Effects of progestagen treatment on concentrations of prostaglandins and oxytocin in plasma from the posterior vena cava of post-partum beef cows

D. A. Cooper, D. A. Carver, P. Villeneuve, W. J. Silvia and E. K. Inskeep

Division of Animal and Veterinary Sciences, West Virginia University, Morgantown, WV 26506, USA

Summary. The role of PGF-2 α in determining the lifespan of corpora lutea in the post-partum beef cow was investigated. In control cows (N = 5) induced to ovulate at Day 28 to 36 *post partum* by injection of 1000 i.u. hCG, corpora lutea had an average lifespan of only 8 days. In cows pretreated with 6 mg implants of a progestagen (norgestomet, N = 4) for 9 days, with implant removal 2 days before injection of hCG, luteal lifespan averaged 17.5 days. Concentrations of PGF-2 α in 9 hourly samples of plasma collected from the posterior vena cava via indwelling catheters were higher on Days 4 through 9 after injection of hCG ($P < 0.05$) in the cows with short-lived corpora lutea. Greater release of PGF-2 α could therefore be a major factor in premature luteal regression. Concentrations of PGFM and oxytocin did not differ between cows with corpora lutea of short or normal lifespan.

In a second experiment, concentrations of PGF-2 α in plasma from the posterior vena cava were examined during treatment with norgestomet (N = 8) or in contemporary controls (N = 7). In progestagen-treated cows, PGF-2 α was higher than in control cows ($P < 0.05$), beginning on Day 3 of treatment and peaking on Day 5. It is concluded that the post-partum uterus increases secretion of PGF-2 α very early after first exposure to endogenous or exogenous progestagen.

Keywords: PGF-2 α ; abnormal corpus luteum; PGFM; oxytocin; progestagen

Introduction

Corpora lutea (CL) with short lifespans (< 14 days) are formed subsequent to ovulation induced by early weaning (Ramirez-Godinez *et al.*, 1981) or by injection of exogenous gonadotrophins or gonadotrophin-releasing hormone (Lishman *et al.*, 1979; Sheffel *et al.*, 1982) in post-partum anoestrous beef cows. Copelin *et al.* (1987) found that hysterectomy prevented regression of bovine CL destined to have short lifespans. Peter *et al.* (1989) reported rises in 13,14-dihydro-15-keto, prostaglandin F-2 α (PGFM), a pulmonary metabolite of PGF-2 α , during luteolysis in both short and normal first post-partum oestrous cycles in dairy cows. Copelin *et al.* (1988) found no difference in concentrations of PGF-2 α in uterine venous plasma on Day 2 after ovulation between beef cows expected to have short or normal luteal lifespans. Likewise, there were no differences in concentrations of PGFM in peripheral venous plasma on several days after induced ovulation in beef cows (Troxel & Kesler, 1984a; Garcia-Winder *et al.*, 1986). Thus, whether or not PGF-2 α rises early during short luteal phases has not been clearly established.

Luteal oxytocin has been implicated in release of PGF-2 α during luteolysis in domestic ruminants (Wathes, 1984; Flint *et al.*, 1986). Exogenous oxytocin elicited greater concentrations of PGFM on Day 5 of the oestrous cycle in beef cows expected to have short rather than normal luteal lifespans (Zollers *et al.*, 1989b). In post-partum dairy cows, Peter *et al.* (1989) reported that increases in oxytocin were associated with increases in PGFM during premature luteolysis.

The present study was designed to test whether increased release of PGF-2 α and/or oxytocin occurred earlier in post-partum cows in which the lifespan of an induced CL was short (< 14 days) than in cows in which luteal lifespan was normal. Because metabolism of PGF-2 α to PGFM by the lungs is less complete in cows than in ewes (Davis *et al.*, 1985), a second objective was to determine whether measurement of PGFM accurately reflected uterine release of PGF-2 α .

