PREPARTUM HORMONE LEVELS RELATED TO DYSTOCIA AND POSTPARTUM REPRODUCTION

by

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ABSTRACT

Dystocia may be described as parturition that is prolonged, difficult, or impossible for the dam without assistance. There have been numerous factors associated with dystocia.

Twelve Holstein heifers were observed during the latter part of gestation for symptoms of dystocia. Seven variables were studied during this period. Factors which apparently did not influence the incidence of dystocia were cow body weight, pelvic area, gestation length, plasma hydroxy-progesterone level, total level of plasma progestins, total level of plasma estrogens, and plasma estrone levels. Factors which appeared to influence the incidence of dystocia were calf weight, calf sex, sire, and the relationship between plasma corticoid levels, plasma progesterone levels, and plasma estradiol levels,
CHAPTER 1

INTRODUCTION

Dystocia may be described as parturition that is markedly prolonged or becomes difficult or impossible for the dam without assistance (13). Calving difficulty is a major factor in calf losses at or near birth (7, 87). Difficult parturition in cattle is costly in terms of labor, medication and losses in cows, saleable calves and herd replacements (13, 26, 47, 61).

Factors reported to be associated with calving difficulty include age of dam (88), sex of calf (61), weight (11, 63) and shape of calf (87), gestation length (25), breed x breed mating system (47), sire of calf (26, 87) and pelvic area of dam (10, 15).

Relatively heavy calves in combination with a low level of estrogen seem to be a predisposition for a difficult birth process (59). As estrogenic hormones are required for the sensitization of receptors in the uterus for normal uterine myometrial contractile activity, one could postulate that when a low quantity of estrogens are present the myometrium of the cow is not stimulated optimally. The consequence would be that the birth canal is
not well prepared, the birth process will be slow and would cause a higher incidence of difficult birth.

The exact mechanism involved in the onset of parturition is not well understood. For a normal parturition to occur there is evidence that a properly timed sequence of hormonal events must take place. The objectives of this study are to determine if the sequential changes in peripheral plasma hormones can be utilized to predict cases of calving difficulty.
Dystocia in cattle may be attributed to various factors. Frequency of calving difficulty varies with the age of the dam (13). Two-year-olds experience the most difficulty (10, 13, 46, 47, 48, 87, 88). Three- and four-year-olds have more difficulty than mature five- through nine-year-olds (13, 48). It appears that there is a highly significant reduction in the incidence of dystocia with increasing age (77).

It has been demonstrated that a major cause of calving difficulty among different ages is due to the smaller pelvic area in two-year-olds as compared to four-year-olds (11). The pelvis grows linearly at a rate of approximately 0.5 cm² per day throughout pregnancy (87). This increase would partially account for the reduction in the occurrence of dystocia in older animals.

It has been reported that breed of dam and breed of sire can significantly influence pelvic area (46). A large percentage of the differences in pelvic size among breeds is due to differences in body weight (46). Thirty-six percent of the variability in pelvic area in Hereford heifers was accounted for by body weight, hip width and rump length.
(10). Also, larger cows tend to have larger pelvic openings (46). Rice and Wiltbank (63) reported that dystocia rates were 68% in cows with pelvic areas less than 200 cm² and 28% for cows with pelvic areas over 200 cm². Other work has shown that the effects of pelvic measurements on dystocia and stratification of cows by pelvic area reveals no threshold points for the influence of pelvic size on dystocia rates (47). Laster and Gregory (48) reported that the relationships of dystocia to pelvic size and other measurements describing cow size, condition and anatomy are too low to accurately predict dystocia in cattle.

Dams of a number of different British Breeds showed no difference in the incidence of dystocia (77). Apparently the greatest calving difficulty arises with first calf heifers, especially when they have male calves (59, 88). Brinks, Olsen, and Carroll (13) have shown that calving difficulty is more pronounced with male births than with births of females. Burfening (16) reported that male calves have a higher incidence of dystocia.

The effect of calf sex on birth weight has been well documented (16, 31, 44, 45, 47, 48, 61). Significant differences in birth weight exist between male and female offspring (26). Calving difficulty has been found to increase for each kilogram increase in birth weight (11, 47, 58, 61, 63, 71). Pattullo (61) found that calves with
high birth weights and those with low birth weights have a higher mortality than calves of an average birth weight. The correlation between calf size and calving difficulty has also been reported to be low (88).

