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Induction of Parturition in Cattle

By Albert D. Barth DVM, MVetSc

Induction of parturition can be a very useful tool for managing calving. In healthy animals, the stages of labour, pelvic relaxation, calf viability, colostrum transfer, and milk production are similar for both induced and natural parturitions. The main limitations are the requirements for known breeding dates and a high incidence of retained placentas. Induction of parturition may be indicated for the treatment of medical conditions to save the life of the fetus or the cow. Since the fetus will gain about 0.5 kg/day in the final weeks of normal gestation and up to 1 kg/day when gestation has progressed beyond the normal due date, induction of parturition may be used to prevent dystocia from an oversized fetus. Additionally, parturition induction may be beneficial when gestation is prolonged, allowing the cow extra time to resume cycling for rebreeding. Potentially, parturition induction can be used to schedule calving to occur during daylight hours on known dates, so that personnel are available to manage calving. This issue of *Large Animal Veterinary Rounds* reviews the physiology of birth and the indications, precautions, and methods for induction of parturition in cows. In addition, this issue examines several comparative experiments on induction methods.

Endocrinological aspects

Progesterone is essential for establishing and maintaining pregnancy in all mammalian species that have been studied. In cattle, the corpus luteum (CL) is the primary source of progesterone throughout gestation and luteal regression is necessary for parturition to occur. After 120 days of gestation, the placenta begins to secrete progesterone and this source alone is sufficient to maintain pregnancy until approximately 240 days. Rising fetal cortisol in the last 4 to 6 weeks of gestation gradually reduces the uteroplacental synthesis of progesterone. Therefore, near the end of gestation, maintenance of pregnancy once again becomes dependent on the CL.¹ If luteolysis occurs prior to the 8th month of gestation, pregnancy would be maintained for a time, but parturition would likely occur several weeks before the normal due date.

High concentrations of progesterone during pregnancy maintain uterine quiescence by hyperpolarizing the myometrial cells. At the end of gestation, falling progesterone and increasing estrogen produce depolarization of the myometrial cells and stimulate the formation of myometrial cell gap junctions that enhance the sensitivity of the myometrium to stimulatory agonists. Declining progesterone and rising estrogen also result in increased expression of oxytocin receptors in the myometrium. It appears that increased estrogen concentrations also stimulate the production and release of prostaglandins. Prostaglandin (PG) production results in the demise of the CL and a precipitous drop in serum progesterone. Smooth muscle activation is associated with endometrial synthesis of PGF_{2α} that augments the force of contraction. PGs are also involved in the mechanisms of cervical dissolution that are essential for parturition.

The trigger for the spontaneous onset of labour is greatly increased cortisol production by the adrenal gland of the maturing fetus. The increase in activity of the fetal hypothalamo-pituitary-adrenal (HPA) axis at the end of gestation is likely caused by programmed maturation in the fetal hypothalamus, rather than a response of the fetal pituitary to chronic stress (eg, possibly caused by the developing inadequacy of space and nourishment within the uterus). Throughout the last 2 to 3 weeks of in utero development, the fetal adrenal gland increases in size relative to body weight and cellular sensitivity to adrenocorticotropic hormone (ACTH) increases. The increase in size and sensitivity of the adrenal gland, combined



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with increasing circulation of ACTH, account for the increased cortisol secretion that triggers parturition. Recent evidence suggests that at least some of the activity of the fetal HPA axis is due to positive feedback from placental estrogen; ie, increasing estrogen in fetal plasma greatly increases ACTH concentrations in fetal plasma.

