

REVIEW OF ESTRUS SYNCHRONIZATION SYSTEMS:CIDR

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Introduction

The CIDR is an intravaginal progesterone insert, used in conjunction with other hormones to synchronize estrus 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 suckled beef cows treated with estrous synchronization protocols containing progestins.

Reference and treatment description	No. of cows	Conception rate ^a , %	Pregnancy rate ^b , %
Stevenson et al., 2000			
Exp. 1			
<i>Select Synch</i>	289	115/175 (66)	115/289 (38)
<i>Select Synch + Norgestomet</i>	289	123/208 (59)	123/289 (42)
<i>2 × PGF_{2α}</i>	294	86/142 (61)	86/294 (28)
Dejarnette et al., 2001			
Exp. 2			
<i>Select Synch</i>	77	40/60 (67)	40/77 (52)
<i>Select Synch + MGA from d -7 to -1</i>	73	43/61 (72)	43/73 (60)
Lamb et al., 2001			
<i>CO-Synch</i>	287	-	138/287 (48)
<i>CO-Synch + CIDR from d -7 to 0</i>	273	-	160/273 (59)
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., 2004) 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).

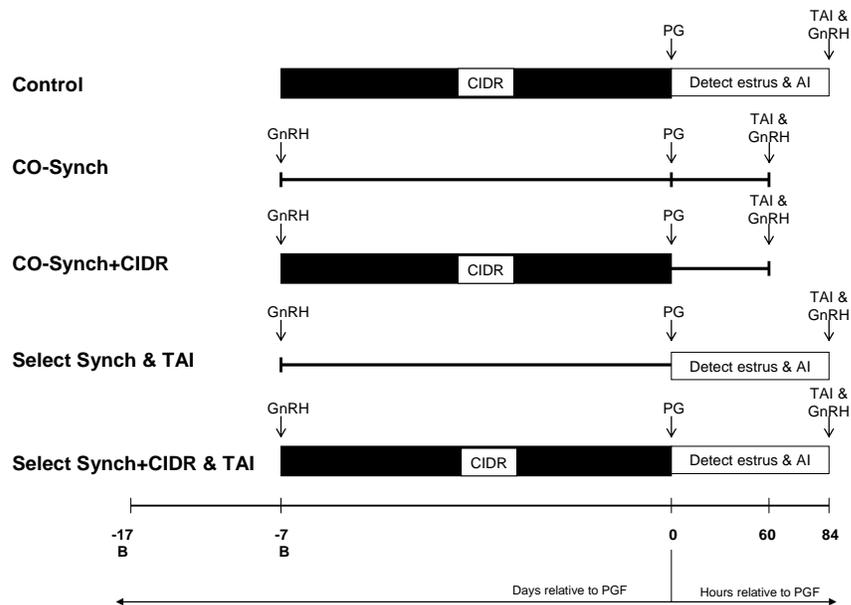


Figure 1. Estrous synchronization protocols using a CIDR (Larson et al., 2005).

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.