Materials and Methods

Two experiments were conducted with anoestrous beef cows which were induced to ovulate. One group received subcutaneous implants of 17 α -acetoxy-11 β -methyl-19 nor-pregn-4-ene-3,20-dione (norgestomet; Ceva Laboratories, Overland Park, KS, USA; 6 mg) for 9 days; another group served as contemporary controls. Treatment with a progestagen has usually resulted in formation of CL with normal functional lifespans after induced ovulation (Ramirez-Godinez *et al.*, 1981; Sheffel *et al.*, 1982; Smith *et al.*, 1987). Cows were fitted with catheters into the posterior vena cava for collection of samples in which PGF-2 α could be measured before its metabolism by the lungs. Therefore, concentrations of PGF-2 α , PGFM and oxytocin could be compared at the same stage *post partum* between lactating cows expected to have short (controls) or normal (progestagen-treated) luteal lifespans.

Experiment 1

Suckling multiparous cows (17–25 days *post partum*) were assigned at random to receive progestagen (N = 4) or remain untreated (N = 5). At 48 h after removal of progestagen implants, 1000 i.u. human chorionic gonadotrophin (hCG; Sigma Chemical Co., St Louis, MO, USA) were injected into each cow i.m. to induce ovulation and formation of a CL. At 3 days after injection of hCG, catheters were placed into the posterior vena cava as described below.

Blood samples (20 ml) were taken from the posterior vena cava every hour for 9 h beginning between 10:00 and 12:00 h on Days 4 through 9 after injection of hCG (during expected luteal regression in control cows). Calves were separated from the cows during each daily sampling period. Each sample was divided equally into 2 chilled tubes, each containing 500 i.u. heparin. One portion was acidified immediately with 0.1 N-hydrochloric acid (HCl) to prevent synthesis or metabolism of prostaglandins (1 ml per 10 ml blood). Plasma was harvested and stored at –20°C until assayed for PGF-2 α (acidified portion) or PGFM and oxytocin. Two random samples collected from each cow on Day 5 were assayed for progesterone to verify placement of catheters beyond entry of uteroovarian venous drainage.

Blood samples were taken via jugular venepuncture at implant insertion, implant removal and injection of hCG and on Days 4 through 10, 13, 16, 19 and 22 after injection of hCG. Serum was collected for assay of progesterone.

Experiment 2

As in Exp. 1, cows (20–31 days *post partum*) from three different groups of available animals were assigned at random to receive progestagen (N = 8) or to serve as controls (N = 7). At 48 h after removal of the implants, 1000 i.u. hCG were injected i.m. into cows in Groups 1 (N = 4, 2 treated and 2 controls) and 2 (N = 6, 3 treated and 3 controls). Weaning of the calf on Day 7 of the implant period induced oestrus and formation of CL in cows in Group 3 (N = 5, 3 treated and 2 controls). The day of implant insertion will be referred to as Day –11 and the day of implant removal as Day –2. Catheters were inserted into the posterior vena cava by the procedure described below on Days –4, –13 and –12 in Groups 1, 2 and 3, respectively.

Blood samples (8 ml) were taken from the posterior vena cava every hour for 9 h beginning between 10:00 and 12:00 h on Days –3 to 0, Days –12 to 0 and Days –11 to 0 in Groups 1, 2 and 3, respectively. Calves were separated from cows during sampling. Samples were placed into chilled tubes containing 500 i.u. heparin and were not acidified. Plasma was harvested immediately for assay of PGF-2 α and PGFM. Jugular blood samples were taken at implant insertion, implant removal and injection of hCG and on Days 4, 8, 12 and 16 after injection of hCG (after oestrus in Group 3). Serum was collected for assay for progesterone.

Catheterization of the posterior vena cava

The method used was similar to that reported by Walters *et al.* (1984). Epidural anaesthesia was achieved by the injection of 8 ml 2% lidocaine hydrochloride. The medial coccygeal vein was isolated between the 3rd and 4th coccygeal vertebrae. Sutures were placed around the vein proximal and distal to the expected point of entry. At catheterization, pressure was applied to the proximal suture to occlude blood flow. An incision was made in the vein with iris scissors and a 100 cm polyethylene catheter (i.d. 0.86 mm, o.d. 1.27 mm; PE-90, Clay-Adams, Parsippany, NJ, USA) was inserted. As pressure on the proximal suture was released, the catheter was passed 70 cm into the vein. Catheter patency was maintained by infusion of 3 ml sterile heparinized saline (250 i.u./ml) after sampling.