Placental maturation may require exposure to elevated cortisol levels for a period of time prior to calving. This hypothesis is supported by a reduction in the incidence of retained placenta when long-acting corticosteroids are used to induce parturition.²

Indications

Induction of parturition may be indicated for the treatment of uterine hydrops, cardiac failure, or other health-related matters in which salvage of the fetus or the life of the cow are being considered. Parturition induction as a calving management tool is ideally suited to producers of purebred cattle who employ artificial insemination with known breeding dates. The procedure facilitates close observation of calving for detection and correction of dystocia and could reduce perinatal calf deaths.³ In a normal gestation, the fetus can gain from 0.45-0.68 kg/day in the final weeks *in utero* and as much as 1 kg per day when gestation is 1 to 2 weeks overdue. It has become common practice to induce parturition after 285 days of gestation rather than allow gestation to be prolonged to prevent dystocia due to fetal oversize. Induction of parturition may also allow the cow extra time to resume cycling for rebreeding. However, despite normal durations of gestation, with induction placental retention rates are elevated, leading to endometritis, delayed onset of estrus, and reduced first cycle pregnancy rates. Nevertheless, end-of-season pregnancy rates are usually not reduced.

In dairy herds, parturition may be induced 1 to 2 weeks early to prevent excessive udder edema and distension that predispose cows to mastitis and difficulty in milking. Induction of parturition with long-acting corticosteroids has gained widespread acceptance with dairy producers in New Zealand and Australia to synchronize lactation with the grazing season.^{4,5} Calving is concentrated at a time of year when grazing is optimal for milk production. In the limited breeding season that follows, it is inevitable that some cows will fail to become pregnant. These cows can be further exposed for breeding to bulls fitted with a chin-ball marking harness. In the following calving season, these cows can be induced to calve 1 to 3 months prematurely. Calves born excessively prematurely will be lost; however, milk yield can be expected to be near normal.

Precautions

Accurate knowledge of breeding dates is necessary to prevent the birth of non-viable calves. Calves born up to 2 weeks preterm have good vitality and are able to attain good maternal immunity derived from colostrum. Cows induced 1 to 2 weeks prematurely usually retain the placenta in >75% of cases; whereas, cows induced within a few days of term, or at term, have a 10%-50% placental retention rate. In most reports, cows with retained placentas did not have reduced end-of-

season pregnancy rates;⁶ however, first service pregnancy rates were reduced.^{7,8}

The effect of induction of parturition on the yield of colostral immunoglobulins and milk in the following lactation depends on how early parturition is induced. When parturition is induced up to 22 days before the expected calving date there is a significant decrease in the yield, but not the concentration of colostral immunoglobulin.⁹ Some calves have lower levels of colostral immunoglobulin when birth occurs 10 to 15 days early. The ability of these calves to absorb immunoglobulin is not reduced and the lower blood immunoglobulin levels are likely due to reduced ingestion, possibly due to calf weakness. In general, when parturition is induced within 2 weeks of normal term, the onset of milk production may be a few days slower than in natural calving, but overall production levels for the entire lactation period are within expected limits.

Induction of parturition may result in reductions in birth weights and, in turn, there would be reductions in weaning weights. In one study, weaning weight was significantly reduced in induced calves (6.9 kg) but, in another study, weaning weights were not significantly lower (2.3 kg).¹⁰

The effect on cow health of inducing parturition on day 274 of gestation was studied in Australian dairy cows. Cows were injected with dexamethasone trimethylacetate with herd mates as controls. Treated cows calved an average of 2.61 days before their due date. There were no differences in the proportion of cows displaying symptoms of milk fever, mastitis, paralysis, or acute metritis and there were no differences between groups for cow mortality or in any parameter of milk yield.¹¹

Methods of induction of parturition

Various types and combinations of hormone treatments have been studied for efficacy and safety in parturition induction, including corticosteroids or prostaglandins in combination with various estrogen preparations and oxytocin. There has been no appreciable reduction in the incidence of placental retention. Dimenhydrate and the hormone, relaxin, in combination with dexamethasone, have been reported to reduce placental retention; however, the number of cows treated with dimenhydrate was small and relaxin is not commercially available. RU-486, a potent antiprogesterone, used alone or in combination with relaxin and administered on day 277 or 278 of gestation, resulted in basal levels of progesterone by 48 hours and calving at 53-55 hours after injection. There were no complications at calving and no retained placentas; however, there were only 2 animals per treatment group and inductions were done very close to normal term. Therefore, a great deal more study is needed before this method can be recommended.

