INDUCING PARTURITION IN BEEF CATTLE WITH DEXAMETHASONE AND OXYTOCIN OR PROSTAGLANDIN $F_{2\alpha}$

by

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Review of Literature

The idea that the conceptus may have a role in determing its own time of birth is shared by numerous researchers (Liggins, 1968; Adams, 1969; Liggins _et al_., 1967; Jochle, 1971; Adams and Wagner, 1970). A functional fetal hypothalamic-pituitary-adrenal (H-P-A) axis appears necessary for a "normal" pregnancy to terminate in the cow or ewe. Wagner _et al_. (1974) described such a hypothetical model involving this axis.

Liggins (1968) demonstrated the fetal influence on the onset of parturition by infusing adreno-corticotrophic hormone (ACTH) or cortisol to fetal lambs which resulted in premature parturition. Conversely, destruction of 70% or more of the fetal pituitary by electrocoagulation led to marked prolongation of gestation (Liggins _et al_. 1967). However, spontaneous delivery of fetuses occurred at term if one fetus in a twin or triplet pregnancy has an intact pituitary. These results substantiated the hypothesis that the mechanism of parturition in the ewe is mediated via the H-P-A axis to enhance the secretion of glucocorticoids from the adrenal cortex. Liggins (1969) further demonstrated that it is glucocorticoid activity of cortisol which is responsible for provoking parturition.

Hormone Levels at Parturition

Progesterone

Prior to day 60 of gestation in the ewe, the corpus luteum was responsible for maintaining progesterone production, but ovarian secretion gradually declined after this time (Edgar and Ronaldson, 1958). Linzell and Heap (1968) found ovariectomy after day 50 did not result in abortion because placental progesterone production adequately maintained pregnancy. A surprisingly small amount of progesterone (0.5-1 ng/ml) was necessary to sustain pregnancy in ovariectomized ewes between days 85-90. Challis et al. (1971) found the blood concentration of progesterone in ewes carrying twins on day 60 to be 4 ng/ml and 10 ng/ml by day 130. Progesterone secretion rate peaked at day 129. Bassett et al. (1969) showed plasma progesterone concentrations decreased over the last 5-15 days of pregnancy to 7-11 ng/ml while Liggins et al. (1972) found the levels on day -3 to parturition was 17-2 ng/ml. The adrenal gland did not appear to supply a significant amount of precursors for placental progesterone synthesis (Thompson and Wagner, 1974).

The corpus luteum appears to be the major site of progesterone production in the cow and corpus luteum regression occurs just prior to the onset of parturition (Thorburn, et al., 1977). Stabenfelt et al. (1970) showed an average of 4.6 mug/ml from day 140 to day 200 and increasing to 6.8 mug/ml by day 250 whereupon it dropped to 4 mug about 10 days antepartum. Twenty-four hours before parturition the level had fallen to less than 1 mug/ml. Similar findings have been reported by Henricks et al. (1972), Smith et al. (1973), and Symons, 1973.

Estrogen

Total unconjugated estrogens in the maternal blood of pregnant ewes remained low until 5 days before parturition when it increased to 25-35 pg/ml (Challis, 1971), and rose sharply during the last 12 hours before delivery (880 pg/ml, Thorburn et al., 1972). Estrone, estradiol-17α and estradiol-17β were the major estrogens in maternal plasma in the ratio of 2:1:1, respectively. Bedford et al. (1972) reported total unconjugated estrogen levels in the uterine vein 16.5 days, 8.5 hours and 17 minutes before parturition of 25.6, 61.4 and 171.8 pg/ml, respectively.

Levels of estrogens in the cow and ewe increased gradually throughout pregnancy with a sharp rise occurring a few days prior to delivery (Garverick et al., 1974; Smith et al., 1973; Thorburn et al., 1972). Hunter et al. (1970) reported gradual increases in urinary excretion of estradiol-17α and estrone as parturition approached. Their study further substantiated the theory that parturition may be initiated by decreasing levels of progesterone and increasing levels of estrogen. The major change in the hormonal pattern of the cow advancing delivery is the 10-fold increase of serum estrogens, 32 ± 6 pg/ml at -26 days, 150 ± 24 pg/ml at -5 days to 295 ± 53 pg/ml at -2 days (Smith et al., 1973).

Corticoids

Circulating levels of fetal sheep plasma corticosteroids elevates sharply a few days before labor and is unrelated to the corticosteroid concentration in the maternal plasma (Bassett and Thorburn, 1969). Thompson and Wagner (1974) showed uterine plasma corticosteroid concentrations greatly increased from day -3 (11.3 ± 3.6 ng/ml) to parturition (32.5 ± 9 ng/ml).

