Ability of intravaginal progesterone inserts and melengestrol acetate to induce estrous cycles in postpartum beef cows[1]

G. A. Perry*†, M. F. Smith*, and T. W. Geary†[2]

*Department of Animal Science, University of Missouri, Columbia 65211 and
†USDA-ARS, Fort Keogh LARRL, Miles City, MT 59301-4016

ABSTRACT: Postpartum anestrous interval in beef cows is a major factor contributing to reproductive failure during a defined breeding season. Our objectives were to determine the ability of a controlled internal drug-releasing device (CIDR, 1.9 g of progesterone), a normal dose of melengestrol acetate (MGA, 0.5 mg·cow^{-1}·d^{-1}), or a high dose of MGA (4.0 mg·cow^{-1}·d^{-1}) to induce ovulation and to eliminate short estrous cycles. Multiparous beef cows (n = 100) were equally assigned to one of four treatments: CIDR, normal MGA, high MGA, or control by age, days postpartum, body condition, and body weight. All cows were fed carrier (0.9072 kg·cow^{-1}·d^{-1}) with (normal MGA, 0.55 mg/kg; high MGA, 4.41 mg/kg) or without MGA for 7 d (d –6 to 0). On d –6, CIDR were inserted and then removed on d 0. Estrous behavior was monitored continuously from d –6 until 29 using HeatWatch electronic mount detectors. Blood was collected on d –13, and three times weekly from d –6 to 29. Treatment influenced ($P = 0.03$) the percentage of cows that were detected in standing estrus. Beginning on d 2, more CIDR-treated cows had exhibited standing estrus compared with high MGA-treated or control cows, but CIDR- and normal MGA-treated cows did not differ. The percentage of CIDR-treated cows that had ovulated was greater ($P < 0.05$) than the percentage of normal MGA-treated, high MGA-treated, or control cows beginning on d 4. The percentage of cows that exhibited standing estrus before the first postpartum ovulation (CIDR = 65%, normal MGA = 57%, high MGA = 35%, control = 30%) did not differ ($P = 0.09$) among treatments. Luteal life span following the first ovulation postpartum and the percentage of cows with a normal luteal life span (i.e., progesterone >1 ng/mL for ≥10 d) was greater ($P < 0.01$) in CIDR-treated cows (14.0 ± 0.8 d; 20/20, 100%) compared with normal MGA-treated (6.2 ± 1.0 d; 3/13, 23%), high MGA-treated (9.6 ± 1.0 d; 8/14, 57%), or control cows (6.1 ± 0.9 d; 4/17, 24%), and greater ($P < 0.03$) in high MGA-treated cows than in normal MGA-treated or control cows. In the present study, treatment of early postpartum suckled beef cows with CIDR induced ovulation and initiated estrous cycles with a normal luteal life span in more cows than did treatment with MGA. Treatment with MGA (normal or high dose) did not induce ovulation earlier than in control cows, but a high dose of MGA increased the percentage of cows with normal luteal life spans following the first ovulation postpartum.

Key Words: Anestrus, Beef Cow, Estrous Cycles, Progestin

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Introduction

The anestrous postpartum interval is a major factor contributing to cows' failing to become pregnant and calving on a yearly interval (Short et al., 1990; Yavas and Walton, 2000b). In addition, a short luteal phase can further delay the interval from calving to conception and usually occurs following the first postpartum ovulation (Perry et al., 1991; Werth et al., 1996) or when ovulation is induced by weaning, GnRH, or hCG (Short et al., 1990; Yavas and Walton, 2000b).

Treatment with some progestins induced ovulation in postpartum anestrous cows (Yavas and Walton, 2000a; Lucy et al., 2001), and treatment with some progestins before the first postpartum ovulation reduced or eliminated the occurrence of a short luteal phase (Smith et al., 1987; Zollers et al., 1989). Therefore, many estrous synchronization protocols have included progestin treatment (Patterson et al., 1989; Odde, 1990; Perry et al., 2002b); however, not all progestins have the same biological response. More specifically, 46% of anestrous beef cows fed melengestrol acetate (**MGA**), an orally

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[2]Correspondence: 243 Fort Keogh Rd. (phone: 406-232-8215; fax: 406-232-8209; e-mail: tom@larrl.ars.usda.gov).

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active progestin, for 5 d before GnRH-induced ovulation had a normal luteal phase, compared with 100% of cows exposed to progesterone for the same 5-d period (Smith et al., 1987). Further evidence for a difference in the biological response of cows to different progestins is based on variations in the affinity of the progesterone receptor for various progestins (Perry et al., 2002c). Because different progestins have been used interchangeably in protocols for the synchronization of estrus, the objectives of the present study were to determine the ability of progesterone and a high or normal dose of MGA to induce ovulation in postpartum anestrous beef cows, and to determine the ability of each treatment to decrease or eliminate the occurrence of a short luteal phase following ovulation.

Materials and Methods

Experimental Design

Postpartum multiparous (n = 100) Hereford- and Angus-based crossbred beef cows of similar genetic composition were divided equally into four treatment groups (normal MGA [0.5 mg·cow^{-1}·d^{-1} for 7 d], high MGA [4.0 mg·cow^{-1}·d^{-}1 for 7 d], controlled internal drug-releasing device [**CIDR**; 1.9 g of progesterone for 6 d; InterAG, Hamilton, NZ], and control) according to age (range 4 to 11 yr), days postpartum (range 9 to 45 d), cow body condition score (1 = emaciated and 9 = obese; range 4 to 6.5), and postcalving BW (range 445 to 704 kg). Calves were maintained with cows at all times and allowed to suckle without restriction. Cows were housed in dry lot confinement and group fed (two pens per treatment) MGA or carrier in bunks before receiving their daily ration. Cows with concentrations of progesterone greater than 1 ng/mL as determined by RIA on d –13 or on d –6 of treatment were removed from the study (normal MGA = 7, high MGA = 4, CIDR = 3, control = 3). In addition, one animal in each of the normal MGA and high MGA groups ovulated during MGA treatment and were removed from the study, but animals that exhibited standing estrus but did not ovulate were left in their respective treatment.

Cows were fed carrier (wheat middlings pellets, United Agri Products, Miles City, MT) at 0.9072 kg·cow^{-1}·d^{-1} with (0.55 mg/kg for normal MGA; 4.41 mg/kg for high MGA) or without MGA for 7 d (d –6 to 0). Controlled internal drug-releasing devices (1.9 g of progesterone per device) were inserted into the vagina of cows on the first day of treatment (d –6) and were removed on d 0. All cows were individually fitted with estrous-detection transmitters and monitored for estrous behavior continuously from d –6 until d 29 with the HeatWatch Estrous Detection System (DDx, Inc., Denver, CO). Cows were considered to be in standing estrus when three mounts of 2 s or longer in duration were recorded within a 4-h period.

