

REVIEW OF ESTROUS SYNCHRONIZATION SYSTEMS:CIDR

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Introduction

The CIDR is an intravaginal progesterone insert, used in conjunction with other hormones to synchronize estrous in beef and dairy cows and heifers. The CIDR was developed in New Zealand and has been used for several years to advance the first pubertal estrus in heifers and the first postpartum estrus in cows. The CIDR is a “T” shaped device with flexible wings that collapse to form a rod that can be inserted into the vagina with an applicator. On the end opposite to the wings of the insert a tail is attached to facilitate removal with ease. The backbone of the CIDR is a nylon spine covered by progesterone (1.38g) impregnated silicone skin. Upon insertion blood progesterone concentrations rise rapidly, with maximal concentrations reached within an hour after insertion. Progesterone concentrations are maintained at a relatively constant level during the seven days the insert is in the vagina. Upon removal of the insert, progesterone concentrations are quickly eliminated.

Retention rate of the CIDR during a seven-day period exceeds 97%. In some cases, vaginal irritation occurs resulting in clear, cloudy or yellow mucus when the CIDR is removed. Cases of mucus are normal and does not have an impact on effectiveness of the CIDR. Caution should be taken when handling CIDRs. Individuals handling CIDRs should wear latex or nitrile gloves to prevent exposure to progesterone on the surface of the insert and to prevent the introduction of contaminants from the hands into the vagina of treated females. The inserts are developed for a one-time use only. Multiple use may increase the incidence of vaginal infections.

CIDR/PGF_{2α} Protocols for Cows

During the seven days of CIDR insertion, progesterone diffusion from the CIDR does not affect spontaneous luteolysis. Assuming all cows have 21 day estrous cycles, there will be two populations of females after six days of CIDR treatment: females without corpora lutea and females with corpora lutea more than six days after ovulation. All females, therefore, have corpora lutea that are potentially responsive to an injection of PGF_{2α}. Although most research data indicates that only about 90% of corpora lutea in cows more than six days after ovulation regress promptly to an injection PGF_{2α}, only about 60% of the females will have corpora lutea at the time of PGF_{2α} treatment (assuming that spontaneous corpora lutea regression beings about 18 days after ovulation). Therefore, about 95% of the females treated with the FDA approved CIDR/PGF_{2α} protocol are synchronized to exhibit estrus within a few days of CIDR insert removal. However, more than 95% of the treated females will be synchronized to exhibit estrus if estrous behavior is monitored for five days after removal of the CIDR insert.

Table 1. Fertility rates in cycling or noncycling suckled beef cows treated with estrous synchronization protocols containing a CIDR.

Reference and treatment description	No. of cows	Conception rate ^a , %	Pregnancy rate ^b , %
Lamb et al., 2001			
<i>CO-Synch - anestrous</i>	56	-	22/56 (39)
<i>CO-Synch - cyclic</i>	172	-	91/172 (53)
<i>CO-Synch + CIDR from d -7 to 0 - anestrous</i>	61	-	36/61 (59)
<i>CO-Synch + CIDR from d -7 to 0 - cyclic</i>	161	-	102/161 (63)
Larson et al., 2004a			
<i>CIDR/PGF_{2α} (PG on d 0) - anestrous</i>	147	-	74/147 (50)
<i>CIDR/PGF_{2α} (PG on d 0) - cyclic</i>	296	-	159/296 (54)
<i>CO-Synch - anestrous</i>	156	-	59/156 (38)
<i>CO-Synch - cyclic</i>	330	-	145/330 (44)
<i>CO-Synch + CIDR - anestrous</i>	180	-	85/180 (47)
<i>CO-Synch + CIDR - cyclic</i>	294	-	169/294 (57)
<i>Hybrid Synch - anestrous</i>	143	-	60/143 (42)
<i>Hybrid Synch - cyclic</i>	308	-	182/308 (59)
<i>Hybrid Synch + CIDR - anestrous</i>	136	-	72/136 (53)
<i>Hybrid Synch + CIDR - cyclic</i>	306	-	180/306 (59)
Lucy et al., 2001			
<i>Control - anestrous</i>	151	6/16 (38)	6/151 (4)
<i>Control - cyclic</i>	134	15/26 (58)	15/134 (11)
<i>PGF_{2α} - anestrous</i>	154	17/30 (57)	17/154 (11)
<i>PGF_{2α} - cyclic</i>	129	44/63 (70)	44/129 (34)
<i>CIDR/PGF_{2α} (PG on d -1) - anestrous</i>	141	36/63 (57)	36/141 (26)
<i>CIDR/PGF_{2α} (PG on d -1) - cyclic</i>	140	64/101 (63)	64/140 (46)

^a Percentage of cows pregnant exposed to AI.

^b Percentage of cows pregnant of all cows treated.