Radioimmunoassays

Progesterone. Concentrations of progesterone in peripheral serum were determined by the procedure of Sheffel *et al.* (1982). Recovery of progesterone after extraction with petroleum ether was $96.3 \pm 1.2\%$ ($n = 3$ assays). The sensitivity of the assay was 0.4 ng/ml with inter- and intra-assay coefficients of variation of 9.8 and 6.7%, respectively.

PGFM. Concentrations of PGFM in posterior vena caval plasma were determined by the procedure described by Silvia & Taylor (1989). Sensitivity of the assay was 34 pg/ml with inter- and intra-assay coefficients of variation of 19.0 and 12.0%, respectively.

PGF-2 α . Before extraction, plasma samples (200 μ l) were acidified by addition of 50 μ l HCl (1 N). PGF-2 α was extracted by addition of 2 ml ethyl ether (anaesthesia grade) and vortexing the tubes for 30 sec. After the gelatinous plasma phase was frozen by placing tubes into a methanol–solid CO₂ bath, the ether phase of each sample was decanted into a 12 $\times$ 75 mm disposable culture tube. Ether was evaporated under a stream of nitrogen at 37°C.

After evaporation of the ether phase, 200 μ l assay buffer (0.05 M-phosphate, 0.9% NaCl, 0.2% bovine serum albumin, 0.1% sodium azide, pH 7.4) were added to all tubes and allowed to equilibrate at 4°C for a minimum of 1 h. Subsequently, 100 μ l tracer (40 pg [5,6,8,9,11,12,14,15-³H]PGF-2 α ; 0.01 μ Ci) and 200 μ l PGF-2 α antiserum were added (RA546C-15, from Dr Lawrence Levine, Brandeis University, Waltham, MA, USA; 1:12 000 dilution). Tubes were vortexed and incubated at 37°C for 5 min followed by a 16-h incubation at 4°C.

Separation of bound and free ligand was accomplished by addition of 1 ml 40% polyethylene glycol (M_r 3000–3700; Fisher Scientific, Fairlawn, NJ, USA). Pellets were formed by centrifugation at 2000 g for 30 min. Supernatant was removed and pellets resuspended in 1 ml distilled H₂O. Tubes were vortexed to ensure a homogeneous suspension and 900 μ l were transferred to a vial containing 2.5 ml scintillation fluid. Recovery of PGF-2 α after extraction was $86.3 \pm 4.3\%$ ($n = 39$ assays). Sensitivity of the assay was 43 pg/tube with inter- and intra-assay coefficients of variation of 11.3 and 10.8%, respectively. Standard curves in assay buffer and in plasma were parallel and amounts of PGF-2 α added to plasma and measured by the assay were correlated ($r = 0.93$, $P < 0.05$). Concentrations of PGF-2 α determined in unknown samples ($n = 50$) by this method and that of Pexton *et al.* (1975) were correlated ($P < 0.001$; $r = 0.93$).

Oxytocin. Concentrations of oxytocin in 200 μ l unextracted plasma were determined by a previously described procedure (Gorewit, 1979; antiserum purchased from Calbiochem, La Jolla, CA, USA), except that bound and free oxytocin were separated by addition of 200 μ l 15% polyethylene glycol. There was no significant deviation from parallelism ($P > 0.10$) between a standard curve in assay buffer and a standard curve in plasma or a number of dilutions of a single plasma sample. Amounts of oxytocin added to plasma and the amounts measured by the radioimmunoassay were correlated ($r = 0.97$; $P < 0.05$). Sensitivity of the assay was 2.8 pg/tube with inter- and intra-assay coefficients of variation of 3.6 and 9.3%, respectively ($n = 3$ assays). Concentrations of oxytocin in unknown samples ($n = 100$) determined by the method of Sheldrick & Flint (1981) and the present method were correlated ($P < 0.001$; $r = 0.98$). The procedure of Gorewit (1979) was chosen for routine use because samples could be processed without extraction.

