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Prediction of parturition and dystocia in holstein-friesian cattle, and cesarean section in dystocic beef cattle

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PREDICTION OF PARTURITION AND DYSTOCIA IN HOLSTEIN-FRIESIAN CATTLE, AND
CESAREAN SECTION IN DYSTOCIC BEEF CATTLE

For the degree of Doctor of Philosophy

Is approved by the final examining committee:

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12/04/2014

Head of the Department Graduate Program

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PREDICTION OF PARTURITION AND DYSTOCIA IN HOLSTEIN-FRIESIAN CATTLE, AND
CESAREAN SECTION IN DYSTOCIC BEEF CATTLE

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of

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by

Wen Han Mark Hiew

In Partial Fulfillment of the

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of

Doctor of Philosophy

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This dissertation is dedicated to my family and to all bovine lovers and enthusiasts out there.

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ABSTRACT

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Dystocia is a major problem in the dairy industry as it causes livestock and economic loss. It is more frequently seen in primiparous cattle compared to their multiparous counterparts due to their smaller stature and the slow maturation of pelvic dimensions. In some instances, human intervention of the parturition process is imperative to avoid pain, injury, and mortality of the neonate and the dam. The ability to accurately predict dystocia and the time of parturition will ensure that timely assistance can be given to animals that are of high risk of dystocia.

The present thesis contains four studies that explore methods to predict dystocia and the time of parturition as well as factors that influence the presentation and outcome of cesarean sections. The first study, presented in chapter three, evaluated the clinical utility of measuring the circumference of the calf front and maternal intrapelvic dimensions to predict the incidence of dystocia in late gestation Holstein-Friesian cattle. The ratio of the calf hoof circumference to the maternal intrapelvic area was identified to have clinical utility in predicting the calving difficulty score. The second study, presented in chapter four, assessed the changes in plasma progesterone concentration, rectal temperature, sacrosciatic ligament relaxation, and feed intake to predict the time of parturition in dairy cattle. Results indicated that plasma progesterone concentration had the highest accuracy in predicting the time of parturition. The third study,

presented in chapter five, explored the clinical utility of blood and plasma glucose concentrations in predicting parturition as well as their relationship with hypercortisolemia and clinical signs associated with the activation of the sympathetic nervous system namely heart rate, respiratory rate, mean arterial blood pressure, hematocrit, and rumen contraction rate. Blood glucose was determined to have the potential to predict parturition due to its accuracy, practicality, and cost effectiveness. In the fourth study, presented in chapter six, a retrospective study was conducted to examine the clinical presentations and outcomes of beef cattle that were admitted into a teaching hospital with dystocia and had cesarean sections performed. Results indicate that cesarean section was a useful method to resolve dystocia with high dam survivability but delays in admitting cattle to the hospital could result in increased calf mortality.

Collectively, the results presented in this thesis provide methods to predict dystocia and parturition in late gestating cattle as well as highlight factors that help ensure favorable outcomes from cesarean sections.

CHAPTER 1. INTRODUCTION

Dystocia remains an important issue in the dairy and beef industries. The primary aims of the research presented in this dissertation were to identify practical and inexpensive methods to: 1) predict dystocia in Holstein-Friesian cattle; 2) predict the time of parturition in Holstein-Friesian cattle; and 3) determine the success rate of cesarean section as a treatment for dystocia in beef cattle.

Chapter two reviews the process of parturition in cattle, the hormonal and physiologic changes that occur in preparation for parturition, and the methods used to predict the time of parturition. The incidence of perinatal mortality is discussed, as well as methods for measuring intrapelvic dimensions in cattle. The causes of dystocia in cattle and their management, including the different techniques and approaches for cesarean section, are also covered.