Short-acting corticosteroids

The most commonly used corticosteroids for inducing parturition are dexamethasone (20-30 mg) or flumethasone (8-10 mg) given as a single intramuscular injection. Parturition is induced with 80%-90% efficacy when the injection is given within 2 weeks of normal term. The interval from injection to parturition is 24-72 hours, with an average of 48 hours.

Induction is considered to have failed if cows have not calved by 72 hours after treatment. Retreatment in such cases is often successful.

Long-acting corticosteroids

Long-acting corticosteroids are used when calf viability is not of primary importance, but lactation (calving) must be synchronized with the grazing season. Dexamethasone trimethyl acetate (25 mg) or triamcinolone acetonide (4–8 mg) may be used and provides similar outcomes. One intramuscular injection is given approximately 1 month prior to the due date for calving and parturition occurs over 4 to 26 days. Usually, the further a cow is from her due date, the longer it takes for a response. The udders of treated cows are consistently engorged with milk about 1 week after injection, although it may be another week before they calve. These cows could be milked prepartum if the udder is obviously full, to prevent regression of secretory tissue. Total milk production per lactation can be expected to be reduced by 4%–7%.

The incidence of retained placentas with the use of long-acting corticosteroids is quite low (9%–22%) compared with short-acting corticosteroids. However, there is a high incidence of calf mortality (7%–45%) due to premature placental separation, increased frequency of uterine inertia, and calf prematurity.

The variability in time-to-calving after treatment can be reduced by administering a short-acting corticosteroid or prostaglandin about 1 week after long-acting corticosteroid treatment. Most cows will calve 2 to 3 days after the 2nd injection; however, calf mortality and the incidence of retained placentas will increase with this method, due to more calf prematurity.

Prostaglandins

Induction of parturition with prostaglandins gives very similar results to induction with short-acting corticosteroids, with a range of 24–72 hours (mean of 45 hours) from treatment to calving. As with short-acting corticosteroids, there is a high incidence of retained placentas and a 10%–20% rate of induction failure when treatments are given within 2 weeks of normal term.¹²

One experiment revealed that cows induced with cloprostenol had a longer interval from appearance of the placental membranes until delivery of the fetus than cows treated with dexamethasone or a combination of dexamethasone and cloprostenol. Compared with cows receiving dexamethasone, cows receiving only cloprostenol had higher concentrations of progesterone at parturition, which may have suppressed uterine contractions.¹²

Corticosteroids and prostaglandins in combination

Hormones used to induce parturition initiate endocrine events normally triggered by fetal cortisol. Corticosteroid injections appear to efficiently remove the placental source of progesterone by inducing enzymes to convert placental progesterone to estrogen. Failure of corticosteroids to induce

parturition may be caused by failure to remove the ovarian source of progesterone. On the other hand, prostaglandin injections efficiently remove the ovarian source of progesterone, but they may fail to induce parturition because of remaining placental progesterone. A combination of the two hormones would remove both sources of progesterone and result in fewer induction failures and less variability in the time from treatment to parturition.

Cows receiving a combination of prostaglandin and dexamethasone calved earlier (25–42 hours after treatment) and the interval from injection to calving was less variable than with dexamethasone alone (29–65 hours) or cloprostenol alone (37–57 hours).¹¹ There were no induction failures with the combination treatment; however, separate dexamethasone or cloprostenol treatments resulted in induction failures of 10.5%–16.6%. The rate of placental retention was significantly higher with all methods of parturition induction than in control cows.

Long-acting corticosteroids, in combination with dexamethasone, and cloprostenol for daylight calving

This combination has been used to induce daylight calving and a low incidence of retained placentas. The main impediments to induction of parturition are the need for known breeding dates, lack of control of the time of calving, and an elevated incidence of retained placentas. Several investigators have made significant progress towards alleviating these impediments.^{7,8} This work is presented here in greater detail to provide readers with a clear understanding of the progress made to date and to provide direction for future research.