Blood Sampling

Blood samples were collected via puncture of a tail vessel on d –13, –6, –3, and 0, and three times weekly following treatment. Plasma was collected during the treatment period (d –6 to 0) and for 2 wk following treatment for determination of plasma concentrations of estradiol and progesterone. Blood was collected in 10-mL EDTA Vacutainer tubes (Fisher Scientific, Pittsburgh, PA) and centrifuged immediately following collection (3,000 × *g* for 30 min) to harvest plasma. For the remainder of the experiment, blood was collected in 10-mL Vacutainer tubes (Fisher Scientific), allowed to clot, stored at 4°C for 24 h, and centrifuged at 3,000 × *g* for 30 min to harvest serum for determination of serum concentrations of progesterone.

Radioimmunoassays

Serum concentrations of progesterone before the initiation of treatment (d –13 and –6) were used to determine whether cows had initiated estrous cycles, and cows with a concentration of progesterone greater than 1 ng/mL were considered to have functional luteal tissue present and were removed from the study. Concentrations of progesterone were analyzed in all plasma and serum samples by RIA (Bellows et al., 1991; Diagnostic Products Corporation, Los Angeles, CA). Intra- and interassay CV for progesterone assays were 1.6 and 8.2%, respectively, and assay sensitivity was 0.04 ng/mL.

Circulating concentrations of estradiol-17β were analyzed in all plasma samples by RIA using methodology similar to Kirby et al. (1997). Duplicate samples (300 μL) were extracted with 4 mL of methyl-tert-butyl ether (HPLC grade; Fisher Chemical Co., Fair Lawn, NJ) for 1 min on a multitube vortexer. Samples were frozen in a dry ice-methanol bath. The solvent fraction was decanted into 12 × 75-mm borosilicate glass tubes and dried at 37°C under air. The extract was dissolved in 100 μL of assay buffer (1% BSA, 0.01% sodium azide, 0.01 *M* PO_4, and 0.9% NaCl; pH 7.2). Redissolved extracts and estradiol standards (0.25, 0.5, 1, 2.5, 5, 7.5, 10, and 20 pg per tube) were incubated with 100 μL of estradiol-17β antisera (ICN, Costa Mesa CA; 1:450,000 vol/vol dilution) at 37°C for 5 min followed by 1 h at 4°C. Following incubation, 100 μL of [^{125}I]estradiol-17β (ICN; 2,000 μCi/μg; adjusted to 5,000 to 6,000 cpm) was added to each tube. Tubes were incubated at 4°C for 20 h. Bound and free estradiol were separated by addition of 0.5 mL dextran-coated charcoal solution (10-min incubation) followed by centrifugation at 3,000 × *g* for 10 min. Supernatants were counted in a gamma counter for 5 min per tube. Cross-reactivities of the antibody have previously been published as 100% for estradiol-17β, 6.5% for estriol, 5.2% for estradiol-17α, 0.6% for estrone, and <0.01% for aldosterone, androstenedione, cholesterol, progesterone, and testosterone (Kirby et al., 1997). Increasing volumes of bovine serum (200,

Table 1. Days postpartum, body condition score, and weight at the initiation of treatment

Item	CIDR[a]	Normal MGA[b]	High MGA[c]	Control
No. of cows	22	17	20	22
Days postpartum	31 ± 1.7	30 ± 2.0	30 ± 1.7	30 ± 1.5
(range)	(12 to 42)	(12 to 45)	(9 to 41)	(9 to 39)
Body condition score	4.9 ± 0.2	4.9 ± 0.2	4.8 ± 0.2	4.9 ± 0.2
(range)	(4 to 6)	(3.5 to 6.5)	(4.5 to 6)	(3.5 to 6)
Weight, kg	581 ± 16.4	583 ± 17.3	580 ± 16.0	571 ± 16.4
(range)	(477 to 684)	(475 to 704)	(450 to 665)	(445 to 692)

[a]Controlled internal drug-releasing device.
[b]Normal dose of melengestrol acetate (0.5 mg MGA·cow^{-1}·d^{-1}).
[c]High dose of melengestrol acetate (4 mg MGA·cow^{-1}·d^{-1}).

300, 400, and 500 μL) produced a displacement curve that was parallel (P = 0.08) to the standard curve (slope = 2.46 ± 0.25 for standard curve; slope = 2.27 ± 0.36 for bovine serum). Addition of known amounts of estradiol-17β (1, 5, and 10 pg/mL) to charcoal-stripped ovariectomized cow serum were accurately recovered (102%; r = 0.94). Intra- and interassay coefficients of variation for estradiol-17β assays were 3.4 and 14.1% respectively, and assay sensitivity was 0.5 pg/mL.

Statistical Analysis

Luteal life span following the first postpartum ovulation was analyzed by ANOVA using SAS (Proc GLM; SAS Inst. Inc., Cary, NC). The preceding variable was analyzed for an effect of treatment. When the F-statistic was significant ($P < 0.05$), a mean separation was performed using the least significant difference test (Snedecor and Cochran, 1989). Percentage of cows exhibiting estrus before an increase in progesterone and percentage of cows with a normal length luteal life span (progesterone >1 ng/mL for ≥10 d) were analyzed using categorical data modeling in SAS (Proc Catmod). The preceding variables were analyzed for an effect of treatment. Plasma concentrations of estradiol-17β were determined by analysis of variance for repeated measures in SAS (Proc Mixed; Littell et al., 1998) and are expressed as means ± SEM. The statistical model consisted of treatment, day, and treatment × day interactions. The effect of treatment on plasma concentrations of estradiol-17β was tested using animal within treatment as the error term, and effects of day and treatment × day on plasma concentrations of estradiol-17β were analyzed using the residual as the error term. To determine differences in the distribution of the response to the different treatments, the percentage of animals detected in standing estrus, and the percentage of animals with elevated progesterone (>1 ng/mL) were analyzed using repeated measures of categorical data (Koch et al., 1977). The preceding variables were analyzed for an effect of treatment, day, and treatment × day interactions by repeated measures analysis in SAS (Proc Catmod; Stanish and Koch, 1984).

