattle Research Report. Progress Report 353. Pp. 31-33.

Patterson, D.J., S.L. Wood, and R.F. Randle. 2000a. Procedures that support reproductive management of replacement beef heifers. Proc. Am. Soc. Anim. Sci., 1999. Available at: http://www.asas.org/jas/symposia/proceedings/0902.pdf. Accessed August 3, 2000.

Patterson, D.J., S.L. Wood, F.N. Kojima, and M.F. Smith. 2000b. Current and emerging methods to synchronize estrus with melengestrol acetate. In: 49th Annual Beef Cattle Short Course Proceedings "Biotechnologies of Reproductive Biology". Pp. 45-66. University of Florida, Gainesville.

Patterson, D.J., J.E. Stegner, F.N. Kojima, and M.F. Smith. 2002. MGA® Select improves estrus response in postpartum beef cows in situations accompanied with high rates of anestrous. Proc. West. Sec. Am. Soc. Anim. Sci. 53:418-420.

Patterson, D.J., F.N. Kojima, and M.F. Smith. 2003. A review of methods to synchronize estrus in replacement heifers and postpartum beef cows. J. Anim. Sci. 81(E. Suppl. 2):E166-E177. Online.Available: http://www.asas.org/symposia/03esupp2/jas2402.pdf. Accessed June 19, 2003.

Perry, G.A., M.F. Smith, and D.J. Patterson. 2002. Evaluation of a fixed-time artificial insemination protocol for postpartum suckled beef cows. J. Anim. Sci. 80:3060-3064.

Perry, G.A, M.F. Smith, and T.W. Geary. 2004. Ability of intravaginal progesterone inserts and melengestrol acetate to induce estrous cycles in postpartum beef cows. J. Anim. Sci. 82:695-704.

Perry, G.A., M.F. Smith, M.C. Lucy, J.A. Green, T.E. Parks, M.D. MacNeil, A.J. Roberts, and T.W. Geary. 2005. Relationship between follicle size at insemination and pregnancy success. Proc. National Academy of Sciences. 102:5268-5273.

Pursley, J.R., M.O. Mee, and M.C. Wiltbank. 1995. Synchronization of ovulation in dairy cows using $PGF_{2\alpha}$ and GnRH. Theriogenology 44:915-924.

Pursley, J.R., M.W. Kosorok, and M.C. Wiltbank. 1997a. Reproductive management of lactating dairy cows using synchronization of ovulation. J. Dairy Sci.80:301-306.
Pursley, J.R., M.C. Wiltbank, J.S. Stevenson, J.S. Ottobre, H.A. Garverick, and L.L. Anderson. 1997b. Pregnancy rates in cows and hiefers inseminated at a synchronized ovulation or synchronized estrus. J. Dairy Sci. 80:295-300.
Pursley, J.R., R.W. Silcox, and M.C. Wiltbank. 1998. Effect of time of artificial insemination on pregnancy rates, calving rates, pregnancy loss, and gender ratio after synchronization of ovulation in lactating dairy cows. J. Dairy Sci. 81:2139-2144.
Rowson, L.E.A., R. Tervit, and A. Brand. 1972. The use of prostaglandin for synchronization of oestrus in cattle. J. Reprod. Fertil. 29:145 (Abstr).
Sartori, R., P.M. Fricke, J.C. Ferreira, O.J. Ginther, and M.C. Wiltbank. 2001. Follicular deviation and acquisition of ovulatory capacity in bovine follicles. Biol. Reprod. 65:1403-1409.
Schafer, D.J. 2005. Comparison of progestin based protocols to synchronize estrus and ovulation in beef cows. M.S. Thesis. University of Missouri, Columbia.
Schafer, D.W., J.S. Brinks, and D.G. LeFever. 1990. Increased calf weaning weight and weight via estrus synchronization. Beef Program Report. Colorado State University. pp. 115-124.
Schmitt, E.J.P., T. Diaz, M. Drost, and W.W. Thatcher. 1996. Use of a gonadotropin-releasing hormone agonist or human chorionic gonadotropin for timed insemination in cattle. J. Anim. Sci. 74:1084-1091.
Seidel, G.E. Jr. 1995. Reproductive biotechnologies for profitable beef production. Proc. Beef Improvement Federation. Sheridan, WY. Pp. 28-39.
Sirois, J., and J.E. Fortune. 1988. Ovarian follicular dynamics during the estrous cycle in heifers monitored by real-time ultrasonography. Biol. Reprod. 39:308-317.
Stegner, J.E., F.N. Kojima, M.R. Ellersieck, M.C. Lucy, M.F. Smith, and D.J. Patterson. 2004a. Follicular dynamics and steroid profiles in cows during and after treatment with progestin-based protocols for synchronization of estrus. J. Anim. Sci. 82:1022-1028.
Stegner, J.E., F.N. Kojima, M.R. Ellersieck, M.C. Lucy, M.F. Smith, and D.J. Patterson. 2004b. A comparison of progestin-based protocols to synchronize estrus in postpartum beef cows. J. Anim. Sci. 82:1016-1021.
Stegner, J.E., J.F. Bader, F.N. Kojima, M.R. Ellersieck, M.F. Smith, and D.J. Patterson. 2004c. Fixed-time artificial insemination of postpartum beef cows at 72 or 80 hours after treatment with the MGA® Select protocol. Theriogenology 61:1299-1305.
Stevenson, J.S., G.C. Lamb, J.A. Cartmill, B.A. Hensley, S.Z. El-Zarkouny, and T.J. Marple. 1999. Synchronizing estrus in replacement beef heifers using GnRH, melengestrol acetate, and $PGF_{2\alpha}$. J. Anim. Sci. 77(Suppl. 1):225.
Stevenson, J.S., G.C. Lamb, S.K. Johnson, M.A. Medina-Britos, D.M. Grieger, K.R. Harmoney, J.A. Cartmill, S.Z. El-Zarkouny, C.R. Dahlen, and T.J. Marple. 2003. Supplemental norgestomet, progesterone, or melengestrol acetate increases pregnancy rates in suckled beef cows after timed inseminations. J. Anim. Sci. 81:571-586.

