Gonadotropin-Releasing Hormone and Prostaglandin $F_{2\,alpha}$ in Early Postpartum Dairy Cows

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Reproductive events in early postpartum dairy cows have been well-characterized. The interval from parturition to the development of ovarian follicles > 1 cm diameter averages about 15 days and the interval to first ovulation about 20 days (Marion and Gier, 1968; Saiduddin et. al., 1968; Morrow, 1969; Oxenreider and Wagner, 1971, and Callahan et. al., 1971). First estrus usually occurs from 30-72 days after calving (Wis. Res. Bull. 270, 1968) and about 15% of dairy cows manifest abnormal ovarian activity (e.g., ovarian follicular cysts, luteinized ovarian follicles and cystic corpora lutea) during the first two months postpartum.

Fertility of dairy cows during the normal breeding period increases in direct proportion to the number of estrous cycles prior to the beginning of breeding (Thatcher and Wilcox, 1973, and Britt et al., 1974). Maximum lifetime production of milk and offspring for dairy cows occurs when average calving interval is 12 months or less. A 12-month or less calving interval results when breeding begins about 40-60 days postpartum (Britt, 1975). Thus, treatments given to induce early postpartum ovulations and to increase the number of estrous cycles prior to breeding may result in increased fertility and shorter calving intervals for dairy cows.

Discovery of a naturally occurring decapeptide which caused release of luteinizing hormone in laboratory species (Schally et al., 1971) led to the availability of gonadotropin releasing hormone (GnRH) which appeared to be potentially useful for inducing LH release and subsequent ovulation in early postpartum cows. Similarily, the discovery that prostaglandin $F_{2\alpha}$ was a potent luteolytic agent (Pharriss and Wyngarden, 1969) led to the availability of another naturally occurring compound considered potentially useful for inducing corpus luteum regression and subsequent estrus and ovulation in diestrous cows. Much of the recent research on these two hormones has been reviewed (Hafs et al., 1974, and Britt, 1975).

The objective of this presentation is to review research conducted: 1) to determine whether gonadotropin-releasing hormone (GnRH) could be used to induce normal estrous cycles and improve fertility in early postpartum dairy cows and 2) to determine whether prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) could be used to synchronize the time of ovulation in groups of heifers. In addition, a model for control of ovulation with GnRH and $PGF_{2\alpha}$ in dairy cattle is presented.

GnRH Experiments

Endocrine and ovulatory responses were studied after GnRH treatment in early postpartum dairy cows (Britt et al., 1974). Twenty lactating Holstein cows were given GnRH (100 μg) or saline via a No. 5 gelatin capsule implanted in an ear on day 14 postpartum. Blood samples were collected from a jugular vein on a schedule designed to detect acute and chronic changes in serum hormones. Changes in ovarian structures and uterine size were monitored by rectal palpation twice weekly until day 65 postpartum.

In a second experiment, reproductive performance was examined in Holstein cows given GnRH at two weeks postpartum in four commercial dairy herds. Cows were randomly assigned at calving to be given 200 μg GnRH (im) or 1 ml saline. All cows which calved during each two week period were treated during a bi-weekly visit to each herd; thus, cows received treatment between 8 and 21 days postpartum. Herd records were used to determine intervals to estrus and conception for these cows as well as reasons for additional postpartum therapy and culling.

In the first experiment serum-luteinizing hormone peaked about 4 hrs. after GnRH treatment on day 14 postpartum but did not change during 6 hrs. after administration of saline (Figure1). Thus, cows at two weeks postpartum were capable of responding to GnRH treatment with increases in blood LH sufficient to induce ovulation. One of 10 GnRH-treated cows had ovulated on day 9 postpartum, the remaining nine cows ovulated on day 15, one day after treatment. Eight of 10 saline-treated cows ovulated before day 40 postpartum (Figure 2). Two cows in the saline-treated group developed ovarian follicular cysts and had not ovulated by day 65 postpartum. Another cow in the saline-treated group developed a luteinized follicle and serum progesterone in this cow did not exceed 0.3 ng/ml in samples collected prior to day 65

