CONTROLLED REPRODUCTIVE MANAGEMENT

by

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Recent research at the University of Florida has led to the development of improved estrous synchronization techniques for use with dairy cattle (Van Cleeff et al., 1989). Synchronization of estrus is an excellent method for improving reproductive efficiency of the herd. It increases the likelihood that cycling animals will be bred, primarily because animals will be in heat within a predictable period of time, and such systems improve the rate of estrous detection. It is estimated that an average 50% of estruses are not detected in artificial insemination programs in which animals are not synchronized. Furthermore, synchronization allows any desired number of animals to be bred on a predetermined schedule, thus concentrating labor and facility resources. Using a controlled internal drug releasing device (the "CIDR"), which is impregnated with the natural hormone progesterone, or the GnRH analogue Buserelin, the Dairy Science Department of the University of Florida has developed and conducted synchronization programs in Florida dairy herds.

The CIDR synchronization system involves insertion of an intravaginal device developed in New Zealand, where it is widely used. The CIDR is constructed of a nylon spine covered with a progesterone-impregnated silicone coating. The total progesterone content of the device is 1.9 grams. The device is inserted into the vagina at any stage of the cycle, and remains in place for 9 days, gradually releasing progesterone into the animal's bloodstream. Treatment with prostaglandin F-2 alpha two days before removal of the device insures that no endogenous progesterone from the corpus luteum will be present when the CIDR is removed. This program, implemented in four field trials at two locations, has resulted in excellent synchronization of heifers. A total of 583 heifers received the treatment described above, and of these 489 (83.9%) were synchronized within a 3 day period. Approximately 89.4% of the observed heats occurred

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on the first day of expected estrus, and 9.8% occurred on the second day (Fig. 1). This is an extremely precise synchronization response. Unsynchronized heifers were often found to be prepubertal or unhealthy.

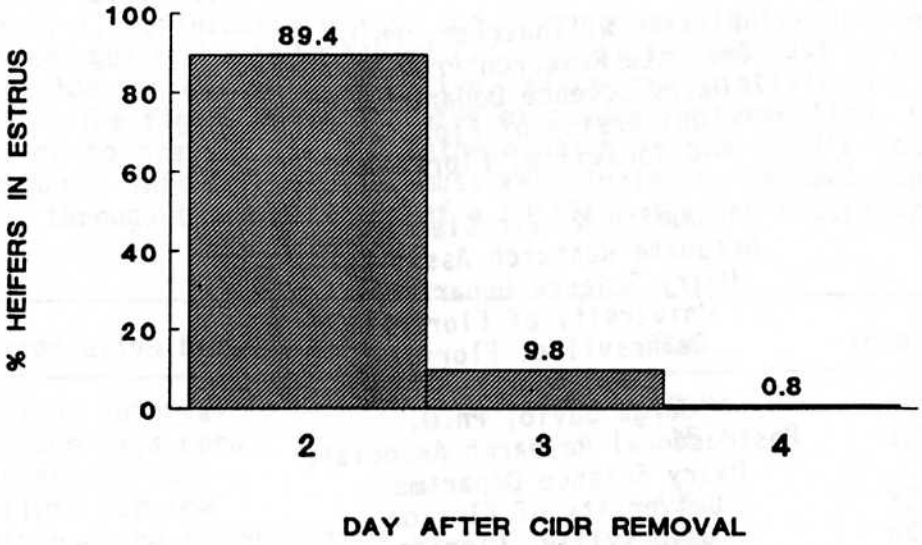

Figure 1. Distribution by day of synchronized estruses after 9-day CIDR, with prostaglandin on day 7.

The 489 synchronized heifers were divided into three treatment (TRT) groups designed to examine various uses for the CIDR device. The three treatment groups were as follows:

TRT 1: Control group. No additional treatment following initial synchronization.

TRT 2: Early Progesterone Supplementation. Either a new CIDR inserted on day 1 following insemination (Trial I), or a used CIDR inserted on day 2 following insemination (Trial II). Both types were removed after a 7 day period.

TRT 3: Resynchronization. A used CIDR inserted from days 17 through 22 of the cycle following insemination.

Fertility for each treatment group is shown separately for all trials in Table 1. Note that Trial I was conducted in midsummer in Florida. Trial II was conducted in late summer, and Trial III was conducted in early fall. Trial IV took place in winter. Acceptable levels of fertility were achieved in TRT 1 heifers, and no overall difference in fertility was found between TRT 1 and TRT 3 (50% vs. 50%).