An advantage of a progestin-based estrous synchronization protocol is that administration of progestins to prepubertal heifers and postpartum anestrous cows have been demonstrated to hasten cyclicity. When suckled beef cows were assigned randomly in replicates to one of three groups (Lucy et al., 2001): 1) untreated controls, 2) a single intramuscular (IM) injection of 25 mg PGF_{2α} (PGF_{2α} alone), or 3) administration of a CIDR insert for 7 d with an IM administration of PGF_{2α} on day 6 of the 7 d CIDR insert administration period (CIDR + PGF_{2α}) no differences were detected between the CIDR + PGF_{2α} treatment group and either the PGF_{2α} alone or control groups for first-service CR for either the first 3 d of AI or the entire 31 d of AI. More cows were pregnant after either 3 d or 7 d of AI in the CIDR + PGF_{2α} group than in either the PGF_{2α} alone or the control group. No differences were detected in PR to first services during the 31 d AI period between the CIDR + PGF_{2α} and either the PGF_{2α} alone or the control group. Therefore, insertion of the CIDR increased the synchronization rates within the first 3 d following PGF_{2α}, resulting in enhanced pregnancy rates. A drawback of the current protocol is that PGF_{2α} was administered on d 6 after CIDR insertion (a day before CIDR removal). For beef producers this tends to be impractical, because the cows need to be handled a minimum of four times including an AI. Therefore, a

more practical modification of this protocol is to inject PGF_{2α} the on the day of CIDR removal.

Advances in Protocols Using the CIDR for Cows

Several alterations of the basic protocol are being evaluated; however, much work is yet to be done since field trials with CIDRs were limited during the FDA approval process. Inclusion of the CIDR in the CO-Synch procedure appears to be the most researched alternative method for synchronizing beef cows. We (Lamb et al., 2001) published data in which the CIDR was included in the CO-Synch estrous synchronization procedure (Table 1). The CIDR was inserted at the time of the first injection of GnRH and removed at the time of the injection of PGF_{2α}. Overall, there was a positive effect of including the CIDR in the CO-Synch protocol; however, this positive effect was not consistent across all locations. Second, the positive effect of including the CIDR was absent in the cows that were cycling and had high progesterone concentrations at the time of PGF_{2α} treatment, which may explain why there was not a positive effect at each location. Along with parity, days postpartum, calf removal, and cow body condition (Table 2) our previous report (Lamb et al., 2001) also indicated that location variables, which could include differences in pasture and diet, breed composition, body condition, postpartum interval, and geographic location, may affect the success of fixed-time AI protocols.

In a more recent study involving 14 locations in 7 states we (Larson et al., 2006) evaluated both fixed-time AI protocols and detection of estrus protocols with a clean-up AI. These protocols were compared to GnRH/ PGF_{2α} protocols. Although the location accounted for the greatest variation in overall pregnancy rates the Hybrid- Synch + CIDR protocol (Figure 1) was the protocol that most consistently yielded the greatest pregnancy rates within each location. However, the CO-Synch protocol (Figure 1) was an effective Fixed-time AI protocol that yielded pregnancy rates of 54%.

Table 2. Pregnancy rates in suckled beef cows after treatment with Cosynch or Cosynch+CIDR (Lamb et al., 2001)

Item	Treatment ^a		Overall
	Cosynch	Cosynch+P	
	----- no. (%) -----		
Body condition ^b			
≤ 4.5	12/40 (30)	11/36 (31)	23/76 ^x (30)
4.5 to 5.5	30/74 (41)	40/80 (50)	70/154 ^y (45)
≥ 5.5	19/32 (59)	11/13 (85)	31/45 ^z (69)
Days postpartum			
≤ 50	23/60 (38)	27/58 (47)	50/118 ^x (42)
51-60	25/62 (47)	36/54 (67)	61/116 ^y (53)
61-70	28/49 (62)	25/44 (57)	53/93 ^y (57)
71-80	18/41 (44)	30/45 (67)	48/86 ^y (56)
> 80	44/75 (59)	42/72 (58)	86/147 ^y (59)
Parity ^c			
Multiparous	61/138 (44)	79/132 (60)	140/270 (52)
Primiparous	25/50 (50)	20/45 (44)	45/95 (47)

^a See experimental design for treatments in Figure 1.

^b Body condition scores from IL and MN only.

^c Parity data from KS and MN only.

^{xyz} Percentages within an item and column lacking a common superscript letter differ ($P < .05$).

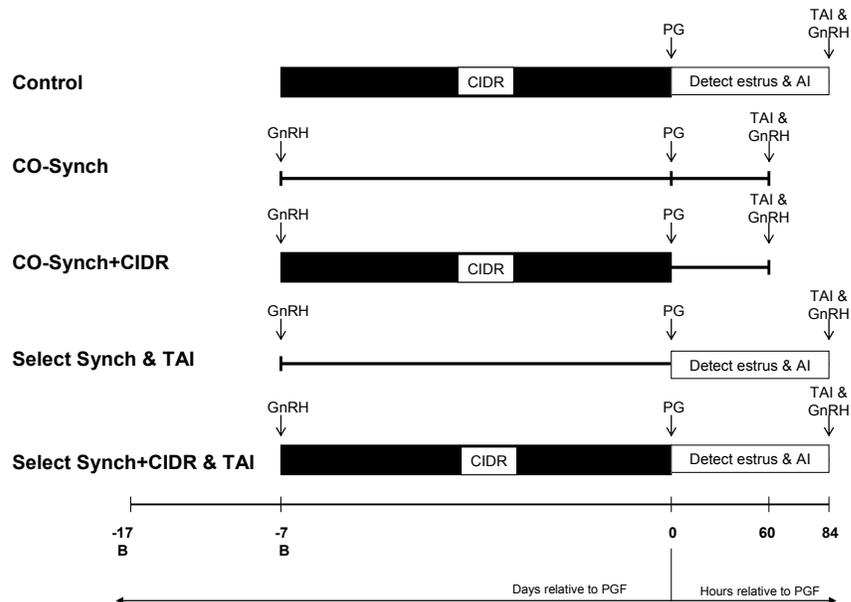


Figure 1. Estrous synchronization protocols using a CIDR (Larson et al., 2006).

