Antibiotic pre-treatment of flumethasone induced parturition
by David Robert Griswold

A thesis submitted in partial fulfillment of the requirements for the degree of MASTER OF SCIENCE in Animal Science
Montana State University

Abstract:
Two-hundred and thirty-five mature beef cows from the fall calving beef herd on the Montana State Prison Ranch were assigned to one of three induction treatments and one of seven induction groups (trials). Treatments were: Control (TO), 10 mg Flumethasone (FLU) i m injection (Tl) and 10 mg FLU i m plus 20 cc long-acting antibiotic i m which consisted of 2,025,000 units each of procaine and benzathine penicillin G plus 1.63 g dihydrostreptomycin (T2). Cows were assigned randomly according to sire of calf and expected calving dates. Analysis of the results showed injection to parturition intervals for Tl and T2 were 48 and 46 hr, respectively, (P<.10). Induction success was 82% in Tl and 90% in T2. Results showed that no significant difference in response or subsequent performance of cows and calves existed between Tl and T2 except that cows in T2 bearing female calves had a 51% incidence of retained placenta whereas the incidence of placental retention was only 21% for T2 cows bearing male calves and 22 to 23% for Tl cows regardless of calf sex (P<.025). Comparison of induced and control cows revealed reductions in gestation length and birth weight due to FLU treatment.. Mean gestation lengths and birth weights were 284, 279 and 278 days (P<.01) and 39, 33 and 33 kg (P<.01) for TO, Tl and T2, respectively. Incidence of retained placenta was significantly greater (P<.01, P<.05) among induced cows with respective means for TO, Tl and T2 being 5, 22 and 36%. The calving season for induced animals was 11 days shorter than that of the controls. Induced parturition did ' not alter calving difficulty in comparison to controls, nor did it significantly reduce calf vigor or 205-day adjusted weaning weights. Mean adjusted weaning weights were 144, 134 and 140 kg for TO, Tl and T2 calves, respectively. Subsequent fertility of induced and control cows was not significantly different. Mean overall pregnancy rates at the end of the breeding season were 91, 83 and 77% for TO, Tl and T2 cows, respectively. Estrus synchronization with PGF2α enhanced overall fertility in Tl and T2 cows, but reduced overall conception during the breeding season in TO animals (P<.025). In general, induced parturition was shown to have no detrimental effects upon the health or subsequent performance of treated animals.

In presenting this thesis in partial fulfillment of the requirements for an advanced degree of Montana State University, I agree that the Library shall make it freely available for inspection. I further agree that permission for extensive copying of this thesis for scholarly purposes may be granted by my major professor, or, in his absence, by the Director of Libraries. It is understood that any copying or publication of this thesis for financial gain shall not be allowed without my written permission.

Signature David R. Griswold

Date August 6, 1975

ANTIBIOTIC PRE-TREATMENT OF FLUMETHASONE INDUCED PARTURITION

by

DAVID ROBERT GRISWOLD

A thesis submitted in partial fulfillment
of the requirements for the degree

of

MASTER OF SCIENCE

in

Animal Science

Approved:

Edward L. Moody
Chairman, Examining Committee

J. L. Van Horn
act Head, Major Department

Henry L. Parsons
Graduate Dean

MONTANA STATE UNIVERSITY
Bozeman, Montana

August, 1975

ACKNOWLEDGEMENTS

To Dr. E. L. Moody, I wish to express my sincere gratitude for the invaluable advice, guidance, encouragement and personal interest which he has extended to me, not only during this project, but throughout my graduate program. I would also like to thank Dr. James McMillan, Dr. Larry Jackson and Dr. J. E. Catlin for their help in preparing this manuscript.

A heartfelt thanks must go to Mr. Paul W. Lambert for his many hours of help and companionship while gathering the data for this study.

Very special thanks are also extended to Mr. Verne A. LaVoie, Mr. Robert L. Friedrich and Mr. Greg Poncelet for their highly valued and appreciated assistance in the designing and analysis of this experiment.

I would like to thank the Montana State Prison for the use of its animals and facilties and extend a special thanks to Mr. Don Smith for his guidance in management of this study.

A special thanks is due to Mrs. Frankie Larson for her advice and for typing this manuscript.

A very deep and special appreciation must also be offered to my wife, Kelley, without her patience, understanding and encouragement this project could not have been completed.

TABLE OF CONTENTS

INDEX TO TABLES

INDEX TO FIGURES

INDEX TO APPENDIX TABLES

ABSTRACT

Two-hundred and thirty-five mature beef cows from the fall calving beef herd on the Montana State Prison Ranch were assigned to one of three induction treatments and one of seven induction groups (trials). Treatments were: Control (TO), 10 mg Flumethasone (FLU) i m injection (T1) and 10 mg FLU i m plus 20 cc long-acting antibiotic i m which consisted of 2,025,000 units each of procaine and benzathine penicillin G plus 1.63 g dihydrostreptomycin (T2). Cows were assigned randomly according to sire of calf and expected calving dates. Analysis of the results showed injection to parturition intervals for T1 and T2 were 48 and 46 hr, respectively, ($P<.10$). Induction success was 82% in T1 and 90% in T2. Results showed that no significant difference in response or subsequent performance of cows and calves existed between T1 and T2 except that cows in T2 bearing female calves had a 51% incidence of retained placenta whereas the incidence of placental retention was only 21% for T2 cows bearing male calves and 22 to 23% for T1 cows regardless of calf sex ($P<.025$). Comparison of induced and control cows revealed reductions in gestation length and birth weight due to FLU treatment. Mean gestation lengths and birth weights were 284, 279 and 278 days ($P<.01$) and 39, 33 and 33 kg ($P<.01$) for TO, T1 and T2, respectively. Incidence of retained placenta was significantly greater ($P<.01$, $P<.05$) among induced cows with respective means for TO, T1 and T2 being 5, 22 and 36%. The calving season for induced animals was 11 days shorter than that of the controls. Induced parturition did not alter calving difficulty in comparison to controls, nor did it significantly reduce calf vigor or 205-day adjusted weaning weights. Mean adjusted weaning weights were 144, 134 and 140 kg for TO, T1 and T2 calves, respectively. Subsequent fertility of induced and control cows was not significantly different. Mean overall pregnancy rates at the end of the breeding season were 91, 83 and 77% for TO, T1 and T2 cows, respectively. Estrus synchronization with $PGF_{2\alpha}$ enhanced overall fertility in T1 and T2 cows, but reduced overall conception during the breeding season in TO animals ($P<.025$). In general, induced parturition was shown to have no detrimental effects upon the health or subsequent performance of treated animals.

INTRODUCTION

During the past five years, extensive research has been devoted to induction of parturition in the domestic animal species. Numerous reports have been published confirming the effectiveness of the synthetic glucocorticoids, especially Flumethasone and Dexamethasone, and establishing their role as a useful tool in management of livestock reproduction.

In cattle, the primary economic side effect of corticosteroid-induced parturition is a significantly increased incidence of retained placental membranes. In most management situations, antibiotic therapy is recommended for this condition in order to insure good postpartum fertility. Where cattle are being fed supplemental silage or concentrates the antibiotic can be administered through oral preparations added to the ration. In many instances, however, antibiotic therapy requires restraint of the cow and injection of parenteral solutions, which can become a major labor requirement.