Corticoid levels in the peripheral plasma of the cow increased significantly 4 days prior to parturition (Adams and Wagner, 1970). Smith et al. (1973) reported a dramatic increase between day -1 (6.4 $\pm$ .9 ng/ml) and day 0 (16.7 $\pm$ 3.5 ng/ml).

Prostaglandins

Because of its effects on various physiological events, prostaglandins have also been studied in connection with the parturition process. Challis et al. (1972) reported an increase 8 hours prepartum of prostaglandin $F_2\alpha$ in the ewe. Similar increases in uterine venous plasma in sheep during normal parturition were observed by Thorburn et al. (1972). Wagner et al. (1974) cites three effects of prostaglandins and their relevance to parturition: 1) prostaglandins E_2 and $F_2\alpha$ have a stimulatory effect on the myometrium; 2) prostaglandin $F_2\alpha$ is a potent luteolytic agent in both the cow and ewe; and 3) prostaglandins E_2 and $F_2\alpha$ are capable of stimulating oxytocin release from the neuro-hypophysis.

Induced Parturition

Corticosteroids

The ability of corticosteroids to cause premature parturition depends on its glucocorticoid rather than its mineralocorticoid activity (Liggins, 1969). Jochle (1973) distinguishes between two classes of corticoids, "short-acting" corticoids (dexamethasone and flumethasone solution) in which premature parturition occurs within 1-5 days, and "long-acting" corticoids (dexamethasone pivalate suspension, flumethasone in suspension and triamcinolone in suspension) in which parturition occurs within 10-15 days.

Since corticoids are routinely used in the veterinary profession to treat conditions such as shock, allergic reactions, infections and musculoskeletal conditions, an additional consequence often observed was that of a premature parturition in cows during late gestation. One of the first to report this inducing effect was Adams (1969) in which dexamethasone administered parenterally to 22 cows caused parturition to occur in 19 cows within 56 hours. Since then, researchers have reported various effective doses. Beardsley et al. (1973) successfully induced parturition in Holstein cows 273 days of gestation with 4.4 mg/100 kg body weight (45.1 ± 11.1 hours after injection). Adams and Wagner (1970) found that when cows were injected earlier in pregnancy, the rate of induction failure and interval from injection to fetal expulsion were increased. Parturition was induced in two cows given 16 and 10 mg doses of dexamethasone (Adams, 1969). When 20 mg of dexamethasone was injected after 255 days of gestation, parturition was successfully induced within 72 hours (Jochle, 1973; Garverick et al., 1974; Wagner et al., 1974; LaVoie and Moody, 1973; Bolte et al., 1977; Adams and Wagner, 1969). Induction at higher doses (30, 50 or 60 mg) was comparative to the 20 mg injection with no additional harmful side effects (Kesler et al., 1976; Wagner et al., 1974).

In New Zealand corticosteroid induced parturition is widely praticed by dairy farmers (Welch et al., 1973).

Welch et al., 1973 reported the results of two field trials comparing three of the longer-acting corticosteroids, dexamethasone trimethylacetate (20 mg), flumethasone suspension (10 mg) and triamcinolone acetonide (30 mg). The interval from injection to calving, taking the three treatments together, averaged 15 ± 8 days. Although calf mortality was high for all three treatments, New Zealand farmers were willing to accept this if the cow becomes pregnant to calve at the optimal time the following year.

When estradiol benzoate (6-12.5 mg) was injected in combination with 20 mg of dexamethasone, the time from treatment to calving was noticeably reduced (Garverick et al., 1972; Schmitt et al., 1975; Bolte et al., 1977). However, LaVoie and Moody (1973) failed to show similar results when varying amounts of estrogen were injected. Flumethasone effectively shortened gestation length by 20 days when injected 30.5 days prior to expected calving at a dose of 10 mg (Welch et al., 1973). Lauderdale (1972) showed that 20 mg of flumethasone (5 mg per day for four consecutive days) to be 100% effective in aborting cows on day 215 of gestation and 90% effective in inducing premature parturition within three days of injection when given on day 268 of gestation.

North et al., (1973) induced parturition in pregnant gilts injected with 75 mg of dexamethasone on days 101, 102 and 103 of gestation. However, Jochle (1971) and Rich et al., (1972) reported unsuccessful attempts to induce premature parturition in swine with flumethasone and dexamethasone with doses less than 75 mg.

Alm *et al.* (1972) injected 12 mares daily for 4 days with 100 mg of dexamethasone starting 18 days before expected foaling. Foaling occurred 10 $\pm$ 1.6 days following injection.