One great advantage of the CIDR is the progesterone-treated device itself will not induce abortion. This fact enables us to use the CIDR to resynchronize nonpregnant heifers that have already been bred following an initial synchronization treatment, even before their pregnancy status is known. Resynchrony is achieved by inserting a second CIDR 17 days after the first insemination. A resynchronization treatment (TRT 3) was applied to 112 of the 489 synchronized and inseminated heifers. Of these,

50% were pregnant (rectal examination at approximately 40 days) to the first insemination (see Table 1, TRT 3), and 53.2% of the nonpregnant heifers returned to estrus in a synchronized manner (within a 3 day period, see Fig. 2). While the heifers which did return to estrus were well synchronized, the overall response to the second CIDR was not as good as it had been to the first. A total of 10 unsynchronized returns were detected, while 17 nonpregnant heifers were not detected in heat within 30 days after removal of the second CIDR. The CIDRs used to resynchronize the TRT 3 heifers were the same CIDRs which had been inserted for 9 days to achieve the initial synchronization. It had been determined previously that CIDRs used for 9 days still contained a significant amount of progesterone. We postulated that, if properly cleaned and stored, the CIDRs could be re-used for resynchronization of heifers. None of the animals showed any pathological response to the used CIDRs. However, it is possible that using new CIDRs to achieve resynchronization may be more effective. In a preliminary trial with lactating cows, a new CIDR inserted for days 17-22 post insemination resulted in the resynchronization of 80% of open cows. Use of new CIDRs for resynchronization has not yet been tested in heifers. In a recently completed experiment, the progesterone concentrations measured in both plasma and milk were lower in ovariectomized-lactating dairy cows fitted with a Used CIDR (previously inserted for a 9-day period) versus the higher concentrations of progesterone measured in the same cows fitted with a New CIDR. Thus, a Used CIDR may indeed not be sufficiently active for effective use.

Table 1. Conception rates by trial and treatment (TRT) group.

Trial	TRT	N	Conception Rate (%)
I	1	69	42.0
	2	59	18.6
	3	51	56.7
II	1	36	52.8
	2	29	17.2
	3	35	31.4
III	1	33	36.4
	3	26	61.5
IV	1	72	62.5
Total	1	210	50.0
	2	88	18.2
	3	112	50.0

Treatment 2 was intended to assess the effect of supplemental progesterone in early pregnancy. It was thought that progesterone may advance development of the embryo, and so enhance embryo survival. This concept was based on recent data from researchers at Oklahoma State University (Garrett et al., 1988). However, progesterone supplementation

via CIDR device during this early period (day 1 or 2 post insemination, for 7 days) was detrimental to fertility (see Table 1, TRT 2). It is possible that, if embryo and/or uterine endometrial advancement did occur, it did not occur at the same rate in both tissues, resulting in an embryo which was not synchronized to its maternal environment. Such a situation may be lethal for the embryo, perhaps due to early regression of the corpus luteum. Another possibility may be that high progesterone levels this early in gestation interferes with transport of the embryo through the oviduct and into the uterus. Poor fertility due to asynchronous embryo transfers is well-documented in commercial embryo transfer (Putney et al., 1989).

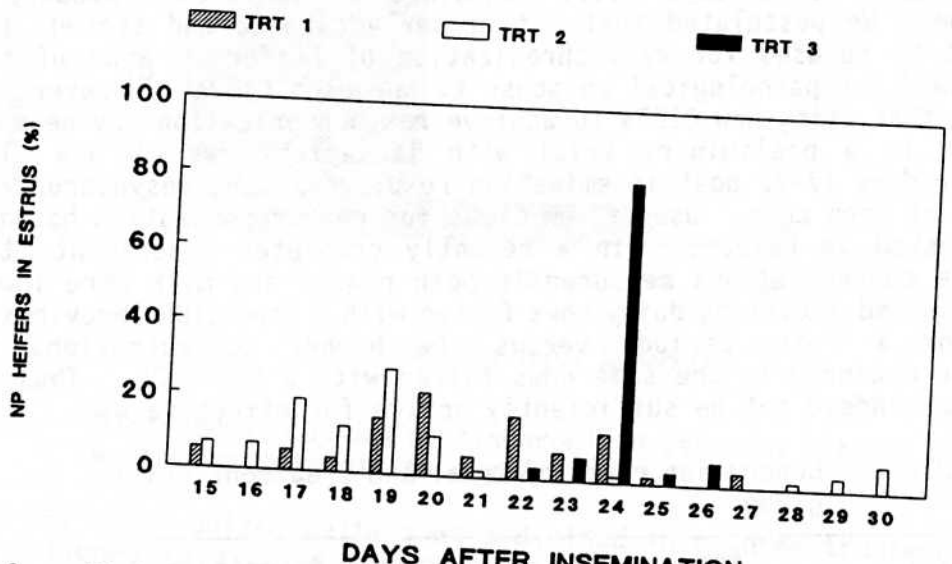

Figure 2. Distribution by day of resynchronized estruses after treatment with used CIDR for days 17-22 post insemination.