This experiment was designed to test the effectiveness of an induction system in which long-acting antibiotic is administered by intramuscular injection at the time of corticosteroid treatment. If effective, this method could elminate the necessity of working the effected cattle a second time and reduce the labor requirements of an induced parturition management scheme.

REVIEW OF LITERATURE

Hormonal Aspects of Parturition

General. Throughout pregnancy in the bovine, plasma progesterone levels remain relatively high, while estrogenic and cortical steroid concentrations are found to be at comparative minimums.

As the full term of gestation is approached, one of the first hormonal changes to occur is that of a decline in plasma progesterone concentrations. Whether or not this decline signifies a reduction in the progesterone synthesis function of the corpus luteum is subject to debate. Although the cow is classified among those species depending upon an ovarian source of progesterone, Turner and Bagnara (1971) report that bovine ovarian function is not essential in the terminal stages of pregnancy and Hafez (1968) describes maintenance of pregnancy in the cow after ovariectomy following the fifth month of gestation.

Diszfalusy, as reviewed by Wagner et al. (1974a) hypothesizes a placental source of progesterone and Jöchle (1971) sites several studies indicating strong involvement of the maternal adrenal as a progesterone source during the third trimester of pregnancy. Hunter et al. (1970) noted mid-cycle levels of plasma progesterone 8 to 13 days postpartum; further suggesting an adrenal progesterone source.

The initial, but gradual, fall in plasma progesterone seems to begin 30 to 34 days prepartum. Hunter et al. (1970) reported a steady drop beginning as early as 34 days before calving in Red Danish and

Holstein cows. Arije et al. (1974) noted a constant decline in progesterone in beef cows throughout the final three weeks of gestation. In contrast, Smith et al. (1973) found no reduction in progesterone levels until three days pre-calving when analyzing blood samples taken from 10 Holstein first-calf heifers. No reason for this variation has been offered.

Despite the conflicting reports concerning initial progesterone decline, these authors are in agreement that a precipitous drop in progesterone occurs 3 to 4 days prepartum and reaches baseline values on or following the day of parturition.

Progesterone levels before and at the time of parturition vary considerably among species and seem to be dependent upon the progesterone source (Wagner et al., 1974a). Those species having a placental progesterone source (sheep and human) have relatively high plasma progesterone levels at parturition while mammals relying on ovarian progesterone (cow and sow) will experience drastic declines in blood concentrations of progesterone at the end of gestation (Wagner et al., 1974a).

Molokwu and Wagner (1973), as reviewed by Wagner et al. (1974a), found plasma progesterone levels to remain constant until 4 to 5 days before farrowing, then dropping abruptly during the final 48 hr in the sow. Killian et al. (1973), as reviewed by the same authors, found much the same relationship, with the rapid decreases beginning

on day -3.

In the sheep, Stabenfeldt et al. (1972) and Thompson (1973), as reviewed by Wagner et al. (1974a), both found that although progesterone levels decline during the last several days prepartum, very low progesterone levels were not reached until as much as 24 hr postpartum and that lambing could occur while fairly substantial plasma progesterone levels still existed. Furthermore, Thompson (1973) showed that ovariectomy of pregnant ewes did not alter progesterone levels, nor did it affect the normal pattern of progesterone decrease seen at parturition.

Anderson et al. (1974) found that placental metabolism of progestigens, when under the influence of high glucocorticoid concentrations similar to the end of gestation, showed an increase of progesterone and pregnenolone catabolism in the ewe. This may partially explain the drop in plasma progesterone seen at that time.

At approximately the same time that plasma progesterone levels begin to descend in the cow, a gradual increase in plasma estrogen concentrations occurs.

Robertson (1974), monitoring individual plasma estrogens in Holstein cows, found plasma estradiol-17$_\alpha$ (E-17$_\alpha$) and estradiol-17$_B$ (E-17$_B$) levels to remain very low until day -19. Plasma estrone concentrations, however, were already 10 times higher than the former estrogens at 40 days before parturition. Parallel rises were seen to

occur in all three of the steroids beginning on day -19.

Plasma estrone and E-17$_B$ levels peaked on the day of parturition reaching levels approximately 20 times those measured on day -40. E-17$_\alpha$ levels peaked on day -4 and then dropped slightly until parturition (Robertson, 1974). The concentration ratio of estrone to E-17$_\alpha$ and E-17$_B$ remained a constant 10:1 throughout the study.

Within 72 hr postpartum, all plasma estrogens had dropped to undetectable levels (Robertson, 1974). Arije et al. (1974) confirmed these results, but Smith et al. (1973) reported precipitous declines in plasma estrogens during the final 2 days before parturition.

Although E-17α concentrations are the lowest of the three plasma estrogens during the final 40 days of gestation (280 pg/ml vs 450 pg/ml (E-17$_B$), 4 ng/ml (estrone)), Hunter et al. (1970) hypothesized it to be the most important of the estrogens. In estrogen excretion studies carried out by these authors, E-17α levels in the urine composed 50% of total urinary estrogens by day -30. At that time, estrone accounted for 44% of total estrogens and E-17$_B$ accounted for the remainder.

At parturition, E-17α levels in the urine had risen to 73% of the urinary estrogens excreted and at 12 hr postpartum it constituted 95% of the total estrogen in the urine. Parallel to Robertson (1974), Hunter et al. (1970) reported bovine urinary estrogens drop to very low levels within 3 days postpartum.

LaVoie and Moody (1973b) used each of the three estrogen compounds

in conjunction with dexamethasone (DEX) in an attempt to reduce incidence of retained placenta resulting from induced parturition. They found that the highest percent response to induction was among those cows which received DEX plus E-17α (100%) and that the response interval among those cows was 11 to 14 hr shorter ($P<.05$) than the estrone and E-17$_\beta$-treated cows. They suggested that this may point to E-17$_\alpha$ as being the most active form of estrogen at the time of parturition.

In the sow, peripheral plasma estrogens (estrone and estradiol) increase substantially during the final week before farrowing. Estrone reaches peak levels 2 days pre-farrowing and remains constant until parturition is completed. Estradiol levels continue to rise until shortly before farrowing. Blood levels of both hormones begin dropping abruptly after parturition and reach baseline values 6 to 7 days pastpartum (Molokwu and Eagner, 1973) as reviewed by Wagner et al. (1974a).

Much later and short-lived rises in plasma estrogens are seen in the ewe. Bedford (1972) and Challis (1971) showed no rise in maternal estrogens until day -3 to -2. Peak levels lasting from 4 to 48 hr were seen around the time of lambing and baseline levels were reached again by 48 hr postpartum.

Austin and Short (1972) described strong involvement of the fetal liver and adrenal glands in placental estrogen production in

the human. Basically, they suggest that maternal cholesterol or pregnenolone is converted into progesterone by the placenta. Progesterone reaching the fetus is converted in the fetal adrenal to adrenocortical steroids and several androgens including dehydroepiandrosterone sulfate (DHAS). The fetal liver adds a hydroxyl group to the DHAS before it is returned to the placenta. Final conversion into estriol, the primary human estrogen, occurs in the placenta. The placenta synthesizes smaller quantities of estradiol-17_B and estrone from the C_{19} androgen precursors.