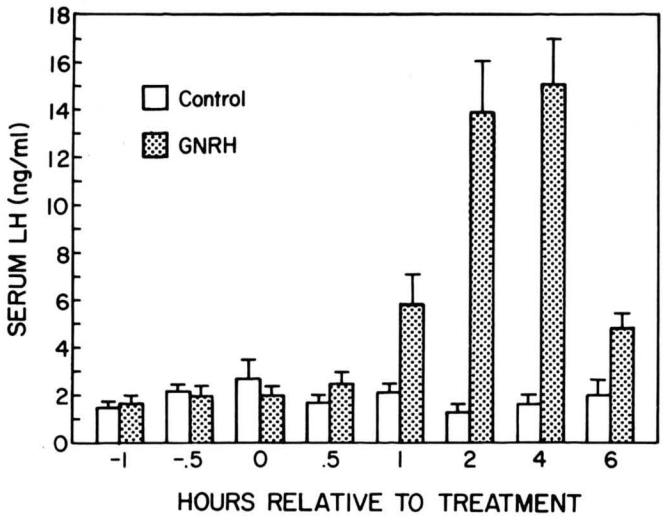


Figure 1. Serum luteinizing hormone after GnRH on day 14 postpartum in Holstein cows.

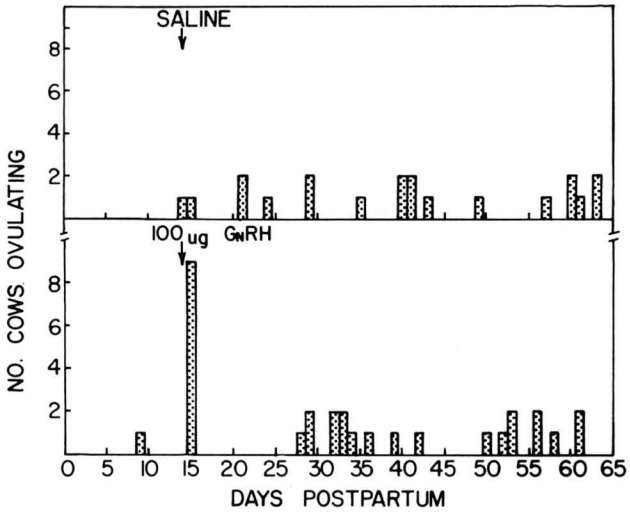


Figure 2. Occurrence of ovulations from day 14 to day 65 postpartum in GnRH- and saline-treated cows (n = 10 for each group).

postpartum, suggesting aberrant ovarian activity. Saline-treated cows averaged 2.0±0.4 ovulations prior to day 65 postpartum compared with 3.1±0.1 ovulations for GnRH-treated cows.

Serum progesterone during three weeks after GnRH treatment was similar to that observed during normal estrous cycles (Figure 3). All cows in the GnRH group exhibited similar responses, suggesting that the corpus luteum formed after GnRH-induced ovulation was capable of normal function.

A summary of reproductive events in GnRH- and saline-treated cows is given in Table 1. The average interval to first ovulation for 10 GnRH-treated cows which had estrous cycles was nine days shorter than for eight saline-treated cows which cycled (14.4 vs. 23.6). The interval from first to second ovulation was slightly shorter in the GnRH-treated group (18.1 vs. 20.9 days) but the interval to first detected estrus was slightly longer (41.0 vs. 37.5 days), indicating that