Statistical analysis

In Exp. 1, mean concentrations of PGF-2 α , PGFM and oxytocin were determined for each day by averaging the 9 hourly samples for each cow. Secretory activity within day for each hormone was defined as the natural logarithm of the variance of that hormone for each cow (ln variance; Ottobre *et al.*, 1980). Mean concentrations and secretory activity of PGF-2 α , PGFM and oxytocin were compared by analysis of variance for a split-plot design (SAS; Barr *et al.*, 1979) with treatment as the main plot variable and day as the subplot variable. Main effects of treatment (differences between means) were tested by the error term, cow within treatment. Interactions of treatment with time (differences in the profiles of concentrations of hormones or of secretory activity) were tested by the residual error term.

Interrelationships between PGF-2 α , PGFM and oxytocin on a simultaneous sample and sample-to-previous sample basis were evaluated by within-cow partial correlations using residual variances after absorbing main effects of treatment and day and the interaction of treatment $\times$ day in the model. Tests for differences between correlation coefficients were done according to the procedure of Snedecor & Cochran (1980).

In Exp. 2, the sampling period was divided into three parts; pretreatment (Day –12), implant period (Days –11 to –3), and post-implant period (Days –2 to 0). Mean concentrations and secretory activity of PGF-2 α were compared by analysis of variance for a split plot design as in Exp. 1.

Results

Validation of experimental conditions

Cows were determined to be anoestrous based upon concentrations of progesterone of <1 ng/ml (mean $\pm$ s.e. = 0.5 ± 0.2 ng/ml in each experiment) at implant insertion (Day –11),

implant removal (Day -2) and injection of hCG (Day 0). All cows formed luteal structures in response to hCG as indicated by plasma concentrations of progesterone on Day 5 after hCG (mean = 3.5 ± 0.6 and 2.9 ± 0.2 ng/ml in Exps 1 and 2, respectively) greater than 3 s.d. above the mean concentrations before hCG. Lifespans of induced CL in Exp. 1, determined as the number of days from injection of hCG until progesterone declined below 1 ng/ml, were increased by treatment with progestagen (17.5 ± 0.6 vs 8.0 ± 0.3 days; Fig. 1). In Exp. 2, 7 of 8 progestagen-treated cows had CL with normal lifespans (> 16 days). In contrast, luteal lifespan in each of 7 control cows was less than 12 days. Data from the progestagen-treated cow with a subsequent short luteal phase were not included in the analysis. Placement of catheters in the posterior vena cava beyond the point of entry of utero-ovarian venous drainage was verified by greater concentrations of progesterone in plasma from the posterior vena cava (23.7 ± 3.2 and 22.3 ± 4.2 ng/ml in Exps 1 and 2, respectively) than from the jugular vein (3.5 ± 0.6 and 2.9 ± 0.4 ng/ml) on Day 5 after injection of hCG.

Fig. 1. Mean concentrations of progesterone in jugular venous plasma in control ($N = 5$: —) and progestagen-treated ($N = 4$: ---) post-partum cows induced to ovulate with 1000 i.u. hCG (Exp. 1).

Experiment 1

Concentrations and secretory activity of hormones in posterior vena cava. Mean concentrations and secretory activity of PGF-2 α on Days 4 through 9 after treatment with hCG were greater in control than in progestagen-treated cows ($P < 0.05$; Fig. 2). Treatment with progestagen had no effect on mean concentrations or secretory activity of PGFM or oxytocin over Days 4 through 9 after injection of hCG ($P > 0.10$; Fig. 2).

