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REVIEW OF ESTROUS SYNCHRONIZATION SYSTEMS:GnRH

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Introduction

Synchronization of estrus contributes to optimizing the use of time, labor, and financial resources by shortening the calving season, in addition to increasing the uniformity of the calf crop. The major limitation of estrus-synchronization programs is their inability to induce a potentially fertile estrus and ovulation in noncycling cattle (i.e., prepubertal heifers and anestrous suckling cattle). Because initial estrus-synchronization programs were not designed for successful treatment of noncycling cattle, their use in cow-calf operations generally has not produced results that would encourage greater A.I. use in beef cattle. Currently, less than 7% of beef cows and an estimated 8 to 10% of beef heifers are A.I.-bred in the U.S. The potential for increasing A.I. in beef cattle is great if a system can resolve successfully the problem of the noncycling female at the beginning of the breeding season.

The premise behind synchronizing cows and heifers is to first control the timing of onset of estrus by controlling the length of the estrous cycle. The choice of approaches for controlling cycle length are: 1) to regress or "kill" the corpus luteum (CL) of the animal before the time of natural luteolysis, and thereby shorten the cycle (by administration of a prostaglandin $F_{2\alpha}$ [$PGF_{2\alpha}$]), or 2) to administer exogenous progestins to delay the time of estrus following natural or induced luteolysis that may extend the length of the estrous cycle. A further approach is to "select" the ovulatory follicle by an injection of GnRH, which should cause premature ovulation of that follicle. Using these concepts, researchers have made tremendous strides in developing numerous system to synchronize the estrous cycle for an A.I. after a detected estrous or a timed-A.I. Table 1 summarizes common products available for use in cattle estrus synchronization systems.

Table 1. Products, commercial names, and doses for synchronization products.

Product	Commercial name	Administration	Dose
Prostaglandins	Lutalyse®	i.m. injection	5 mL
	Estrumate®	i.m. injection	2 mL
	In-Synch®	i.m. injection	
	Prostamate®	i.m. injection	
Progestins	Melengestrol Acetate	Feed	0.5 mg/hd/d
	CIDR	Vaginal implant	1 implant
Gonadotropin Releasing Hormone	Cystorelin®	i.m. injection	2 mL
	Factrel®	i.m. injection	2 mL
	Fertagyl®	i.m. injection	2 mL

Initial estrous synchronization systems focused on altering the estrous cycle by regressing the CL with an injection of $PGF_{2\alpha}$ followed by a detected estrus between 18 and 80 hours after the injection. After systems involving a single injection of $PGF_{2\alpha}$ became successful, researchers focused on multiple injections of $PGF_{2\alpha}$ to further reduce the days required for heat detection and AI (Lauderdale et al., 1974; Seguin et al., 1978). The next generation of estrous synchronization systems involved progestins, which (while administered) prevent estrus from occurring. Progestins were used to delay the time of estrus following a natural or induced luteolysis and extend the length of the estrous cycle. The use of progestins will be covered extensively by Dr. Dave Patterson (MGA) and Darrel Kesler (CIDR) and their written reports.

Until recently researchers primarily have focused on the timing ofestrus; however, the availability of GnRH has given researchers an opportunity to aim their efforts at timing ovulation rather than the event of estrus alone. The obvious advantage is the development of time-A.I. protocols allowing cattlemen to inseminate cows that have no visible signs of estrus. These efforts should optimize the use of time, labor, and financial resources and allow more cattle to become pregnant to A.I. This paper will specifically cover ovulation synchronization protocols emphasizing the use of GnRH.