Evidence for maternal adrenal involvement in estrogen synthesis for the human comes from Siiteri and MacDonald (1966), as reviewed by Wagner et al. (1974a), who estimated that 40% of the precursors for placental estradiol production was DHAS originated in the maternal adrenal. According to the same authors, placental estrone was produced from precursors, half of which were of maternal origin, the other half being of fetal origin. Reports substantiating this showed low estrogen concentrations in plasma of pregnant adrenalectomized women. Sixty mg dosages of DHAS given to these women near term significantly increased estrone and estradiol production (Charles et al., 1970), and Guipide and Vande Wiele (1971) as reviewed by Wagner et al. (1974a).

Adrenalectomy of the pregnant ewe also resulted in reduced estradiol and estrone levels during the final 10 days of gestation

and lower peak levels of these hormones at parturition, suggesting that maternal adrenal function is involved in estrogen sythesis (Thompson, 1973), as reviewed by Wagner et al. (1974a). Similar reports for the cow have not been found by the author.

In many species, progesterone acts to reduce the excitability and contractility of uterine muscle (Austin and Short, 1972). Estrogen, on the other hand, at elevated levels seems to increase activity of myometrial tissue. As the estrogen:progesterone ratio increases, Marshall (1959) noted increased responsiveness of myometrial cells to stimuli as well as development of rhythmic pacemaker activity resulting in regular, productive contractions of the uterine wall.

Roberts and Schare (1969) demonstrated that vaginal distention of estrogen-treated non-pregnant ewes caused increased oxytocin release whereas vaginally stimulated progesterone-treated animals showed a greatly depressed level of oxytocin release.

This so-called "progesterone block" on oxytocin may exist at the hypothalamic, as well as the myometrial level, Wagner et al. (1974a). Jochle (1971) referred to the existence of the progesterone block effect in cattle, but discounted its existence in sheep and expressed considerable doubt concerning the importance of its role in the sow.

Evans (1971) showed cows failing to respond to dexamethasone-induced parturition had plasma progesterone levels twice as high as those cows responding when both groups were tested 24 hr postpartum. Again in 1973, Evans showed cows failing to respond to DEX-induced parturition had significantly higher blood progesterone levels than responding cows at the time that the responding cows were giving birth (reviewed by Wagner et al., 1974a).

Jöchle (1972) successfully prevented flumethasone-induced parturition by giving 100 mg progesterone injections daily starting 3 days before and ending 5 days after injection of flumethasone. Resultant calving did not occur until 4-5 days after the progesterone treatment was ended. Among the cattle responding to the corticoid despite progesterone therapy, all experienced dystocia and 50% of the calves were stillborn.

The change from progesterone to estrogen dominance, at least in the cow, is an important, if not essential, step in readying the uterus for expulsion of the fetus.

Several days prior to parturition in many of the domestic animals, plasma corticosteroid levels begin to increase. In the cow, fluctuations cease and a steady rise begins on day -5 (Arije et al., 1974) or day -4 (Adams and Wagner, 1970) and reaches a peak at parturition. Smith et al. (1973) found no corresponding increase until day -1 in Holstein heifers. The reason for the discrepancy is not mentioned.

Jöchle (1971) suggests that this corticoid rise may not be entirely due to corticoid production by the maternal organism. Work cited by Jöchle (1971) has shown that although maternal corticosteroids cannot pass the placenta to the fetus during most of gestation, fetal corticoids can be passed across the placenta to the dam.

In the ewe, at least, Wagner et al. (1974a) found fetal corticoid levels to increase 4 to 6 days prepartum. No concommitant rise was seen in maternal blood levels, however. It is not known whether reports have been published which challenge Jöchle's theory for other species.

It is widely believed now that corticosteroid production by the fetal adrenal is the trigger signalling the proper time for parturition in many species. Further discussion of this subject will be taken up in the next section which deals with induced parturition.

Several possibilities have been suggested to explain the increase in fetal corticoid production. Wagner et al. (1974a) theorized three possible stimuli: Maturation of the fetal hypothalamic centers; maturation of vital tissues and organs e.g., lung, liver, kidney, possibly in combination with hypothalamic maturation; or new stresses on the fetus.

Gwazduskas et al. (1974) showed that administration of 3 mg estradiol-17_B in dairy heifers during the luteal phase of the estrous cycle caused a decrease of .3 to .8° C in the temperature of the

uterus. Similar changes near term would present the possibility of thermal stress on the fetus.

Wagner et al. (1974a) cited the work of Comline and Silver (1970) in which fetal lamb blood pH, gas tensions, glucose, fructose and lactic acid levels were monitored. Beginning 2 to 4 days before birth, declining fructose levels indicative of early placental failure were noted, thus proposing the possibility of nutritional stress on the fetus.

Plasma corticoid levels are seen to rise at a very late stage in the sow. Killian et al. (1974) demonstrated a cessation of diurnal rhythms and steady rise only during the final 24 hr before farrowing. Peak levels occurred at parturition and then dropped sharply.

Maternal corticoid levels in the ewe follow a pattern very similar to the sow with increases beginning during the final 24 to 48 hr of gestation (Wagner et al., 1974a).

In the sheep and goat, one of the last hormonal changes to occur in association with parturition is that of an increase in plasma prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) concentrations (Thornburn et al., 1972).

Monitoring of uterine vein blood in the ewe showed a rise in plasma estrogens 30 hr prepartum followed in 10 hr by increased $PFG_{2\alpha}$ levels (Challis et al., 1972). Furthermore, administration of progesterone followed by estradiol elicits a similar $PGF_{2\alpha}$ rise in the ewe (Challis et al., 1972). Flint et al. (1973) found similar effects

from exogenous estrogen and also reported simultaneous rises in utero-ovarian vein estrogens and PGFa concentrations 4 to 36 hr prepartum. This same group, using manual cervical stimulation per vaginum 24 hr before lambing, was able to evoke large utero-ovarian venous surges of PGF in 6 out of 11 tests. These results suggest a similar response may be elicited by cervical stimulation by the fetus.

Jöchle (1971) proposed that prostaglandins seem to be the hormones directly responsible for uterine contractions resulting in labor and delivery and that oxytocin plays only a secondary role. Zerobin et al. (1973); inducing abortion and early parturition in Brown Swiss cows and heifers with PGE_2 and $F_{2\alpha}$, found that strong uterine contractions comparable to those recorded at parturition were evinced 20 to 45 minutes post-injection. These contractions vanished, however, and parturition did not usually occur for several days.

In a similar study (Lamond et al., 1973) found no such contractions were witnessed in response to $PGF_{2\alpha}$ treatment of first trimester heifers. The discrepancy between these reports may be the result of a lack of uterine sensitivity to prostaglandins during the first trimester of pregnancy, as Zerobin et al. (1973) tested only animals in the second and third trimesters.

Vandeplassche et al. (1974) hypothesized the effectiveness of $PGF_{2\alpha}$ for terminating pregnancy in the bovine lies in its luteolytic potency.