Burfening (16), in an attempt to relate some measurements of the calf to calving difficulty, used the following measurements: birth weight, gestation length, length of head, width of head, circumference of front feet, heart girth and length of calf. The trait which showed the greatest relationship to calving difficulty, although not significant, was the circumference of the front feet. Laster et al. (47) reported that calf shape measurements, independent of birth weight, has no effect on dystocia. Birth weight and head size were not found to influence the incidence of stillbirths (26).

Frequency of calving difficulty appears to be related to the breed of sire (20, 26, 47). Laster et al. (47) found breed of sire significantly affected dystocia in male and female calves. Sagebiel et al. (71) reported that breed of sire affected dystocia score in male births but not in female births. However, Nelson and Huber (58) indicated that breed of sire was not a source of significant variation in calving difficulty. The range and variation of a sire's progeny seem to be more meaningful than their average (87). The incidence of dystocia in sheep was
reduced to a low level by selection of sires and dams that were free from any record of this defect (60).

Heterosis has not been found to significantly affect calving difficulty (16, 47). Male crossbred calves have been shown to have a higher incidence of dystocia, while female crossbred calves have had a decreased incidence of dystocia when compared to straight breds (47). Sagebiel et al. (71) reported that female crossbred calves have more calving difficulty than straight breds.

Animals on a low energy diet have exhibited the same degree of difficulty as animals on high energy diets (20). Little difference has been found between heifers that calved normally and those that exhibited dystocia in either rate of gain or final calving weight (25). Increased levels of nutrition for a ninety day period before calving increased birth weights but did not significantly affect the percentage of cows requiring assistance at parturition (47). A sub-maintenance ration during the last three months of pregnancy has been reported to reduce the incidence of dystocia (61). Conversely, calving problems have been increased by feeding a ration containing 85% of the National Research Council (NRC) recommendations (15). It has been concluded that losses at or near calving cannot be decreased markedly by placing heifers on a low plane of nutrition prior to calving (87).
The mean gestation period of difficult births has not been shown significantly different from normal animals (15). Little relationship appears to exist between gestation length and the weight of the fetus (25).

Parturition studies have revealed that 60% of the calves assisted during parturition are presented normally, 20% posteriorly and 20% show a postural abnormality (61). Dystocia encountered by posteriorly presented fetuses has been attributed to several factors: at the start of labor there is a delay in the onset of regular and well defined straining bouts (26), the more bulky parts of the fetus are delayed in entering the cervix (90) and as a result pressure receptors in the cervix are not stimulated and there is little reflex straining by the dam (70).

Genetic and environmental factors that affect the condition and tone of the birth canal may have an impact on calving difficulty (48). Low uterine tone adversely affects the expulsive efforts of the dam and predisposes the animal to dystocia (25). Levels of inbreeding of the calf and of the dam have been shown to affect calving difficulty (13). Low levels of inbreeding are associated with reduced calving difficulty, while highly inbred animals are associated with increased calving difficulty (13).

Stillbirths in calves have been attributed to dystocia of maternal origin (25). Stricture of the posterior genital tract and irregular or weak straining have been
indicated as causes of maternal dystocia (25). Various factors have been indicated as causes of vulval constriction or stenosis (64). These factors include hypoplasia in underdeveloped heifers as a result of poor nutrition, congenital or heritable defects and scarring following vulval trauma (25). Sympathetic nerve stimulation and adrenalin injection result in posterior vaginal constriction (53). The point of constriction occurs at the junction of the vulva and the vagina, and forms a band beyond which the fetal cranium cannot easily pass (25). Incomplete relaxation of the posterior genital tract or vulval stenosis can be associated with dystocia (86).

The exact mechanism involved in the onset of parturition in the bovine is not well understood (5, 50). Circulating estrogen levels have been considered the governing factors in the initiation of parturition (36). Evidence from sheep has indicated that the onset of labor is chiefly controlled by corticosteroids secreted by the adrenals of the fetus (5, 50). The rise in plasma corticoids seen just prior to parturition in the cow may be a result of an increase in steroid secretion by the fetal adrenal system with transport across the placenta to the maternal circulation (5). Prevention of parturition by fetal adrenalectomy in sheep (24), and the corticoid and adrenocorticotropic hormone (ACTH) infusions of Liggins (50) indicate an important role for the adrenal in parturition.
Fetal adrenals have been shown capable of producing cortisol or corticosterone (40, 54).