Interestingly, the distribution of estrus among the Control, Select Synch & TAI, and the Select Synch + CIDR & TAI protocols was similar (Figure 2) as was the average interval from PGF_{2α} to estrus or AI was similar to among all three treatments (Figure 3). Since the estrus response was greater in the Hybrid Synch+CIDR protocol overall pregnancy rates were greater.

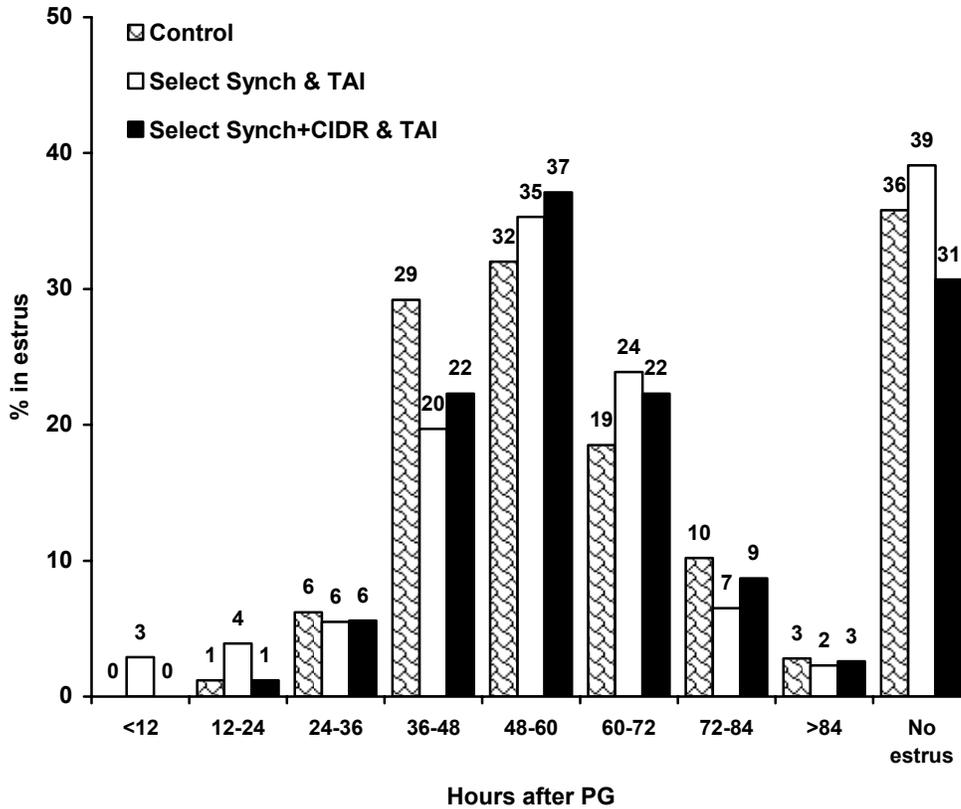


Figure 2. Percentage of cows treated with Control, Select Synch & TAI, Select Synch + CIDR & TAI that were observed in estrus, separated by hours from PG injection to AI (Larson et al., 2004a).

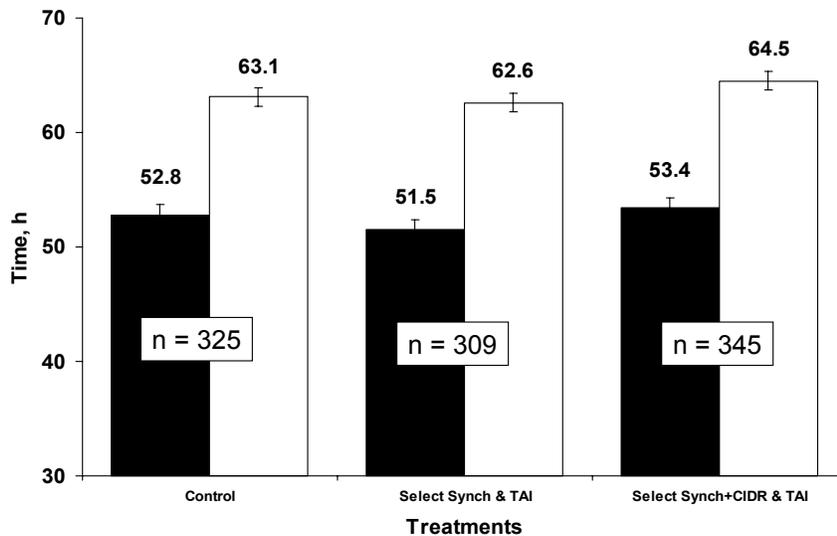


Figure 3. Time from PG injection to estrus (black bar) and time from PG injection to AI (white bar) for those cows exhibiting estrus in Control, Select Synch & TAI, Select Synch + CIDR & TAI treatments (Larson et al., 2006).