Calves that are born within the last 2 weeks of gestation are usually very vital and adjust well to extrauterine life. There is opportunity to develop methods for detecting this safe 2-week period, and to adapt methods of induction that result in early maturation of the placenta and more precise control of the time of parturition. Prediction of the last 2 weeks of gestation could be based on breeding season dates and physical signs in the dam. In an unpublished study using 80 beef cows and heifers done at the Western College of Veterinary Medicine, a scoring system for teat, udder, and vulval changes in late gestation had a positive predictive value of 72% for the last 2 weeks of gestation. However, the predictive value was considered too low to be used to determine a safe induction time. Nevertheless, induction of parturition of 70 cows and heifers by 2 commercial beef producers, after application of the same scoring system and without known breeding dates, resulted in the loss of only 3 calves due to prematurity at birth. Future efforts should likely be directed toward developing an adjunct test to the physical scoring system based on blood endocrine parameters. For example, a chute side test for blood estrogen might be useful to increase predictive values for the last 2 weeks of gestation.

Long-acting corticosteroids for induction of parturition result in the lowest incidence of retained placentas compared to other induction methods. It appears that long-acting corticosteroids more closely mimic the natural gradual rise in fetal

Table 1: Interval from induction to calving, calving to placental release and incidence of retained placenta

Group	n	Induction to calving (hours)	Placental release (hours)	Retained placenta (%)
I OPT	45	–	23.2±8.7 ^{ab}	11
II OPT-DEX	8	34.1 ± 2.6	57.6±3 3.9 ^{bc}	25 ^a
III OPT-DEX + CLO	8	28.3 ± 0.8 ^a	30.2±23.4 ^{ab}	13 ^a
IV DEX + CLO	24	38.1 ± 2.2 ^b	105.8±19.9 ^c	79 ^b
V Control	36	–	13.6 ±5.9 ^a	6 ^a

Values within columns with different superscripts are significantly different (p<0.05)

OPT = optocortenol, dexamethasone trimethyl acetate

DEX = dexamethasone

CLO = cloprostenol

cortisol levels over a sufficient period of time to allow for placental maturation; however, the interval from treatment to calving was highly variable. Cows receiving a combination of dexamethasone and cloprostenol had the least variability in the interval from injection to calving and there were no induction failures. Therefore, an induction regime using a long-acting corticosteroid pretreatment, followed by combined dexamethasone and cloprostenol treatment, might reliably induce parturition for calving in daylight hours with a low incidence of retained placentas.

Several experiments were done to determine the optimum dosages of 2 different long-acting corticosteroids and the optimum time interval from pretreatment with the long-acting corticosteroid and induction with a combined dexamethasone – cloprostenol treatment.^{7,8} The following paragraphs and tables summarize this important work.

Experiment 1

On day 270 of gestation, cows in groups I, II and III received 25 mg of Opticortenol (OPT, dexamethasone trimethyl acetate), a long-acting corticosteroid. Cows that had not calved by day 277 received 25 mg dexamethasone (DEX, Group II) or a combination of DEX and 500 µg cloprostenol (CLO, Group III). Cows in Group IV received only DEX and CLO on day 277. The results are shown in Table 1.

The length of stage II labour, birth weights, and calving difficulty scores were not different between groups. Two calves in group I, 3 in group II, and 1 each in groups III, IV, and V, were considered to be premature based on their size and on the incomplete eruption of their incisors. These calves required assistance to nurse. In the following breeding season, the first-service conception rates and pregnancy rates did not differ between groups; however, first-service conception rates and overall pregnancy rates were lower in cows with retained placentas.

Table 2: Interval from induction to calving, percentage of cows calving between 0700 and 1900 hours, interval from calving to placental release and incidence of retained placenta.

Group	n	Induction to calving (hours)	% calving 0700-1900 (hours)	Placental release (hours)	Retained placenta (%)
High dose 4-day	18	30.8 ± 0.6 ^{bc}	100	87.7 ± 20.0 ^c	67 ^c
High dose 6-day	24	27.8 ± 0.7 ^a	92	29.4 ± 8.2 ^{ab}	29 ^{ab}
Low dose 4-day	12	31.8 ± 0.8 ^c	100	150 ± 24.7 ^d	100 ^d
Low dose 6-day	23	29.0 ± 0.8 ^{ab}	95	47.9 ± 8.1 ^{bc}	57 ^{bc}
Control	22	–	68	16.1 ± 10.7 ^{bc}	5 ^a

