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# DIAMETER OF OVARIAN FOLLICLES, ESTRADIOL AND PROGESTERONE CONCENTRATIONS, AND PREGNANCY RATES IN CATTLE TREATED WITH PROGESTINS AND $PGF_{2\alpha}$

*M. W. Smith and J. S. Stevenson*


## Summary

Holstein cows and virgin heifers were treated with progestins and $PGF_{2\alpha}$ before first service to determine their influence on reproductive traits. Control cows were given two injections of $PGF_{2\alpha}$ 14 days apart and inseminated at estrus after the second injection. Two groups received a norgestomet ear implant (N1) or a progesterone-releasing intravaginal device (PRID; P1) 8 days after one injection of $PGF_{2\alpha}$, followed the next day by $PGF_{2\alpha}$ to regress the corpus luteum, and the progestin source was removed 7 days later. The last two treatments were similar except the second injection of $PGF_{2\alpha}$ was given 14 days after the first and norgestomet (N6) or PRID (P6) sources were removed 1 day later. Inseminations were performed at estrus in the latter four treatments. Pregnancy rates and serum progesterone were higher and serum estradiol and follicular diameters were lower in controls, P6, and N6 treatments, where the corpus luteum was functional during progestin treatments, than in those treatments where the corpus luteum was absent (P1 and N1). Follicle turnover occurred more consistently in control, P6, and N6 treatments, whereas when follicular diameter and serum estradiol were greater (N1 treatment), turnover did not occur as often and pregnancy rates at first service were reduced markedly. Treatments with progestins must control follicular growth, or fertility will be reduced.


(Key Words: $PGF_{2\alpha}$, Progestins, Follicles, Fertility.)

## Introduction

During the past 8 years, much has been learned about the dynamics and control of follicular growth in cattle because of our ability to visualize and monitor the development of individual follicles by transrectal ultrasonography. It is now recognized that either two, three, or four waves of follicles develop during the course of the estrous cycle. These waves develop at various stages of the cycle, with the first wave always beginning shortly after estrus. Follicles (2 to 4 mm in diameter) are recruited by identifiable increases in follicle-stimulating hormone in blood serum. These follicles begin to increase in diameter until one grows more quickly and dominates or suppresses the growth of the remaining emerging follicles. Longer estrous cycles (>21 days) are associated with three or four waves of follicular growth. The first large follicle, which dominates the remaining follicles in both ovaries, reaches its maximal diameter around day 6 to 8 of the cycle and is capable of ovulating, if the corpus luteum is regressed by administering $PGF_{2\alpha}$ (Lutalyse® or Estrumate®). If a dominant follicle is exposed to various sources of progestin before and after natural or induced regression of the corpus luteum, the follicle continues to increase in diameter and, when it ovulates, subsequent fertility seems to be impaired. Our study was designed to determine the effect of two sources of progestin on changes in ovarian follicular growth, concentrations of progesterone and estradiol, and fertility in virgin heifers and lactating Holstein cattle exposed to five different treatments designed to increase or decrease fertility.

## Procedures

Five treatments were employed to test our hypothesis that holding a follicle after regression of the corpus luteum would reduce pregnancy rates in association with increased concentrations of estradiol and larger-diameter follicles. Treatments were applied to virgin heifers (minimum body weight of 800 lb and 13 months of age) and to lactating cows (minimum of 50 days in milk) before first service. All cattle received 25 mg of $PGF_{2\alpha}$ (Lutalyse®) on day O of the experiment, and controls were given a second injection of $PGF_{2\alpha}$ 14 days later. Two groups were given norgestomet (6-mg ear implants) for 7 days, beginning on day 8, with $PGF_{2\alpha}$ being injected either 1 (Nl) or 6 days (N6) after implant insertion. The remaining two treatments consisted of two groups receiving a progesterone-releasing intravaginal device (PRID) containing 1.5 mg of progesterone for 7 days, beginning on day 8, with $PGF_{2\alpha}$ being given either 1 (Pl ) or 6 days (P6) after PRID insertion.

Blood samples were collected on days O, 1, and 8 to 16 of the experiment in all cattle, and follicles in both ovaries were monitored daily by ultrasonography from day 8 of the experiment until ovulation was detected. All cattle were inseminated when detected in estrus following the second injection of $PGF_{2\alpha}$ or after removal of the norgestomet ear implants or PRID. Pregnancy diagnoses were made by transrectal ultrasonography at day 28 and were confirmed later by palpation of the uterus per rectum between days 40 and 54.

## Results and Discussion

Resulting pregnancy rates are summarized in Table 1. Pregnancy rates at ultrasound determination or by palpation were greater (P < .05) in the control, N6, and P6 treatments than in the N1 treatment. Fertility in the P1 treatment was intermediate between that in N1 and the other three treatments. Embryonic survival rates ranged from 81 to 93%, with 16 embryos (7.6910) failing to survive between day 28 and days 40 to 54 of pregnancy. This late embryonic loss probably was associated with failure of the placenta to attach to the uterine wall.

Concentrations of progesterone for the five treatments are illustrated in Figure 1.