Chapters three, four, and five utilized a convenience sample of more than 100 late gestation dairy cattle that were examined daily at the Purdue University Dairy Research and Education Center over an 11 month period in 2012-13. Chapter three describes a study conducted on 103 late gestation Holstein-Friesian cattle that investigated the clinical utility of using pelvimetry and morphometric measurements of the fetus to predict dystocia and calving difficulty score. Chapters four and five evaluated the ability of selected factors and measurements to predict the time of parturition in 106 late gestation Holstein-Friesian cattle. Evaluated factors included plasma progesterone concentration, rectal temperature, feed intake, the extent of sacrosciatic ligament relaxation, and blood and plasma glucose concentration. Evidence for activation of the sympathetic nervous system was investigated by measuring heart

rate, mean arterial blood pressure, respiratory rate, plasma cortisol concentration, rumen contraction rate, and hematocrit.

Chapter six reports a retrospective study of 173 beef cattle admitted to the Purdue University College of Veterinary Medicine's Veterinary Teaching Hospital for the surgical management of dystocia using cesarean section.

Chapter seven presents a brief summary of the findings, their inferences, study weaknesses, and suggestions for future research.

CHAPTER 2. LITERATURE REVIEW

Parturition

Parturition occurs at the end of the gestation period and is defined as “the act or process of giving birth” (Blood, Studdert et al. 2007). It is an event that must be timed to match fetal maturation and its ability to survive outside of the uterus (Wood 1999). In Holstein-Friesian cattle, the physiological gestation length ranges from 278 to 280 days (Knott 1932, Silva, Wilcox et al. 1992, Meyer, Berger et al. 2000, Johanson and Berger 2003, Hansen, Lund et al. 2004, Norman, Wright et al. 2009), but gestation length exhibits breed variations in cattle (Table 2.1).

Table 2.1 Gestation length of various dairy cattle breeds.

Author	Breed	Gestation length (days)
(Norman, Wright et al. 2009)	Holstein	277.8 – primiparous 279.4 – multiparous
	Jersey	278.4 – primiparous 280.0 – multiparous
	Milking Shorthorns	279.3 – primiparous 281.1 – multiparous
	Ayrshires	281.6 – primiparous 281.7 – multiparous
	Guernseys	284.8 – primiparous 285.7 – multiparous
	Brown Swiss	287.2 – primiparous 287.5 – multiparous
(Silva, Wilcox et al. 1992)	Jersey	278
	Holstein	280
	Guernsey	282
(Dessouky and Rakha 1961)	Friesian	282.3

Table 2.1: Continued

(DeFries, Touchberry et al. 1959)	Ayrshire	277.7
	Jersey	279.5
	Holstein-Friesian	279.6
	Guernsey	284.7
	Brown Swiss	291.5
(Brakel, Rife et al. 1952)	Ayrshire	278.2
	Brown Swiss	288.4
	Guernsey	282.7
	Holstein-Friesian	278.6
	Jersey	277.9

Physiology of parturition in cattle

The corpus luteum and placenta both produce progesterone to maintain uterine quiescence by hyperpolarizing myometrial cells and therefore supporting pregnancy in the dam. At the time of parturition, an increase in estradiol production and a decline in progesterone is essential for calving to occur (Streyl 2011) as these hormonal changes combine to depolarize uterine myometrial cells and thereby increase uterine motility (Wood 1999).

Three stages of parturition are identified in cattle in North America: stage I, initiation of myometrial contractions and relaxation and dilation of the cervix; stage II, expulsion of the fetus; and stage III, expulsion of the fetal membranes.