In the ewe, dosages of dexamethasone between 8-20 mg were effective in inducing parturition within 72 hours of injection (Adams and Wagner, 1970; Bosc, 1972; Jochle, 1973; Shevah, 1974). Liggins *et al.* (1973) reported that doses of dexamethasone as low as 0.06 mg/24 hours (approximately equivalent to 1.8 mg of cortisol/24 hours) were effective to induce premature birth. Abortion during the second trimester was induced in 2 of 5 ewes with 10 mg of dexamethasone per day for 5 days (Fylling *et al.*, 1973).

Another study utilizing flumethasone (Skinner *et al.*, 1970) induced lambing but in lower doses than dexamethasone.

Jochle *et al.* (1972) showed 100 mg of progesterone counteracted the corticoid effect when administered 3 days prior to and 5 days after a 10 mg injection of flumethasone on day 270 of gestation.

Prostaglandin

One biological activity of prostaglandin is the alteration of smooth muscle contractility. Lauderdale (1974) demonstrated that levels of prostaglandins increased in maternal cotyledons, myometrium and the amniotic fluid just prior to parturition and were capable of inducing abortions. When $PGF_2\alpha$ was administered at various dosages to 30 cows an average of 267 days of gestation, calving occurred in an average of 3 days (Lauderdale, 1972).

Treatment with 30 mg of $PGF_2\alpha$-THAM salt (intramuscularly) caused 7 of 12 beef heifers to calve within 72 hours when injected on day 267 of gestation (Henricks et al., 1977).

Based on a few recent studies (Spears et al., 1974; Zerobin et al.,1973; Lauderdale, 1974) $PGF_2\alpha$ is as effective in inducing parturition as the corticoids. Kordts and Jochle (1975) reported a shorter interval from treatment to parturition in flumethasone-treated cows (2 x 5 mg, 10 to 14 hours apart, 42.5 hours) versus $PGF_2\alpha$-treated cows (20 mg, i.v., 57.2 hours). This altered response could be attributed to either age (9 of 9 heifers and 5 of 7 cows responded) or weight differences. Bosc et al. (1975) compared dexamethasone (16 mg) to an analog of $PGF_2\alpha$ (I.C.I. compound No. 79939) 4 to 10 mg about one week prior to expected calving. When the analog-$PGF_2\alpha$ was combined with dexamethasone, the interval between treatment and calving was not shortened (38.3 ± 6.4 hours) as compared to giving either dexamethasone (32.58 ± 9.06 hours) or analog-$PGF_2\alpha$ (29.3 ± 12.1 hours) alone.

Killian and Day (1974) reported the mean interval from injection to farrowing for gilts and sows treated on either day 111, 112 or 113 of gestation to be 44.7 hours when given 5 mg and 28.0 hours with 10 mg. Results of Diehl et al. (1977) are in contrast to studies reporting high proportions of females responding to $PGF_2\alpha$. Mean interval from injection to farrowing for 5 mg was 82 ± 14 hours and 90.8 ± 15.5 hours for 10 mg $PGF_2\alpha$-THAM salt.

Godke *et al*. (1975) successfully induced lambing with 8 mg $PGF_{2}\alpha$-THAM salt injected 7 days prior to expected day of lambing. For 8 of 9 ewes treated, the average time to lambing was 41.7 ± 3.6 hours compared to 20 mg dexamethasone in which lambing occurred in 45.3 ± 3.6 hours.

Side Effects of Induced Parturition

Retained Placenta

The biggest deterrent to using corticosteroids to induce premature birth is the incidence of retained fetal membranes (Jochle, 1971; Adams and Wagner, 1970; Garverick *et al*., 1974). Carroll (1974) defined retained placenta as the observance of fetal membranes attached to the cow longer than 24 hours following delivery. Retained placentas occurred in more than 80% of cows treated with dexamethasone (Jochle *et al*., 1972). Several investigators are in agreement with these findings (Kesler *et al*., 1976; Welch *et al*., 1973). Since corticoid-induced parturition accelerates the time to calving, expected peak of estrogen is not attained (Carroll, 1974). Results on the use of exogenous estrogens had no effect on the incidence of retained membranes (Garverick *et al*., 1972; LaVoie and Moody, 1973), while Garverick *et al*. (1974) showed a significant decrease in the number of cows retaining membranes.

Because of the high incidence of retained placenta, acceptance of corticoid-induced parturition as a management tool in the cattle industry has been slow. A 20% decrease in the incidence of placental retention is associated with the "long-acting" preparations; however, the rate of stillbirths is significantly higher. Most researchers have used antibiotic therapy to avoid the secondary effects which may be associated with retained membranes, i.e. metritis. However, cows have had normal post-parturient recovery even when no treatment was administered (Lauderdale, 1972).