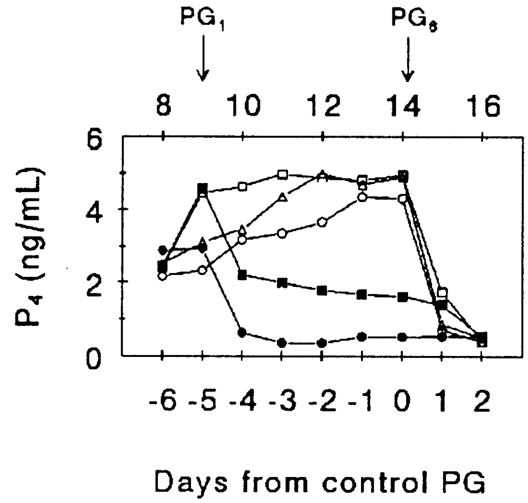


**Figure 1. Progesterone in Serum in Control (△), P6 (□), N6 (○), P1 (■), and N1 (●) Treatments from Day of $PGF_{2\alpha}$ (PG) Injection (day 14)**

Progesterone between days 8 and 16 was greater (P < .01) in control, N6, and P6 treatments because of the continued presence of a functional corpus luteum compared to concentrations of progesterone in the N 1 treatment in which the corpus luteum was regressed by administering $PGF_{2\alpha}$ on day 9. Concentrations of progesterone were intermediate in the P1 treatment. The PRID in the P1 treatment maintained low (~2 ng/mL) concentrations of progesterone, whereas the progestin activity of the N1 or N6 treatments was not assessed and is not reflected by the concentrations of progesterone shown in Figure 1.

Table 2 illustrates concentrations of estradiol and maximal diameter of the dominant follicle on day 14 of the experiment (time of $PGF_{2\alpha}$ in the controls, N6, and P6 and 1 day before removal of the progestin sources). Diameter of the follicles was greater (P < .05) in the N 1 and P1 treatments (corpus luteum regressed 5 days earlier) than in the control, N6, or P6 treatments. These differences in diameters among treatments are reflected mostly by concentrations of estradiol in blood serum. The N1 treatment had greater (P < .05) concentrations of estradiol than any of the other treatments, which was associated with its significantly lower fertility (Table 1).

In the absence of adequate concentrations of progesterone or a functional corpus luteum, the dominant follicle fails to turn over and normal patterns of follicular growth (waves) are not maintained during the estrous cycle. Our study demonstrates that in the absence of the corpus luteum (N1 and P1 treatments) or adequate concentrations of progesterone (N1), follicles continue to grow to larger diameters and secrete more estradiol. These characteristics of follicular development were related to reduced pregnancy rates (Table 1). High concentrations of estradiol and(or) increased retention time of the dominant follicle had adverse effects on the subsequent pregnancy rates. The lower fertility may be associated with aging of the follicle or the egg cell found within it. Either aging of the egg cell that eventually ovulated and(or) the effects of high concentrations of estradiol adversely altered factors related to normal fertility. These negative effects might include alterations in the oviductal and uterine environment as they prepare to nourish the fertilized egg and developing conceptus. Other recent studies have suggested that improved fertility, or prevention of lowered fertility in some cases, is achieved by manipulating the presence of the dominant follicle while estrus is synchronized. Treatments with progestins and $PGF_{2\alpha}$ must synchronize follicular growth, or reduced fertility will occur.

**Table 1. Pregnancy Rates and Embryo Survival in Cattle Treated with Progestins and $PGF_{2\alpha}$ at First Services**

| | | Pregnancy rates | | |
|---|---|---|---|---|
| Treatment | No. of cows | Ultrasound[1] | Palpation[2] | Embryo survival[3] |
| | | ---------- % ---------- | | |
| Control | 43 | $66^{x}$ | $53^{x}$ | 81 |
| P6 | 41 | $58^{x}$ | $56^{x}$ | 93 |
| N6 | 41 | $58^{x}$ | $51^{x}$ | 89 |
| P1 | 41 | $48^{xy}$ | $41^{xy}$ | 83 |
| N1 | 45 | $26^{z}$ | $27^{y}$ | 91 |

[1]Day 28 after insemination.
[2]Between days 40 and 54 after insemination.
[3]Survival of viable embryos between day 28 and days 40 to 54 after insemination.
[x,y,z]Means within a column without a common superscript letter differ ($P < .05$).

**Table 2. Concentrations of Estradiol and Diameter of Ovulatory Follicle**

| Treatment | No. of cows | Estradiol[1] | Diameter of follicle[1] |
|---|---|---|---|
| | | ---- pg/mL ---- | ---- mm ---- |
| Control | 12 | $7.3 \pm 0.9^{x}$ | $16.4^{x}$ |
| P6 | 9 | $7.7 \pm 1.0^{x}$ | $16.4^{x}$ |
| N6 | 8 | $7.6 \pm 1.1^{x}$ | $15.8^{x}$ |
| P1 | 9 | $8.4 \pm 1.0^{x}$ | $18.4^{y}$ |
| N1 | 9 | $11.5 \pm 1.0^{y}$ | $18.2^{y}$ |

[1]Determined on day 14 of the experiment when the second injection of $PGF_{2\alpha}$ was administered to the control, P6, and N6 treatments.
[x,y]Means within a column without a common superscript letter differ ($P < .05$).