The adrenal secretes corticoids in response to circulating levels of pituitary adrenocorticotropic hormone (ACTH), which in turn may be inhibited by increased levels of circulating corticoids. Neural responses to environmental stimuli which indirectly affect ACTH secretion via neuroendocrine pathways involving the hypothalamus have been reported (85). Rapid fluctuations in the levels of corticoids in the plasma due to nonspecific external stimuli may mask the importance of biological events.

Increased levels of endogenous corticoids in cattle is considered a signal for the initiation of luteolysis and termination of pregnancy (5, 37). Plasma corticoid levels begin to rise shortly before parturition and reach peak values at parturition (19, 27, 51). Cortisol and corticosterone have been identified as the principal glucocorticoids in bovine jugular plasma (32). Maternal cortisol has been shown to be higher than fetal cortisol throughout pregnancy (51). Cows with male fetuses have higher cortisol levels (51). Pregnancy has shown no effect on the daily rhythm of corticoid production, although increased levels of corticoids have been found during gestation (51).

Parturition has successfully been induced with injections of Dexamethasone (5, 39, 42, 82). A side effect of this procedure has been the retention of fetal membranes
(5, 42, 82). Calving difficulty has been reported to be greater in Dexamethasone induced cows (8), while birth weights have decreased (8, 49). Welch (83) implicated corticoid treatment with the death of cows in which parturition was induced.

Injections of 17-hydroxyprogesterone have resulted in significant drops in plasma corticosteroids (73). Hydroxyprogesterone-17a increases in the latter part of pregnancy in the human (79, 81). The fetus appears to provide the bulk of 17-hydroxyprogesterone precursors at term (80). An increase in the amnionic fluid content of 17-hydroxycorticoid during pregnancy in women has been reported (4). The fetal adrenal has the potential to act as a source of C19 steroids (73). The bulk of the circulating 17-hydroxyprogesterone appears to be provided by the feto-placental unit (73). There is a lack of information concerning 17-hydroxyprogesterone in cattle.

Progestogens can produce adrenal atrophy and impair adrenal function in rats (34). Progestogens have also been shown to alter levels of plasma and urinary corticoids (34). The luteolytic effect of a glucocorticoid injection can be overcome by simultaneously injecting progesterone (41). In cows with normal parturitions, together with the decrease in progesterone, an increase of perpherial corticoid values has been observed (37). Dystocia occurs in most progesterone treated animals which respond to corticoid injections with
induced parturition (41). This indicates that a proper timing of the sequence of hormonal events has not occurred.

A rise in plasma estrogen in the presence of a declining progesterone level has been shown to be required for initiation of parturition in cattle (17, 27, 28, 64, 66, 67). Estrogen increases the spontaneous activity of the myometrium (21). High levels of progesterone antagonize the action of estrogens on the uterus (12, 21). Failure of progesterone to decrease prior to parturition may be overcome by increasing levels of estrogen in the blood (68).

The concentration of unconjugated estrone in the plasma is relatively high forty days prior to parturition (66, 67). Peak blood estrone in a given cow has been indicated to occur sometime between five days prepartum and parturition (66). Estradiol-17α (66) and estradiol-17β (22, 23, 37, 66, 78) are much lower at this time. A steady increase in estradiol-17β has been determined during the last days of parturition (19, 22, 23, 37, 56, 66, 67, 78). Estradiol-17α has been shown to plateau approximately five days prepartum (66). Estrogen levels are reported to drop dramatically after parturition (30).

Injections of 17α-estradiol have resulted in a significant decrease in interval from Dexamethasone injection to parturition (49). Estrogen pretreatment of Dexamethasone induced cows has been reported to increase
dystocia (58) and has not alleviated the problem of retained placenta (49). Birth weight has been reported to be significantly related to dystocia (46) and to circulating estradiol levels (58). This indicates that estrogen levels may be related to dystocia.