Stage I of parturition

The process of parturition or stage I is initiated by the fetus and is highly dependent on the activation of the fetal hypothalamus-pituitary-adrenal (HPA) axis (Hunter, Fairclough et al. 1977, Wood 1999). However, it is debatable whether the critical event that initiates the process is a fetal neuroendocrine event or a response of the fetal neuroendocrine system to external stimuli such as increased fetal stress caused by decreases in nutrient delivery, manifest as changes in blood gas tension or plasma glucose concentration, or an increase in placental hormone concentrations. It is

hypothesized that the fetus at term identifies that fetal blood oxygen tension and plasma glucose concentration are decreasing to critically low levels. Part of the fetal response to the decrease in nutrient delivery is activation of the fetal HPA axis which initiates a cascade of events leading to parturition (Wood 1999). When the HPA axis is activated, corticotrophin releasing factor (CRF) is released by the hypothalamus which stimulates the anterior pituitary gland to produce the adrenocorticotrophic hormone (ACTH), a peptide hormone produced in response to stress, which in turn stimulates the fetal adrenal cortex to produce cortisol (Broom and Johnson 1993, Wood 1999). Fetal cortisol promotes the production and activation of 17α -hydroxylase, 17 - 20 desmolase, and aromatase that convert and aromatize progesterone (that has high concentrations at the placental interface) to 17α -hydroxyprogesterone, androstenedione, and ultimately estradiol. This conversion accounts in part for the decrease in progesterone and increase in estradiol concentrations during stage I of parturition (Senger 2003, Kindahl, Kornmatitsuk et al. 2004).

The HPA axis is important in the fetus because adrenal hypoplasia leads to prolonged gestation and large post-mature fetuses (Holm, Parker et al. 1961). Experimental studies done in sheep have demonstrated the importance of functioning fetal adrenal glands for normal parturition to proceed because parturition was prevented when fetal adrenalectomy was performed (Drost and Holm 1968). On the other hand, stimulation of the adrenal gland with corticotrophin leads to premature calving (Comline, Hall et al. 1974).

Additionally, fetal hypercortisolemia induces intrauterine prostaglandin synthesis via estrogen-independent and estrogen-dependent pathways (Whittle, Holloway et al. 2000). The estrogen-independent pathway occurs within the trophoblastic tissue and leads to elevations in fetal plasma prostaglandin E_2 (PGE_2) concentrations, while the estrogen-dependent pathway occurs within the maternal endometrium leading to increases in the production and release of maternal plasma prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$). Placental PGE_2 production is deemed to play a role in mediating the fetal HPA activation and placental steroidogenesis at the beginning of

labor. On the other hand, $\text{PGF}_{2\alpha}$ acts in an autocrine and paracrine manner to initiate smooth muscle contraction and induction of corpus luteum regression (Wood 1999, Streyl 2011) which further facilitates the drop in progesterone (Senger 2003). $\text{PGF}_{2\alpha}$ also helps abolish the progesterone block to myometrial contractions. In ruminants, elevations in plasma cortisol concentration induce cytochrome P450_{c17} in the placenta which permits a rise in the synthesis rate of estradiol at the expense of the rate of synthesis of progesterone (Wood 1999).

As both estradiol and $\text{PGF}_{2\alpha}$ concentrations increase, the myometrium begins to become more motile and contractions become more noticeable. As intrauterine pressure increases, the fetus rotates so that its head and front feet are pointed toward the caudal aspect of the dam. This rotation is important to facilitate a proper delivery and any abnormalities to this rotation may result in a dystocia (Senger 2003, Norman and Youngquist 2007).

Cervical dilation is divided into two phases. The preliminary phase is the passive phase whereby the caudal cervix opens (Taverne, Breeveld-Dwarkasing et al. 2002) due to a decrease in the muscular tone of the smooth muscle cells (Streyl 2011). The dilation begins at the external cervical os and extends toward the internal cervical os. The second phase is the active phase and begins once the external os has dilated adequately to allow the introduction of a hand. The strong initial contractions of the myometrium pull the cervix open and force the fetus and its membranes into the cervical canal (Norman and Youngquist 2007). The first stage of parturition is complete once the fetus enters the cervical canal at which stage the chorioallantoic sac usually ruptures (Senger 2003, Norman and Youngquist 2007). Stage I of parturition usually lasts approximately 6 h but variation among cattle occurs and this stage may last longer in heifers.