Calving data during the subsequent calving season was also assessed. Of the 1,752 calvings, 994 calves (56.7%) were the result of AI after estrus synchronization. Average duration of gestation among all AI sired calves was 281.9 ± 5.2 d ($\bar{x} \pm$ SD), and the range was 258 to 296 d. Duration of gestation was similar among treatments, but a location effect ($P < 0.0001$) was detected, which may have included breed, sire and management differences. Period of gestation was greater ($P < 0.001$) for male (282.9 ± 0.2 d) than female calves (280.9 ± 0.2 d), and single calves were carried 3.0 d longer ($P < 0.05$) than multiple calves.

For those cows from which calving data was recorded, the average interval from the $\text{PGF}_{2\alpha}$ injection (Day 0 of the study) to calving among all cows was 297.3 ± 17.7 d ($\bar{x} \pm$ SD) with a range of 258 to 373 d (Figure 4). Although average calving interval was similar among treatments, a ($P < 0.001$) location effect was detected.

At calving, gender was recorded in 1,490 calves, with 770 (52.2%) male calves compared with 704 females. In addition, 15 sets of twins and a single set of triplets were recorded. Gender ratio of calves that conceived to AI at estrus synchronization favored ($P < 0.01$) bulls (i.e., 52.7% of 841 calves born were male). Similarly, of the 635 calves that conceived to clean-up bulls, 51.7% were male. No difference was detected in gender ratio for AI compared with natural-sired calves. Multiple birth rate for AI-sired calves [1.1% (9 of 850)] was similar to that of calves sired by clean-up bulls [0.9% (6 of 641)].

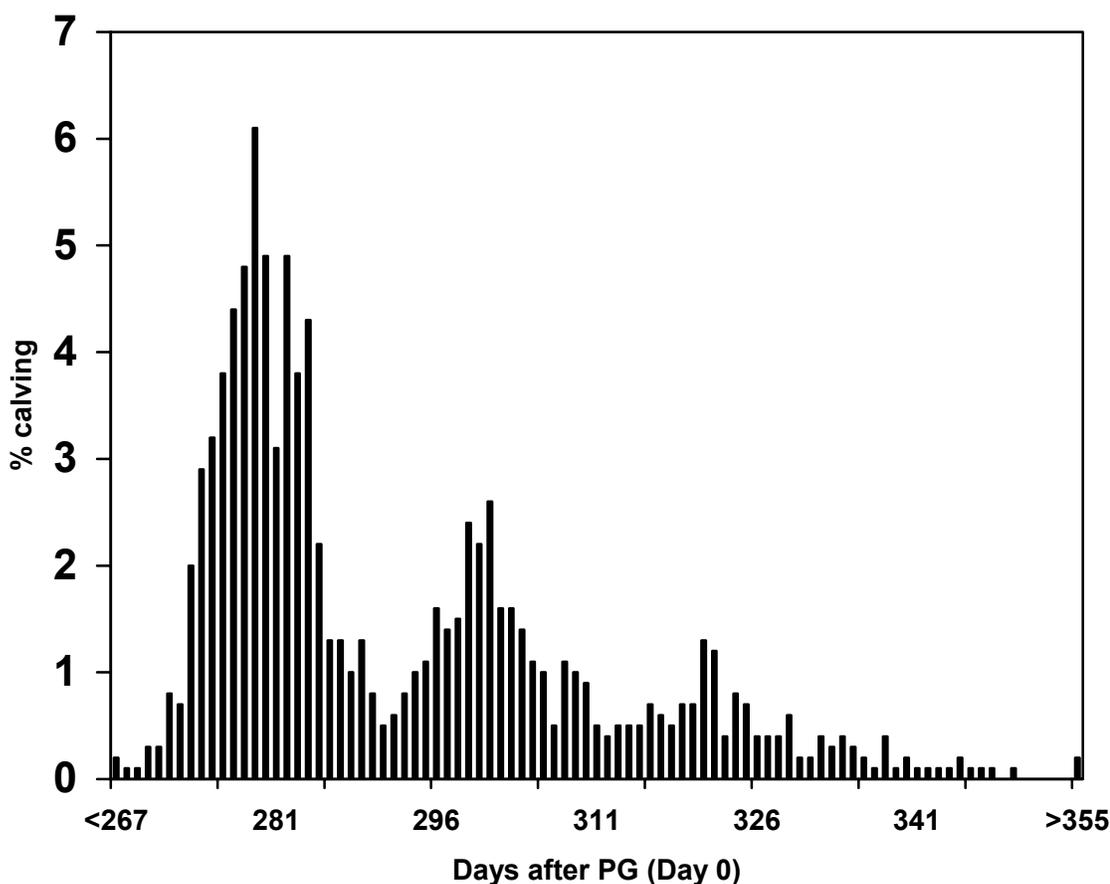


Figure 4. Distribution of calving during the subsequent calving season after synchronization of estrous with GnRH, PGF_{2α}, and (or) a CIDR.