Retained placenta occurs at a lesser frequency in cows, induced to calve, which are closer to natural term. Wagner *et al*. (1971) showed the relationship between stage of pregnancy and occurrence of placental retention for dexamethasone treated cows 270, 270-274, 275-280 and 280 days pregnant to be 61.9%, 57.0%, 48.7% and 30.8%, respectively.

Fertility

With the proper antibiotic treatment to induced cows with retained placentas, subsequent postpartum uterine involution and fertility was no different than control cows (Jochle, 1971; Wagner *et al*., 1974; Beardsley *et al*., 1973).

Milk Production

Jochle (1973) confirmed observations noted by other researchers in which the onset of milk production was slower for induced cows versus controls. Beardsley *et al*. (1973) showed a nonsignificant difference in milk production and amount of milk fat between induced (24.8 kg) and control cows (27.8 kg).

Birth Weight and Growth of Offspring

The birth weight of calves born to induced cows is less when compared to controls (Beardsley *et al*., 1973;

Wagner *et al.*, 1974; LaVoie and Moody, 1973) while viability of induced calves was not significantly different from control calves (LaVoie and Moody, 1973). Carroll (1974) attributes a shorter length of gestation for induced calves to their lighter birth weights.

Weaning weights between induced and non-induced calves were comparable (LaVoie and Moody, 1973).

Introduction

Within the last fifteen years the idea of controlling the time of parturition in domestic animals has become of great importance, not only to obtain further knowledge of the complexities related to the reproductive processes, but also to minimize economic losses to producers of livestock.

In order to more precisely control the time of parturition certain compounds have been found to effectively begin the birth process; however, the exact mechanisms have not been determined. Grouping parturitions of domestic animals leads to homogeniety of animal lots and a reduction in work time. Successful artifical stimulation of a link in the mechanism of birth may employ the properties of corticoids, estrogens, prostaglandins ($PGF_2\alpha$) or oxytocin, which are all involved with the end of pregnancy. Although these compounds have been widely researched, the time range is still too wide to pratically depend on any of them. In addition, the major complication following induced birth in cattle is retained placenta, however this hasn't become a health hazard to the dam as long as antibiotics are administered to avert infectious bacteria. The degree of calving difficulty is the same or worse and calf birth weights are decreased. Nevertheless, calf survival rate and growth to weaning age is comparable to non-induced calves. In order to safeguard this period, the livestock producer needs to maintain strict supervision such that the consequences of possible economic risks are minimized.

The objectives of this study were to:

(1) Determine if flumethasone would induce lambing in ovariectomized ewes.

(2) Attempt to narrow the time interval from parturition to calving by combining prostaglandin $F_2\alpha$ or oxytocin with dexamethasone.

(3) Determine if estradiol cypionate would reduce the incidence of retained placenta after induction of calving.

(4) Determine if epinephrine inhibits the ability of prostaglandin to induce labor.

Materials and Methods

Experiment 1: Six crossbred Western ewes were used in this experiment. A vaginal pessary was inserted into each ewe for sixteen days to synchronize estrus. Ewes were bred naturally by appointment or at estrus. All ewes were laparatomized 60 days post-breeding to verify conception dates and perform bilateral ovariectomy. Four ewes were left intact and two were ovariectomized. All ewes were injected (im) with 2 mg of flumethasone[1] on day 142 of gestation. Close observation was maintained to determine the exact time of lambing.

Experiments 2 through 5 used either prostaglandin $F_2\alpha$ ($PGF_2\alpha$) or oxytocin (OXY) as an adjunct to dexamethasone in an attempt to induce calving at a predictable time. Cows were allotted to treatments 40 hours after dexamethasone according to day of gestation. Over a four-year period 138 multiparous Polled Hereford cows ranging from 3 to 9 years old were injected with 20 mg of dexamethasone intramuscularly, at 275 $\pm$ 1 days after breeding. The range of injection times for each experiment is shown in table 1. All cows were maintained on range pasture and bred either artifically or naturally. Breeding dates were verified by pregnancy diagnosis which was performed twice between 55 and 120 days post-breeding. Cows were rectally palpated just prior to injection and only those cows approaching parturition were used.