Supplemental progesterone later in the cycle warrants investigation. Recent results by Dr. Jock Macmillan in New Zealand (personal communication), indicate that insertion of a CIDR device between 6 to 9 days postinsemination, for either a 6 or 12-day period, increased pregnancy rates. A field trial is currently underway at the University of Florida to confirm this important beneficial effect. It is indeed clear from the present results that a CIDR-prostaglandin synchronization program allows precise synchronization of estruses such that inseminations can be conducted at a predetermined time of the week with a high proportion of estruses detected.

Our laboratory also has investigated an alternative approach to estrous synchronization in which not only is regression of the corpus luteum synchronized but ovarian follicle development also is synchronized (Thatcher et al., 1989). Injection of Receptal (Hoechst-Roussel), a potent GnRH analogue (Buserelin), causes either ovulation, luteinization or atresia of many existing antral follicles (> 3 mm). This response is due to the induced release of LH from the pituitary. Following the injection of Receptal (8 ug), a new follicle wave occurs in approximately 7 days. This newly recruited follicle can continue to develop and become the ovulatory follicle if prostaglandin is injected to regress any original CL or an induced CL due to the initial injection of Receptal.

Such a program involves two injections 7 days apart (8 ug of Receptal followed by 25 mg of Lutalyse [Upjohn Co.]).

The efficiency of such a program is documented in the following experiments. In experiment I, a total of 189 heifers received an injection of Receptal (8 ug) followed by prostaglandin F-2 alpha (25 mg) 8 days later. Following the synchronized estrus and inseminations, half of the heifers received an additional injection of Receptal at day 12 post estrus and half of the heifers received no additional injection. This treatment at day 12 was to test whether luteinization of ovarian follicles would increase conception rates. Luteinization of a potential developing dominant follicle should delay the time of CL regression (an estrogen-dependent process) such that the incidence of 17 to 19 day cycle lengths is reduced. This will permit some embryos a longer period to grow before having to exert an antiluteolytic effect.

The same protocol was repeated in Experiment II with 175 heifers except that the interval between Receptal injection (8 ug) and prostaglandin F-2 alpha (25 mg) was reduced to a 7 day interval. Following the synchronized estrus and inseminations, half of the heifers received an additional injection of Receptal (8 ug) at day 12 post estrus and half of the heifers received no additional injection.

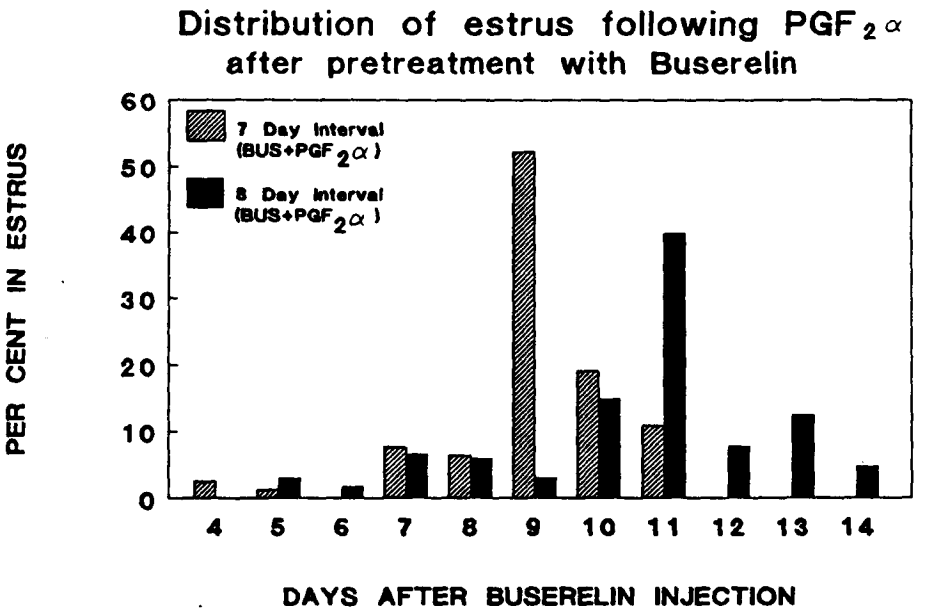

Figure 3. Distribution of estrus following $PGF_2\alpha$ (25 mg) injection after pretreatment with Receptal (8 μg) at 7 or 8 day intervals.