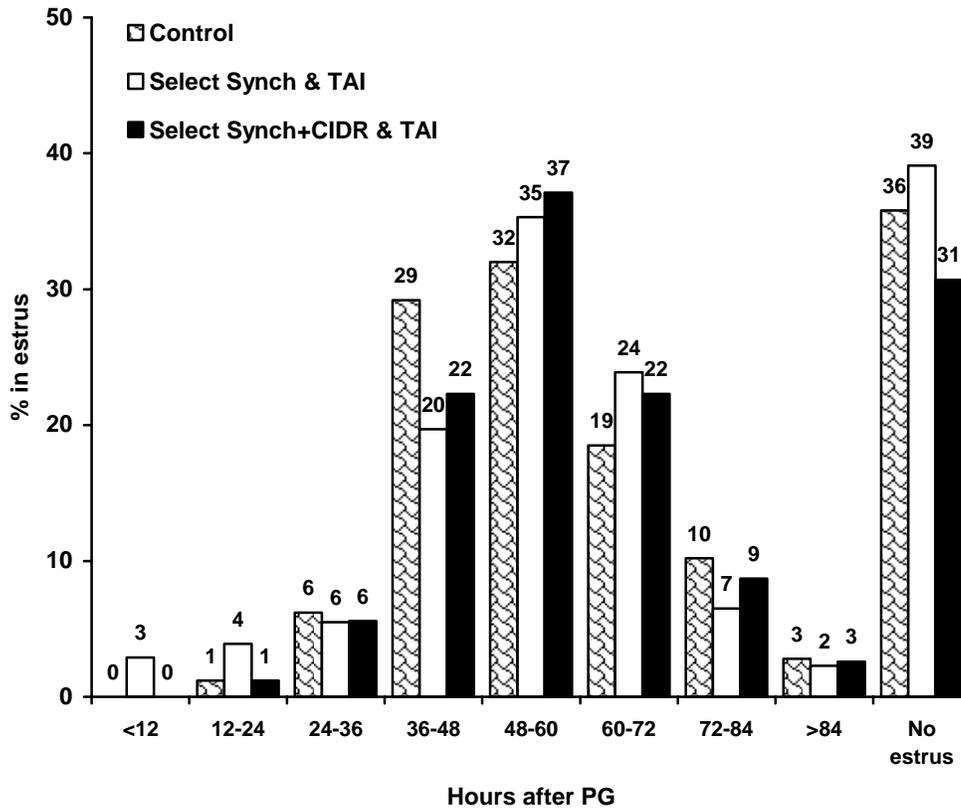


Figure 2. Percentage of cows treated with Control, Select Synch & TAI, Select Synch + CIDR & TAI that were observed in estrus, separated by hours from PG injection to AI (Larson et al., 2004a).