[1]Flucort, Diamond Laboratories, Inc., Des Moines, Iowa

TABLE 1. STAGE OF GESTATION AT TIME OF DEXAMETHASONE TREATMENT FOR COWS IN EXPERIMENTS 2 TO 5

Experiment	No. of Cows	Average Days Gestation at Dexamethasone Injection (Range)
2	45	274 (269-282)
3	39	276 (268-283)
4	26	277 (274-281)
5	28	275 (263-287)

Close observation was made on all cows to determine the exact time of calving. Abnormal presentations were noted and assistance was given when necessary. Birth weights for all calves were recorded within 12 hours after birth. Cows that had not expelled the placenta 24 hours following parturition were treated with 10 cc combiotic once daily for three consecutive days.

Experiment 2: Forty-five cows were injected with 20 mg of dexamethasone[2] (DEXA) and 10 mg of estradiol cypionate[3] (ECP). Cows failing to calve within 40 hours after DEXA + ECP were injected with either ECP or $PGF_2\alpha$[4] + ECP.

Experiment 3: Thirty-nine cows were injected with 20 mg of DEXA and 10 mg of ECP. Cows failing to calve within 40 hours after DEXA were allotted into one of the following treatments: $PGF_2\alpha$, $PGF_2\alpha$ + epinephrine[5] (EP) or no further treatment.

Experiment 4: Twenty-six cows were injected with 20 mg of DEXA. Cows failing to calve within 40 hours after DEXA were allotted into groups that received either OXY[6] or no further treatment.

Experiment 5: Twenty-eight cows were injected with 20 mg of DEXA. Cows failing to calve within 40 hours after DEXA were injected with either ECP or OXY + ECP.

[2] Azium, Schering Corp., Kenilworth, New Jersey.
[3] ECP, The Upjohn Co., Kalamazoo, Michigan.
[4] PGF_2 -THAM-salt, The Upjohn Co., Kalamazoo, Michigan.
[5] Adrenalin, Parke-Davis, Detroit, Michigan.
[6] Oxytocin, Med Tech, Inc., Elwood, Kansas.

All injections were given intramuscularly and dosages for hormones used were: $PGF_{2}\alpha$, 30 or 33.3 mg THAM-salt; OXY, 100 u.s.p. units and EP, 1 mg/100 pounds of body weight.

Results and Discussion

Experiment 1: Results of experiment 1 are shown in table 2. The interval from flumethasone injection to lambing for the ovariectomized and intact groups was not different (56.33 vs 57.75 hrs, respectively). It has been hypothesized that corticoid-induced parturition is due to drug action on the the corpus luteum (CL) to cause regression (Jochle, 1973). In view of the results obtained in this experiment with ewes, it is concluded that in sheep the ovaries are not essential for normal parturition and flumethasone induces parturition equally as well in ewes without a CL as in those with a CL. The primary function of corticoids in triggering lambing is not one of CL regression. The earlier hypothesis is not correct for ewes, but further work is needed to establish this point in cows.

Cows Calving By 40 Hrs Post Dexamethasone (Experiments 2-5)

Results of cows calving within 40 hrs to dexamethasone (DEXA) or DEXA + estradiol cypionate (ECP) are shown in table 3. Prostaglandin $F_2\alpha$ ($PGF_2\alpha$) was given 40 hrs after DEXA in light of results of Morrison (1975). His results indicated that it takes 40 hrs for DEXA to initiate the changes necessary for labor in the cow and additional treatments involving $PGF_2\alpha$ are not effective until after this time. The average hrs from DEXA injection to fetal expulsion between experiments are not different. Percent of cows calving by 40 hrs post DEXA varied considerably between experiments. Percent of cows calving before 40 hrs in experiments 2 through 5 were 35.5,

TABLE 2. INDUCTION OF LAMBING WITH FLUMETHASONE[a] (EXPERIMENT 1)

	No. of Ewes	Hours From Injection To Lambing (Avg)
Ovariectomized Ewes[b]	2	56.33
Intact Ewes	4	57.75

[a]Two mg flumethasone (Flucort, Diamond Laboratories Inc., Des Moines, Iowa) injected im on day 142 of gestation.

[b]Ovariectomy performed 60 days post-breeding.

TABLE 3. DATA SUMMARY FOR COWS THAT CALVED WITHIN 40 HOURS AFTER DEXAMETHASONE (DEXA) INJECTION

Experiment	No. of Cows Treated With DEXA	No. of Cows Calving by 40 Hrs. Post DEXA Injection	Hrs. From DEXA To Calving (Mean[c] ± S.D.)	No. of Cows With Retained Placentas[b]
2	45[a]	16 (35.5%)	32.4 ± 7.20	10 (62.5%)
3	39[a]	12 (30.7%)	37.1 ± 7.85	5 (41.6%)
4	26	12 (46.1%)	33.0 ± 5.07	2 (16.6%)
5	28	5 (17.8%)	31.7 ± 6.08	0 (0%)

[a]10 mg of estradiol cypionate injected at the time of DEXA.