For both experiments, 88.9% and 89.7% of the heifers had a detected estrus over ranges of 9 (days 5 to 14 following Buserelin insertion) and 7 (days 4 to 11) days for Experiments I and II, respectively (Figure 3; Table 2). The 8 day interval for Experiment I was not considered optimal in that 17.26% (29 heifers; 11 on day 7 and 10 on day 8) of the heifers detected in estrus were in estrus by the day of prostaglandin F-2 alpha injection. By going to a 7 day interval between injections in Experiment

II, only 11.46% (18 heifers; 12 on day 7) of the detected heifers were in heat by day 7 (time of prostaglandin F-2 alpha injection). The probable reason for heifers coming into estrus prior to prostaglandin F-2 alpha injection is that the newly recruited follicle in heifers without a corpus luteum will come into estrus earlier than those with a CL that is induced to regress by prostaglandin F-2 alpha injection.

Fertility to the synchronized estrus was very good being 61.4% and 57.6% for Experiments I and II, respectively (Table 2). There was no statistical difference in conception rate for either experiment relative to Receptal injection at 12 days post insemination versus control groups (Table 2). The interestrous interval was slightly longer (2.2 and 5.5 days for Experiments I and II, respectively) in Receptal-injected animals (Table 2). This is primarily due to a higher incidence of extended interestrous intervals (> 27 days) of the Receptal groups (overall: 1 heifer in Control and 10 heifers in Receptal treatments). Perhaps this greater frequency of extended interestrous intervals is related to a rescue of embryos destined to an early embryo death, but which did perish later. Injection of Receptal on day 12 should not have compromised ability of a follicle to induce estrus in nonpregnant animals, since 90% of heifers receiving Receptal for initial synchronization had an induced estrus. Of interest was the observation that conception rate to the return service was lower in animals pretreated with Receptal at 12 days post insemination. No heifers conceived that had an extended interestrous interval greater then 27 days. This is an interesting phenomenon that warrants additional investigation.

Table 2. Effect of Receptal (8 μg) on conception rate when given at +12 days post estrus in heifers synchronized with Receptal (8 μg) followed by $PGF_2\alpha$ (25 mg) at 8 or 7 day intervals.

Responses	Synchronization: Buserelin + $PGF_2\alpha$	
	8 day interval	7 day interval
Heifers treated	189	175
Heifers in estrus	168 (88.9%)	157 (89.7%)
Conception rate to synchronized estrus		
Control	61.9 (n=71)	56.5 (n=76)
Buserelin at +12 days	60.9 (n=69)	58.7 (n=75)
Interestrus interval (days)		
Control	21.0 (n=18)*	22.3 (n=26)**
Buserelin at +12 days	23.2 (n=19)	27.8 (n=26)
Conception rate to return service		
Control	75.0 (n=16)*	66.6 (n=26)**
Buserelin at +12 days	55.5 (n=18)	42.3 (n=26)

**P < .01; *P < .05.

The CIDR + prostaglandin F-2 alpha program gives a more precise synchrony of estruses compared to the Receptal + prostaglandin F-2 alpha program. Nevertheless, both systems are manipulating the estrous cycle in a slightly different manner and provide alternative systems for synchronization that contribute to a reproductive management program. With our current acquisition of new knowledge and experience, relative to these novel systems of reproductive management, it is likely that in the future we will be able to: synchronize both follicle development and CL regression to maximize fertility at a preplanned insemination that occurs at a time most efficient for the farm manager, to treat animals following insemination to reduce embryo mortality and thus increase pregnancy rates, to synchronize returns to service in those animals that did not conceive. Our current knowledge of the mechanisms controlling these reproductive processes makes these goals achievable and applicable to the management system of Florida dairy producers.

Our research with reproductive management systems described in this report have been supported partially by the Florida Dairy Producer's Milk Check-off Grant Program. Based on the promising research results achieved in both Florida and New Zealand with the CIDR and Buserelin products, commercial companies are in the process of conducting various field trials across the United States (including Florida) that will hopefully lead to the registration and marketing of these agents to the producer.

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