CIDR/PGF_{2α} Protocols for Heifers

As with cows, beef heifers have 21-day estrous cycles and respond to the CIDR in a similar fashion to cows, resulting in a majority of heifers that should be synchronized using the FDA approved CIDR/PGF_{2α} protocol. Heifers tend to be an easier population of females to synchronize for estrus, because they are not nursing calves, tend to express estrus well, and most of the heifers usually are cycling, and can be maintained in areas where they can be fed allowing them to respond well to the MGA/PGF_{2α} system (Wood et al., 2001; Brown et al., 1988; Lamb, et al., 2000). In addition, MGA delivered in feed has the ability to induce puberty in some peripubertal heifers (Patterson et al., 1992). However, the length of time to apply this system (31 to 33 d) is a drawback. During a late spring/early summer breeding season, MGA must be delivered in a grain carrier when cattle tend to be grazing forage pastures. Thus, the challenge is to ensure that each heifer receives the required MGA dose. Therefore, producers could benefit from an alternative estrous synchronization system that eliminates the use of MGA.

First attempts focused at synchronizing estrus in heifers with a CIDR and PGF_{2α}. The study by Lucy et al., (2001; Table 2) demonstrates the pregnancy rates of heifers synchronized with

the FDA approved CIDR/ PGF_{2α} protocol. As in cows, the CIDR/PGF_{2α} protocol yielded greater pregnancy rates in heifers than for heifers that were untreated or for heifers treated with PGF_{2α} alone. Therefore, insertion of the CIDR increased the synchronization rates within the first 3 d following PGF_{2α}, resulting in enhanced pregnancy rates. Again, the drawback of the current protocol is that PGF_{2α} was administered on d 6 after CIDR insertion, which requires an additional day of handling the heifers. Therefore, consideration should be to inject PGF_{2α} the on the day of CIDR removal.

The CIDR + PGF_{2α} treatment reduced the interval to first estrus (2 d) compared with either the control (15 d) or PGF_{2α} alone (16 d) treatments. Similarly, for heifers that were prepubertal when the study was initiated the CIDR + PGF_{2α} shortened the interval to first estrus (14 d) compared to control (27 d) and PGF_{2α} alone (31 d). The CIDR + PGF_{2α} treatment improved the synchrony of estrus compared with the PGF_{2α} alone, with 60% vs. 25%, of heifers in estrus over 3 d after CIDR inserts were removed.

Advances in Protocols Using the CIDR for Heifers

Although excellent pregnancy rates can be achieved with the MGA/PGF_{2α} protocol and acceptable pregnancy rates can be achieved with the CIDR/PGF_{2α} protocol, no system short duration system has managed to successfully synchronize estrus in replacement beef heifers that consistently yields pregnancy rates that match the MGA/PGF_{2α} protocol. In addition, there has not been a no reliable fixed-time AI protocol exists for synchronizing estrus in beef heifers. Therefore, in a more recent study involving 12 locations in 8 states we (Larson et al., 2004b) focused on developing a study to determine whether: 1) a TAI protocol could yield fertility similar to a protocol requiring detection of estrus; and 2) an injection of GnRH at CIDR insertion enhances pregnancy rates.

To evaluate our objectives, estrus in beef heifers was synchronized and artificial insemination occurred after four treatments (Figure 5): 1) ETAI; 2) G+ETAI; 3) TAI; and 4) G+TAI. The percentage of heifers cycling at the initiation of estrous synchronization was 91.0%. Percentages of cycling heifers among locations ranged from 78 to 100%. Overall pregnancy rates were at days 30 to 35 after AI ranged from 38 to 74%. Although no differences in pregnancy rates were detected among treatments, heifers that were inseminated in the estrus-detection treatments had greater pregnancy rates than heifers in the fixed-time AI treatments (56 vs. 51%, respectively). However, the the G+TAI treatment provides a reliable fixed-time AI protocol for beef producers (Figure 6).