Additionally, estradiol elevations at parturition facilitate relaxation of the birth canal (Wood 1999) and increase vascular permeability, which may contribute to edema formation in the udder (Janowski, Zduńczyk et al. 2002). It also initiates secretory activity, especially at the cervix, to produce mucus that washes out the cervical seal of pregnancy and lubricates the cervical and vaginal canal (Senger 2003). The synthesis of

the hormone relaxin (stimulated by $\text{PGF}_{2\alpha}$) also plays a role in successful parturition as it causes the softening of connective tissues in the cervix increasing its dilatation, facilitates pelvic area expansion, and increases the relaxation in the pelvic ligaments (Musah, Schwabe et al. 1988, Bagna, Schwabe et al. 1991, Beagley, Whitman et al. 2010) but this has been controversial and questionable (Shah, Nakao et al. 2006).

Stage II of parturition

The increasing pressure caused by the fetus in the cervix activates pressure sensitive neurons that synapse in the spinal cord and ultimately synapse with oxytocin producing neurons in the maternal hypothalamus. Oxytocin facilitates myometrial contractility and its secretion increases as the pressure against the cervix continues to increase (Senger 2003) due to the Ferguson reflex (Hydbring, Madej et al. 1999). Each bout of straining consists of 5 to 7 contractions and increases to 8 to 10 contractions as the process advances. Dystocia that delays or prevents entry of the head or limbs of the fetus into the cervix to stimulate the pressure receptors result in little to no abdominal straining by the dam. The conical shape of the fetal head as it enters the cervical canal is essential as it gradually dilates the cervix with mechanical pressure. The intact amniotic sac appears at the vulva shortly after the rupture of the chorioallantois (Norman and Youngquist 2007). A sign of progress in stage II of parturition is a recumbent dam that is straining intermittently but strongly. The cow may occasionally go through bouts of standing and recumbency. Progressively, the fetal head and legs will emerge at the vulva (Mee 2004). As contractions become more forceful, the dam will be in lateral recumbency with the head, hindquarters, and uppermost limbs lifted. Maximal force is needed to deliver the fetal head through the vulva and in larger calves, additional abdominal pressure is needed to deliver the shoulders and hindquarters. On average, the second stage of parturition lasts 2 to 4 h in multiparous cows, but it can be longer in heifers as additional effort is required to dilate the birth canal (Norman and Youngquist 2007). Calving time (hour of delivery) is defined as the time when the calf was fully visible outside of the dam. For dams that stand during calving, it is the moment the calf

hits the ground, while for dams that are recumbent, it is the time when the hindlegs of the calf are fully visible outside the dam (Proudfoot, Huzzey et al. 2009).

Stage III of parturition

Detachment and expulsion of the fetal membranes requires the separation of cotyledon villi from the caruncle crypts and is facilitated by vasoconstriction of the villi arteries associated with continued myometrial contractions. The majority of cattle will pass their placenta within 6 h after parturition (Van Werven, Schukken et al. 1992) and the placenta is considered retained if it has not been expelled within 12 h of calving (Berglund and Philipsson 1987).

Stages of parturition (German doctrine)

Alternatively, the German doctrine describes the process of parturition in 5 stages (Streyll 2011). The first stage is the preparatory stage (occurs two to three weeks before parturition with hormonal and clinical changes) followed by the opening stage (opening of the cervix), dilatation stage (rupture of chorioallantois and front of fetus passing through the vulva), expulsion stage (delivery of calf), and placental expulsion stage.

Dystocia

The terms dystocia comes from the Greek 'dys' meaning difficult and 'tokos' meaning birth (Mee 2008). Dystocia also carries the meaning "difficult parturition to the point of needing human intervention" (Blood, Studdert et al. 2007) and "calving difficulty resulting from prolonged spontaneous calving or prolonged or severe assisted extraction" (Mee 2004). Eutocia or normal calving, on the other hand, is defined as spontaneous calving of normal duration (Mee 2008).