[b]Includes only cows that calved by 40 hrs. post-DEXA injection.

[c]Values not different ($P > .05$).

30.7, 46.1 and 17.8, respectively. These results are in agreement with Morrison (1975) where he reported calving occurred in 8 of 9 cows within 40 hrs and also with Adams, 1969; Adams and Wagner, 1970; Wagner et al., 1974 and Garverick et al., 1974. Average days gestation for 45 cows calving within 40 hrs after DEXA injection was 276.7 versus 268.1 for 75 cows responding to the various treatments in experiments 2 through 5.

Experiment 2: Sixteen of 45 cows calved before 40 hrs post DEXA. Calving time in response to $PGF_2\alpha$ + ECP or ECP for 29 cows treated 40 hrs post DEXA injection is shown in table 4. The interval to calving was reduced by the prostaglandin injection, 47.8 vs 61.2 hrs. Three cows in the ECP group and two cows in the $PGF_2\alpha$ group did not calve by 72 hrs post DEXA treatment, thus were not included in subsequent data. This procedure was followed in order to compare data with previous data of researchers using the same procedure (Adams and Wagner, 1970). Although data are not available for DEXA and $PGF_2\alpha$ combined in this way, it is well established that $PGF_2\alpha$ can terminate pregnancy (Spears et al., 1974; Lauderdale, 1974; Henricks et al., 1977). In an attempt to further synchronize calving, Morrison (1975) administered $PGF_2\alpha$ 30 hrs following DEXA injection. However, labor was not induced in a shorter time period as indicated by a larger standard deviation, 10.85, versus 5.37 hrs for $PGF_2\alpha$ given 40 hrs post DEXA. It was shown by Dufty (1972) that when heifers were confined in a shed when parturition was impending or had actually begun a prolonged time to parturition occurred. In the present experiment it was

TABLE 4. DATA SUMMARY FOR COWS IN EXPERIMENT 2 THAT DID NOT CALVE BY 40 HOURS POST DEXAMETHASONE (DEXA) AND WERE INJECTED WITH ESTRADIOL CYPIONATE (ECP) OR ECP AND PROSTAGLANDIN $F_2\alpha$ ($PGF_2\alpha$). (EXPERIMENT 2)

Treatment[a]	No. of Cows	No. of Cows Calving by 72 Hrs Post DEXA	Hrs. From DEXA To Calving (Mean ± S.D.)	No. of Cows With Retained Placentas
ECP	14	11 (78.5%)[b]	61.2 ± 13.20	8 of 11 (72.7%)
$PGF_2\alpha$ + ECP	15	13 (86.6%)[c]	$47.8^{d} \pm 8.46$	11 of 13 (84.6%)

[a] Injected 40 hrs. after DEXA treatment.

[b] Three cows calved 6, 6.5 and 12 days after ECP injection.

[c] Two cows calved 6 and 8 days after DEXA treatment.

[d] Different ($P < .01$) than ECP treatment. Includes only those cows calving by 72 hrs. post-DEXA.

observed that when 8 of the prostaglandin treated cows were returned to pasture to calve a significantly shorter interval and standard deviation to parturition resulted, 2.9 $\pm$ .94 hrs. Seven cows in this group were with-held in a corral for closer observation. However, only 5 of the 7 calved within 72 hrs after DEXA and they calved an average of 15.7 hrs after $PGF_2\alpha$ injection. It was hypothesized that cows delayed the parturition process and possibly $PGF_2\alpha$ did not override the effects of a stress-related situation. ECP did not reduce the occurrence of retained placentas as previously reported by Garverick <u>et</u> <u>al</u>., 1974 but is in agreement with LaVoie and Moody (1973).

<u>Experiment 3:</u> Twelve of 39 cows calved before 40 hrs post DEXA. Epinephrine was injected along with $PGF_2\alpha$ in an attempt to mimic the results obtained in experiment 2 (table 4). It was hypothesized that by elevating the cows epinephrine level via an injection, the same response could be obtained if indeed the cows were stressed (held in a corral). From these results it appeared that epinephrine (EP) with $PGF_2\alpha$ delayed the time to parturition, 18.1 hrs after injection (table 5). However, the interval to calving for cows treated with $PGF_2\alpha$ alone was only slightly lower, 20.2 hrs after injection and that for cows receiving no furhter treatment calved 14.4 hrs following the time $PGF_2\alpha$ and $PGF_2\alpha$ + EP were given. Since $PGF_2\alpha$ did not shorten the interval to calving in this experiment as it had in experiment 2 the hypothesis was not properly tested. The ability of $PGF_2\alpha$ to initiate labor is variable and may depend on the exact physiological state of the cow at the time of injection or how close