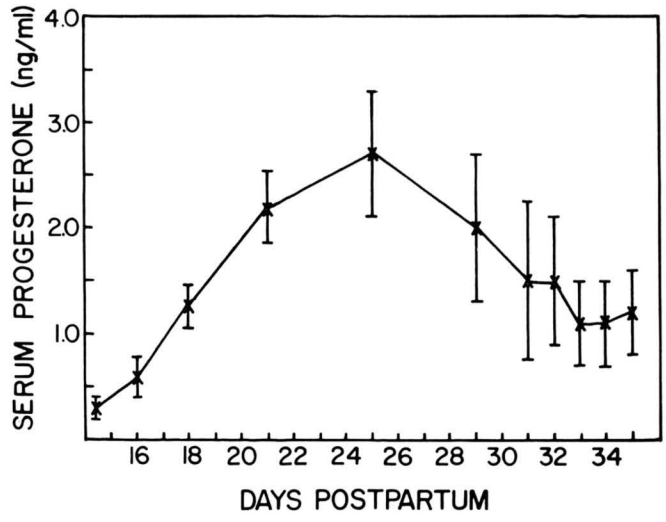


Figure 3. Serum progesterone after administration of GnRH on day 14 postpartum in Holstein cows.

some estrous periods may not have been detected in the GnRH-treated cows.

None of the 10 GnRH-treated cows were detected in estrus around the time of the induced ovulation but two of eight saline-treated cows were in estrus the day prior to their first ovulation (Table 2). More saline-treated cows exhibited first estrus at first or second ovulation than GnRH-treated cows, suggesting that occurrence of estrus may be related to the postpartum interval as well as steroid hormone concentration. First ovulation in both cases occurred more frequently on the ovary opposite the previously gravid uterine horn.

Reproductive performance of cows given GnRH or saline at two weeks postpartum in four commercial dairy herds is summarized in Table 3. While intervals to first estrus, first insemination and conception and inseminations per conception did not differ among GnRH- and saline-treated cows which conceived, fewer GnRH-treated cows were culled for infertility (24 vs. 55%) and fewer GnRH-treated cows developed ovarian follicular cysts (5.7 vs. 15.2%). Thus, while GnRH treatment did not result in improved reproductive performance for cows which conceived, it did decrease the incidence of ovarian follicular cysts and reduce the percent of cows which were culled for reproductive reasons. Presumably this allowed dairymen to cull low milk producers rather than cows which were repeat-breeders or which had other reproductive problems.

$PGF_{2\alpha}$ Experiment

Six Holstein heifers each in diestrus were given: 1) 30 mg $PGF_{2\alpha}$ (Tham salt, i.m.), 2) two 15 mg injections of $PGF_{2\alpha}$ at 6-hr. intervals, or 3) 60 mg $PGF_{2\alpha}$. Blood samples were collected via a jugular canulae for determination of acute and chronic changes in progesterone and estradiol and LH. Heifers were observed for estrus at 12-hr. intervals and the ovaries were palpated *per rectum* to determine the time of

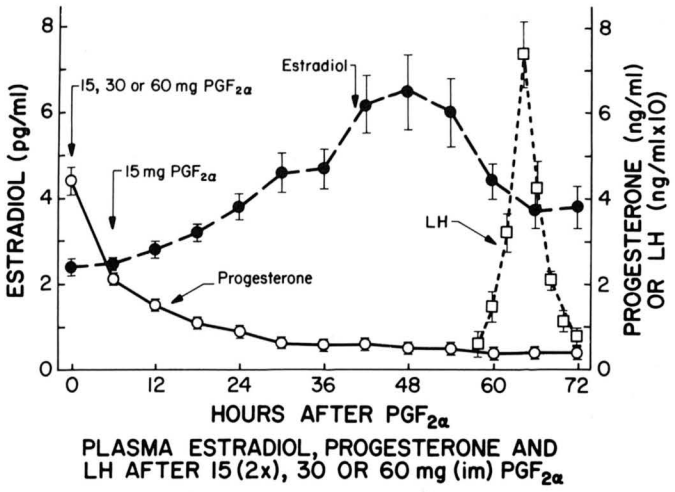


Figure 4. Serum progesterone, estradiol and luteinizing hormone after $PGF_{2\alpha}$ administration to diestrous Holstein heifers.