Thatcher, W.W., M. Drost, J.D. Savio, K.L. Macmillan, K.W. Entwistle, E.J. Schmitt, R.L. De La Sota, and G.R. Morris. 1993. New clinical uses of GnRH and its analogues in cattle. Anim. Reprod. Sci. 33:27-49.

Thimonier, J., D. Chupin, and J. Pelot. 1975. Synchronization of estrus in heifers and cyclic cows with progestogens and prostaglandin analogues alone or in combination. Ann. Biol. Anim. Biochim. Biophys. 15:437-449.

Twagiramungu, H., L.A. Guilbault, J. Proulx, and J.J. Dufour. 1992a. Synchronization of estrus and fertility in beef cattle with two injections of Buserelin and prostaglandin. Theriogenology 38:1131-1144.

Twagiramungu, H., L.A. Guilbault, J. Proulx. P. Villeneuve, and J.J. Dufour. 1992b. Influence of an agonist of gonadotropin-releasing hormone (Buserelin) on estrus synchronization and fertility in beef cows. J. Anim. Sci. 70:1904-1910.

Twagiramungu, H., L.A. Guilbault, and J.J. Dufour. 1995. Synchronization of ovarian follicular waves with a gonadotropin-releasing hormone agonist to increase the precision of estrus in cattle: A review. J. Anim. Sci. 73:3141-3151.

Ulberg, L.C., R.E. Christian, and L.E. Casida. 1951. Ovarian response in heifers to progesterone injections. J. Anim. Sci. 10:752-759.

Vasconcelos, J.L., R. Sartori, H.N. Oliveira, J.G. Guenther, and M.C. Wiltbank. 2001. Reduction in size of the ovulatory follicle reduces subsequent luteal size and pregnancy rate. Theriogenology 56:307-314.

Wood, S.L., M.C. Lucy, M.F. Smith, and D.J. Patterson. 2001. Improved synchrony of estrus and ovulation with addition of GnRH to a melengestrol acetate-prostaglandin $F_{2\alpha}$ estrus synchronization treatment in beef heifers. J. Anim. Sci. 79:2210-2216.

Wood-Follis, S.L., F.N. Kojima, M.C. Lucy, M.F. Smith, and D.J. Patterson. 2004. Estrus synchronization in beef heifers with progestin-based protocols. I. Differences in response based on pubertal status at the initiation of treatment. Theriogenology 62:1518-1528.

Zimbelman, R.G. 1963. Maintenance of pregnancy in heifers with oral progestogens. J. Anim. Sci. 22:868.

Zimbelman, R.G., and L.W. Smith. 1966. Control of ovulation in cattle with melengestrol acetate. I. Effect of dosage and route of administration. J. Reprod. Fertil. (Suppl.1):185.

Zimbelman, R.G., J.W. Lauderdale, J.H. Sokolowski, and T.G. Schalk. 1970. Safety and pharmacologic evaluations of melengestrol acetate in cattle and other animals. A review. J.A.V.M.A. 157:1528-1536.