Values within columns with different superscripts are significantly different (p<0.05)

High dose = OPT 1mg/25 kg BW (OPT= optocortenol)

Low dose = OPT 1 mg/50 kg BW

4-day = induction with DEX+CLO 4 days after OPT

(DEX= dexamethasone, CLO= cloprostenol)

6-day = induction with DEX + CLO 6 days after OPT

Experiment 2

Cows were assigned, in a 2 x 2 factorial design, to 1 of 4 treatment groups and a control group. On day 270 of gestation cows in the treatment groups received either a high dose (1 mg/25 kg body weight [BW]) or a low dose (1 mg/50 kg BW) of OPT. The cows were further subdivided for induction with DEX+CLO on day 274 (4-day) or day 276 (6-day). Induction treatments were performed at 0900 hours in order to achieve daylight calvings. The results are shown in Table 2.

The length of stage II labour, birth weights, calving difficulty, and calf viability were not different between groups and no premature calves were born in this experiment. Calf immunoglobulin concentrations at 48 hours of age were not different, whether the calves were born to induced cows or to untreated control cows, and there was no increase in neonatal illness in calves born to induced cows. In the following breeding season, the first-service conception rates and pregnancy rates did not differ between groups. However, first-service conception rates and overall pregnancy rates tended to be lower in cows with retained placentas than in cows that did not.

The results of experiments 1 and 2 suggest that the use of a long-acting corticosteroid on day 270 of gestation as a pretreatment for a short-acting induction treatment results in a reduced incidence of retained placentas and no increase in calf losses. The poor predictability of calving time observed in experiment 1, when induction treatments were scheduled at day 277 (7 days after OPT) was overcome in experiment 2, when cows were induced either 4 or 6 days after OPT pretreatment. In experiment 2, 95% of cows pretreated with OPT and induced 4 or 6 days later with DEX+CLO, calved between 0700 and

Table 3: The effect of the day of dexamethasone plus cloprostenol (DEX+CLO) treatment following triamcinolone (TRI) pretreatment (1 mg/60 kg BW) on day 270 on the intervals (h) from DEX+CLO to calving, calving to placental release, and the incidence of retained placenta

Group	n	Day of DEX + CLO	DEX + CLO to calving (h)	Placental release (h)	RP (%)
Ia*	24	275	30.4 ± 0.9	43.4 ± 13.4 ^{bc}	29 ^b
Ib**	1	–	–	6.0	0
IIa*	21	276	30.8 ± 1.0	68.4 ± 19.4 ^c	33 ^b
IIb**	6	–	–	7.7 ± 1.2	0
IIIa*	19	277	29.3 ± 1.0	22.2 ± 9.8 ^{ab}	11 ^{ab}
IIIb**	7	–	–	9.8 ± 1.8	0
Control	24	–	–	6.1 ± 0.8 ^a	0 ^a

Means and percentages within a column with different superscripts are significantly different (P<0.05)

*Cows that calved 24 to 48 h after DEX+CLO

**Cows that calved early (prior to or < 24h after DEX+CLO)

h = hours BW = body weight RP = retained placenta

1900 hours. The interval from treatment to calving was shorter in cows induced to calve with the combination of DEX+CLO after OPT pretreatment than when DEX+CLO was used without the benefit of OPT pretreatment. The OPT dosage and the interval from OPT pretreatment to the DEX+CLO induction treatment are inversely related to the interval from induction to calving and the incidence of retained placenta. For example, cows exposed to higher dosages of OPT for a longer period of time (6 days) had a shorter interval from induction to calving than cows exposed for a shorter period of time (4 days) to either the high or low OPT dosage. In addition, the incidence of retained placenta in the high-dosage, 6-day group was not different from that in the control group.