The methods used to quantify estrogens range from the measurement of total estrogens to the measurement of compounds following purification and chromatographic separation. Therefore, values for estrogen concentration in bovine peripheral plasma vary greatly from different laboratories. Quantification of bovine peripheral plasma hormone levels during late pregnancy has been undertaken in this study to help clarify these differences.
CHAPTER 3

MATERIALS AND METHODS

Twelve two-year-old Holstein heifers were observed from approximately day 260 of gestation until parturition. A total of seven variables were studied during this period. They included dystocia, pelvic area, calf sex, calf birth weight, gestation length, sire and plasma hormone levels. Hormones measured included corticosteroids, progesterone, 17-hydroxyprogesterone, estrone and estradiol-17β.

Dystocia was classified according to Laster (46). Cows that calved with no assistance and those given minor hand assistance were classified as no difficulty. Animals requiring assistance with a mechanical calf puller or cesarean removal were classified as dystocia. Twin births and abnormal presentation were not included in this study.

Pelvic height and width measurements were obtained by the procedure described by Bellows (9). Calipers were designed and built to make the necessary measurements. The parameters were multiplied together to estimate the pelvic area. The pelvic measurements were made at 260 days of gestation.

All calves were sexed at parturition. The calves were also weighed within twelve hours of birth.
The heifers were fed the same ration, alfalfa ad libitum, which provided a high plane of nutrition prior to parturition. The animals were fed and maintained in a common drylot prior to calving.

Blood samples were obtained every day at approximately 0730 hours. Thirty milliliter samples were taken via venipuncture of the middle coccygeal vein or artery. The samples from each cow were separated by centrifugation and the plasma was stored frozen. The samples were saved until the end of the study, at which time they were analyzed for their hormone content.

Plasma corticosteroid levels were determined by the modified protein binding method of Murphy (57). Plasma progesterone (1), 17-hydroxyprogesterone (2), estrone and estradiol-17β (3) were measured by Radioimmunoassay. Details of the methods used for measurement have been previously described (1, 2, 3, 57).

Standard statistical procedures (75) were used for the analysis of data. Comparison of means was done by "t" tests. Correlation between the various hormones were computed.
CHAPTER 4

RESULTS AND DISCUSSION

Dystocia requiring the use of a mechanical calf puller occurred in 6 of the 12 animals in the experiment. The amount of dystocia (50%) encountered in this period is slightly higher than has been reported by other workers (46, 87). This may be attributed to the relatively small sample size.

Assisted cow mean body weights (1331 lbs.) taken 2 days postpartum were not significantly different from normal mean cow body weights (1306 lbs.) recorded at 2 days postpartum. This indicates that cow body weight had little effect on dystocia.

Pelvic area of assisted heifers was an average of 35 cm² greater than the pelvic area of normal heifers. Mean pelvic area in cases of dystocia was 340 ± 42 cm², while the mean pelvic area in normal parturition was 305 ± 34 cm². From this it is apparent that pelvic area measurements cannot be used to accurately predict dystocia in dairy heifers. Laster et al. (47) was also unable to relate pelvic area to calving difficulty in beef heifers. On the other hand, pelvic area has been used to identify beef heifers which showed dystocia (62, 87).
Numerous studies have related calf weight to calf sex (31, 44, 45, 48). Results of this study revealed that male calves were heavier at birth than female calves. However, all calves, regardless of sex, that experienced dystocia showed increased birth weights. Calving difficulty occurred more often with male births (33%) than with female births (17%). Several investigators have elucidated the influence of calf sex on dystocia (10, 47, 58, 71). It has also been well documented by several researchers that male calves are heavier at birth than female calves, and that male calves experience more dystocia than female calves (7, 10, 11, 31, 44, 45, 47, 48, 63, 88, 89).

Mean gestation length in assisted parturitions was approximately 283 ± 6 days, while mean gestation of normal births was of a shorter duration, occurring at approximately 280 ± 4 days. These results were skewed in the assisted group by one cow having a prolonged gestation period which required termination via cesarean operation. Otherwise, gestation length in the two groups was approximately equal. Other investigators could not find significant differences between mean gestation lengths of heifers (16, 25, 26). Male calves in this study had longer gestation periods, whereas Dufty (26) reported longer gestation periods with females.