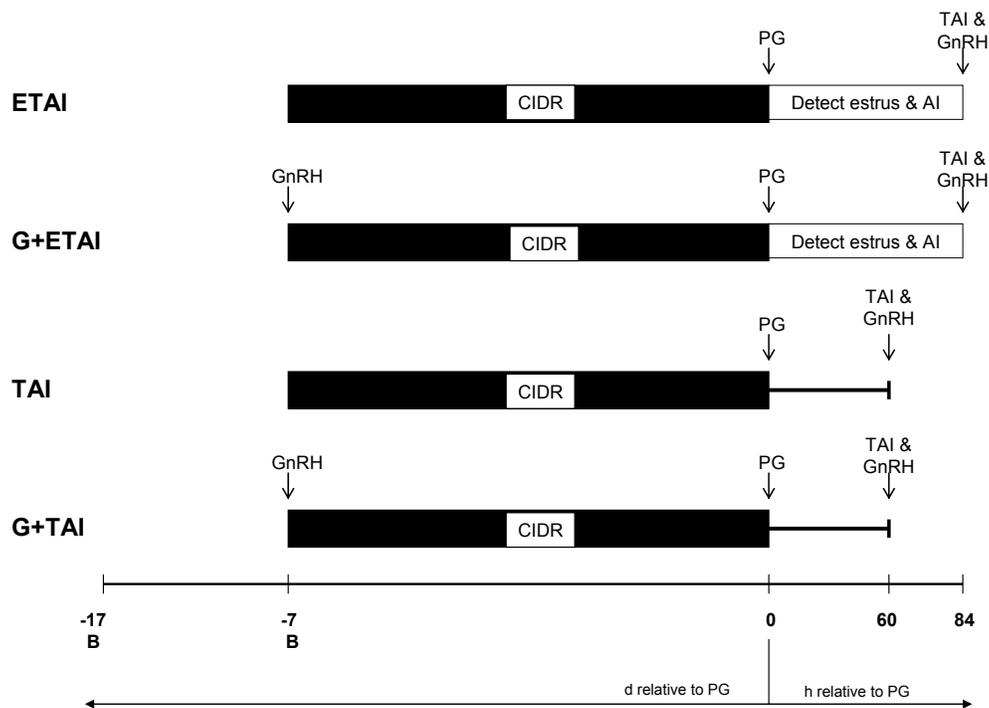


Figure 5. Experimental protocol for estrous synchronization treatments. Blood (B) samples were collected on d -17, and -7. PG = PGF_{2α}; CIDR = controlled internal drug release; TAI = timed AI.

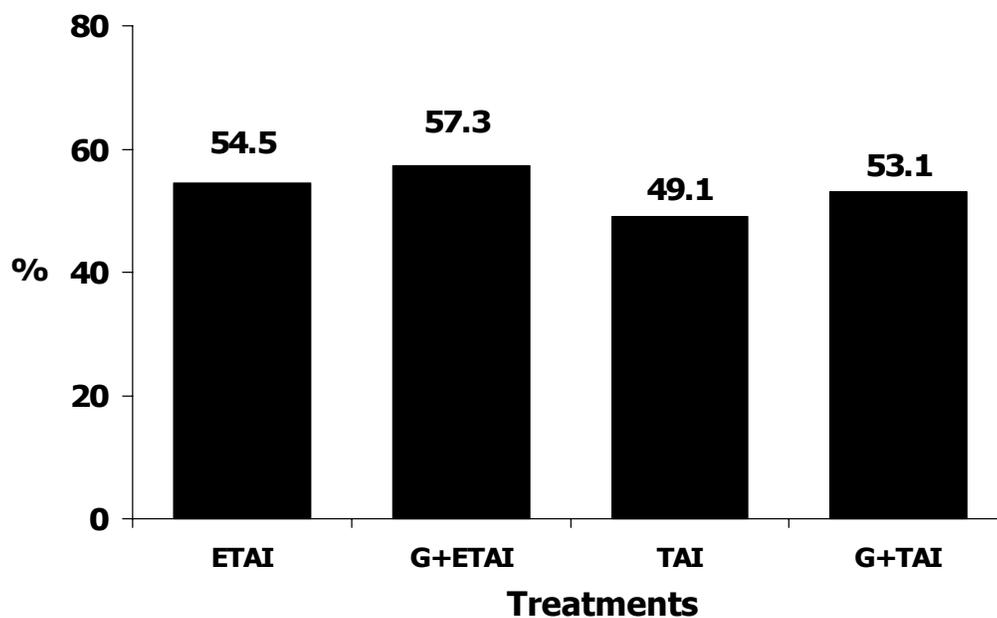


Figure 6. First service pregnancy rates in heifers after receiving one of four CIDR treatments (Larson et al., 2004).

For the two estrus-detection protocols, ETAI and G+ETAI, pregnancy rates for heifers detected in estrus before 84 hr were 44.6 and 45.0%, respectively. Therefore, the clean-up TAI at 84 hr enhanced pregnancy rates by 9.9 and 12.3 percentage points for ETAI and G+ETAI protocols, respectively. These results indicate that TAI after a period of estrus detection enhances the potential for improving pregnancy rates to exceed those of estrus detection alone (Figure 7).

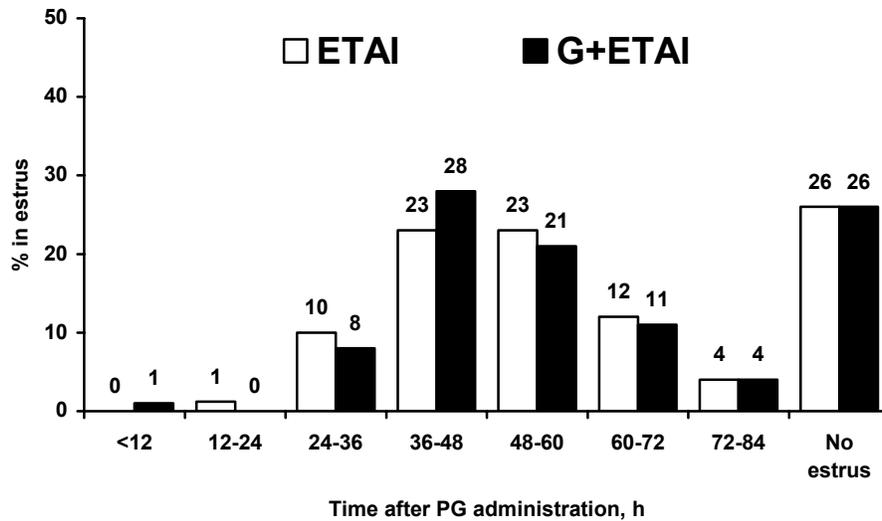


Figure 7. Percentage of heifers treated with CIDR/ PGF_{2α}, or Hybrid Synch+CIDR that were observed in estrus, separated by hours from PG injection to AI (Larson et al., 2004b).