Correlations between PGF-2 α , PGFM and oxytocin. Concentrations of PGF-2 α , PGFM and oxytocin in the posterior vena cava were correlated positively ($P < 0.001$) on a simultaneous sample and sample-to-previous sample basis when calculated from residual variances within cow (Table 1). Correlations of oxytocin with PGFM (0.51 to 0.87) were higher ($P < 0.05$) than correlations of oxytocin with PGF-2 α (0.18 to 0.30) or those of PGFM with PGF-2 α (0.21 to 0.35).

Experiment 2

Concentrations and secretory activity of PGF-2 α in posterior vena cava. No differences ($P > 0.10$) in daily mean concentrations or secretory activity of PGF-2 α were detected between cows suckling calves throughout the study (Groups 1 and 2) and those which had their calves weaned on the 7th day of the implant period (Group 3). Therefore, values obtained from cows in all three groups were pooled for further analyses.

Fig. 2. Mean and ln variance of early luteal-phase concentrations of (a) PGF-2 α , (b) PGFM and (c) oxytocin in control (N = 5) and progesterone-treated (N = 4) post-partum beef cows induced to form CL by injection of 1000 i.u. hCG.

During the pretreatment period (Day -12), neither mean concentrations nor secretory activity of PGF-2 α differed between progesterone-treated and control cows ($P > 0.10$). An interaction of treatment $\times$ day was detected during the implant period (Days -11 to -3) for mean concentrations and secretory activity of PGF-2 α with peak concentrations of PGF-2 α occurring on Day -6 (Day 5 of progesterone treatment) in progesterone-treated cows ($P < 0.05$; Fig. 3). After implant

Table 1. Within-cow partial correlation coefficients for PGF-2 α , PGFM and oxytocin in plasma from the posterior vena cava, on a sample and previous sample basis, utilizing residual variances with effects of treatment, treatment $\times$ day, and day absorbed into the model: all correlations are significant ($P < 0.001$; d.f. = 345)

Variable	Previous PGF-2 α	PGFM	Previous PGFM	Oxytocin	Previous oxytocin
PGF-2 α	0.17	0.28	0.31	0.24	0.30
Previous PGF-2 α		0.21		0.18	
PGFM			0.80	0.64	0.83
Previous PGFM				0.51	
Oxytocin					0.52

Fig. 3. Mean and ln variance of concentrations of PGF-2 α in control (—) and progestagen-treated (---) post-partum beef cows during 13 days before induction of formation of CL by injection of 1000 i.u. hCG ($N = 3-6$ per day).

removal (Days -2 to 0), mean concentrations and secretory activity of PGF-2 α were increased in progestagen-treated compared to control cows ($P < 0.05$).

Discussion

Concentrations of PGF-2 α in plasma from the posterior vena cava on Days 4–9 after injection of hCG were greater in cows undergoing premature luteal regression than in cows with normal luteal phases. Zollers *et al.* (1989a) found that more PGF-2 α and PGFM were secreted *in vitro* by endometrial samples from cows expected to have a short luteal phase compared with progestagen-treated animals. Treatment with indomethacin, a potent prostaglandin endoperoxide synthetase inhibitor, extended luteal lifespan in post-partum beef cows induced to ovulate by injection of GnRH (Troxel & Kesler, 1984b). The uterus was required for regression of short-lived CL (Copelin

et al., 1987, 1988) and active immunization against PGF-2 α prevented premature regression of first post-partum CL (Copelin *et al.*, 1989). All of these data strongly implicate an early increase in secretion of PGF-2 α as the major cause of premature luteolysis. Whether the uterus is the only source of that PGF-2 α may be questioned, since Hu *et al.* (1990) showed that short-lived CL produced more prostaglandins, especially PGF-2 α , than did CL with a normal lifespan.