Several reports have been presented on the effects of sire on dystocia (20, 26, 46, 57, 70). In this study,
due to the small number of progeny per sire, no significant indication was found. However, a definite trend developed that showed that the sire may produce an effect on the incidence of dystocia. Progeny from the 8 sires were either found in the assisted group or in the normal group, but not in both. Three bulls sired 2 or more calves in this study. Progeny of two bulls accounted for 5 unassisted calvings, while progeny from a third sire accounted for 2 assisted calvings.

Results of hormone analysis of blood samples were pooled for 3-day periods to give a mean value. It was thought that this would present a more meaningful illustration since there is a rather wide variation in hormone concentration from sample to sample, due to probable uncontrolled environmental factors and to normal rhythmic fluctuation in hormone secretion (52).

The analysis of peripheral plasma for corticoids during late gestation and parturition are shown in Fig. 1. Normal animals exhibited an elevated corticoid level throughout the entire sampling period when compared to assisted animals. The greatest observable difference is seen between day 20 and day 12 prepartum with normal heifers showing a rise in corticoid output, while assisted heifers demonstrated a decrease in corticoid output. Corticoid production increased during the last 11 days of gestation in normal and assisted animals. The rise of cortocoids
Fig. 1. Circulating Corticoid Levels in Late Gestation

- Assisted
- Normal
- One Std. Dev.

Days Prepartum: 23-21, 20-18, 17-15, 14-12, 11-9, 8-6, 5-3, 2-0

Corticoid Levels (NG/ML)
in late gestation follows closely with results reported in other papers (5, 17, 33, 35, 37, 42, 43, 55, 74). Increased levels of endogenous corticoids is considered a signal for the initiation of luteolysis (5, 14, 36). A depressed circulating level of corticoids might therefore delay the onset of luteolysis and thus predispose the animal to a difficult parturition.

Progesterone analysis (Fig. 2) indicates that the greatest difference between assisted and unassisted animals occurs in the period of day 20 to day 15 prepartum. During this period normal animals exhibit a significantly depressed progesterone level when compared to the assisted animals. Thereafter progesterone levels of normal animals increased above that of the assisted animals at approximately 12 days prepartum. Concentrations of progesterone in both groups then declined until parturition. Other studies have shown that progesterone levels decline prior to parturition and continue to decline in the postpartum period (18, 19, 29, 30, 33, 36, 37, 39, 65, 74). Since progesterone has been shown to antagonize the action of corticoids (42) and estrogens (12, 21), it may be postulated that high levels of progesterone may increase a cow's susceptibility to dystocia.

Plasma hydroxyprogesterone-17 (Fig. 3) appears to follow approximately the same pattern in normal and assisted heifers. This is especially evident during the
Fig. 2. Circulating Progesterone Levels in Late Gestation
Fig. 3. Circulating Hydroxyprogesterone Levels in Late Gestation
last 2 weeks of pregnancy. However, a nonsignificant increase was noticed between days 15-17 and between days 21-23 in assisted heifers. Hydroxyprogesterone-17 has been shown to increase in the human in the latter part of pregnancy (38, 79, 81). The opposite of this appears to occur in the bovine, with the exception of a rise seen just prior to parturition in both groups of animals.

Estradiol-17β (Fig. 4) during the last 11 days of gestation shows a parallel trend for normal and for assisted heifers. Three-day group combinations exhibited a continuous rise in estradiol-17β during the last 3 weeks of gestation in both groups of heifers. A decrease in estradiol-17β was observed approximately one day prepartum in both groups when compared on a daily basis. An increase in circulating levels of estradiol-17β during the final stages of gestation has been shown by several investigators (6, 17, 19, 22, 39, 66, 67, 69, 72, 76, 78, 84). A significant elevation (p .05) of estradiol-17β appeared in the normal heifers compared to assisted heifers between day 15 and day 20 prepartum. The normal heifer may, therefore, be optimally stimulated well in advance of parturition by the elevated estradiol, whereas the assisted heifer may not be adequately prepared for the onset of parturition.

No significant differences were noted between levels of total progestins (progesterone + hydroxyprogesterone-17) in normal or assisted animals. Total estrogen
Fig. 4. Circulating Estradiol-17β Levels in Late Gestation
(estradiol-17β + estrone) were not significantly different. Estrone (Fig. 5) showed small but nonsignificant differences during the sampling period.