Table 1

Intervals to Ovulation and Estrus in Dairy Cows Treated with Gonadotropin-Releasing Hormone on Day 14 Postpartum

Variable	Saline	GnRH
No. cows	10	10
No. cows which cycled[1]	8	10
Interval (days):		
Calving to 1st ovulation[2]	23.6±2.6	14.4±0.6
1st ovulation to 2nd ovulation	20.9±0.9	18.1±1.0
Calving to 1st estrus	37.5±4.0	41.0±4.0
Avg. ovulations prior to Day 65	2.0±0.4	3.1±0.1
Percent of cows exhibiting 1st estrus at:		
1st ovulation	25	0
2nd ovulation	62	50
3rd ovulation	13	40
4th ovulation	0	10
1st ovulation in relation to previously gravid uterine horn:		
Same side	2	3
Opposite side	6	7

[1]Two control cows developed ovarian follicular cysts and were not included in these calculations.
[2]Mean ± SE.

ovulation. Details of the procedures have been published (Hafs et al., 1974 and Stellflug et al., 1975).

Serum progesterone declined from 4.4 ng/ml at the time of administration of 15, 30 or 60 mg $PGF_{2\alpha}$ to 1.5 ng/ml at 12 hrs., then continued to decline until reaching a nadir of about 0.5 ng/ml from 48 to 72 hrs. (Figure 4). Estradiol increased from 2.4 pg/ml at $PGF_{2\alpha}$ treatment to 6.5 pg/ml at 48 hrs. after $PGF_{2\alpha}$. Thus, luteolysis manifested as a decline in serum progesterone was accompanied by a concurrent increase in serum estradiol. Blood LH peaked at 64 hrs. after $PGF_{2\alpha}$ treatment.

The onset of estrus in six heifers given 60 mg $PGF_{2\alpha}$ averaged 54±4 hrs. after treatment compared with 56±2 and 66±7 hrs. for heifers given 30 or 2x15 mg $PGF_{2\alpha}$ (Table 3). Serum LH peaked from 61±5 to 67±6 hrs. after $PGF_{2\alpha}$ and ovulation occurred at 78±5 to 92±8 hrs. following treatment. Apparently the largest dose of $PGF_{2\alpha}$ resulted in slightly shorter intervals to estrus, LH peak and ovulation.

Model for Control of Ovulation

Since GnRH is effective in inducing ovulation and subsequent formation of a functional corpus luteum in early postpartum cows and $PGF_{2\alpha}$ will effectively synchronize the onset of estrus and ovulation in diestrous cows, it is logical that these two products be used in a scheme for synchronizing inseminations in early postpartum cows. A model for ovulation control with GnRH and $PGF_{2\alpha}$ is presented in Figure 5.

Cows which calve during a three-week interval are grouped, and 12 days later each is given a single injection of GnRH to induce ovulation. This is followed by injections of $PGF_{2\alpha}$ at 10 and 22 days after the GnRH treatment and all cows are inseminated at 80 hrs. after the second $Pgf_{2\alpha}$ treatment. The double treatment of $PGF_{2\alpha}$ has been used effectively to synchronize ovulations in beef heifers and cows and fertility of inseminations at 80 hrs. after the second $PGF_{2\alpha}$ is equal to that in heifers and cows inseminated 12 hrs. after observed estrus (Hafs et al., 1975).