Results

There were no significant differences among treatments in days postpartum, body condition score, or weight at the initiation of treatment (Table 1). A significant treatment (P = 0.03), day ($P < 0.01$), and treatment × day ($P < 0.01$) interaction was detected in the cumulative percentage of cows that exhibited standing estrus (Figure 1). A greater ($P < 0.05$) percentage of CIDR-treated cows had exhibited standing estrus on d 2 after treatment withdrawal compared with high MGA-, or control-treated cows, but beginning on d 14 no significant difference was detected between CIDR- and control-treated cows. There was a tendency (P = 0.07), from d 4 through 10, for the cumulative percentage of CIDR-treated cows that had exhibited estrus to be greater than the cumulative percentage of normal MGA-treated cows that had exhibited estrus. The cumulative percentage of normal MGA- and control-treated cows that exhibited standing estrus did not differ significantly on any day of the experiment.

Treatment also influenced ($P < 0.01$) the percentage of cows that had ovulated (Figure 2). Ovulation was defined as occurring 4 d before circulating concentrations of progesterone were greater than 1 ng/mL. The cumulative percentage of CIDR-treated cows that ovulated was greater ($P < 0.05$) than the cumulative percentage of normal MGA-, high MGA-, or control-treated cows that ovulated beginning on d 4 after treatment withdrawal. On d 18, the cumulative percentage of CIDR- and control-treated cows that had ovulated did not differ (P = 0.08), and no difference was detected between CIDR-treated cows and normal MGA- (P = 0.19) and high MGA-treated (P = 0.58) cows on d 22 (Figure 2). The cumulative percentage of cows that ovulated was not different among control-, high MGA-, and normal MGA-treated cows except on d 4, when more ($P < 0.01$) normal MGA- and control-treated cows had ovulated compared to high MGA-treated cows (Figure 2). In addition, a more synchronous rise in concentration of progesterone occurred following treatment in CIDR-treated cows compared with other treatments (Figure 3). However, no difference (P = 0.32) was detected among treatments in the percentage of cows that

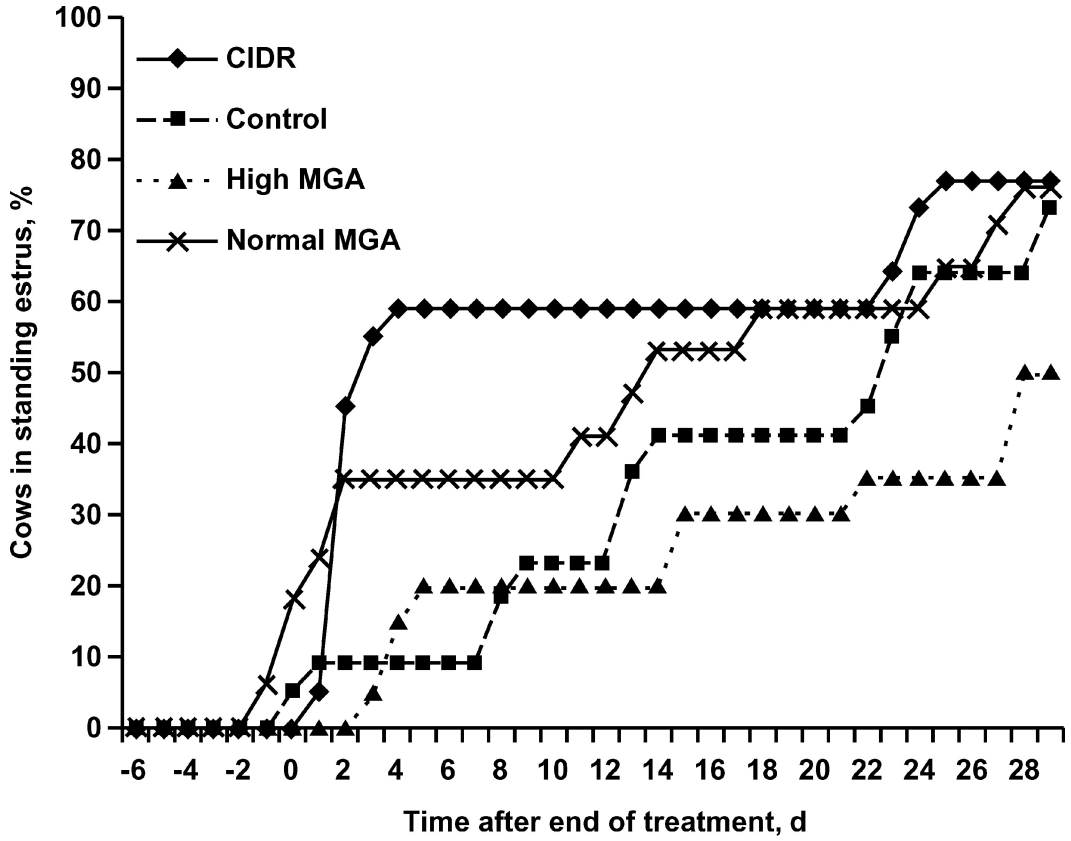

Figure 1. Effect of treatment on cumulative percentage of cows detected in standing estrus by day of treatment (d 0 = last day of feeding melengestrol acetate [MGA], and day of controlled internal drug-releasing device [CIDR] removal). Treatment $P = 0.03$; day $P < 0.01$; treatment × day $P < 0.01$.

exhibited standing estrus before an increase in progesterone (65%, 35%, 57%, and 30% for CIDR, high MGA, normal MGA, and control, respectively).

Only cows that had progesterone >1 ng/mL were used to determine luteal life span and the percentage of cows with a normal length luteal life span (progesterone >1 ng/mL for ≥10 d). Following the first ovulation postpartum, CIDR-treated cows had a longer luteal life span than did normal MGA-, high MGA-, or control-treated cows (Table 2), and the percentage of cows that had a normal length luteal phase (≥10 d) was greater ($P < 0.01$) in CIDR-treated cows than in normal MGA-, high MGA-, or control-treated cows (Table 2). Cows treated with high MGA had a longer ($P < 0.02$) luteal life span, and a greater ($P < 0.03$) percentage of high MGA-treated cows had a normal luteal life span compared with normal MGA- and control-treated cows. Treatment-induced ovulation was defined as ovulation occurring within 5 d of treatment withdrawal (increase in concentration of progesterone >1 ng/mL on d 5 to 10) for CIDR-, normal MGA-, and high MGA-treated cows and all ovulations in control-treated cows. Following treatment-induced ovulation, a longer luteal life span ($P < 0.01$) was detected in CIDR- and high MGA-treated cows than in normal MGA- or control-treated cows, with a tendency ($P = 0.06$) for CIDR-treated cows to have a longer luteal life span than high MGA-treated cows (Table 2). The percentage of cows with a normal (≥10 d) luteal life span following treatment-induced ovulation was greater ($P < 0.01$) in CIDR- and high MGA-treated cows than normal MGA- or control-treated cows, and greater ($P = 0.05$) in CIDR-treated cows than high MGA-treated cows.