In Exp. 2, progestagen-treated cows began to secrete more PGF-2 α after 3–4 days of exposure to progestagen, just as control cows in Exp. 1 exhibited increased concentrations of PGF-2 α on Days 4–9 after injection of hCG. It therefore appears that early after first exposure to endogenous or exogenous progestagen, the post-partum uterus increases secretion of PGF-2 α . The one progestagen-treated cow which failed to have a subsequent normal luteal phase had low concentrations of PGF-2 α throughout the implant period. Approximately 80% of post-partum cows treated with progestagen have normal luteal phases (Sheffel *et al.*, 1982; Garcia-Winder *et al.*, 1986; Breuel *et al.*, 1988). One could speculate that a short luteal phase after treatment with progestagen may be due in part to failure of uterine secretion of PGF-2 α to increase during the implant period.

The site(s) of action of PGF-2 α secreted during treatment with progestagen remains in question. Villeneuve *et al.* (1988) have shown that continuous infusion of PGF-2 α on Days 2–13 after parturition increased development of large non-atretic follicles in beef cows. Similar findings were reported for post-partum ewes; 3 days of exogenous PGF-2 α increased development of large follicles (Villeneuve *et al.*, 1989). In progestagen-treated cows, increases in diameter of the pre-ovulatory follicle, and in follicular contents of oestradiol and receptors for LH (Garcia-Winder *et al.*, 1987; Inskeep *et al.*, 1988), as well as higher peripheral concentrations of oestradiol (Sheffel *et al.*, 1982; Garcia-Winder *et al.*, 1986, 1987; Garverick *et al.*, 1988), may be due to an action of PGF-2 α on the follicle.

In contrast with results for PGF-2 α after induced formation of CL, concentrations of PGFM were not altered by pretreatment with progestagen. Rises in PGFM were found during short luteal phases in dairy cows (Peter *et al.*, 1989) and in association with 'abnormal' corpora lutea in anoestrous ewes (Hunter *et al.*, 1989), but neither Troxel & Kesler (1984a) nor Garcia-Winder *et al.* (1986) could detect differences in PGFM between beef cows expected to have short or normal luteal lifespans. Concentrations of PGF-2 α and PGFM in the posterior vena cava were correlated positively in sheep, but effects found with PGF-2 α were not always found with PGFM (Vallet *et al.*, 1988).

Concentrations of PGFM have been utilized as an indicator of uterine release of PGF-2 α in the cow by several workers (e.g. Kindahl *et al.*, 1976; Guilbault *et al.*, 1984). However, only 31% of [3 H]PGF-2 α was present as PGFM after one passage in the cow (Davis *et al.*, 1985) and, after three circulations, 16% of injected PGF-2 α remained unmetabolized. In addition, PGFM was released by endometrial explants from post-partum cows (Zollers *et al.*, 1989a) and bovine endometrium metabolized PGF-2 α into PGFM *in vitro* (Lewis *et al.*, 1982; Lewis & Waterman, 1983) and *in vivo* (Meyer *et al.*, 1989). Therefore, measurement of concentrations of PGFM may not be adequate to detect all or subtle changes in PGF-2 α in certain physiological states.

Watkins & Moore (1987) reported that exogenous PGFM had biological activity in ewes (see below). PGFM can be metabolized in women (Bygdeman *et al.*, 1974) to 13,14-dihydro-PGF-2 α , a compound which had the same potency as PGF-2 α to induce uterine contractions in women (Bygdeman *et al.*, 1974) or luteal regression in cyclic heifers (Milvae & Hansel, 1983). However, H. Kindahl (unpublished, cited by Kindahl *et al.*, 1976) could not detect 13,14-dihydro-PGF-2 α in the cow and conversion of exogenous PGFM to 13,14-dihydro-PGF-2 α was relatively low in women (Bygdeman *et al.*, 1974).

Oxytocin has been implicated in luteolysis in domestic ruminants (Wathes, 1984). Blockade of oxytocin action by immunization (Sheldrick *et al.*, 1980; Schams *et al.*, 1983; Cooke & Homeida, 1985) or down-regulation of oxytocin receptors (Flint & Sheldrick, 1985; Gilbert *et al.*, 1989) prolonged the luteal phase. Cyclic heifers treated with oxytocin during the first week of the oestrous

cycle returned to oestrus 8–12 days after the previous oestrus (Armstrong & Hansel, 1959). The presence of the uterus was required for this luteolytic effect. Additionally, exogenous oxytocin elicited a release of PGF-2 α from the uterus both *in vivo* (Sharma & Fitzpatrick, 1974; Mitchell *et al.*, 1975; Milvae & Hansel, 1980; Cooke & Homeida, 1982) and *in vitro* (Roberts *et al.*, 1976; Silvia & Homanics, 1988).