Cows which do not conceive to the timed artificial insemination should exhibit their second estrus during the time of first expected estrus for cows in the next three-week calving group. Pregnancy diagnosis via rectal palpations is conducted at about 35 days after the initial AI and cows found non-pregnant are grouped with those receiving their second $PFG_{2\alpha}$

Table 2

Reproductive Performance of Cows Given GnRH or Saline at Two Weeks Postpartum in Four Commercial Dairy Herds

Variable	GnRH	Saline
No. cows treated	105	99
No. cows culled	33	29
Low milk production	21 (64%)	9 (31%)
Injury or disease	4 (12%)	4 (14%)
Infertility*	8 (24%)	16 (55%)
No. cows pregnant	72	70
Avg. interval (days) to:		
1st recorded estrus	67	63
1st insemination	90	86
Conception	117	119
Inseminations/Conception	1.8	1.7
No. cows with ovarian follicular cysts	6 (5.7%)	15 (15.2%)
Eventually culled	3	6
Eventually conceived	3	9

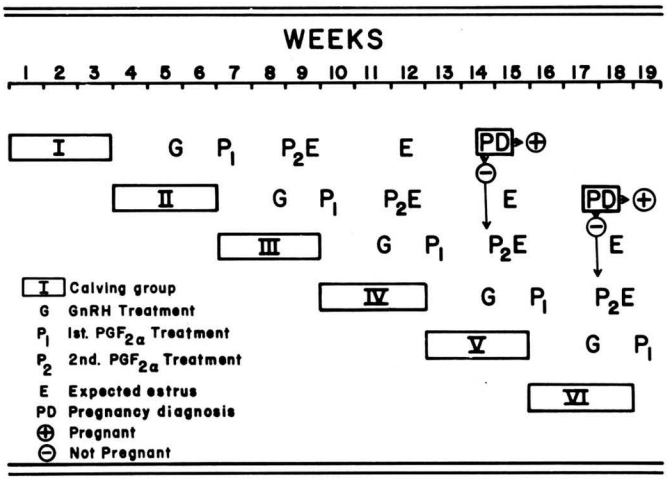
*2 GnRH-treated cows and 1 saline-treated cow were considered reproductive culls because interval from calving to conception for each was greater than 250 days.

Table 3

Intervals from $PGF_{2\alpha}$ to Estrus, Peak LH and Ovulation in Holstein Heifers

$PGF_{2\alpha}$ (mg)	Interval (hr.) from $PGF_{2\alpha}$ to: Onset of estrus	Peak LH	Ovulation
30	56±2[1]	65±5	90±5
2x15	66±7	67±6	92±8
60	54±4	61±5	79±5

[1]x±S.E. for 6 heifers.



Model For Ovulation Control With GnRH and $PGF_{2\alpha}$ In Dairy Cows

Figure 5. Model for synchronization of ovulation with GnRH and $PGF_{2\alpha}$ in lactating dairy cows.

treatment in order to re-synchronize ovulations. With this scheme, estrus detection and inseminations are concentrated to a three-day period every three weeks.

To work best it appears that such a scheme be supervised by trained technicians working under the direction of a veterinarian. Furthermore, since inseminations have to be properly timed in relation to $PGF_{2\alpha}$ treatment, it seems logical that the entire reproductive management program be conducted through an organization which would provide semen and GnRH and $PGF_{2\alpha}$ treatments in addition to maintaining reproductive performance records and providing a pregnancy diagnosis service.

While application of these procedures in lactating cows awaits approval of the Food and Drug Administration, it seems plausible to expect that such a regime will be used to manage reproductive performance in dairy herds in the future.

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Questions

Items 1 through 3 are to be answered with the most correct response from the list below.

A. Increased; B. Decreased

____ 1. Serum luteinizing hormone concentrations during first four hours after GnRH treatment on day 14 postpartum in dairy cows.

____ 2. Serum estradiol during 48 hours after $PGF_{2\alpha}$ treatment in diestrous heifers.

____ 3. Serum progesterone during 10 days after administration of GnRH on day 14 postpartum in dairy cows.

4. Estrus begins at about ____ hours and LH peaks at about ____ hours after $PGF_{2\alpha}$ treatment in diestrous heifers.

5. The incidence of ovarian follicular cysts (increased, decreased) after GnRH treatment on day 14 postpartum in Holstein cows.