In various species, prostaglandins E_2 and $F_{2\alpha}$ have been shown to have effects which include: Stimulation of the myometrium; luteolysis; stimulation of oxytocin release from the posterior pituitary; and initiation of estrogen synthesis in the placenta (Wagner et al., 1974a) In the bovine, the role of prostaglandins and parturition is not yet defined.

Oxytocin levels in the cow and ewe remain unchanged even through labor and rise only during delivery, at which time peak levels are reached. Decline is rapid and immediately follows fetal expulsion (Chard, 1972) as reviewed by Winter (1974).

Serum prolactin levels also remain low until the last 1 to 2 days of gestation (Ingalls et al., 1973), as reviewed by Winter (1974). At that time, concentrations increase sharply, peaking 24 hr prepartum.

Induction of Parturition with Corticosteroids

General. Evidence has mounted over the past 10 years which strongly indicates that, in many species, the signal to end pregnancy and begin the birth process comes from corticosteroid production by the fetal adrenal. Maturity of the fetus alone, or in combination with intrauterine stresses (Wagner et al. 1974a) which prompt the fetal pituitary-adrenal axis into action initiates production of adrenal corticosteroids.

Findings which support this theory are numerous. In humans, fetuses aborted for no diagnosed reason are found to have significantly

heavier adrenals than fetuses aborted due to diagnosed conditions unrelated to adrenal conditions (Anderson et al., 1971). Anencephalic fetuses, which possess degenerated or severely underdeveloped brains (Arey, 1965), are generally associated with prolonged gestations (Pokoly, 1973). Cyclopic lambs, resulting from maternal ingestion of Veratrum californicum often lack functional pituitaries and suffer from adrenal dysfunction. Associated gestations are typically extended well past normal term (Wagner et al., 1974a).

Holm (1967), studied the prolonged gestation syndrome in Guernsey and Holstein cattle and noted that affected calves, once removed from the dam (at the end of normal gestation periods), exhibited marked hypoadrenalism and could not survive independently of replacement therapy.

In essence, the associated facts show that hyperadrenalism in the fetus is often associated with early termination of pregnancy and hypoadrenalism is strongly linked with prolongation of the gestation period in cattle, sheep, humans and probably other species as well.

Wagner et al. (1974a), in their review of artificially altered gestations in the sheep, cited studies by several teams of researchers (Liggins et al., 1966, 1967 and Drost and Holm, 1968) which showed that inhibition of fetal adrenal function before day 134 of gestation lengthened gestation and/or prevented parturition. Stimulation of the fetal adrenal shortened the time until parturition.

In the cow, Adams and Wagner (1970) report ACTH injections were found to depress formation of the corpus luteum. Jöchle (1971) noted that corticosteroids seem to shut off sources of progesterone in the corpus luteum (CL) and the adrenal in the pregnant cow and Carroll (1974) also suggested that corticoids may cause decline of the CL's function.

In the 1960's, veterinarians and many researchers found that glucocorticoid therapy in ruminants often resulted in premature parturition when the animals being treated were in later stages of pregnancy (Jöchle, 1971).

The ability of a particular corticoid to induce premature parturition in the sheep was shown to depend on its biological acitivity (Liggins, 1969). Mineralocorticoids such as deoxycorticosterone and corticosterone would not induce labor whereas glucocorticoids such as dexamethasone, when given at comparable times to the fetus or the dam produced the desired parturition. Furthermore, administration of a mineralocorticoid with dexamethasone did not shorten the interval to response in comparison to dexamethasone treatment alone (Liggins, 1969).

Three effective glucocorticoids are mentioned by Jöchle (1971): Betamethasone, dexamethasone and flumethasone. Of the three, dexamethasone and flumethasone are commonly used in the United States (Winter, 1974). Flumethasone is the most potent of the three; having an activity 4 times greater than dexamethasone (Jöchle, 1971). All three of the efficacious compounds have a methyl or hydroxyl substitution at

the 16_{α} position (Jöchle, 1973).

Jöchle (1973) describes two major types of induced parturition. The first type, premature parturition, involves delivery of a live fetus, but extrauterine survival is often dependent upon special care by those attending the offspring. The second type, precocious parturition, also occurring before term, produces a live fetus which is capable of survival without any further attention. In cattle, both types of parturitions can be induced, although the precocious variety is more easily evoked and seems to be more reliable (Jöchle, 1973).

Premature parturition in the ewe can be induced only by glucocorticoid infusion of the fetus on or later than day 100 (Liggins, 1969). Treatment of the ewe does not result in parturition until approximately two weeks preterm (Jöchle, 1973 and Skinner et al., 1970) or day 136 (Lindahl and Terril, 1974).

Both gilts and sows have been shown to respond to dexamethasone with precocious parturition near term (North et al., 1972) and First and Stagmiller, (1972). However response is not elicited using dosages of 10 to 20 mg, which would be effective in cattle and sheep (Rich et al., 1972). Response in gilts occurred at dosages of 75 mg/day on days 101 through 103 (North et al., 1972) and sows farrowed after receiving 100 mg DEX/day on days 101 through 104 of gestation (First and Stagmiller, 1972). No minimum effective dosages were mentioned.

Dosages similar to those required by the sow are found to be

necessary for induction in the mare. Alm et al. (1972) showed 100 mg DEX/day for four days beginning on the 18th day prepartum would cause precocious parturition in all horses treated. No difficulties were noted in parturition and foals were normal in all respects except for a reported weakness in the fetlocks which disappeared after the first week of age.

A general tendency noticed in all species is an increased sensitivity to glucocorticoid induction as treatment is scheduled closer to term (Jöchle, 1973).

The corticosteroids discussed in this section all have important side effects which must be carefully considered when deciding upon their use for induced parturition.

Corticoids, as a group, are suppressors of the inflammatory responses of the body. Vascular permeability is reduced, as is exudation and inflammatory cell migration (Carroll, 1974). In addition, corticosteroids reduce the production of lymphocytes which further reduce the body's ability to produce an inflammatory response to injury and infection (Guyton, 1971). Fever and symptoms of toxemia may also be suppressed and a general feeling of well-being and an increased tolerance to pain developed. Poor appetite, lethargy and fevers indicating the presence of infection in the animal may thus be disguised (Carroll, 1974).

The overall picture is one of reduced defense against disease or

infection due to injury and a possible reduction of symptoms for a pathological condition which already exists.

Carroll (1974) also brings out the point that some work (Sheffy and Davies, 1972) has shown corticosteroids to allow reactivation of latent viral infections, in this case, infectious bovine rhinotracheitis (IBR). This same effect could certainly apply to latent and chronic bacterial infections, as well.

Carroll (1974) suggests that whenever suspicions of latent or undetected disease exists in a herd, corticoid therapy should be withheld until diagnosis has been completed. Use of corticoid drugs in a herd where disease is known to exist should be weighed carefully against the possible consequences, especially in the case of viral diseases where no specific anti-viral drugs are available.

In the bovine. Responsiveness of the cow to glucocorticoid-induced parturition is very time dependent. Administration of flumethasone to the pregnant heifer during the first trimester of pregnancy evokes no abortion. Estrogen treatment during the same period of pregnancy, however, will affectively terminate pregnancy (Jöchle, 1973).

