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#### **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 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 do 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<sub>2a</sub> 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 potentially responsive to an injection of  $PGF_{2\alpha}$ . Although most research data indicates only about 90% of corpora lutea in cows more than six days after ovulation regress promptly to an injection of  $PGF_{2\alpha}$ , only about 60% of the females will have corpora lutea at the time of  $PGF_{2\alpha}$  treatment (assuming spontaneous corpora lutea regression begins about 18 days after ovulation). Therefore, about 95% of the females treated with the FDA approved CIDR/PGF<sub>2\alpha</sub> 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.

Reference and treatment description	No. of cows	Conception rate <sup>a</sup> , %	Pregnancy rate <sup>b</sup> , %
Stevenson et al., 2000			
Exp. 1			
Select Synch	289	115/175 (66)	115/289 (38)
Select Synch + Norgestomet	289	123/208 (59)	123/289 (42)
$2 \times PGF_{2\alpha}$	294	86/142 (61)	86/294 (28)
Dejarnette et al., 2001			
Exp. 2			
Select Synch	77	40/60 (67)	40/77 (52)
Select Synch + MGA from d -7 to -1	73	43/61 (72)	43/73 (60)
Lamb et al., 2001			
CO-Synch	287	-	138/287 (48)
CO-Synch + $CIDR$ from $d$ –7 to $0$	273	-	160/273 (59)
Larson et al, 2004a			
<b>CIDR/PGF</b> <sub>2<math>\alpha</math></sub> (PG on d 0) - anestrous	147	-	74/147 (50)
<b>CIDR/PGF</b> <sub>2<math>\alpha</math></sub> (PG on d 0) - cyclic	296	-	159/296 (54)
CO-Synch - anestrous	156	-	59/156 (38)
CO-Synch - cyclic	330	-	145/330 (44)
CO-Synch + CIDR - anestrous	180	-	85/180 (47)
CO-Synch + CIDR - cyclic	294	-	169/294 (57)
Hybrid Synch - anestrous	143	-	60/143 (42)
Hybrid Synch - cyclic	308	-	182/308 (59)
Hybrid Synch+CIDR - anestrous	136	-	72/136 (53)
Hybrid Synch+CIDR - cyclic	306	-	180/306 (59)
Lucy et al., 2001			
Control - anestrous	151	6/16 (38)	6/151 (4)
Control - cyclic	134	15/26 (58)	15/134 (11)
$PGF_{2\alpha}$ - anestrous	154	17/30 (57)	17/154 (11)
$PGF_{2\alpha}$ - cyclic	129	44/63 (70)	44/129 (34)
<b>CIDR/PGF</b> <sub>2<math>\alpha</math></sub> (PG on $d-1$ ) - anestrous	141	36/63 (57)	36/141 (26)
$CIDR/PGF_{2\alpha}(PG on d - 1) - cyclic$	140	64/101 (63)	64/140 (46)

**Table 1.** Fertility rates in suckled beef cows treated with estrous synchronization protocols containing progestins.

<sup>a</sup> Percentage of cows pregnant exposed to AI.

<sup>b</sup> 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 (Table 1; Lucy et al., 2001): 1) untreated controls, 2) a single intramuscular (IM) injection of 25 mg PGF<sub>2α</sub> (PGF<sub>2α</sub> alone), or 3) administration of a CIDR insert for 7 d with an IM administration of PGF<sub>2α</sub> on day 6 of the 7 d CIDR insert administration period (CIDR + PGF<sub>2α</sub>); no differences were detected between the CIDR + PGF<sub>2α</sub> treatment group and either the PGF<sub>2α</sub> alone or control groups for first-service conception rate 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<sub>2α</sub> alone or control group than in either the PGF<sub>2α</sub> alone or control group. No differences were detected in pregnancy rate to first services during the 31 d AI period between the CIDR + PGF<sub>2α</sub> and either the PGF<sub>2α</sub> alone or control group. Therefore, insertion of the CIDR increased the synchronization rates

within the first 3 d following  $PGF_{2\alpha}$ , resulting in enhanced pregnancy rates. A drawback of the current protocol is  $PGF_{2\alpha}$  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  $PGF_{2\alpha}$  on the day of CIDR removal.