A treatment × day interaction influenced plasma concentrations of estradiol. Cows in the CIDR-treated group had greater ($P < 0.05$) concentrations of estradiol than other treatments on d 1, and high MGA-treated cows had greater ($P < 0.05$) concentrations of estradiol than other treatments on d 3 and 5. No significant peak in estradiol concentration occurred in normal MGA- or control-treated cows (Figure 4). In addition, cows that had greater ($P = 0.03$) concentrations of estradiol before ovulation exhibited a longer luteal phase compared to cows that had lower concentrations of estradiol before ovulation (Figure 5).

Discussion

Treatment of early postpartum cows (see review by Yavas and Walton, 2000a) and peripubertal heifers (Hall et al., 1997) with a synthetic progestin (norgestomet) has been reported to induce ovulation; however, the response to other progestins has been variable. In addition, when peripubertal beef heifers were treated

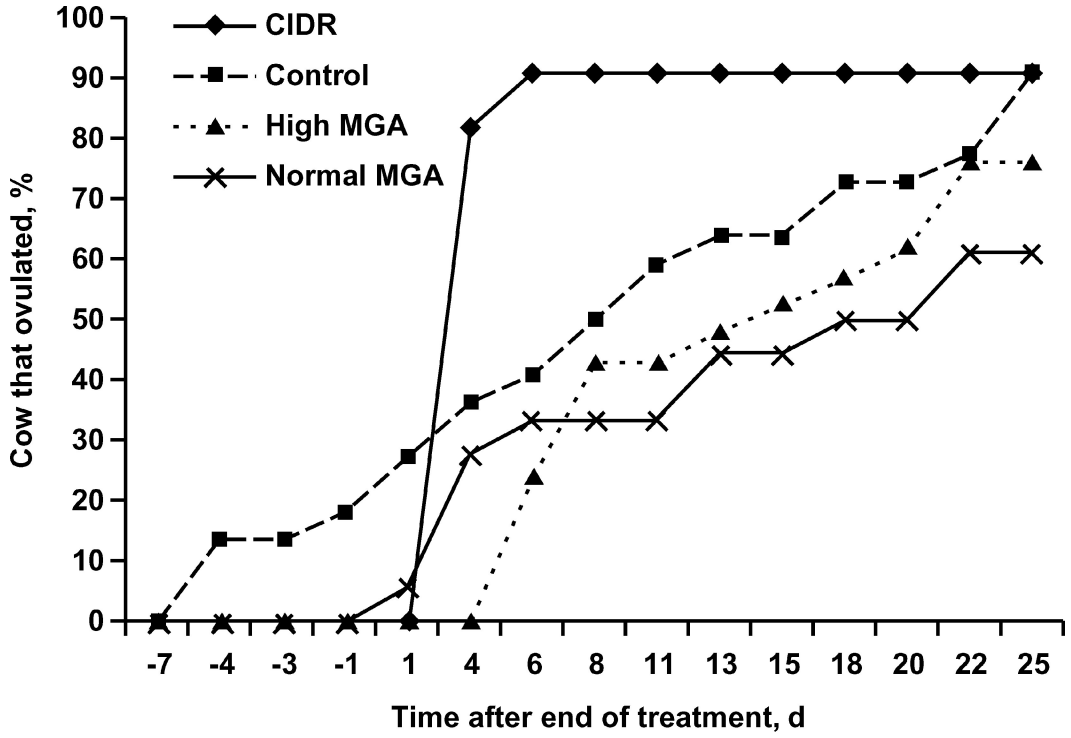

Figure 2. Effect of treatment on the cumulative percentage of animals that had ovulated (ovulation is shown as having occurred 4 d before the first day on which circulating concentrations of progesterone were >1 ng/mL) by day of treatment (d 0 = last day of feeding melengestrol acetate [MGA], and day of controlled internal drug-releasing device [CIDR] removal). Treatment $P < 0.01$; day $P < 0.01$; treatment × day $P < 0.01$.

with MGA for 8 d, an increased proportion of heifers initiated estrous cycles following treatment withdrawal compared with untreated controls (Imwalle et al., 1998). In contrast, when postpartum anestrous beef cows were treated with MGA for 14 d, only 13% ovulated, as determined by transrectal ultrasonography and serum concentrations of progesterone, within 7 d of treatment withdrawal (2/16, Perry et al., 2002a). In the present study, a greater percentage of cows treated with CIDR had ovulated by d 4 after treatment withdrawal compared with the two MGA or the control treatments, as determined by increased circulating concentrations of progesterone. In addition, no differences were detected in the cumulative percentage of control- and normal MGA-treated cows that had ovulated throughout the study. The CIDR used in the present study contained 1.9 g of progesterone compared to 1.38 g of progesterone, which is contained in CIDR currently available in the United States. However, the type of progesterone contained in the two types of CIDR is the same and release rates are similar among the two types of CIDR (Rathbone et al., 2002). Therefore, results from the use of CIDR containing 1.38 g of progesterone and CIDR containing 1.9 g of progesterone would likely be similar. Furthermore, more anestrous cows treated with a CIDR containing 1.38 g of progesterone and receiving an injection of $PGF_{2\alpha}$ on the day before CIDR removal were detected in standing estrus during the first 3 d of the breeding season compared to anestrous control cows or anestrous cows treated with $PGF_{2\alpha}$ alone (Lucy et al., 2001).

Differences in the response of early postpartum anestrous beef cows to different progestins may be explained by the ability of progestins to increase LH pulse frequency and cause the formation of a persistent follicle. Early work demonstrated that a low dose of progesterone increased LH secretion and increased the sensitivity of the pituitary to GnRH in estrogen primer rats (McPherson and Mahesh, 1979), and, when early postpartum anestrous unsuckled (Williams et al., 1983) and anestrous suckled (Garcia-Winder et al., 1986) beef cows were treated with low doses of a progestin, LH pulse frequency increased compared to untreated controls. In addition, exposure of peripubertal heifers to a lose dose of norgestomet increased LH pulse frequency, stimulated follicular development, and resulted in formation and ovulation of persistent follicles (Anderson et al., 1996). Treatment of peripubertal heifers with MGA (0.5 $mg \cdot cow^{-1} \cdot d^{-1}$) for 7 d increased LH pulse frequency following treatment withdrawal (Imwalle et al., 1998), but feeding MGA (0.5 $mg \cdot cow^{-1} \cdot d^{-1}$) for 14 d to early postpartum anestrous beef cows did not result in formation of persistent follicles, even though persistent follicles were observed in MGA-treated cows that had previously initiated estrous cycles and had undergone luteolysis at the beginning of MGA treatment (Perry et al., 2002a). In contrast, treatment of early postpartum anestrous dairy cows with low concentrations of proges-