Correlations were determined involving estradiol-17β, progesterone and corticoids during the last 23 days of gestation (Table 1). Assisted heifers showed a highly negative correlation (.98), while normal heifers showed a moderately negative correlation (.47) when estradiol-17β and progesterone were compared. Positive correlations were obtained between estradiol-17β and corticoids. Assisted animals were highly correlated (.90) and normal animals were moderately correlated (.71). A highly negative correlation was involved in both groups when progesterone and corticoids were compared. This pattern is in agreement with results of other workers (5, 8, 19, 22, 30).

Due to the apparent differences in hormone levels prior to day 12 prepartum, the sampling period was divided into two sections. Correlations were then run on estradiol-17β, progesterone and corticoids from day 12 through day 23 prepartum and also from day 11 prepartum to parturition (Table 2).

During the period from parturition to day 11 prepartum, high negative correlations were found between estradiol-17β and progesterone and also between corticoids and progesterone in assisted and in normal heifers. No difference was observed between estradiol-17β and corticoids
Fig. 5. Circulating Estrone Levels in Late Gestation
Table 1. Hormone correlations during the last 23 days of gestation.

<table>
<thead>
<tr>
<th>Hormones</th>
<th>Assisted Animals</th>
<th>Normal Animals</th>
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<tbody>
<tr>
<td>Estradiol-17β to Progesterone</td>
<td>-.98</td>
<td>-.47</td>
</tr>
<tr>
<td>Estradiol-17β to Corticoids</td>
<td>+.90</td>
<td>+.71</td>
</tr>
<tr>
<td>Progesterone to Corticoids</td>
<td>-.87</td>
<td>-.90</td>
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Table 2. Hormone correlations during the last 23 days of gestation when observed as two sampling periods.

<table>
<thead>
<tr>
<th>Sampling period: Day 23 prepartum to day 12 prepartum;</th>
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<tr>
<td>Hormones</td>
</tr>
<tr>
<td>Estradiol-17β to Progesterone</td>
</tr>
<tr>
<td>Estradiol-17β to Corticoids</td>
</tr>
<tr>
<td>Progesterone to Corticoids</td>
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<table>
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<tr>
<th>Sampling period: Day 11 prepartum to parturition;</th>
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<tbody>
<tr>
<td>Hormones</td>
</tr>
<tr>
<td>Estradiol-17β to Progesterone</td>
</tr>
<tr>
<td>Estradiol-17β to Corticoids</td>
</tr>
<tr>
<td>Progesterone to Corticoids</td>
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during this period, both normal and assisted animals being highly positive correlated.

High negative correlations were observed between estradiol-17β and progesterone in assisted animals that were 12 to 23 days prepartum. Only moderately negative correlations were found between estradiol-17β and progesterone in normal animals during this time.

When comparing levels of estradiol-17β and corticoids between day 12 through day 23 prepartum, a contrasting picture was observed. Normal animals possessed a low positive correlation (.37), while assisted animals exhibited a moderately negative correlation (.53). These results show that in the period preceding 11 days prepartum there is an increase in both estradiol and corticoids in normal animals. On the other hand, corticoids decrease in assisted animals while estradiol-17β increases during this period. When comparing progesterone with corticoids during this time, the reciprocal of this trend was observed. Progesterone in normal animals showed a high negative correlation to corticoids, conversely progesterone showed a high positive correlation with corticoids in assisted animals. The combination of these results may represent an improper timing of events which predispose animals to dystocia.
CHAPTER 5

CONCLUSIONS

Results from this experiment indicate that cow body weight, pelvic area and gestation length have very insignificant influence on calving difficulty. Calf birth weight demonstrated a definite effect on dystocia. Heavier calves, regardless of sex, exhibited greater calving difficulty. A trend developed among sire groups which pointed out that the sire may influence calving difficulty.

Plasma hormone analysis revealed several differences between heifers that calved normally and heifers that showed dystocia. The greatest difference between assisted and normal animals appears approximately between day 20 and day 15 prepartum. Normal animals have higher blood levels of corticosteroids and estradiol-17β when compared to assisted animals, while progesterone levels are lower in normal animals than in assisted animals. Estrone levels and 17-hydroxyprogesterone levels in peripheral blood in normal animals was approximately the same as in animals experiencing calving difficulty. The difference in the levels of the various hormones suggests that the proper timing in the sequence of hormonal events leading to parturition is not attained in cases of dystocia.
LIST OF REFERENCES