GnRH Ovulation Synchronization Protocols

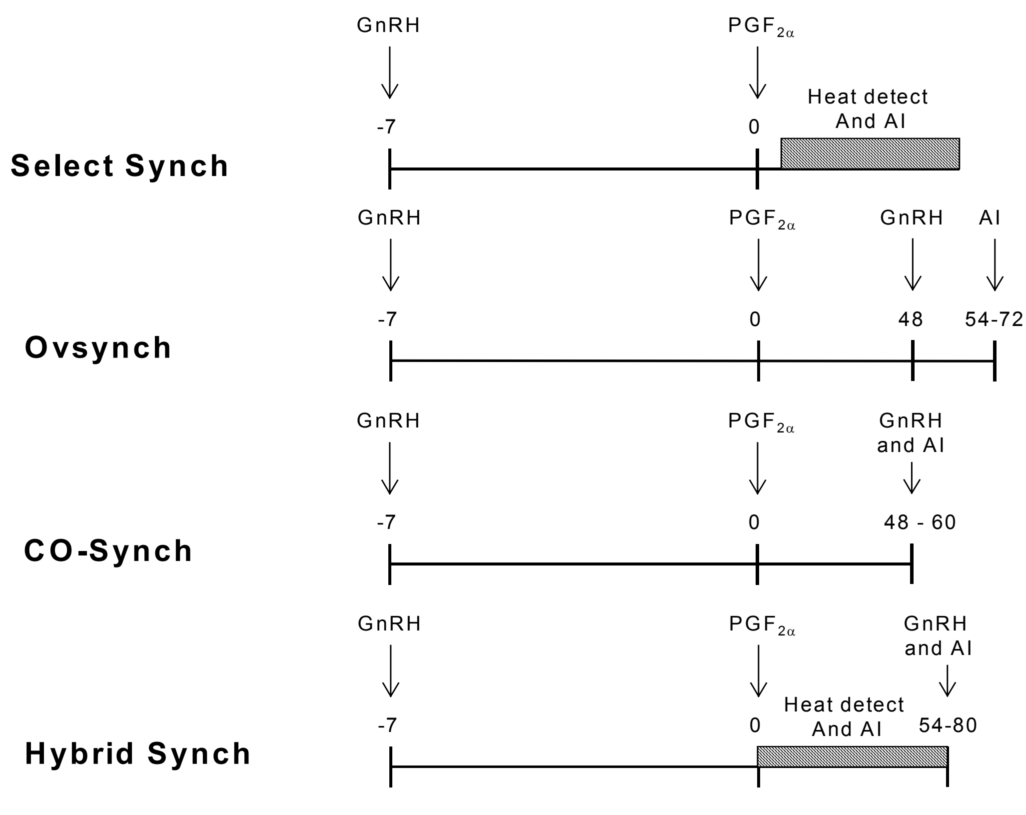

Figure 1. GnRH protocols frequently used for synchronizing beef cattle.

Refer to Figure 1 for GnRH protocol descriptions.

- ***Select Synch.*** Select Synch effectively initiates estrous cycles in postpartum cows that are not cycling. The duration of the system only requires one week from the start of synchronization until cows begin showing signs of estrus. As many as 5-20% of cows may exhibit estrus at least three days before the $PGF_{2\alpha}$ injection so insemination of these cows will improve overall response. For cows that are inseminated before the $PGF_{2\alpha}$ injection, there is no need to inject those cows with $PGF_{2\alpha}$ on day 0.

- ***Ovsynch.*** A protocol developed for lactating dairy cows that can be used with success in beef cattle operations. A drawback of Ovsynch is that cows are required to be processed through the working facility a minimum of four times; however, in smaller, more intensive cow/calf operations this protocol can be effective in obtaining excellent overall pregnancy rates.

- ***CO-Synch.*** In beef cattle operations that are fairly extensive, or would like to incorporate an AI program into their operation, and feel that labor and time associated with heat detection are limiting opportunities for AI use, then using the CO-Synch protocol is a good option. CO-Synch was modified from Ovsynch to reduce the total number of times the cows were to be processed. Even so, pregnancy rates around 50% can be consistently achieved in well-managed herds that use this system.

- ***Hybrid Synch.*** By using the benefits of Select Synch and CO-Synch, Hybrid Synch maximizes the opportunity for obtaining the greatest overall pregnancy rates. Detection of estrus for two to three days followed by a fixed-time A.I. should increase overall pregnancy rates. As with Select Synch, estrus detection at least three days before the $PGF_{2\alpha}$ injection and inseminating cows then will increase the heat detection rate by between 5 and 20%.

Advantages and Disadvantages of GnRH Ovulation Synchronization Protocols

Cows

Table 2 summarizes the conception and pregnancy rates of numerous reports evaluating GnRH based synchronization systems. Thompson et al. (1999) scanned the ovaries of 40 early postpartum, suckled beef cows before, during, and after treatments of GnRH and (or) norgestomet and reported that luteal structures were induced from dominant follicles in 75% of the noncycling cows treated, resulting in elevated progesterone after 7 d. In contrast, Stevenson et al. (2000) reported that the rates of induced ovulation for noncycling cows treated with Select Synch were 38% and 49% in two experiments.