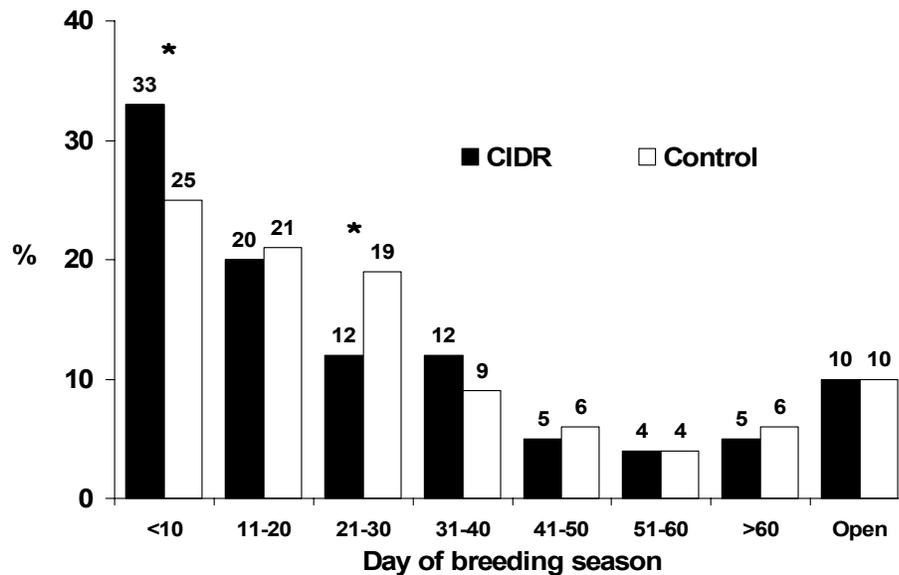
The time from PG injection to detection of estrus and AI for those heifers exhibiting estrus was similar among ETAI (49.9 and 61.7 hr, respectively) and G+ETAI (49.8 and 61.3 hr, respectively). These results demonstrate that estrus in heifers can be synchronized effectively with GnRH, PG, and a CIDR. The G+ETAI treatment most frequently produced the greatest pregnancy rates and provided a reliable alternative to an MGA/PGF_{2α} protocol.

Utilization of the CIDR for bull breeding

To many producers artificial insemination is too technical or time consuming, yet many producers feel that with the development of fixed-time AI (TAI) protocols AI might be a technology that can be utilized to generate a greater proportion of genetically superior beef cattle. The primary reason US beef producers cite for the lack of widespread AI use to breed heifers and cows is limited time and labor (NAHMS, 1998). However, the step from using natural service without estrous synchronization to using TAI is a large jump that few producers are willing to take. Therefore, there is reason to believe that estrous synchronization for bull breeding herds is a suitable step towards altering the calving season, decreasing the breeding season length, and initiating noncycling cows to start cycling.

Estrous synchronization in bull breeding herds has the potential to impact a greater number of producers, because greater than 90% of producers do not utilize AI in their current management systems. In fact, only 8.1% of beef cattle operations in the U.S. use AI management procedures regularly on replacement beef heifers or postpartum beef cows to improve reproductive management of their herds and ultimately improve profitability (NAHMS, 1997).

When estrous was synchronized for bull breeding with a single injection of PGF2a administered at initiation of the breeding season the percentage of females detected in estrus and pregnancy rates were greater than saline treated controls (Whittier et al., 1991). In addition, when heifers were estrous synchronized with melengestrol acetate and PGF2a and exposed to bulls, the desirable bull:heifer ratio was 1:25 or less (Healy et al., 1993). Under this premise, we (Dahlen et al., 2006) designed a study to determine whether insertion of a CIDR for 7 d prior to the breeding season and removing the CIDR on the day bulls were introduced to the cowherd would alter the overall pregnancy rates, average days to conception, and the subsequent calving distribution.



* Treatments differ within period (P < 0.05)

Figure 8. Proportion of cows conceiving at various intervals of the breeding season for cows in Control or CIDR treatments.

Overall pregnancy rates ranged from 59.3 to 98.9% among the 13 locations. Pregnancy rates within the first 30 days of the breeding season were similar between CIDR (64.4%) and Control (64.7%), and overall pregnancy rates were similar between CIDR (89.7%) and Control (89.6%). The average day of conception after initiation of the breeding season was shorter (P < 0.05) for CIDR (20.1 ± 0.8 d) compared to Control cows (23.2 ± 0.8 d). Of cows conceiving during the breeding season, more (P < 0.05) CIDR cows (43%) conceived during the first ten days of the breeding season than Control cows (35%; Figure 8). Therefore,

insertion of a CIDR prior to the breeding season failed to increase overall pregnancy rates, but did influence the average day of conception in earlier calving cows.