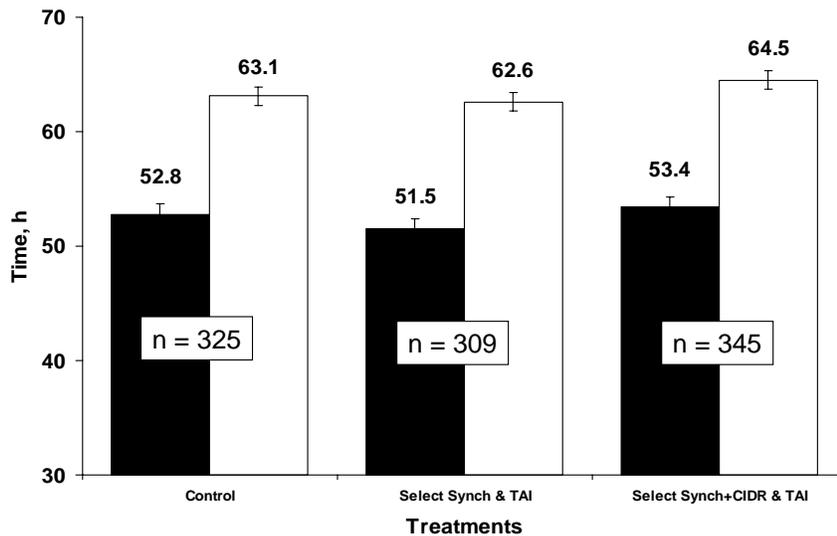
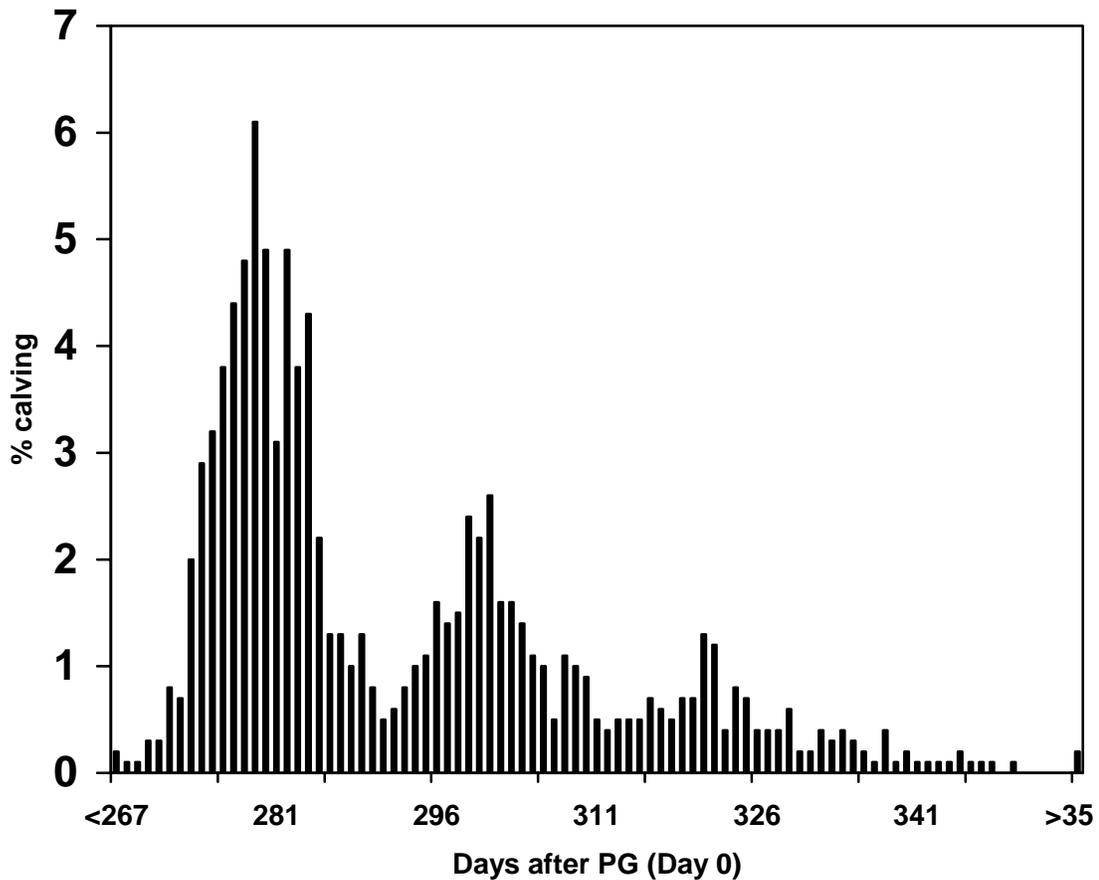


Figure 3. Time from PG injection to estrus (black bar) and time from PG injection to AI (white bar) for those cows exhibiting estrus in Control, Select Synch & TAI, Select Synch + CIDR & TAI treatments (Larson et al., 2005).

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 ($\times \pm$ 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 ($\times \pm$ 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)].



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 (Table 3). 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.

Table 3. Interval to estrus, synchrony of estrus and fertility of beef heifers following treatment with PGF_{2α} or CIDR and an injection of PGF_{2α} (Lucy et al., 2001).

Criterion	Untreated controls	PGF _{2α} ¹	CIDR/PGF _{2α} ²
Interval ³ to estrus, d (n)			
All heifers	15*	16*	2
Anestrous heifers ⁵	27**	31**	14
Estrus d 1-3, %	12**	25**	60
FSCR ⁴ , % (n)			
D 1-3	57	52	60
D 1-31	58	52	58
FSPR ⁵ , % (n)			
D 1-3	7**	14**	36
D 1-7	14**	18**	38
D 1-31	42	36*	47

¹25 mg prostaglandin F_{2α}

²CIDR insert administered intravaginally for 7 days with PGF_{2α} administered on day 6.

³ Median interval in days from removal of CIDR inserts.

⁴ First-service conception rate (number of heifers).

⁵ First-service pregnancy rate (number of heifers).

* Different from CIDR/PGF_{2α}, *P* < 0.05.