During the second trimester, estrogen sensitivity per se is lost and responsiveness shifts to a combination of estrogen and glucocorticoids. Jöchle (1973) theorizes that this is a protective mechanism against early abortion resulting from rising maternal estrogen

levels at this time.

Estrogens are of no value for inducing parturition during the third trimester of a normal pregnancy, but response to glucocorticoids is generally good, with best results being obtained near the end of gestation (Jöchle, 1973 and Winter, 1974). Jöchle proposed that parturition is triggered by a rise in fetal and maternal corticosteroids with the requirement of a functional placenta.

Of considerable interest are the findings of Vandeplassche et al. (1974) concerning termination of pathological pregnancies in cattle. Cases of hydrops allantois or amnion in which a live fetus was involved, were successfully terminated with corticoids although parturitions were sometimes slow and accompanied by insufficient dilation. Cases of fetal mummification did not respond to corticoids, however diethylstilbestrol (DES) or intrauterine infusion of $PGF_{2\alpha}$ caused luteolysis and fetal expulsion. Finally, where fetal maceration with associated uterine damage was involved, DES proved effective only where uterine damage was minimal and $PGF_{2\alpha}$ was successful as long as uterine condition was sufficient for fetal expulsion.

Vandeplassche et al. (1974) concluded from these results that parturition is primarily a response to increased $PGF_{2\alpha}$ levels and resultant myometrial response in the bovine. Furthermore, corticosteroids mediate their effect through stimulation of the fetal-placental unit to increase estrogen synthesis which, in turn, increases

endometrial $PGF_{2\alpha}$ production. Thus they require a live fetus and a functional placenta. According to the same authors, estrogens induce parturition by stimulating endometrial $PGF_{2\alpha}$ production which requires relatively healthy uterine tissue, but does not rely on placental function.

The blood hormone levels seen during induced parturition in the cow are relatively the same as in natural births. Plasma progesterone levels drop sharply after corticoid administration. Estrogens rise sharply, but drop equally as fast and there is an absence of the marked rise in plasma corticoid levels usually seen 48 hr prepartum (Jöchle, 1973). LaVoie (personal communication) felt that the low corticoid levels reported may be the result of an inability of the assay method to detect the synthetic exogenous corticosteroids in the blood at the same time with the endogenous maternal corticoids.

Corticosteroid-induced parturition has been accomplished in the bovine as early as day 246 of gestation (Adams and Wagner, 1970). Although response does occur at this early time, there is a general reduction in calf viability, especially in births occurring before day 260 (Carroll, 1974). It has been found that results are generally most satisfactory when births occur on or later than day 270 since no reduction in calf vigor is encountered at this time and response to corticoid treatment is relatively rapid (Carroll, 1974).

Minimal effective dose levels (single injection) for dexamethasone and flumethasone seem to be 8 and 5 mg, respectively (Bosc, 1971 and

Brown et al., 1971), as reviewed by Carroll (1974). This varies, however, according to how far from term the treatment is given (Winter, 1974).

Winter (1974) found no difference in response between intramuscular and intravenous administration of dexamethasone. Hagg and Schlitz (1973), as reviewed by Carroll (1974), induced parturition with intramammary infusion of 10 mg dexamethasone per quarter.

When parturition is induced on or later than day 270 of gestation, calving difficulty generally is not increased in comparision to natural birth and in some instances of overly large fetuses, may even be decreased (Carroll, 1974 and Winter, 1974).

Aside from reduced birth weight of induced calves, performance of the offspring is not altered and comparison of weaning weights shows no significant difference between induced and non-induced calves (Winter, 1974 and LaVoie and Moody, 1973a).

The most commonly encountered disadvantage presented by induced calving is the highly significant increase in the incidence of retained placental membranes. Although unsightly, no real harm results from this condition when systemic or intrauterine antibiotic therapy is given to the affected animals and no attempt is made at manual cleansing of the uterus (LaVoie and Moody, 1973; Jöchle, 1971; Wagner et al., 1974a; Carroll, 1974).

The majority of experiments reported show no decrease in subsequent fertility resulting from retained placenta (LaVoie and Moody, 1973a;

Wagner et al., 1974b and Poncelet, 1974). Lauderdale (1972) showed no difference in postpartum fertility even when antibiotic therapy was withheld following placental retention.

Attempts to reduce the occurrence of placental retention with estrogen treatments 6 days before through 1 day following corticoid injection (LaVoie and Moody, 1973b) and with 100 mg progesterone 3 days prior through 5 days post-injection (Jöchle, 1972) proved to be fruitless. Jöchle (1973) lowered the number of retained placentas with the use of a "long-acting" corticoid suspension, however, response intervals were significantly increased and the number of stillbirths was also greater.

A possible decrease in milk production due to induced parturition was studied by Beardsley et al. (1974) in Holstein cows. No significant difference in yield was found between induced and control cows, however, the treated group did have slightly lower production. When comparison of lactations was made starting on day 280 of gestation, thus standardizing the treatments and controls, no difference was found in milk production. The same authors also found that milk yield of induced cows during the next lactation was higher than that in the lactation subsequent to the induced parturition. Milk composition between the two groups was identical except for casein levels which were slightly higher in the control cows. No difference in colostrum composition was found (Beardsley et al., 1974).

Induction of Parturition with Prostaglandins

Results of recently published induced parturition studies employing certain of the prostaglandins have established their effectiveness in several of the domestic animal species.

In the bovine, Lamond et al. (1973) have induced abortion during the first trimester of pregnancy using $PGF_{2\alpha}$. Zerobin et al. (1974) have successfully terminated pregnancy during the second and third trimesters with both PGE_2 and $F_{2\alpha}$ injections. The same authors report parturitions to be uncomplicated, however the typical signs of approaching parturition i.e., vulvar edema and pelvic relaxation are absent. Swelling of the udder is reported to occur rapidly following PG injection and calf survival is good (Zerobin et al., 1974) when birth occurs later than 260 days gestation.

$PGF_{2\alpha}$, while inducing parturition in the ewe, does not seem to be as effective as the corticosteroids. Harman and Slyter (1974) reported induction success of only 33% in ewes treated with $PGF_{2\alpha}$ versus 87% responding to flumethasone when both compounds were administered on day 141 of gestation. The same authors reported that response intervals for the flumethasone-treated ewes were also significantly shorter.

Currie and Thorburn (1974) have shown efficacious results with $PGF_{2\alpha}$ in the goat.

Gilts receiving 10 hr infusions of 2.1 mg $PGF_{2\alpha}$ 5 to 7 days

prepartum gave birth 29± 2 hr after the start of the infusion. Gestation lengths and response intervals were shortened in comparison to saline-infused controls. All gilts displayed abundant colostrum at farrowing and survival of piglets was good for both groups (Diehl and Godke, 1974).

At the end of the 10 hr $PGF_{2\alpha}$ infusion, plasma progesterone levels of the treated gilts had dropped to one-thrid of orginal values whereas no change was seen for controls. Saline-infused gilts displayed elevated plasma cortisol levels by the onset of parturition, but no corresponding change was seen in the $PGF_{2\alpha}$ group (Diehl and Godke, 1974).