Postinsemination Utilization of CIDR

Previous reports have demonstrated that Post-insemination progesterone supplementation on d 5 after AI enhanced pregnancy rates in Holstein cows, but suppressed fertility when administered within 2 d of first insemination (Van Cleeff et al., 1996). In addition, heifers receiving a CIDR insert on d 2 after AI had shorter estrous cycles than controls (Lynch et al., 1999).

Resynchronization of estrous in nonpregnant cows after an initial AI reduces the period required for detection of estrus and AI of nonpregnant females. When cows were resynchronized with a progestin the synchronized return rates of nonpregnant females was greater than controls (Stevenson et al., 2003). Therefore, we conducted a study to determine whether resynchronization of an estrus could be accomplished in nonpregnant cows without compromising pregnancy in cows pregnant from a previous synchronized estrus or to those inseminated to the resynchronized estrus. Ovulation was synchronized in 937 suckled beef cows at 6 locations using a CO-Synch + CIDR protocol. After initial TAI cows were assigned randomly to 4 treatments; 1) untreated (control; n = 237); 2) CIDR inserted 5 d after TAI and removed 14 d after TAI (CIDR5-14; n = 234); 3) CIDR inserted 14 d after TAI and removed 21 d after TAI (CIDR14-21; n = 232); or 4) CIDR inserted 5 d after TAI and removed 14 d after TAI and then a new CIDR inserted at 14 d and removed 21 d after TAI (CIDR5-21; n = 234). After TAI, cows were observed twice daily until 25 d after TAI for estrus and inseminated according to the AM-PM rule. Pregnancy was determined at 29 and 59 d after TAI to determine conception to first- and second-service AI.

Pregnancy rates to TAI were similar for control (55%), CIDR5-14 (54%), CIDR14-21 (48%), and CIDR5-21 (53%; Table 3). A greater proportion of nonpregnant cows were resynchronized during a 2-d peak period in the CIDR5-21 (76/109, 70%) and CIDR14-21 (77/119, 65%) than controls (44/106, 42%) and CIDR5-14 (39/109, 36%) cows. Although overall pregnancy rates after second AI service were similar, conception rates of nonpregnant cows detected in estrus and inseminated seemed to be compromised ($P < 0.05$) in CIDR5-21 (41/76, 54%) and CIDR14-21 (71/77, 53%) compared with CIDR5-14 (28/39, 72%) cows, whereas controls (29/44, 66%) were intermediate. Insertion of a CIDR 5 d after a TAI did not compromise or enhance pregnancy rates to TAI, however, conception rates were compromised in nonpregnant cows that were resynchronized with a CIDR from d 5 or 14 until 21 d after TAI.

Supplementation of progesterone to postpartum suckled beef cows on d 5 after AI does not appear to enhance fertility. In addition, resynchronization of estrus in nonpregnant cows with a CIDR until d 21 after TAI improves synchronized return rates, but decreases conception rates at the resynchronized estrus.

Table 3. Fertility rates and estrous response to cows resynchronized with a CIDR after an initial fixed-time AI (Thielen et al., 2006).

Item	Treatments			
	Control	CIDR5-14	CIDR14-21	CIDR5-21
1 st service pregnancy rates, no./no. (%) ^a	130/237 (55)	126/234 (54)	111/232 (48)	124/234 (53)
2 nd service pregnancy rates, no./no. (%) ^b	159/237 (67)	159/234 (68)	155/232 (67)	161/234 (69)
Non-pregnant cows exhibiting estrus, no./no. (%) ^c	44/106 (42) ^x	39/109 (36) ^x	77/119 (65) ^y	76/109 (70) ^y
Conception rates, no./no. (%) ^d	29/44 (66) ^{xy}	28/39 (72) ^x	41/77 (53) ^y	41/76 (54) ^y

^a Percentage of cows pregnant to fixed-time AI compared to all cows treated.

^b Percentage of cows pregnant to fixed-time AI and resynchronized estrus compared to all cows treated.

^c Percentage of non-pregnant cows that exhibited estrus between d 5 and 26 after fixed-time AI.

^{xyz} Percentages within a row lacking a common superscript letter differ ($P < .05$).

Summary

To achieve optimal pregnancy rates with CIDR based estrous synchronization protocol, cows should be in good body condition ($BCS \geq 5$) and treatments should be initiated only when cows are at least 50 days postpartum. Treatment of suckled cows and replacement beef heifers with a CIDR and GnRH will yield industry accepted pregnancy rates. Results of the most recent CIDR based studies indicate that for a fixed-timed AI protocol the CO-Synch+CIDR protocol yields the most impressive pregnancy rates for a fixed-time AI protocol, whereas the Hybrid Synch+CIDR treatment yields the best overall pregnancy rates. Similarly, heifers can be synchronized effectively with GnRH, PG, and a CIDR. The Select Synch+CIDR protocol most frequently yields the greatest pregnancy rates and provides a reliable alternative to an MGA/PGF_{2 α} . In addition, a fixed-time AI CIDR-based estrous synchronization protocol has been developed to inseminate both suckled beef cows and replacement heifers with acceptable pregnancy rates.

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