** Different from CIDR/PGF_{2α}, *P* ≤ 0.01.

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: 1) CIDR/PGF_{2α}; 2) Hybrid Synch+CIDR; 3) CO-Synch+CIDR; and 4) CIDR/PGF_{2α} + 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 CO-Synch+CIDR treatment provides a reliable fixed-time AI protocol for beef producers (Figure 5).

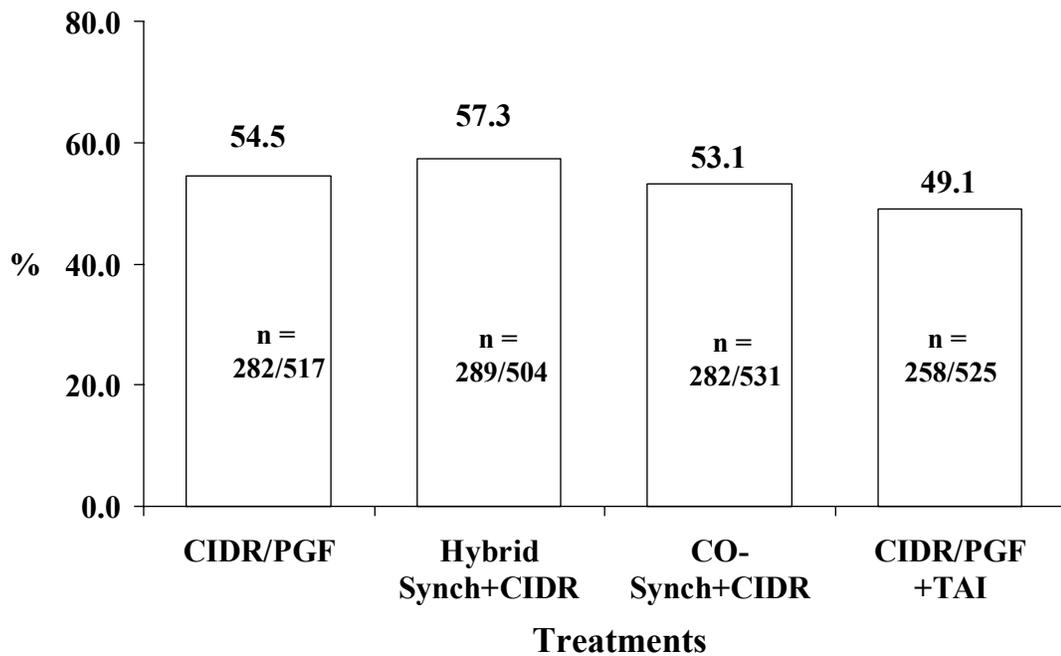


Figure 5. First service pregnancy rates in heifers after receiving one of four CIDR treatments (Larson et al., 2004).

For the two estrus-detection protocols, CIDR/PGF_{2α} and Hybrid Synch+CIDR, 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 CIDR/PGF_{2α} and Hybrid Synch+CIDR 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 6).