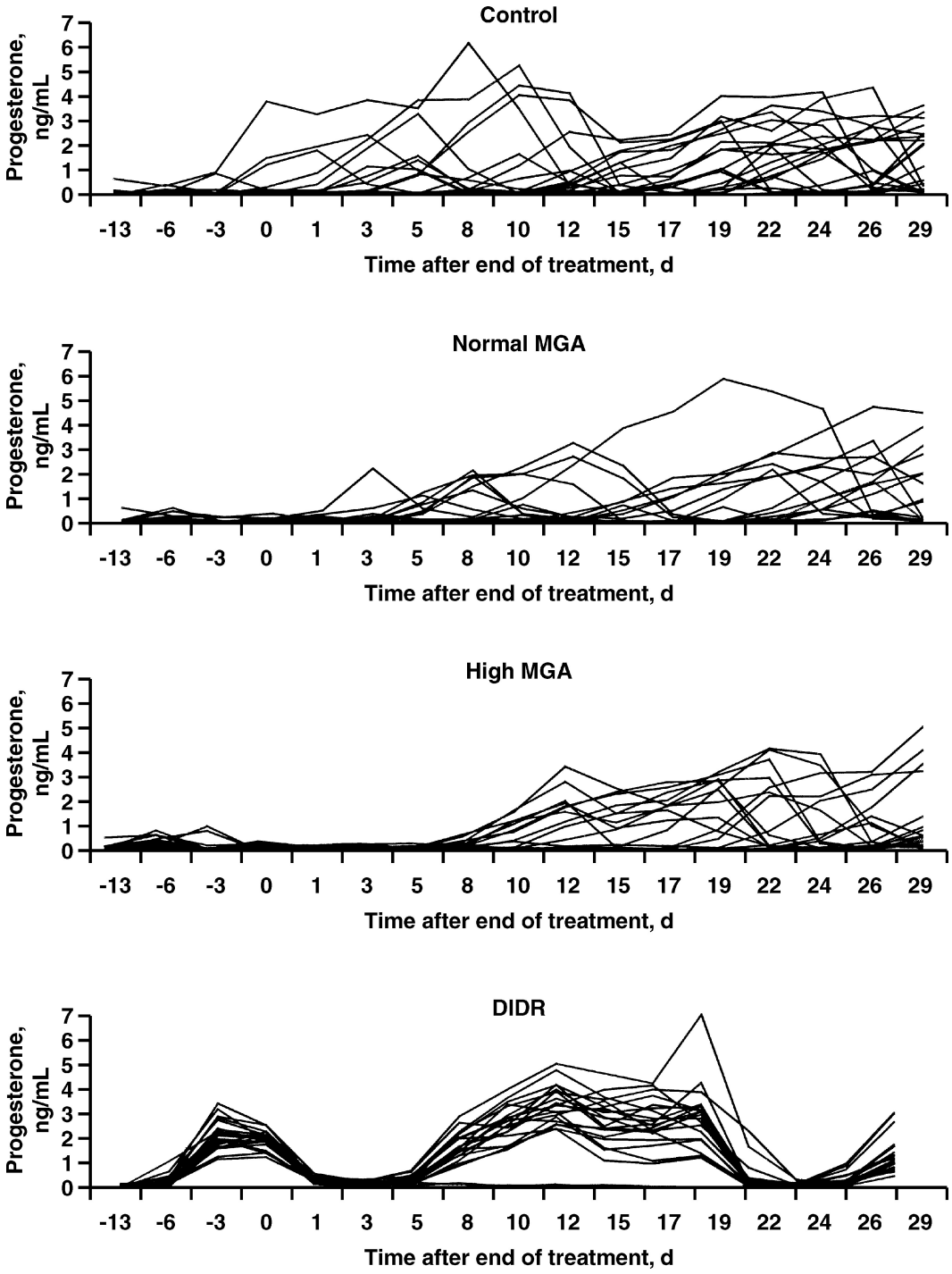

Figure 3. Circulating concentrations of progesterone (collected three times weekly) for cows receiving no treatment (control), 0.5 mg melengestrol acetate (MGA)·cow^{-1}·d^{-1} (normal MGA), 4 mg MGA·cow^{-1}·d^{-1} (high MGA) or controlled internal drug-releasing device (CIDR; from d –6 to 0). Day 0 = last day of feeding MGA and day of CIDR removal.

terone (CIDR) resulted in increased LH pulse frequency compared with untreated controls (Rhodes et al., 1997).

In addition to differences in the ability of different progestins to induce ovulation in postpartum anestrous cows, differences were also detected in the ability of progesterone and MGA to eliminate the occurrence of short estrous cycles. Progesterone treatment is necessary for establishment of the normal timing of uterine $PGF_{2\alpha}$ secretion. Following the first postpartum exposure to progesterone, oxytocin receptors were down-regulated and normal length luteal phases were established (Zollers et al., 1993). In the present study, cows that ovulated following CIDR treatment had a normal length luteal life span, but the majority of cows that ovulated in the normal MGA and control groups experienced a short luteal life span. This is consistent with

Table 2. Effect of treatment on luteal life span and percentage of cows with a normal luteal life span following their first ovulation postpartum and ovulation within 5 d of treatment withdrawal

Item	CIDR[a]	Normal MGA[b]	High MGA[c]	Control[d]	Comparisons, *P*-value <[e] CIDR vs normal MGA	CIDR vs high MGA	CIDR vs control	Normal MGA vs high MGA	Normal MGA vs control	High MGA vs control
	First postpartum ovulation									
No. of cows	20	13	14	17						
Luteal life span, d[f]	14.0 ± 0.8	6.2 ± 1.0	9.6 ± 1.0	6.1 ± 0.9	0.01	0.01	0.01	0.02	0.98	0.02
Cows with normal luteal life span, %[g]	100	23	57	24	0.01	0.01	0.01	0.07	0.97	0.06
	Ovulation within 5 d of treatment									
No. of cows	20	5	7	17						
Luteal life span, d[f]	14.0 ± 0.8	4.4 ± 1.1	11.3 ± 1.0	6.1 ± 0.9	0.01	0.06	0.01	0.01	0.29	0.01
Cows with normal luteal life span, %[g]	100	0	71	24	0.01	0.05	0.01	0.01	0.15	0.01

[a]Controlled internal drug-releasing device.
[b]Normal dose of melengestrol acetate (0.5 mg MGA·cow^{-1}·d^{-1}).
[c]High dose of melengestrol acetate (4 mg MGA·cow^{-1}·d^{-1}).
[d]Control animals.
[e]The less-than values given are *P*-values for the pairwise comparisons indicated.
[f]Interval from first day on which concentrations of progesterone were >1 ng/mL to the day on which concentrations of progesterone decreased to <1 ng/mL.
[g]Percentage of animals with a luteal life span (i.e., concentrations of progesterone >1 ng/mL) of 10 d or longer.