MATERIALS AND METHODS

Two-hundred and thirty-five mature Hereford and Hereford cross-bred beef cows were divided into three treatment groups: Controls (TO), and two induction treatments, T1 and T2. Cows in treatment 1 (T1) received a 10 mg injection of Flumethasone[1] i m 6 to 12 days before expected calving date. Any TO or T1 cows having retained placental membranes 24 hr postpartum received a 20 cc injection i m of long-acting broad spectrum antibiotic containing 2,025,000 units each of procaine and benzathine penicillin G plus 1.63 g dihydrostreptomycin. Treatment 2 (T2) cows received identical dosages of Flumethasone and antibiotic, but the antibiotic was administered at the time of Flumethasone injection. Therefore all T2 cows received antibiotic therapy regardless of their postpartum condition. T2 cows received no further antibiotic treatment unless illness at a later date warranted it.

Seven induction trials were carried out during the fall 1974 calving season. Cows were randomly assigned to treatments and to induction groups (G1-G7) according to their expected calving dates and the bull to which they were bred. Expected calving dates were calculated using a 285-day gestation length and the known or estimated date of conception as determined by breeding records and pregnancy test data gained from rectal palpation. To induction group seven (G7) were added all unassigned cows which had not yet calved and were determined to be carrying full-term fetuses. Each one of these cows

[1](Flucort Solution Veterinary, a product of Diamond Laboratories, Inc.).

was then randomly designated to one of the three treatments.

Induction trials were scheduled to begin every seven days and each of the seven groups was composed of animals due to calve during the seven day time period 6 to 12 days following the Flumethasone injection. This schedule allowed induction of parturition to occur, in responding cows, from 4 to 10 days before their expected calving dates.

Beginning approximately 24 hr post-injection, T1 and T2 cows were observed every 2 hr for signs of approaching parturition and dystocia. The observation schedule for T0 animals was on a 4 to 6 hr interval.

Control animals were kept on pastures ranging in size from 300 to 640 acres throughout the calving season. T1 and T2 cows in each induction group were gathered out of the fall herd at the beginning of the week in which they were scheduled to be treated. Except for those T1 and T2 cows in G1, which were turned back out on pasture with the rest of the herd, all T1 and T2 cows were confined within a one-half acre corral. This period of confinement lasted from 1 day prior to treatment until 24 to 48 hr postpartum depending on the condition of the cow and calf. At 24 hr after calving, examination was made for presence of retained placental membranes and antibiotic therapy was given to those T1 cows requiring it.

Any T1 or T2 cows not calving within 96 hr after Flumethasone injection were pregnancy tested and those found to be pregnant full term were considered as having failed to respond to treatment.

Failures in T1 were designated as T3 cows and those not responding in T2 were designated T4 so that in subsequent data analysis they could be compared as distinct and separate treatment groups.

Date of birth was recorded for all animals and time of birth was also recorded for T1 and T2 cows. Calving difficulty was noted and scored on a scale from 1.0 to 4.5. Normal, or physiological birth was 1.0; mild dystocia requiring manual assistance was scored as 2.0; 3.0 designated difficulty necessitating mechanical traction and births which required surgical procedures for delivery of the fetus were scored as 4.0. An additional .5 was added to the score of any delivery accompanied by a fetal malpresentation.

Inspection 24 hr postpartum and again 5 to 7 days after calving was made for the presence of visibly retained placental membranes and the findings were noted for every cow. T0 and T1 cows having retained placenta received antibiotic therapy 24 hr postcalving. No further treatment was administered unless subsequent developments warranted it. No intrauterine manipulation or treatment was attempted.

Sex of calf and birth weight were recorded. Vigor at 24 and 48 hr of age was scored on a scale of 1 to 3 with a normal-to-vigorous calf receiving a score of 1, a weak calf receiving a score of 2 and 3 designating an extremely weak or dead calf. Weakness was judged on a comparative basis using general altertness, amount of activity and length of time passing before the calf first rises to suckle as the basic criteria for comparison.

Approximately one-third of all calves received a 2 cc i m injection of a commercially available vitamin A, D and E preparation soon after birth. This treatment was given to every calf receiving an even numbered ear tag (every other calf) and began approximately one-third of the way through the calving season. Analysis was later done to compare adjusted 205-day weaning weights of the A, D and E treated calves against the non-treated calves.

The subsequent breeding season was begun 45 days after the calving season ended and lasted for a total of 48 days. Breeding was done by artificial insemination for the first 28 days and by natural service for the remaining time. Semen was supplied by American Breeder's Service, DeForest, Wisconsin. Imposed upon the AI season were two Prostaglandin $F_{2\alpha}$($PGF_{2\alpha}$) estrus synchronization trials. The first trial utilized cows calving during the first half of the calving season and the second trial was done with cows from the second half. Animals were randomly assigned to the $PGF_{2\alpha}$ control or treatment groups according to age, sex of calf, induction treatment in the previous calving season and, as mentioned earlier, date of calving.

Control cows were gathered when found to be in standing estrus and bred 12 hr later. Cows receiving $PGF_{2\alpha}$ and responding with standing estrus before 72 hr post-injection were bred identically to the controls. Those treated cows not found in estrus by 72 hr post-treatment were gathered as a group and bred approximately 80 hr after receiving the injection.

Forty-five days following termination of the breeding season, all cows were gathered and pregnancy tested by means of rectal palpation. On the basis of breeding records from the AI season and estimation of fetal age, sire and conception date were determined. Cows were then scored as being pregnant or open and also as being AI or bull bred.

Calves were weaned at approximately six months of age and weighed. Their adjusted 205-day weaning weights were then calculated.

Gestation lengths were calculated for each cow having a known conception date and injection to parturition intervals were computed for all T1 and T2 animals responding to treatment.

Mean values for injection to parturition intervals, calving difficulty, percent incidence of retained placenta at 24 hr and 7 days postpartum, calving date, gestation length, calf vigor at 24 and 48 hr of age, calf birth weight, percent of cows pregnant to AI, overall percent pregnant to the subsequent breeding season, and actual and adjusted 205-day weaning weights were analyzed in respect to effects of induction treatment, induction group, calf sex, sire, $PGF_{2\alpha}$ treatment (for subsequent fertility analysis), and significant main effect interactions. The one exception to this was the analysis of the T3 and T4 groups. Since there were very few animals in T3 and T4 and the cows were not distributed across all groups and sires, analysis was made by calculation and comparison of arithmetic means for the measured parameters.

To analyze sire effects in the data, cows were grouped according to sire of calf. As a result, five groups were formed. B1 and B2 consisted of cows pregnant to each of the two Simmental AI sires, B3 and B4 cows were those conceiving to the two Polled Hereford AI bulls, and B5 animals were those cows bred to one of the 15 bulls used for natural service during the last 20 days of the fall 1973 breeding season. B5 bulls were primarily Hereford and Hereford-Simmental crossbreds.

All data, except mean percent response to treatment, were analyzed by the method of least squares means (Harvey, 1960). Where analysis of variance showed significant differences, further analysis was carried out using the Student-Newman-Keuls test to determine where the real differences existed and these were then reported.