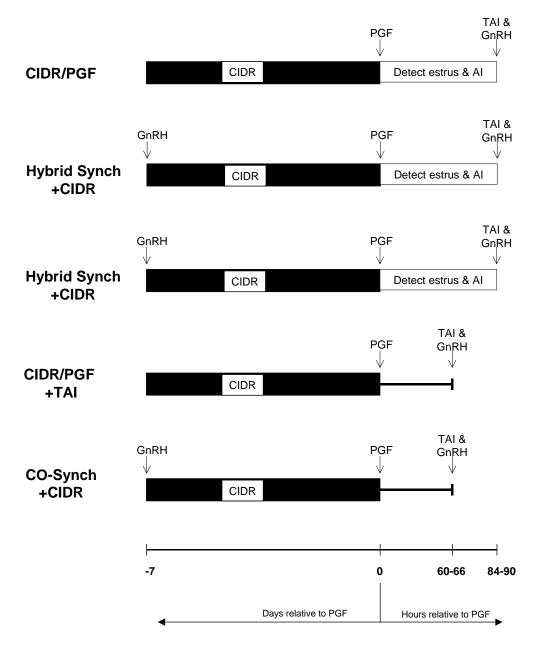


Figure 1. Estrous synchronization protocols using a CIDR.

### **Recent 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<sub>2α</sub>. 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 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 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.

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

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

<sup>a</sup> See experimental design for treatments in Figure 1.

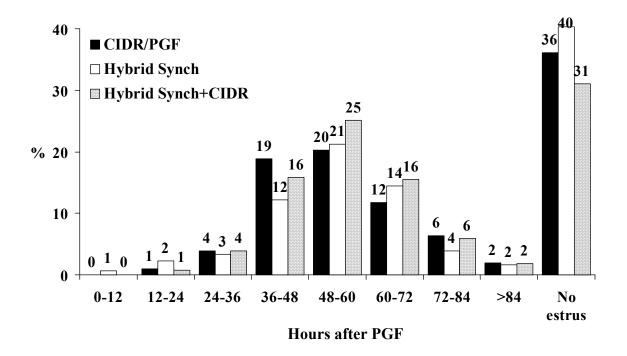
<sup>b</sup> Body condition scores from IL and MN only.

<sup>c</sup> Parity data from KS and MN only.

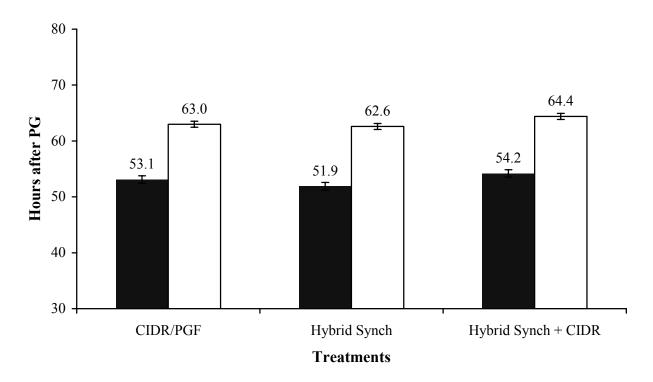
<sup>xyz</sup>Percentages within an item and column lacking a common superscript letter differ (P < .05).

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<sub>2a</sub> 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%.

Interestingly, the distribution of estrus among the CIDR/  $PGF_{2\alpha}$ , Hybrid Synch and Hybrid Synch+CIDR protocols was similar (Figure 2) and the average time from  $PGF_{2\alpha}$  to estrus or AI was similar 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 CIDR/  $PGF_{2\alpha}$ , Hybrid Synch, or Hybrid Synch+CIDR 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, Hybrid Synch, and Hybrid Synch+CIDR treatments (Larson et al., 2004a).

#### CIDR/PGF<sub>2a</sub> 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<sub>2a</sub> 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<sub>2a</sub> 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 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  $PGF_{2\alpha}$ . The study by Lucy et al., (2001; Table 2) demonstrates the pregnancy rates of heifers synchronized with the FDA approved CIDR/  $PGF_{2\alpha}$  protocol. As in cows, the CIDR/ $PGF_{2\alpha}$  protocol yielded greater pregnancy rates in heifers than for untreated heifers or for heifers treated with  $PGF_{2\alpha}$  alone. Therefore, insertion of the CIDR increased the synchronization rates within the first 3 d following  $PGF_{2\alpha}$ , resulting in enhanced pregnancy rates. Again, the drawback of the current protocol is  $PGF_{2\alpha}$  was administered on d 6 after CIDR insertion, which requires an additional day of handling the heifers. Therefore, consideration should be to inject  $PGF_{2\alpha}$  on the day of CIDR removal.

