OVARIAN ACTIVITY IN BEEF HEIFERS IMMUNIZED AGAINST GONADOTROPIN-RELEASING HORMONE (GnRH)

D. K. Bishop[1], R. P. Wettemann[2], J. V. Yelich[1] and L. J. Spicer[3]

Story in Brief

Angus x Hereford heifers (n = 23) were used to determine if the ovaries of heifers immunized against GnRH would respond to exogenous gonadotropins. Heifers were immunized against GnRH conjugated to human serum albumin (HSA) or HSA, then half the heifers in each group were treated with gonadotropin (GTH; 2000 IU PMSG + 1000 IU hCG) or saline (control). All heifers were given PGF2α (i.m.) on d 2 (d 0 = start of GTH treatment) and 2000 IU of hCG (i.m.) on d 4. Blood samples were collected and ovaries were evaluated by ultrasound during the 14 day trial. Concentrations of estradiol and progesterone in plasma, and the number of follicles $\geq$ 6 mm were increased by gonadotropin treatment of heifers but the response was reduced by immunization against GnRH. We conclude that anestrus occurs in heifers immunized against GnRH because of reduced secretion of gonadotropins since the ovary of heifers immunized against GnRH will respond to gonadotropins.

(Key Words: GnRH, Gonadotropins, Heifers, Immunization, Ultrasound.)

Introduction

Immunization against GnRH effectively isolates the anterior pituitary from hypothalamic stimulation and results in cessation of estrous cycles in beef heifers (Wettemann and Castree, 1988; O'Connell and Wettemann, 1989) and prolongs the anestrous period after parturition in beef cows (O'Connell and Wettemann, 1990). These authors monitored concentrations of progesterone and luteinizing hormone and concluded that immunization against GnRH blocked the ovulatory surge of gonadotropins necessary to cause ovulation of follicles and formation of a corpora lutea. As antibody titers against GnRH decreased with time after immunization, the females returned to estrus.

---

[1]Graduate Student [2]Regents Professor [3]Assistant Professor

The objective of this experiment was to determine if exogenous gonadotropins will stimulate follicular growth in heifers that are anestrus as a result of active immunization against GnRH.

Materials and Methods

Angus x Hereford heifers (n = 23; 491 ± 23 kg) that were 24 mo of age and exhibiting normal estrous cycles were used. Twelve of the heifers had been previously immunized against GnRH conjugated to human serum albumin (HSA) and eleven of the heifers had been immunized against HSA as controls. GnRH immunized heifers were given a booster immunization (GnRH-Imm) to enhance antibody production and cause cessation of estrous cycles. Control heifers received a booster immunization against HSA (HSA-IMM).

Blood samples were collected weekly commencing on the day that the booster immunization was given and continuing until the heifers immunized against GnRH became anestrus (concentrations of progesterone < 1 ng/mL for 3 weeks). Estrous cycles of HSA-IMM heifers were synchronized with prostaglandin $F_{2\alpha}$ (PGF) and heifers were treated between d 9 and 11 (d 0 = estrus) of the subsequent cycle.

Gonadotropin treatments were arranged in a 2 x 2 factorial design. Half of the anestrous (GnRH-IMM; n = 6) heifers and six of the control (HSA-IMM) immunized heifers received gonadotropins (2000 IU PMSG + 1000 IU hCG; P.G. 600, Intervet America Inc.; GTH). The remaining heifers were given saline (control). Treatments (10 mL) were administered (s.c.; 40, 30 and 30% of the total dose) at 6 h intervals on d 0. All heifers were given PGF on d 2 (i.m.) and 2000 IU hCG (i.m.) on d 4.

Blood samples were collected prior to treatment (d 0), daily through d 8 and every second day through d 14, and progesterone and estradiol were quantified in plasma. Ovaries of heifers were examined with an Aloka 210 portable ultrasound scanner equipped with a 5 Mhz transducer designed for intrarectal examinations. Both ovaries of each heifer were evaluated just prior to treatment on d 0 and on d 2, 4, 6, 8 and 14. The size, location, and numbers of follicles and corpora lutea (CL) were determined and relationships between ultrasound data and hormone concentrations were determined.

Results and Discussion

Heifers immunized against GnRH were anestrus (first of three consecutive samples with progesterone < 1 ng/mL plasma) by 3.3 ± .1 wk after the booster was given. GTH treatment was initiated within 5 wk after the

onset of anestrus. At treatment, antibody titers against GnRH (^{125}I-GnRH bound at 1:1000 dilution) were 69.5 ± 3.2 % in GnRH-IMM heifers and non-detectable in HSA-IMM heifers. Similar to a previous report (Wettemann and Castree, 1988), concentrations of progesterone in plasma indicated that the CL present at the time of the booster immunizations had normal lifespans but subsequent ovulations were inhibited. Additionally, none of the heifers immunized against GnRH had CL present on the ovaries prior to GTH treatments.