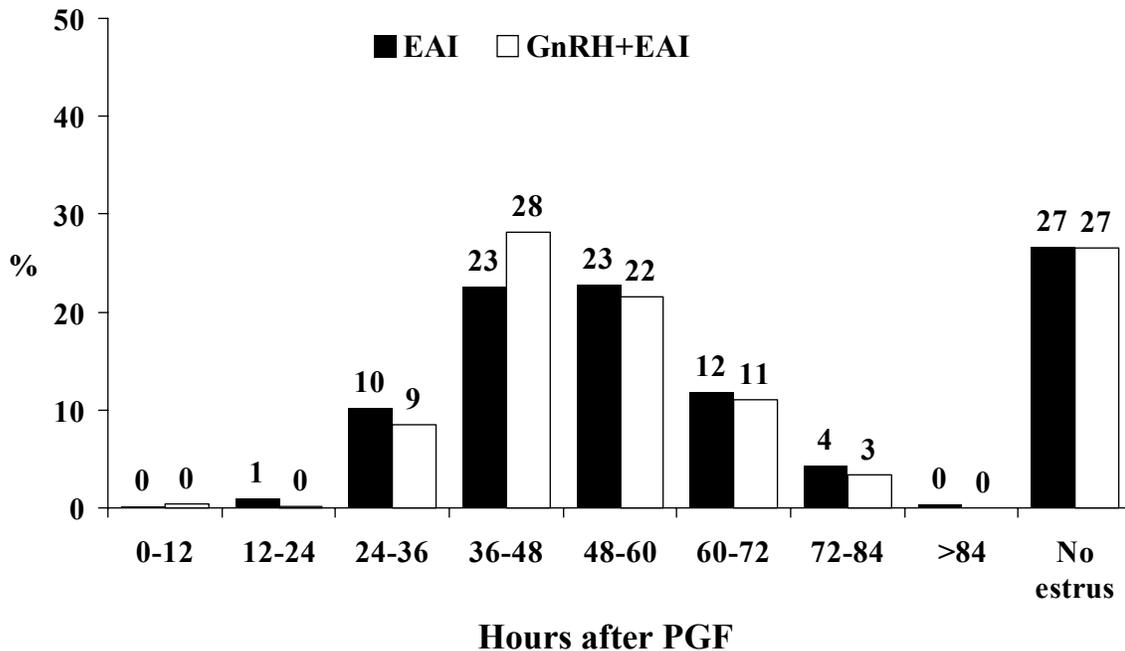


Figure 6. Percentage of heifers treated with CIDR/ PGF_{2α}, or Hybrid Synch+CIDR that were observed in estrus, separated by hours from PG injection to AI (Larson et al., 2004b).

The time from PG injection to detection of estrus and AI for those heifers exhibiting estrus was similar among CIDR/PGF_{2α} (49.9 and 61.7 hr, respectively) and Hybrid Synch+CIDR (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 hybrid Synch+CIDR treatment most frequently produced the greatest pregnancy rates and provided a reliable alternative to an MGA/PGF_{2α} protocol.

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_{2α}. 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.

Literature Cited

- DeJarnette, J.M., R.A. Wallace, R.B. House, R.R. Salverson, and C.E. Marshall. 2001b. Attenuation of premature estrous behaviour in postpartum beef cows synchronizaed to estrus using GnRH and PGF_{2α}. *Theriogenology* 56:493-501.
- 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_{2α} for ovulation control in postpartum suckled beef cows. *J. Anim. Sci.* 79:2253-2259.
- Larson, J.E., G.C. Lamb, T.W. Geary, J.S. Stevenson, S.K. Johnson, M.L. Day, D. J. Kesler, J.M. DeJarnette, and D. Landblom. 2004. Synchronization of estrus in replacement beef heifers using GnRH, prostaglandin F_{2α} (PG), and progesterone (CIDR): a multi-location study. *J. Anim. Sci.* 82(Suppl. 1):368.
- 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. Arseneau. 2005. Synchronization of estrus in suckled beef cows for detected estrus and artificial insemination and (or) timed AI using gonadotropin-releasing hormone (GnRH), prostaglandin F_{2α} (PG), and progesterone (CIDR): *J. Anim. Sci.* 83 (In Press).
- Lucy, M. C., H. J. Billings, W. R. Butler, L. R. Ehnes, M. J. Fields, D. J. Kesler, J. E. Kinder, R. C. Mattos, R. E. Short, W. W. Thatcher, R. P. Wettemann, J. V. Yelich, and H. D. Hafs. 2001. Efficacy of an Intravaginal Progesterone Insert and an Injection of PGF_{2α} for Synchronizing Estrus and Shortening the Interval to Pregnancy in Postpartum Beef cows, Peripubertal Beef Heifers, and Dairy Heifers. *J. Anim. Sci.* 79: 982-995
- Stevenson, J. S., K. E. Thompson, W. L. Forbes, G. C. Lamb, D. M. Grieger, and L. R. Corah. 2000. Synchronizing estrus and (or) ovulation in beef cows after combinations of GnRH, norgestomet, and prostaglandin F_{2α} with or without timed insemination. *J. Anim. Sci.* 78:1747-1758.