Table 2. Fertility rates in suckled beef cows treated with GnRH protocols

Reference and treatment description	No. of cows	Conception rate[a], %	Pregnancy rate[b], %
Geary et al., 1998			
Ovsynch + calf removal	220	-	119/220 (54)
Syncromate-B	216	-	91/216 (42)
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 × $PGF_{2\alpha}$	294	86/142 (61)	86/294 (28)
Exp. 3			
Select Synch	184	80/115 (70)	80/184 (44)
CO-Synch	175	-	58/175 (33)
Hybrid Synch	177	60/177 (34)	60/184 (34)
Dejarnette et al., 2001			
Exp. 1			
Select Synch (6 day interval)	24	17/22 (77)	17/24 (71)
Select Synch (7 day interval)	27	19/25 (76)	19/27 (70)
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)
Dejarnette et al., 2001			
Exp. 1			
Hybrid Synch (72h)	45	15/20 (75)	20/45 (71)
Hybrid Synch (72h)+ GnRH on d-16	42	19/24 (79)	23/42 (55)
Exp. 2			
Hybrid Synch (72h)	638	278/467 (60)	299/632 (47)
Hybrid Synch (72h)+ GnRH on d-16	638	287/447 (64)	333/634 (53)
Greiger et al., 2001			
Select Synch + horn bred	118	47/64 (73)	47/118 (40)
Select Synch + body bred	119	46/66 (70)	46/119 (39)
CO-Synch + horn bred	108	-	45/108 (42)
CO-Synch + body bred	115	-	61/115 (53)
Geary et al., 2001			
Ovsynch	123	-	64/123 (52)
Ovsynch + calf removal	114	-	70/114 (61)
CO-Synch	117	-	63/117 (54)
CO-Synch + calf removal	119	-	75/119 (63)
Geary et al., 2001			
CO-Synch (GnRH)	117	-	57/117 (49)
CO-Synch (GnRH) + calf removal	121	-	56/121 (46)
CO-Synch (hCG)	114	-	39/114 (34)
CO-Synch (hCG) + calf removal	115	-	40/115 (35)
Lamb et al., 2001			
CO-Synch	287	-	138/287 (48)
CO-Synch + CIDR from d –7 to 0	273	-	160/273 (59)

[a] Percentage of cows pregnant exposed to AI.
[b] Percentage of cows pregnant of all cows treated.

Response of ovaries to GnRH is dependent on the stage of follicular growth that GnRH is administered (Geary et al., 2000). A high percentage of cows during the later stages of their estrous cycle (d 15 to 17) failed to ovulate a follicle after administration of GnRH and exhibited estrus prior to an injection of $PGF_{2\alpha}$ (Geary et al., 2000). In addition, Moreira et al. (2000) observed that day of the estrous cycle in which the Ovsynch protocol was initiated in dairy heifers affected dynamics of follicular development, plasma progesterone profiles, and occurrence of premature ovulation. We (Lamb et al., 2001) determined that when treatments were initiated (d -7), 99 of 333 cows (29.7%) considered to be cycling subsequently had low concentrations of progesterone on d 0. In this class of cows treated by Cosynch, 43.3% (26/60) were pregnant after AI.

Of the estrus or ovulation synchronization protocols currently used for suckled beef cows, CO-Synch tends to be more cost effective and less labor intensive than other timed-AI synchronization protocols (Twagiramungu et al., 1995; Geary et al., 2001; Kojima et al., 2000). A disadvantage of this protocol is that approximately 10 to 20% of suckled beef cows exhibit estrus prior to and immediately after the $PGF_{2\alpha}$ injection. Unless these cows are detected in estrus and inseminated, they will fail to become pregnant after the CO-Synch protocol.