The finding that exogenous PGF-2 α will cause release of oxytocin (Flint & Sheldrick, 1982; Lamsa *et al.*, 1989) and measurement of concomitant pulses of PGF-2 α and oxytocin during luteolysis (Fairclough *et al.*, 1980, 1983; Flint & Sheldrick, 1983; Vighio & Liptrap, 1986) led Flint *et al.* (1986) to conclude that an essential aspect of luteal regression was participation by oxytocin and PGF-2 α in a positive feedback loop. An infusion of PGFM caused release of oxytocin-associated neurophysin from CL in cyclic ewes (Watkins & Moore, 1987). Addition of oxytocin to uterine endometrium collected from post-partum cows resulted in the release of PGFM *in vitro* (Del Vecchio *et al.*, 1988). Daily samples collected by Peter *et al.* (1989) revealed early rises in concentrations of oxytocin in peripheral sera from dairy cows undergoing premature luteal regression compared with cows having normal luteal phases. In Exp. 1, no differences in concentrations of oxytocin were detected between cows having short or normal lifespans of induced CL. In Exp. 2, release of PGF-2 α did not appear to depend on luteal oxytocin; increases in concentrations of PGF-2 α were observed in cows without CL (progesterone < 0.5 ng/ml). Although uterine release of PGF-2 α was more responsive to exogenous oxytocin on Day 5 after oestrus in cows expected to have short luteal phases (Zollers *et al.*, 1989a, b), there was no evidence in the present work that endogenous oxytocin is important in regression of induced CL in post-partum beef cows.

Although concentrations and secretory activity of PGFM and oxytocin did not differ between progestagen-treated and control cows on Days 4 through 9 after injection of hCG, there were significant positive correlations between these two molecules and of each of them with PGF-2 α . Correlations between oxytocin and PGFM ($r = 0.51$ – 0.87) were higher ($P < 0.05$) than correlations between oxytocin and PGF-2 α ($r = 0.18$ – 0.30). The half-lives of both oxytocin (Gorewit, 1979) and PGFM (Kindahl *et al.*, 1976; Meyer *et al.*, 1989) are longer than for PGF-2 α (Ferreira & Vane, 1967); considering the sampling frequency of 1 h, this may explain the higher correlations of oxytocin with PGFM than with PGF-2 α . Many workers reporting simultaneous pulses of oxytocin and PGF-2 α (Fairclough *et al.*, 1980, 1983; Vighio & Liptrap, 1986) and oxytocin-induced release of PGF-2 α (Mitchell *et al.*, 1975; Milvae & Hansel, 1980) have utilized measurements of PGFM as an indication of release of PGF-2 α or antisera which were unable to differentiate among prostaglandins of the F series. Therefore, oxytocin might stimulate secretion of PGFM or metabolism of PGF-2 α to PGFM by the endometrium, thereby accounting for the high correlation between oxytocin and PGFM, seen also by Peter *et al.* (1989) in dairy cows.

In conclusion, increased concentrations of PGF-2 α were detected during regression of short-lived CL, but did not occur at that early time in cows with CL of normal lifespan. Release of PGF-2 α was observed during treatment with progestagen, which may be important for subsequent normal patterns of secretion of PGF-2 α and normal luteal function to occur. No differences in mean concentrations or secretory activity of PGFM were detected between cows with short and normal luteal lifespans. Concentrations of oxytocin were not different between cows having short or normal lifespans of induced CL; therefore, a role for oxytocin in controlling the release of PGF-2 α during premature luteolysis seems doubtful.

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