TABLE 5. EFFECT OF INJECTING PREGNANT COWS WITH $PGF_2\alpha$ OR $PGF_2\alpha$ AND EPINEPHRINE (EP) 40 HRS AFTER DEXAMETHASONE (DEXA). (EXPERIMENT 3)

Treatment[a]	No. of Cows	No. of Cows Calving by 72 Hrs Post DEXA	Hrs. From DEXA To Calving (Mean[b] $\pm$ S.D.)	No. of Cows With Retained Placentas
None	9	8 (88.8%)[c]	54.4 ± 10.12	8 of 8 (100%)
$PGF_2\alpha$ [a]	8	6 (75.0%)[d]	50.2 ± 9.49	4 of 6 (66.6%)
$PGF_2\alpha$ + EP[a]	10	8 (80.0%)[e]	58.1 ± 9.66	5 of 8 (62.5%)

[a]Injected 40 hrs after DEXA treatment.

[b]Values not different ($P > .05$).

[c]One cow calved 9 days after DEXA treatment.

[d]Two cows calved 5 days after DEXA treatment.

[e]Two cows calved 5 and 5.5 days after DEXA treatment.

to actual labor she was at the time of injection. Challis et al., (1972) has proposed that prostaglandin is involved in labor and has shown a drastic increase in $PGF_2\alpha$ near the time of labor. $PGF_2\alpha$ may be involved in releasing oxytocin or may elicit an oxytocic effect directly on the myometrium.

Experiment 4: Since $PGF_2\alpha$ was not commercially available and the possibility exists that its affect was oxytocic, oxytocin was tested in conjunction with DEXA. Prostaglandins have been shown to have both luteolytic and oxytocic properties (Lauderdale, 1974). Also, oxytocin is more readily available and cheaper than $PGF_2\alpha$. Twelve of 26 cows calved before 40 hrs post DEXA. Table 6 shows the results of 7 cows responding to oxytocin 40 hrs after DEXA. Oxytocin significantly reduced the interval to calving following DEXA injection, 4.6 $\pm$ 3.72 hrs ($P < .05$). All 7 cows were returned to the pasture to calve which was similar to the handling procedure for 8 of the $PGF_2\alpha$-treated cows in experiment 2. From these results it appears that prostaglandin in experiment 2 acted in an oxytocic-like manner. These results support the suggestion made by Lauderdale (1974) that for species not requiring a functional CL for pregnancy maintenance the primary action of prostaglandin may be oxytocic.

Experiment 5: Oxytocin in experiment 4 appeared to work similar to $PGF_2\alpha$ in experiment 2. Since $PGF_2\alpha$ was quite variable in its ability to hasten parturition when used after DEXA (compare experiments 2 and 3) another experiment was designed to repeat the conditions of experiment 2 but to substitute oxytocin for $PGF_2\alpha$. Five of 28 cows calved before 40 hrs post DEXA. Calving time in response to oxytocin (OXY) + ECP or ECP

TABLE 6. EFFECT OF INJECTING PREGNANT COWS WITH OXYTOCIN 40 HRS AFTER TREATMENT WITH DEXAMETHASONE (DEXA). (EXPERIMENT 4)

Treatment[a]	No. of Cows	No. of Cows Calving by 72 Hrs Post DEXA	Hrs. From DEXA To Calving (Mean ± S.D.)	No. of Cows With Retained Placentas
Oxytocin	7	7 (100%)	44.6[c] ± 3.72	5 of 7 (71.4%)
None	7	6 (85.7%)[b]	54.4 ± 10.12	4 of 6 (66.6%)

[a]Injected 40 hrs after DEXA treatment.

[b]One cow calved 6 days after DEXA treatment.

[c]Different ($P < .05$) than no treatment.

for 23 cows treated 40 hrs post DEXA injection is shown in table 7. The interval from OXY treatment to parturition for 12 cows was 9.16 hrs. The results obtained in this experiment do not confirm results from the previous experiment. Seven of the 8 OXY + ECP treated cows were returned to the pasture and calving occurred in 10.5 hrs. Five of the 8 cows remaining in this group were with-held in a corral. Average hrs to parturition was 16.0. Again ECP did not affect the percent of cows with retained placentas. Oxytocin as well as $PGF_2\alpha$ was not consistent in shortening the interval to calving after DEXA. Stress factors may be involved but the confinement used in this experiment was not great enough to be a factor.