Significant correlations were determined by analysis of correlation coefficients using Table A.11 from Statistical Methods, Snedecor and Cochran, 1967.

RESULTS

Induced Parturition

Response. A combined analysis across all seven induction groups showed the mean percentage of cows in T1 and T2 which responded to treatment by calving within 96 hr post-injection to be 82.3 and 89.7%, respectively. The highest response rates were obtained in group 7 (G7) where 94.4 and 100% of the cows in T1 and T2, respectively, calved following injection. Response was lowest in G4 with only 50% (4/8) and 57% (4/7), respectively, of T1 and T2 cows having induced births (tables 1, 3).

Injection to parturition interval. Least squares means analysis of injection to parturition intervals was carried out to test for significant differences due to main effects i.e., induction treatment, induction group, sex and sire of calf, and included all animals responding to treatment with induced parturition. Mean response intervals for T1 and T2 were 48.2 and 46 hr, respectively, and were not significantly different ($P>.10$). Differences due to calf sex were also at the $P>.10$ level of significance (tables 1, 3, 5).

Among induction groups, the injection to parturition interval ranged from 36 hr in G7 to 58 hr in G3 ($P<.005$). Group 7 cows had a mean response interval significantly shorter than all other groups ($P<.10$, $P<.05$, $P<.01$), except G4. Mean response interval for G3 cows, although the longest, was significantly longer than only G7 ($P<.01$), G4 and G1 ($P<.05$), (table 3).

Cows bred to the Simmental AI sires (B1, B2) and the natural service bulls (B5), many of which were Simmental crossbreds, had significantly longer response intervals ($P<.10$, $P<.05$ and $P<.01$) than did the cows bred to the Polled Hereford AI sires (B3, B4). No real differences existed between the two groups of Simmental bred cows, or between the Simmental and natural service bred groups ($P<.10$), (table 6).

Even though cows in G7 had the shortest injection-parturition interval, analysis of all seven groups showed a positive correlation between date of calving and length of response interval ($r=.4827$, $P<.01$). Among cows responding to Flumethasone treatment, longer response intervals were associated with increased incidence of retained placental membranes at 24 hr postpartum ($r=.2377$, $P<.05$), (table 2).

Calving difficulty. The mean calving difficulty score for the entire fall herd was a very low 1.06 on a scale of 1.0 to 4.5. No significant differences were found among any sets of main effects (treatment, group, sex of calf and sire). Calving difficulty was affected by the day of the calving season on which birth occurred. Births early in the calving season were accompaned by a higher degree of difficulty than were those occurring late in the season ($r=.1594$, $P<.05$).

Increased calving difficulty was also associated with depression of calf vigor at both 24 and 48 hr of age. Correlation coefficients for calving difficulty and calf vigor scores at 24 and 48 hr of age were $r=.2471$ ($P<.01$) and $r=.1859$ ($P<.05$), respectively.

Retained placenta. The incidence of cows suffering from retained placental membranes was considerably higher among the induced cows than the controls ($P<.025$) and was highest in the T2 animals. Mean percent retained placenta at 24 hr was 5.2, 22.4 and 35.9 for TO, T1 and T2, respectively. Differences between T1 and T2 were at the $P<.10$ level of significance, (table 1).

Analysis also showed the existence of a treatment x sex interaction ($P<.025$), but no real differences in placental retention due to sex of calf alone. Treatment 2 cows bearing heifer calves showed a least squares mean incidence of retained placenta 30% greater than T2 cows bearing males, 29% higher than all T1 cows and (an average of) 45% higher than the TO cows, (table 9).

The effect of treatment and the treatment x sex interaction disappeared when analysis was done on the incidence of retained placenta 7 days postpartum. Significant variation was found only among induction groups ($P<.05$), with G1 having the highest incidence (14%) and differing significantly from all groups ($P<.01$, $P<.05$, $P<.10$) except G6, (table 3).

A positive correlation was found between occurrence of retained placenta at 24 hr and at 7 days ($r=.3408$, $P<.01$).

Calving date. Cows responding to Flumethasone treatments had mean calving dates significantly earlier in the calving season than did controls ($P<.001$). Both T1 and T2 had a mean calving date of day 255, while the mean for TO was day 260, (table 1).

An increase in calf birth weight and vigor was associated with later calving dates. The correlation coefficient for birth weight was .2102 ($P<.05$) and was -.1553 ($P<.05$) for calf vigor score at 24 hr of age. Cows having long gestation periods were also found to have later mean calving dates as a group ($r=.9444$ ($P<.01$)), (tables 1, 3).

Gestation length. Analysis of gestation length by the method of least squares means showed a strong effect of induction treatment. T1 and T2 cows had respective mean gestation periods 5 and 6 days shorter than that of T0 animals, with means for T0, T1 and T2 being 284, 279 and 278 days, respectively, ($P<.001$). T0 was significantly longer than both T1 and T2 ($P<.01$), but no significant variation existed between T1 and T2 ($P<.10$), (table 1).

No effect on gestation length due to induction group was found (table 3).

The data were then reanalyzed excluding T1 and T2 animals to test for real differences in gestation length due to sex of calf or sire effects. Among cows having normal (not induced) births, sex of calf had no real effect on the length of the gestation period ($P>.10$). However, respective mean gestation lengths for pregnancies involving male and female calves were 283 and 285 days and analysis of variance showed the difference to be very close to the $P<.10$ level (table 5).

Among cows grouped according to sire of calf, those bred to bull 3, a Polled Hereford AI sire, had the shortest mean gestation length.

B3 cows had shorter gestations than both the Simmental-bred groups ($P<.01$), the other Polled Hereford group (B4) ($P<.05$), and the natural service-bred group of cows ($P<.05$). No differences existed among any of the other four groups ($P>.10$), (table 6).

Among controls and those cows not assigned to any treatment group, gestation length was significantly correlated to calving difficulty; the relationship being that those cows having naturally shorter gestation periods experienced a greater amount of calving difficulty ($r=-.2448$, $P<.05$). This relationship did not exist, however, among cows in T0, T1 and T2.

Across the three induction treatments, reduced gestation lengths caused a reduction in calf vigor, i.e. an increased vigor score. Correlations between gestation length and vigor scores at 24 and 48 hr, respectively, were -.2288 ($P<.01$) and -.2392 ($P<.01$), (table 2).

A positive correlation was also found between gestation length and birth weight ($r=.2235$, $P<.05$).

Calf Performance

Vigor. Analyses across all treatments and across only T0 and unassigned cows showed no significant differences among any set of main effects for calf vigor scores both at 24 and 48 hr of age. Mean vigor scores for 24 and 48 hr, respectively, across all treatments and groups, were $1.1\pm.3$ and $1.1\pm.5$ on a scale of 1 to 3, (tables 2, 4, 5 and 7).

No interactions among main effects existed which had any influence on calf vigor. A positive correlation of .7225 ($P<.01$) was found between vigor score at 24 hr and vigor at 48 hr.

Birth weight. Induction treatments 1 and 2 were both shown to significantly reduce calf birth weight in comparison to controls when the data were analyzed for treatment and group effects on birth weights. Birth weight means for T0, T1 and T2 were 38.9, 32.5 and 32.5 kg, respectively, ($P<.001$). No group effects were found (tables 2, 4).