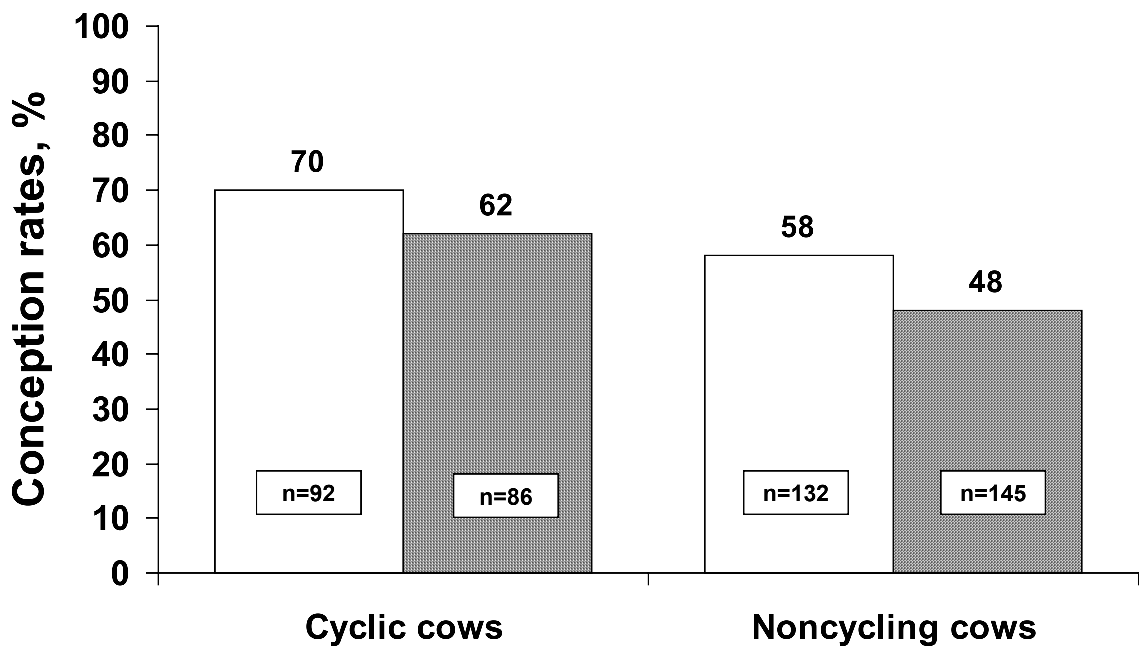

Figure 2. Conception rates in suckled beef cows treated with CO-Synch or Ovsynch (Geary et al., 2001).

Comparison of the CO-Synch and CO-Synch with a CIDR insert from day –7 to day 0 treatments indicated that addition of a CIDR for progesterone supplementation improved pregnancy rates after a fixed time AI (Lamb et al., 2001). But progesterone did not seem to improve pregnancy rates in suckled beef cows cycling at the initiation of treatments. Progesterone seemed to be more effective in at enhancing pregnancy rates in cows that were cycling but in the later stages of the estrous cycle at first injection of GnRH and subsequently no luteal structure at the $PGF_{2\alpha}$ injection or in noncycling cows. Along with parity, days postpartum, calf removal, and cow condition (Figure 2, Table 3;) 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. Therefore, a sound strategy for utilizing a GnRH protocol in the absence of progesterone may be to select cows that calved earlier in the calving season that tend to be in good body condition. A high percentage of these cows should be cycling, resulting in acceptable fertility rates.

Reports by Dr. Dave Patterson and Darrel Kesler will address additional GnRH protocols that also utilize a progestin for enhancing fertility rates.

Table 3. Pregnancy rates in suckled beef cows after treatment with CO-Synch, Select Synch, and 2 × $PGF_{2\alpha}$.

Lamb et al., 2001		*Stevenson et al., 2001*		
Item	Cosynch	Item	Select Synch	2 × $PGF_{2\alpha}$
	---- no. (%) ----		---------- no. (%) ----------	
Body condition		Body condition		
≤ 4.5	12/40 (30)	≤4.0	14/50 (28)	5/30 (17)
4.5 to 5.5	30/74 (41)	4.5	19/49 (39)	15/51 (29)
≥ 5.5	19/32 (59)	≥5.0	38/76 (50)	23/61 (38)
Days postpartum		Days postpartum		
≤ 50	23/60 (38)	≤ 60	12/52 (23)	1/56 (2)
51-60	25/62 (47)	61-70	31/67 (46)	26/77 (34)
61-70	28/49 (62)	71-80	42/106 (40)	37/106 (35)
71-80	18/41 (44)	> 80	31/70 (44)	21/63 (33)
> 80	44/75 (59)			

Advantages and Disadvantages of GnRH Ovulation Synchronization Protocols

Heifers

Heifers are an easier group of females to synchronize within a beef herd. Because heifers are not nursing calves and can be maintained in areas where they can be fed they have responded extremely well to the MGA/$PGF_{2\alpha}$ 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.

Table 4. Occurrence of Estrus Before, During, and After the Target Breeding Week (days 0 to 7; day 0 = $PGF_{2\alpha}$; Stevenson et al., 1999).