Two further experiments were designed to determine whether pretreatment with a different long-acting corticosteroid – triamcinolone acetonide (TRI) – before induction of parturition with combined dexamethasone and cloprostenol (DEX+CLO) could be used to reduce the incidence of retained placenta and produce a predictable calving time.⁸

Experiments 3 and 4

In experiment 3, 1 mg/60 kg BW was found to be the optimum dosage of TRI. Experiment 4 was conducted to determine more precisely the optimum interval from pretreatment to induction treatment with the chosen dose of TRI. All cows in groups I, II, and III were pretreated with TRI (1 mg/60 kg) on day 270 of gestation and received DEX+CLO on days 275, 276, or 277, respectively. Group IV cows served as untreated controls. The results are shown in Table 3.

All induced cows calved between 24 and 48 h after DEX+CLO and 94% began to calve between 0700 and 1900, whereas only 58% of control cows began to calve during the same time period. The length of stage II labour, birth weights, calving difficulty, and calf viability did not differ among groups. Overall, none of the early

calving cows had a retained placenta and the mean interval from calving to placental release was not different from the control cows. In the following breeding season, first-service pregnancy rates and final pregnancy rates in cows with retained placentas were somewhat lower than in cows that did not retain their placentas, but the differences were not statistically significant.

The results of these studies support the hypothesis that exposure to elevated blood corticosteroid levels prior to induction with DEX+CLO results in a reduced incidence of retained placenta compared to induction with DEX+CLO alone which, in the same laboratory, resulted in a 61.4% incidence of retained placenta. In addition, it appears that a period of 7 days is required between pretreatment with TRI and induction with DEX+CLO for placental maturation and prevention of placental retention. Unfortunately, this required time period causes some loss of precision in predicting the time of calving after DEX+CLO. Although TRI pretreatment (1 mg/60 kg BW) appears to be near the optimum dose, 18% of cows calved prior to, or <24 hours after induction with DEX+CLO.

Summary

In these experiments, the use of long-acting corticosteroids to induce placental maturation, followed by DEX+CLO to ensure parturition at a predictable time, was quite successful in meeting the goals of calving in daylight, with a low incidence of retained placentas. Work needs to be done to combine this concept of parturition induction with a test to predict the final 2 weeks of gestation in cows without known breeding dates. The level of blood estrogens at the time of induction treatment with DEX has shown a negative correlation with the incidence of placental retention and induction failures. Therefore, estrogen concentrations near term may serve as a useful indicator of placental maturity and the temporal proximity to parturition for subsequent induction of parturition experiments.

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Dr. Barth has stated that he has no disclosures to announce in association with the contents of this issue.

Abstracts of Interest

Induction of abortion in feedlot heifers with a combination of cloprostenol and dexamethasone

BARTH AD, ADAMS WM, MANNs JG, KENNEDY KD, SYDENHAM R G, MAPLETOFT R J

A field trial was conducted to assess the efficacy of a combined prostaglandin F₂ analogue (cloprostenol) and dexamethasone treatment as an abortifacient in feedlot heifers. Heifers were grouped according to stage of gestation as follows: GP1, 1-4 mo, n=37; GP 2, 4-6 mo, n=40; GP3, 6-8 mo, n=40; GP 4, 1-8 mo, n=29. Heifers in groups 1, 2, and 3 received a simultaneous IM injection of 500 µg Cloprostenol and 25 mg Dexamethasone at the time of rectal palpation for pregnancy. Heifers in GP 4 were 1-8 mo pregnant, but received no treatments. Heifers aborting were: GP 1, 37/37; GP 2, 37/40; GP 3, 37/40; GP 4, 0/20. In each of groups 2 and 3 there was one pregnancy and 2 fetal mummies. A combination of Cloprostenol and Dexamethasone induced abortion at all stages of pregnancy.

Can Vet J 1981; 22(3):62-64.

Chemical structure of glucocorticoids and induction of parturition in cattle.

BALLARINI G, BONOMINI S.

IM injection of 145 healthy and diseased pregnant cows with difluoroprednisolone-21-disodium phosphate, a potent anti-inflammatory steroid with a non-substituted C-16, at 10-20 mg per animal on 2-3 occasions at intervals of 2-3 days did not induce abortion nor premature parturition. Abortion did occur in three of the cows, but it was ascribed to their diseased state. It is concluded that the hydrogen at C-16 must be replaced for a corticosteroid to induce abortion in cattle.

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