Concentrations of estradiol were similar in all heifers on d 0 prior to treatments. Concentrations of estradiol in heifers (Figure 1) increased after GTH but the response was reduced by immunization against GnRH. Similarly, the number of follicles on ovaries (Figure 2) was increased by injection of GTH and GnRH-IMM decreased the number of follicles. Estradiol concentrations in plasma, adjusted for day of treatment, were related to the number of follicles > 6mm detected with ultrasound ($r = .54$, $P < .01$).

In agreement with the number of CL (Figure 3) on the ovaries, concentrations of progesterone at treatment (d 0) were 6.2 ± .3 and 0.5 ± .3

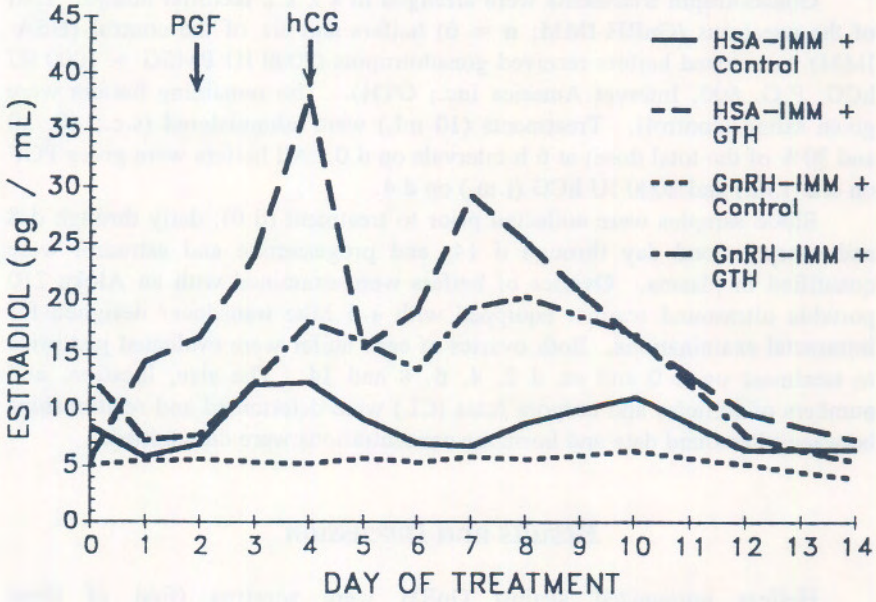

Figure 1. Concentrations of estradiol in plasma of heifers immunized against GnRH (GnRH-IMM) or HSA (HSA-IMM) and treated with gonadotropins (GTH) or saline.

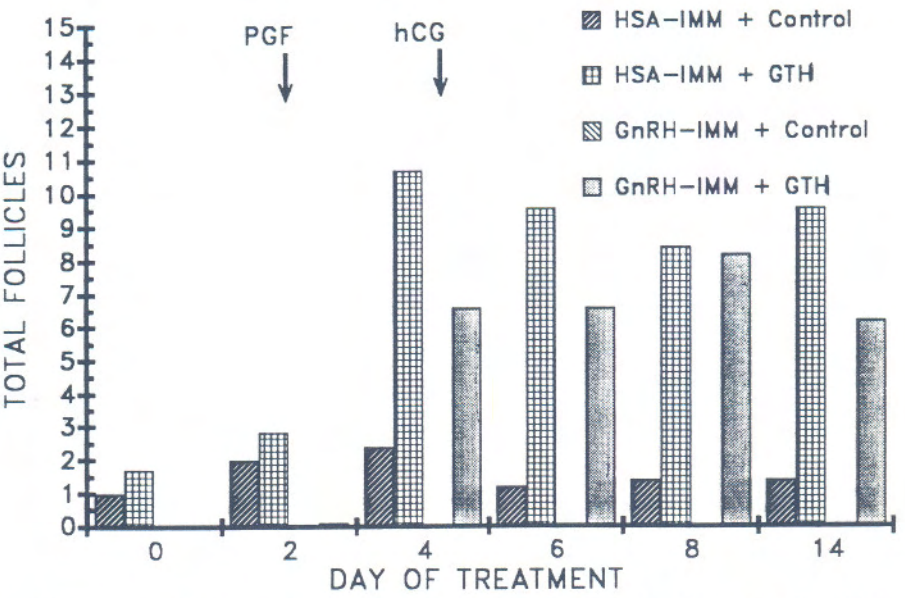

Figure 2. Total number of follicles > 6 mm on ovaries of heifers immunized against GnRH (GnRH-IMM) or HSA (HSA-IMM) and treated with gonadotropins (GTH) or saline.