	Treatment		
Item	$2\times PGF_{2\alpha}$	$MGA+PGF_{2\alpha}$	Select Synch
No. of heifers	139	289	160
	------------ % (no.) -------------		
Before: days -5 to -1	8.6 (12)	5.9 (17)	12.5 (20)
During: days 0 to 7	74.8 (104)	82.0 (237)	72.5 (116)
(Average days to estrus)	(3.0 ± .1)	(3.2 ± .1)	(2.3 ± .1)
After: >day 7	8.6 (12)	8.3 (24)	8.7 (14)
No estrus	7.9 (11)	3.8 (11)	6.2 (10)

More recently researchers have incorporated gonadotropin-releasing hormone into (GnRH) estrus synchronization systems, which can induce preovulatory LH surges in prepubertal heifers (Skaggs et al., 1986) and consistently induce ovulation of large follicles (≥ 10 mm) present at the time of injection (Thompson et al., 1999; Wood et al., 2001). The majority of these systems have relied on visual detection of estrus for suitable results (Cassady et al., 1999; Stevenson et al., 1999). In most cases heifers have failed to achieve the fertility rates in a GnRH protocol that equals the fertility of the standard MGA/PGF system. In addition, synchrony of estrus after $PGF_{2\alpha}$ in an MGA system tends to be tighter with more heifers being artificially inseminated during a shorter period of time than when using a GnRH protocol (Table 4; Stevenson et al., 1999; Funston et al., 2002). Nonetheless, fertility in heifers that are estrus detected and inseminated after a detected estrus does not appear to be compromised over a normal $2 \times PGF_{2\alpha}$ system (Table 5), whereas heifers inseminated after a fixed time with or without an additional injection of GnRH before the CO-Synch protocol appears to have improved fertility over a $2 \times PGF_{2\alpha}$ system, especially in heifers with poorly developed reproductive tracts (Table 6; Dahlen et al., 2001).

Table 5. Rates of Estrus, Conception, and Pregnancy for Heifers Detected during the Target Breeding Week (days 0 to 7; day 0 = $PGF_{2\alpha}$; Stevenson, et al., 1999).

Item	Treatment[1]		
	2 × $PGF_{2\alpha}$	MGA+$PGF_{2\alpha}$	Select Synch
No. of heifers	139	289	160
Estrus detection[2], %	74.8	82.0	72.5
Conception rate[3], %	69.2	68.2	63.8
Pregnancy rate[4], %	51.8	56.0	46.2

[1] Percent of heifers expressing estrus of all heifers synchronized
[2] Percent of heifers conceiving of heifers inseminated
[3] Percent of heifers pregnant of all heifers synchronized

Table 6. Synchronized Pregnancy rates of heifers synchronized with prostaglandin $F_{2\alpha}$ and GnRH (Dahlen et al., 2001)

Reproductive tract score	Treatment						Overall	
	2 × $PGF_{2\alpha}$ (d –12 and 0)		CO-Synch (GnRH on d –6)		CO-Synch (GnRH on d –12 and –6)			
	--------no. (%)--------							
2	0/53	(0)	6/55	(11)	9/53	(17)	15/161	(9)[p]
3	12/72	(17)	12/71	(17)	21/73	(29)	45/216	(21)[q]
4	6/38	(16)	17/38	(45)	12/35	(34)	35/111	(32)[q]
5	4/10	(40)	3/8	(38)	1/8	(13)	8/26	(31)[pq]
Total	22/173	(13)[x]	38/172	(22)[y]	43/169	(25)[y]	103/514	(20)

[a] RTS = Reproductive tract scores.
[p,q] Percentages within a item and column lacking a common superscript differ ($P < 0.01$).
[x,y] Percentages within a row lacking a common superscript differ ($P < 0.05$).

Implications

Most beef herds in the mid-western United States initiate the breeding season with between 25 and 70% of their cows in an anestrus state. For most AI programs to work, a sound nutrition program is essential to ensure a high percentage of cows are cycling. Synchronization does decrease the labor associated with AI programs; additional benefits include a shorter breeding season and consequently a shorter calving season. In essence, the value of progeny is greater due to a more uniform calf crop and more older calves at weaning.

To achieve optimal pregnancy rates with a GnRH synchronization protocol, cows should be in good body condition (BCS ≥5) and treatments should be initiated only when cows are at least 50 days postpartum. Treatment of suckled cows with GnRH 7 d before an injection of $PGF_{2\alpha}$ partially resolved the problem of anestrus before the beginning of the breeding season that cannot be resolved with $PGF_{2\alpha}$ systems alone.