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

Criterion	Untreated controls	$PGF_{2\alpha}^{1}$	$CIDR/PGF_{2\alpha}^{2}$
Interval <sup>3</sup> to estrus, d	1 5 4	1.7.*	2
All heifers Anestrous heifers <sup>5</sup>	15* 27**	16* 31**	2 14
Estrus d 1-3, %	12**	25**	60
FSCR <sup>4</sup> , %			
D 1-3	57	52	60
D 1-31	58	52	58
FSPR <sup>5</sup> , %			
D 1-3	7**	14**	36
D 1-7	14**	18**	38
D 1-31	42	36*	47

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

<sup>1</sup>25 mg prostaglandin  $F_{2\alpha}$ 

<sup>2</sup>CIDR insert administered intravaginally for 7 days with PGF<sub>2 $\alpha$ </sub> administered on day 6.

<sup>3</sup> Median interval in days from removal of CIDR inserts.

<sup>4</sup> First-service conception rate (number of heifers).

<sup>5</sup> First-service pregnancy rate (number of heifers).

\* Different from CIDR/PGF<sub>2 $\alpha$ </sub>, P < 0.05.

\*\* Different from CIDR/PGF<sub>2 $\alpha$ </sub>,  $P \leq 0.01$ .

# **Recent Advances in Protocols Using the CIDR for Heifers**

Although excellent pregnancy rates can be achieved with the MGA/PGF<sub>2 $\alpha$ </sub> protocol and acceptable pregnancy rates can be achieved with the CIDR/PGF<sub>2 $\alpha$ </sub> protocol, no short duration system has managed to successfully synchronize estrus in replacement beef heifers that consistently yields pregnancy rates matching the MGA/PGF<sub>2 $\alpha$ </sub> protocol. In addition, there has been no reliable fixed-time AI protocol that 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 1): 1) CIDR/PGF<sub>2α</sub>, 2) Hybrid Synch+CIDR, 3) CO-Synch+CIDR, and 4) CIDR/PGF<sub>2α</sub> + TAI. The percentage of heifers cycling at the initiation of estrous synchronization was 91%. Percentages of cycling heifers among locations ranged from 78 to 100%. Overall pregnancy rates at days 30 to 35 after AI ranged from 38 to 74%. Although no differences in pregnancy rates were detected among treatments, heifers inseminated in the estrus-detection treatments had greater pregnancy rates than heifers in the fixed-time AI treatments (56 vs. 51%, respectively). However, the CO-Synch+CIDR treatment provides a reliable fixed-time AI protocol for beef producers (Figure 4).

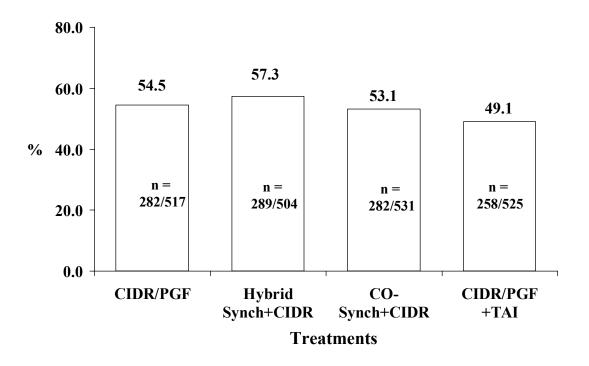
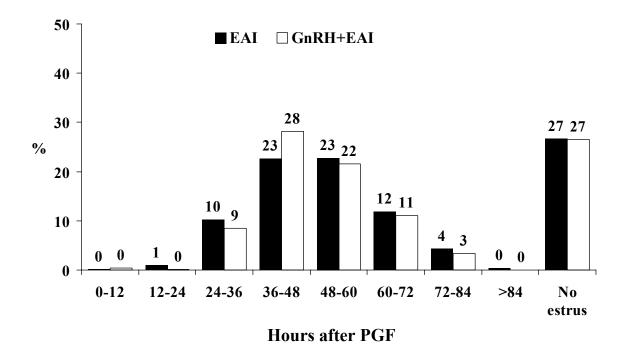


Figure 4. First service pregnancy rates in heifers after receiving one of four CIDR treatments (Larson et al., 2004).

For the two estrus-detection protocols, CIDR/PGF<sub>2 $\alpha$ </sub> 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<sub>2 $\alpha$ </sub> and Hybrid Synch+CIDR protocols, respectively. These results indicate TAI after a period of estrus detection enhances the potential for improving pregnancy rates to exceed those of estrus detection alone (Figure 5).



**Figure 5.** Percentage of heifers treated with CIDR/  $PGF_{2\alpha}$ , or Hybrid Synch+CIDR 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<sub>2 $\alpha$ </sub> (49.9 and 61.7 hr, respectively) and Hybrid Synch+CIDR (49.8 and 61.3 hr, respectively). These results demonstrate 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<sub>2 $\alpha$ </sub> 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 for a fixed-timed AI protocol the CO-Synch+CIDR protocol yields the most impressive pregnancy rates, 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<sub>2 $\alpha$ </sub>. 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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