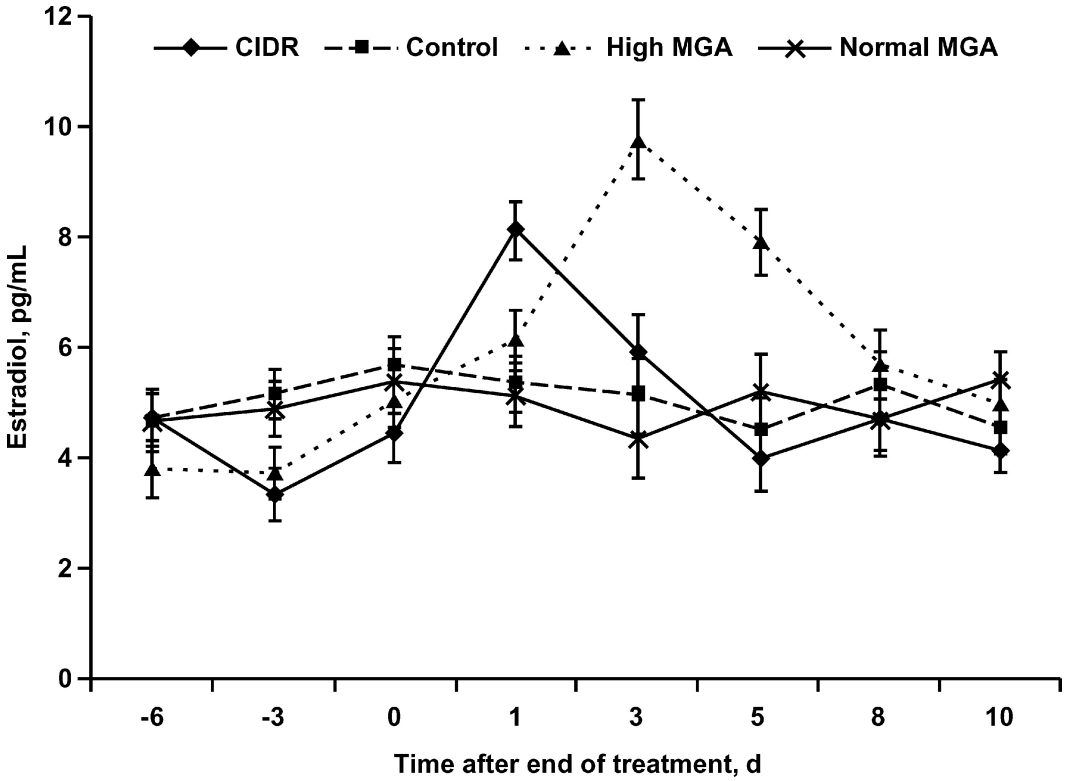

Figure 4. Effect of treatment on mean plasma concentrations of estradiol (treatment $P = 0.07$; day $P < 0.01$; treatment × day $P < 0.01$). Day 0 = last day of feeding melengestrol acetate (MGA), and day of controlled internal drug-releasing device (CIDR) removal.

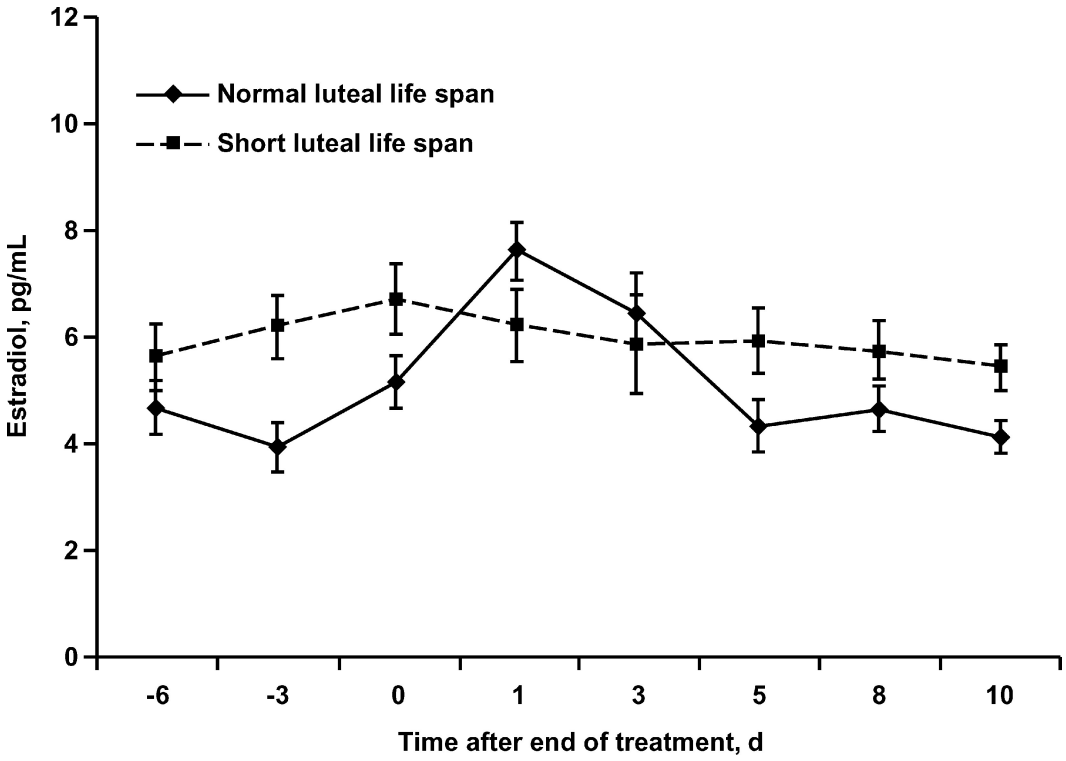

Figure 5. Mean plasma concentrations of estradiol for cows exhibiting normal (≥10 d) and short luteal life span (luteal life span, $P = 0.03$; day, $P < 0.01$; luteal life span × day, $P = 0.04$). Day 0 = last day of feeding melengestrol acetate (MGA), and day of controlled internal drug-releasing device (CIDR) removal.

previous reports in which treatment of anestrous postpartum beef cows with 0.5 mg·cow^{-1}·d^{-1} of MGA for 5 d before GnRH-induced ovulation resulted in only 46% of cows having a normal luteal phase, but treatment with progesterone for 5 d before GnRH-induced ovulation resulted in 100% of cows having a normal luteal phase (Smith et al., 1987). In addition, Fralix et al. (1996) reported that up to 20% of anestrous postpartum beef cows fed MGA (0.5 mg·cow^{-1}·d^{-1}) for 14 d experienced a short luteal phase following MGA withdrawal. Thus, the normal dose of MGA (0.5 mg·cow^{-1}·d^{-1}) is not adequate to prevent the earlier secretion of uterine $PGF_{2\alpha}$ following the first postpartum ovulation.