Literature Cited

Brown, L.N., K.G. Odde, M.E. King, D.G. Lefever, and C.J. Neubauer. 1988. Comparison of melengestrol acetate-prostaglandin $F_{2\alpha}$ to Synchro-Mate B for estrus synchronization in beef heifers. *Theriogenology* 30:1.

Cassady, J.M., J.E. Wheaton, C.M. Zehnder, A. DiCostanzo, G.C. Lamb, and B. Seguin. 1999. Estrous synchronization in beef heifers using MGA and $PGF_{2\alpha}$, or GnRH and $PGF_{2\alpha}$. *J. Anim. Sci.* 77(Suppl. 1):226.

Cassady, J.M., J.E. Wheaton, C.M. Zehnder, A. DiCostanzo, G.C. Lamb, and B. Seguin. 1999. Estrous synchronization in beef heifers using MGA and $PGF_{2\alpha}$, or GnRH and $PGF_{2\alpha}$. *J. Anim. Sci.* 77(Suppl. 1):226.

Dejarnette, J.M., M.L. Day, R.B. House, R.A. Wallace, C.E. Marshall. 2001a. Effect of GnRH pretreatment on reproductive performance of postpartum suckled beef cows following synchronization of estrus using GnRH and PGF2alpha. *J. Anim. Sci*. 9:1675-82.

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 $PGF_{2\alpha}$. *Theriogenology* 56:493-501.

Funston, R. N., R. P. Ansotegui, R. J. Lipsey, and T. W. Geary. 2002. Evaluation of melengestrol acetate/prostaglandin (MGA/PGF), Select Synch, and 7 d MGA/Select Synch estrous synchronization protocols in beef heifers. *Proc. Westwern Section, Am. Soc. Anim. Sci.* 53: 405-406.

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

Geary, T.W., J.C. Whittier, D.M. Hallford, and M.D. MacNeil. 2001. Calf removal improves conception rates to the Ovsynch and CO-Synch protocols. *J. Anim. Sci.* 79:1-4.

Grieger, D.M., G.C. Lamb, T.G. Rozell, K.E. Thompson, and J.S. Stevenson. 1998. Site of semen deposition and fertility in beef cows inseminated according to estrus or at a fixed time after synchronization with GnRH-$PGF_{2\alpha}$. *J. Anim. Sci.* 76(Suppl. 1):279.

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.

Lamb, G.C., D.W. Nix, J.S. Stevenson, and L.R. Corah. 2000. Increasing the interval to prostaglandin $F_{2\alpha}$ from 17 to 19 days in an MGA-prostaglandin synchronization system for beef 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.

Lauderdale, J.W., B.E. Seguin, J.N. Stellflung, 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.

Moreira, F., R.L. de la Sota, T. Diaz, and W.W. Thatcher. 2000. Effect of day of the estrous cycle at the initiation of a timed artificial insemination protocol on reproductive responses in dairy heifers. *J. Anim. Sci.* 78:1568-1576.

Patterson, D. J, R.C. Perry, G.H. Kiracofe, R.A. Bellows, R.B. Staigmiller, L.R. Corah. 1992. Management considerations in heifer development and puberty. *J Anim. Sci.* 70:4018-4035.

Seguin, B.E., B.K. Gustafson, J.P. Hurtgen, E.C. Mather, K.R. Refsal, R.A. Wescott, and H.L. Withmore. 1978. Use of the prostaglandin $F_{2\alpha}$ analog cloprostenal (ICI 80,996) in dairy cattle with unobserved estrus. *Theriogenology* 10:55-64.

Skaggs, C. L., B. V. Able, and J. S. Stevenson. 1986. Pulsatile or continuous infusion of luteinizing hormone-releasing hormone and hormonal concentrations in prepubertal beef heifers. *J. Anim. Sci.* 62:1034-1048.

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., 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 $F_{2\alpha}$ with or without timed insemination. *J. Anim. Sci.* 78:1747-1758.

Thompson, K. E., J. S. Stevenson, G. C. Lamb, D. M. Grieger, and C. A. Löest. 1999. Follicular, hormonal, and pregnancy responses of early postpartum suckled beef cows to GnRH, norgestomet, and $PGF_{2\alpha}$. *J. Anim. Sci.* 77:1823-1832.

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.

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

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