Reanalysis excluding induced animals was performed to evaluate sex and sire effects. Male calves averaged 36.6 kg at birth and were not significantly heavier ($P>.10$) than the females whose mean birth weight was 35.9 kg. (table 3).

The progeny of bull 1 (Simmental) had the heaviest mean birth weight of the five sire-based groups. B1 calves were significantly heavier than calves sired by bull 3 ($P<.01$), bull 4 and bull 5 ($P<.05$), but were only slightly larger than offspring of bull 2 ($P>.10$). The group with the lightest mean birth weight consisted of calves sired by bull 3. Although the lightest, weight differences were significant only between B3 and those of B1 and B2, at $P<.01$ and $P<.05$ levels, respectively, (table 7).

No significant interactions on birth weight were found between any sets of main effects in either analysis.

Weaning weight. Differences in calf weights which had been found between treatment groups at birth no longer existed at the time of

weaning. Two-hundred and five day adjusted weaning weight means for TO, T1 and T2 were 144, 134, and 140 kg, respectively (table 2). Existing differences between treatments were found to be at statistically nonsignificant levels ($P>.10$).

Analysis showed no significant effects on weaning weight due to group.

Bull calves weaned an average 2 kg heavier than heifers ($P<.10$) with respective means being 145 and 143 kg when analysis was performed excluding T1 and T2 animals (table 5).

Analysis by bull showed B2 calves to be significantly heavier at weaning than all others ($P<.01$). The B1 Simmental calves were heavier than all except the B2 calves ($P<.01$) and B4 offspring were the lightest by 4 to 18 kg ($P<.01$, $P<.05$), (table 7).

Analysis including vitamin A, D and E treatment showed no significant differences in mean adjusted weaning weights between calves receiving the vitamin complex and those from which it was withheld. Mean weaning weights for treated and nontreated calves were 136 ± 5.1 and 142 ± 6.2 kg, respectively ($P>.10$). No significant effect was shown to result from a treatment x vitamin interaction (table 12).

No significant main effect interactions were indentified in either analysis of adjusted weaning weights.

Even though the effect of induction treatment had disappeared at weaning, analysis of birth weight and weaning weight together

showed a significant and positive correlation (r=.4073, P<.01). Adjusted weaning weight was also correlated to the total percent of cows conceiving during the subsequent breeding season (r=.1942, P<.05).

Subsequent Fertility

Pregnancy rates. The conception rates to AI service during the first 28 days of the fall 1974 breeding season for TO, T1 and T2 cows were 47, 47 and 51%, respectively (P>.10). No significant effect was found on AI pregnancy rates due to induction group, sex or sire of calf (table 1).

Least squares analysis of overall conception rates for the 48-day fall 1974 breeding season did not show any significant variations among sets of main effects. Mean overall conception rates for TO, T1 and T2 cows were 91, 83 and 71%, respectively, (P>.10), (tables 3, 5, and 6).

$PGF_{2\alpha}$ effects. Across all treatments, cows receiving Prostaglandin $F_{2\alpha}$ prior to AI service had a 19% higher mean AI conception rate than did cows which were designated as $PGF_{2\alpha}$ controls (P<.10). Mean AI conception percentages were 39 and 58 for Prostaglandin treatments and controls, respectively (table 8).

The same analysis also revealed a significant interaction between Flumethasone and Prostaglandin treatments (P<.025). Among TO cows, those which were also prostaglandin controls had a mean overall conception rate which was 14% higher than those cows receiving $PGF_{2\alpha}$. The trend reversed, however, among T1 and T2 cows. The animals receiving $PGF_{2\alpha}$ in T1 and T2 had respective mean overall conception

rates 20 and 23% higher than did their prostaglandin control counterparts (table 10).

Performance of T3 and T4 Cows

Analysis of the cows failing to respond to the two Flumethasone treatments was done arithmetically by treatment and the two groups compared. No analysis of variance or correlation coefficients were calculated.

Parturitions in the two groups were not only similar to each other, but very comparable to those of the T0, T1 and T2 cows. Calves in T3 had noticeably lower vigor scores than any other treatment (table 11). While birth weights were comparable to the rest of the herd, weaning weights of both T3 and T4 calves were far below those of the other three treatment groups; being 115.8 and 106.1 kg, respectively. This may, however, be partially due to the fact that only five calves in each of the two failure groups had recorded weaning weights. The reason for this is not clear.

Subsequent fertility of the T4 cows was very comparable to that of the induced and control cows. Means for AI and overall pregnancy rates were 42.9 and 85.7%, respectively. Fertility in T3, however, was very poor. AI conception was fully 22% below T4, the mean being 20%. The overall pregnancy rate was 50%; 35.7% below T4 and approximately 30% below the other three treatments.

TABLE 1. EFFECT OF FLUMETHASONE (FLU) TREATMENT ON MEASURED PARAMETERS FOR INDUCED PARTURITION AND SUBSEQUENT FERTILITY

Measured parameters	Means for Treatments		
	TO Control	T1 10 mg FLU	T2 10 mg FLU + antibiotic
No. of cows	61	51	62
Induction success (%)*	--	82.3	89.7
Injection to parturition interval (hr)	--	48.2 (5.44)	46 (5.96)
Calving difficulty (1.0-4.5)	1.14 (.08)	1.11 (.10)	1.09 (.11)
Retained placenta 24 hr postpartum (%)	5.2 (11.42)^{a,m}	22.4 (13.06)^{n}	35.9 (14.35)^{b}
Retained placenta 7 days postpartum (%)	1.7 (4.84)	3.4 (5.54)	3.6 (6.07)
Calving date (day of year)	260 (1.3)^{a}	255 (1.5)^{b}	255 (1.6)^{b}
Gestation length (days)	284 (.8)^{a}	279 (.8)^{b}	278 (.7)^{b}
Percent pregnant to AI service	47.3 (14.6)	47.3 (17.7)	51 (18.6)
Total percent pregnant in breeding season	90.7 (9.7)	82.6 (11.8)	77 (12.4)

* Numbers on this line are arithmetic means.
Numbers in parentheses are standard errors.
All averages are least squares means.

a,b Means on the same line having unlike superscripts differ significantly ($P<.01$).

m,n Means on the same line having unlike superscripts differ significantly ($P<.05$).

TABLE 2. EFFECT OF FLUMETHASONE (FLU) TREATMENT ON MEASURED PARAMETERS FOR CALF PERFORMANCE

Measured parameters	Means for Treatments T0 Control	T1 10 mg FLU	T2 10 mg FLU + antibiotic
No. of calves	61	51	62
Calf vigor @24 hr of age (1-3)	1.05(.1)	.98(.12)	1.02(.13)
Calf vigor @48 hr of age (1-3)	1.01(.14)	1.01(.16)	1.05(.17)
Birth weight (kg)	38.9(1.2)[a]	32.5(1.5)[b]	32.5(1.6)[b]
205 day adjusted weaning wt. (kg)	143.7(5.6)	134.4(7.3)	139.7(7)

Numbers in parentheses are standard errors.
All averages are least squares means.
ab Means on the same line having unlike superscripts differ significantly (P<.01).