Differences in the ability of progesterone (CIDR) and MGA to induce a normal length luteal phase might be explained by estradiol concentrations following treatment withdrawal. Estradiol-17β increased uterine progesterone receptors in sheep (Zelinski et al., 1980) and may permit progesterone to coordinate the timing of $PGF_{2\alpha}$ secretion (Zollers et al., 1993). In postpartum beef cows, preovulatory concentrations of estradiol-17β were lower preceding a short compared with a normal length luteal phase (Garcia-Winder et al., 1986; Garverick et al., 1988; Braden et al., 1989), and reduced concentrations of estradiol-17β during the preovulatory period have been associated with decreased numbers of endometrial progesterone receptors during the early luteal phase (Zollers et al., 1993). Expression of endometrial oxytocin receptors was greater on d 5 in cows expected to have a short luteal phase compared with cows expected to have a normal luteal phase (Zollers et al., 1993), and a greater release of $PGF_{2\alpha}$ in response to oxytocin occurred on d 5 in cows expected to have a short luteal phase (Zollers et al., 1989). In addition, treatment of ovariectomized cows with progesterone alone resulted in a large $PGF_{2\alpha}$ release in response to oxytocin on d 6 after treatment (Lamming and Mann, 1995b), but exposure of ovariectomized cows to progesterone (14 d) and estradiol (2 d), resulted in oxytocin receptors not being detectable in the uterus from d 8 to 12 following treatment, and a $PGF_{2\alpha}$ release in response to oxytocin was not observed until d 16 (Lamming and Mann, 1995a,b).

In the present study, CIDR-, normal MGA- and high MGA-treated cows were exposed to a progestin during the treatment period. Following treatment withdrawal, an increase in circulating concentrations of estradiol was detected in cows in the CIDR and high-MGA treatments, but not in the normal-MGA or control treatments. The lack of a rise in estradiol may explain the increased incidence of short estrous cycles among normal MGA- and control-treated cows. In addition, cows that exhibited a normal length luteal life span experienced a peak of estradiol before ovulation, but cows exhibiting a short luteal life span did not. The reason for the lack of an increase in concentrations of estradiol in normal MGA-treated cows is not known.

No cows in the high-MGA-treated group were detected in standing estrus before d 3 or had progesterone concentrations >1 ng/mL until 10 d after treatment withdrawal. This delay in estrus and ovulation may partially be explained by the extended period of time necessary for a greater dose of MGA to be metabolized and removed from the body. The half-life of radiolabeled MGA in cattle has been estimated to be 2½ to 3 d (Lauderale et al., 1977), and the average interval from withdrawal until estrus increased from 2.7 d, for a dose of 0.2 mg·cow^{-1}·d^{-1}, to 6.3 d, for a dose of 2.0 mg·cow^{-1}·d^{-1} (Zimbelman and Smith, 1966). Therefore, differences in interval from treatment withdrawal until the first estrus and ovulation are likely due to a longer interval from the last day of feeding until clearance and, thus, a longer period of inhibition of ovulation by the higher dose of MGA.

Implications

The anestrous postpartum period and the occurrence of short estrous cycles are major factors in cows not conceiving during a defined breeding season, and treatment with some progestins before the breeding season has successfully induced ovulation and eliminated the occurrence of short estrous cycles. However, in the current study, neither a high nor a normal dose of melengestrol acetate was as effective at inducing ovulation in early postpartum anestrous beef cows as was a progesterone-releasing controlled internal drug-releasing device. In addition, treatment with a controlled internal drug-releasing device resulted in a normal luteal life span following ovulation compared with a short luteal phase in cows treated with a normal dose of melengestrol acetate, and an intermediate luteal phase in cows treated with a high dose of melengestrol acetate. Therefore, we conclude that not all progestins are equally effective at inducing ovulation and eliminating short estrous cycles in early postpartum anestrous cows.

Literature Cited

Anderson, L. H., C. M. McDowell, and M. L. Day. 1996. Progestin-induced puberty and secretion of luteinizing hormone in heifers. Biol. Reprod. 54:1025–1031.

Bellows, R. A., R. B. Staigmiller, J. M. Wilson, D. A. Phelps, and A. Darling. 1991. Use of bovine FSH for superovulation and embryo production in beef heifers. Theriogenology 35:1069–1082.

Braden, T. D., M. E. King, K. G. Odde, and G. D. Niswender. 1989. Development of preovulatory follicles expected to form short-lived corpora lutea in beef cows. J. Reprod. Fertil. 85:97–104.

Fralix, K. D., D. J. Patterson, K. K. Schillo, R. E. Stewart, and K. D. Bullock. 1996. Changes in morphorlogy of corpora lutea, central luteal cavities and steroid secretion patterns of postpartum suckled beef cows after melengestrol acetate with or without prostaglandin $f_{2\alpha}$. Theriogenology 45:1255–1263.

Garcia-Winder, M., P. E. Lewis, D. R. Deaver, V. G. Smith, G. S. Lewis, and E. K. Inskeep. 1986. Endocrine profiles associated with life span of induced corpora lutea in postpartum beef cows. J. Anim. Sci. 62:1353–1362.

Garverick, H. A., J. R. Parfet, C. N. Lee, J. P. Copelin, R. S. Youngquist, and M. F. Smith. 1988. Relationship of pre- and post-ovulatory gonadotropin concentrations to subnormal luteal function in postpartum beef cattle. J. Anim. Sci. 66:104–111.

Hall, J. B., R. B. Staigmiller, R. E. Short, R. A. Bellows, M. D. MacNeil, and S. E. Bellows. 1997. Effect of age and pattern of gain on induction of puberty with a progestin in beef heifers. J. Anim. Sci. 75:1606–1611.

Imwalle, D. B., D. J. Patterson, and K. K. Schillo. 1998. Effects of melengestrol acetate on onset of puberty, follicular growth, and patterns of luteinizing hormone secretion in beef heifers. Biol. Reprod. 58:1432–1436.

Kirby, C. J., M. F. Smith, D. H. Keisler, and M. C. Lucy. 1997. Follicular function ni lactating dairy cows treated with sustained-release bovine somatotropin. J. Dairy Sci. 80:273–285.