TABLE 7. EFFECT OF INJECTING PREGNANT COWS WITH ESTRADIOL CYPIONATE (ECP) OR OXYTOCIN (OXY) AND ECP 40 HRS AFTER DEXAMETHASONE (DEXA). (EXPERIMENT 5)

Treatment[a]	No. of Cows	No. of Cows Calving by 72 Hrs Post DEXA	Hrs. From DEXA To Calving (Mean[b] $\pm$ S.D.)	No. of Cows With Retained Placentas
ECP	7	4 (57.1%)[c]	65.3 $\pm$ 10.16	4 of 4 (100%)
OXY + ECP	16	12 (75.0%)[d]	49.1 $\pm$ 8.04	11 of 12 (91.6%)

[a]Injected 40 hrs after DEXA treatment.

[b]Values not different ($P > .05$).

[c]Three cows calved 3.5, 4 and 15 days after ECP injection.

[d]Four cows calved 4, 5, 5.5 and 10 days after DEXA treatment.

Summary

Table 8 presents a summary for cows responding to various treatments given 40 hrs after DEXA injection.

TABLE 8. DATA SUMMARY FOR COWS THAT CALVED WITHIN 72 HRS AFTER DEXAMETHASONE AND OXYTOCIN, PROSTAGLANDIN $F_2\alpha$ OR EPINEPHRINE INJECTION

Treatment	No. of Cows	Hrs. From DEXA To Calving
ECP or Nothing	29	56.34 ± 10.28
$PGF_2\alpha$	19	48.60 ± 8.61
OXY	19	47.47 ± 7.02
$PGF_2\alpha$ + EP	8	58.12 ± 9.66

Oxytocin (OXY, 100 usp units) and $PGF_2\alpha$ (30 or 33.3 mg) appear to hasten calving when given 40 hrs after DEXA treatment (20 mg). An injection of epinephrine (EP, 1 mg/ 100 lbs body weight) in conjunction with $PGF_2\alpha$ may not be effective in the presence of increased levels of epinephrine. Estradiol cypionate (ECP) did not hasten time to calving nor did it reduce the incidence of retained placenta as it occurred in 80% of the induced cows.

Cows were 275 ± 1.5 days gestation at the time of DEXA injection. Average days gestation for forty-five cows calving within 40 hrs of DEXA injection was 276.7 days. Seventy-five cows responding to the various treatments given 40 hrs after DEXA injection calved at an average of 268.1 days gestation.

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INDUCING PARTURITION IN BEEF CATTLE WITH DEXAMETHASONE AND OXYTOCIN OR PROSTAGLANDIN $F_2\alpha$

by

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Oxytocin (100 usp units) or prostaglandin $F_2\alpha$ (30 or 33.3 mg THAM-salt) was injected into pregnant Polled Hereford cows 3-9 years old that had been given 20 mg of dexamethasone on 275 $\pm$ 1.5 days gestation. In this study, 138 injections were given. Forty-five cows calved before 40 hours post injection (average of 33.5 hours). The remaining 93 cows were allotted to one of the following treatment groups: group-1 prostaglandin $F_2\alpha$ and estradiol cypionate and returned to pasture (16 cows); group 2- prostaglandin $F_2\alpha$ and estradiol cypionate and held in confinement (5 cows); group 3- oxytocin and estradiol cypionate and returned to pasture (15 cows); group 4- oxytocin and estradiol cypionate and held in confinement (8 cows); group 5- prostaglandin $F_2\alpha$ and epinephrine (1 mg/100 lbs body weight) and returned to pasture (10 cows); group 6- no further injection and returned to pasture (31 cows). All injections were given intramuscularly. Average hours from dexamethasone injection to fetal expulsion for groups 1-6 were 46.1, 55.7, 47.5, 47.2 58.1 and 56.3, respectively. Two cows in group 1, one cow in group 3, three cows in group 4 and two cows in groups 5 and 6 did not calve in response to the injection. Estradiol cypionate did not affect parturition time. The incidence of retained placenta was similar for all treatments. Prostaglandin $F_2\alpha$ or oxytocin, given 40 hours after dexamethasone and returned to pasture (groups 1 and 3) effectively shortened the interval to parturition. Mean time of calving for cows in group 2 was slightly longer suggesting that the stress of confinement delays the onset of parturition. Although the average time to calving for cows in group 4 was similar to cows in group 3, oxytocin was not as effective since only 5 of 8 cows responded. The addition of group 5 further demonstrates that prostaglandin $F_2\alpha$ may not be effective in the presence of increased levels of epinephrine.