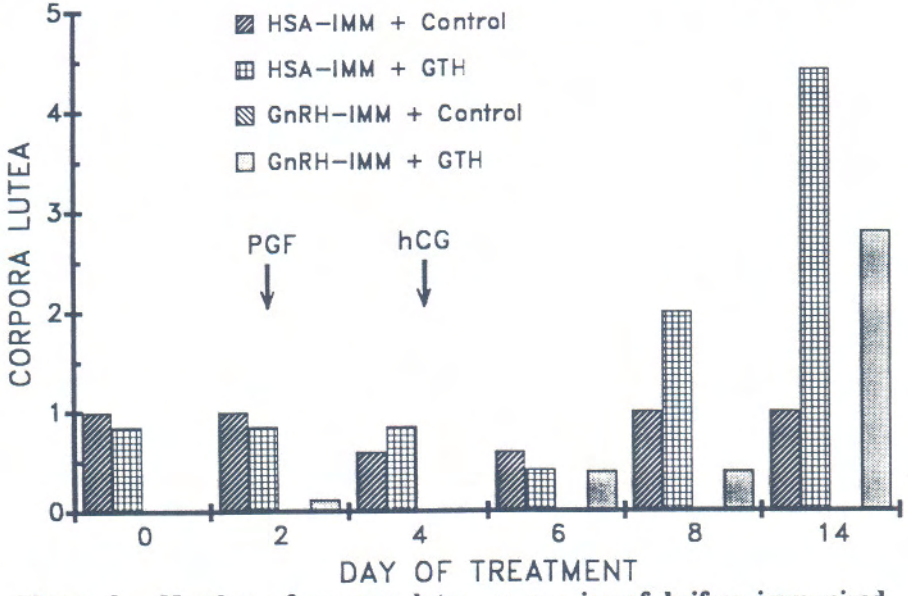

Figure 3. Number of corpora lutea on ovaries of heifers immunized against GnRH (GnRH-IMM) or HSA (HSA-IMM) and treated with gonadotropins (GTH) or saline.

ng/mL for HSA-IMM and GnRH-IMM heifers, respectively. After administration of PGF to cause luteal regression (d 2), concentrations of progesterone in control immunized heifers decreased and on d 8 concentrations of progesterone were similar among all heifers. Treatment with GTH increased concentrations of progesterone between d 8 and d 14 (Figure 4). The number of CL was closely related to concentrations of progesterone ($r = .82$; $P < .001$). Although concentrations of progesterone were not influenced by immunization against GnRH, the number of CL was less in GnRH-IMM heifers compared with control immunized heifers.

We conclude that treatment with exogenous gonadotropins will cause increased concentrations of estradiol, follicular growth and ovulation in anestrous heifers immunized against GnRH. Increased antibody titers against GnRH that are sufficient to prevent ovulation and/or development of corpora lutea, do not prevent the ovary from responding to exogenous gonadotropins.

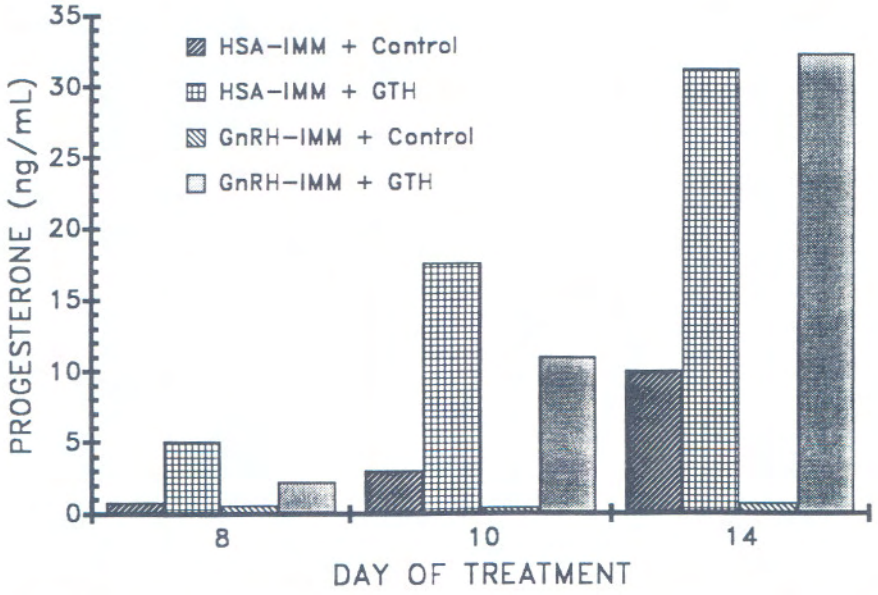

Figure 4. Least squares mean concentrations of progesterone in plasma of heifers immunized against GnRH (GnRH-IMM) or HSA (HSA-IMM) and treated with gonadotropins (GTH) or saline.

Literature Cited

Wettemann, R. P. and J. W. Castree. 1988. Immunization of heifers against luteinizing hormone releasing hormone delays puberty and causes anestrus. Okla. Agr. Exp. Sta. Res. Rep. MP-125:17.

O'Connell, C. and R.P. Wettemann. 1989. Effects of active immunization against LHRH in beef heifers on the onset of ovarian activity. Okla. Agr. Exp. Sta. Res. Rep. MP-127:242.

O'Connell, C. and R.P. Wettemann. 1990. Immunization of postpartum cows against gonadotropin releasing hormone influences the onset of luteal activity and establishment of pregnancy. Okla. Agr. Exp. Sta. Res. Rep. MP-129:334.