Koch, G. G., J. R. Landis, J. L. Freeman, D. H. Freeman, Jr., and R. C. Lehnen. 1977. A general methodology for the analysis of experiments with repeated measurement of categorical data. Biometrics 33:133–158.

Lamming, G. E., and G. E. Mann. 1995a. Control of endometrial oxytocin receptors and prostaglandin $f_{2\alpha}$ production in cows by progesterone and oestradiol. J. Reprod. Fertil. 103:69–73.

Lamming, G. E., and G. E. Mann. 1995b. A dual role for progesterone in the control of cyclicity in ruminants. J. Reprod. Fertil. Suppl. 49:561–566.

Lauderdale, J. W., L. S. Goyings, L. F. Krzeminski, and R. G. Zimbelman. 1977. Studies of a progestogen (MGA) as related to residues and human consumption. J. Toxicol. Environ. Health 3:5–33.

Littell, R. C., P. R. Henry, and C. B. Ammerman. 1998. Statistical analysis of repeated measures data using SAS procedures. J. Anim. Sci. 76:1216–1231.

Lucy, M. C., H. J. Billings, W. R. Butler, L. R. Ehnis, M. J. Fields, D. J. Kesler, J. E. Kinder, R. C. Mattos, R. E. Short, W. W. Thatcher, R. P. Wettemann, J. V. Yelich, and H. D. Hafs. 2001. Efficacy of an intravaginal progesterone insert and an injection of $PGf_{2\alpha}$ for synchronizing estrus and shortening the interval to pregnancy in postpartum beef cows, peripubertal beef heifers, and dairy heifers. J. Anim. Sci. 79:982–995.

McPherson, J. C., 3rd, and V. B. Mahesh. 1979. Dose related effect of a single injection of progesterone on gonadotropin secretion and pituitary sensitivity to LHRH in estrogen-primed castrate female rats. Biol. Reprod. 20:763–772.

Odde, K. G. 1990. A review of synchronization of estrus in postpartum cattle. J. Anim. Sci. 68:817–830.

Patterson, D. J., G. H. Kiracofe, J. S. Stevenson, and L. R. Corah. 1989. Control of the bovine estrous cycle with melengesterol acetate (MGA): A review. J. Anim. Sci. 67:1895–1906.

Perry, G. A., F. N. Kojima, B. E. Salfen, J. F. Bader, D. J. Patterson, and M. F. Smith. 2002a. Effect of an orally active progestin on follicular dynamics in cycling and anestrous postpartum beef cows. J. Anim. Sci. 80:1932–1938.

Perry, G. A., M. F. Smith, and D. J. Patterson. 2002b. Evaluation of a fixed-time artificial insemination protocol for postpartum suckled beef cows. J. Anim. Sci. 80:3060–3064.

Perry, G. A., W. V. Welshons, and M. F. Smith. 2002c. Basis of melengestrol acetate as a progestin in cattle. Bio. Reprod. 66(Suppl. 1):336. (Abstr.)

Perry, R. C., L. R. Corah, G. H. Kiracofe, J. S. Stevenson, and W. E. Beal. 1991. Endocrine changes and ultrasonography of ovaries in suckled beef cows during resumption of postpartum estrous cycles. J. Anim. Sci. 69:2548–2555.

Rathbone, M. J., C. R. Bunt, C. R. Ogle, S. Burggraaf, K. L. Macmillan, C. R. Burke, and K. L. Pickering. 2002. Reengineering of a commercially available bovine intravaginal insert (CIDR insert) containing progesterone. J. Control. Release 85:105–115.

Rhodes, F. M., B. A. Clark, M. L. Day, and K. L. Macmillan. 1997. Can persistent ovarian follicles be induced in young postpartum dairy cows? Page 103 in Proc. of the Aust. Soc. of Reprod. Biol., Canberra, Australia.

Short, R. E., R. A. Bellows, R. B. Staigmiller, J. G. Berardinelli, and E. E. Custer. 1990. Physiological mechanisms controlling anestrus and infertility in postpartum beef cattle. J. Anim. Sci. 68:799–816.

Smith, V. G., J. R. Chenault, J. F. McAllister, and J. W. Lauderdale. 1987. Response of postpartum beef cows to exogenous progestogens and gonadotropin releasing hormone. J. Anim. Sci. 64:540–551.

Snedecor, G. W., and W. G. Cochran. 1989. Statistical Methods. 8th ed. Iowa State University Press, Ames.

Stanish, W. M., and G. G. Koch. 1984. The use of catmod for repeated measurement analysis of categorical data. Pages 761–770 in Proc. 9th Annu. SAS Users Group, Hollywood Beach, FL.

Werth, L. A., J. C. Whittier, S. M. Azzam, G. H. Deutscher, and J. E. Kinder. 1996. Relationship between circulating progesterone and conception at the first postpartum estrus in young primiparous beef cows. J. Anim. Sci. 74:616–619.

Williams, G. L., F. Talavera, B. J. Petersen, J. D. Kirsch, and J. E. Tilton. 1983. Coincident secretion of follicle-stimulating hormone and luteinizing hormone in early postpartum beef cows: Effects of suckling and low-level increases of systemic progesterone. Biol. Reprod. 29:362–373.

Yavas, Y., and J. S. Walton. 2000a. Induction of ovulation in postpartum suckled beef cows: A review. Theriogenology 54:1–23.

Yavas, Y., and J. S. Walton. 2000b. Postpartum acyclicity in suckled beef cows: A review. Theriogenology 54:25–55.

Zelinski, M. B., N. A. Hirota, E. J. Keenan, and F. Stormshak. 1980. Influence of exogenous estradiol-17 beta on endometrial progesterone and estrogen receptors during the luteal phase of the ovine estrous cycle. Biol. Reprod. 23:743–751.

Zimbelman, R. G., and L. W. Smith. 1966. Control of ovulation in cattle with melengestrol acetate. I. Effect of dosage and route of administration. J. Reprod. Fertil. 11:185–191.

Zollers, W. G., Jr., H. A. Garverick, and M. F. Smith. 1989. Oxytocin-induced release of prostaglandin $f_{2\alpha}$ in postpartum beef cows: Comparison of short versus normal luteal phases. Biol. Reprod. 41:262–267.

Zollers, W. G., Jr., H. A. Garverick, M. F. Smith, R. J. Moffatt, B. E. Salfen, and R. S. Youngquist. 1993. Concentrations of progesterone and oxytocin receptors in endometrium of postpartum cows expected to have a short or normal oestrous cycle. J. Reprod. Fertil. 97:329–337.