The incidence of dystocia in Holstein-Friesian cattle in France, Spain, the United Kingdom, Ireland, and New Zealand ranges from 2 to 11% (Fourichon, Beaudeau et al.

2001, McDougall 2001, Lopez de Maturana, Legarra et al. 2006, Rumph and Faust 2006, Mee, Berry et al. 2011). In the United States, 19% of primiparous and 11% of multiparous dairy cattle were reported to experience dystocia (NAHMS 2009a) while in beef cattle dystocia was reported in 12% of primiparous and 4% of multiparous cattle (NAHMS 2009b). The high dystocia rates in dairy cattle compared to beef cattle are due to the fact that dairy animals are not usually selected for calving ease and breeding strategies are not fully directed to reducing dystocia risk or effects on newborn calves. Although dairy artificial insemination sires are evaluated for calving ease, most producers typically choose bulls based on their production traits (Garry 2004).

Calving difficulty score

There is no common system established to determine the level of calving difficulty in cattle (Zaborski, Grzesiak et al. 2009). As a result, the categorical scoring of dystocia has ranged from a two-point (Johanson and Berger 2003) to a seven-point system (McClintock, Beard et al. 2005). These scores typically have no consistent defined intervals between each category but generally higher scores are associated with more severe dystocia or a higher amount of assistance (Meijering 1984, Mee 2008). Johanson and Berger (2003) used a two-point system that categorized animals into assisted and unassisted calving which may be a good and clear cut method to analyze and compare animals without ambiguity. A three-point scoring has been used which grouped calvings into unassisted, requiring light traction, and requiring heavy traction (Jacobsen, Schmidt et al. 2000) as well as one that used the categories 1 = normal, 2 = hard pull, and 3 = complicated (Fiedlerová, Řehák et al. 2008). There were many variants of the four-point system – those that were based off a 0 to 3 scale: 0 = no assistance with normal delivery of a live calf, 1 = no assistance with delivery of a stillborn calf, 2 = some assistance required for extraction of the calf, and 3 = difficult calving with forced extraction of the calf (Ettema and Santos 2004), and those that used a 1 to 4 scale: 1 = easy, 2 = easy with assistance, 3 = difficult but without veterinary assistance, and 4 = difficult with veterinary assistance (Hansen, Lund et al. 2004). There were other scoring

systems that used the highest score to denote surgical intervention such as seen in: 1 = no assistance, 2 = minor dystocia requiring manual (hand traction) assistance, 3 = severe dystocia requiring use of a mechanical calf puller, 4 = major dystocia requiring cesarean section (Bellows and Lammoglia 2000); and 1 = calving without assistance, 2 = calving with easy pull, 3 = calving with mechanical assistance) to 4 = cesarian section or fetotomy (Phocas and Laloë 2004). For the five-point system, one study (Dematawewa and Berger 1997) used the scoring system of: 1 = no problem, 2 = slight assistance, 3 = needed assistance, 4 = considerable force needed, and 5 = extreme difficulty that was introduced by the National Association of Animal Breeders (NAAB). Another form of a five-point system based scores on the amount of assistance provided during parturition (Lombard, Garry et al. 2007) whereby 1 = no assistance, 2 = required intervention by one person without the use of mechanical assistance (mild dystocia), 3 = required the assistance of 2 or more people, 4 = mechanical extraction was used, and 5 = surgical procedure was done. The seven-point system used by the Australian Dairy Herd Improvement Scheme (ADHIS) consisted of two calving classes that was made up of observed and unobserved which was then subdivided into seven groups namely unobserved – not ok, unobserved – ok, observed – ok, observed – easy pull, observed – very difficult, observed – surgical, and observed – malpresentation (McClintock, Beard et al. 2005). Twin births are typically excluded from analysis to simplify the experimental procedures although they do influence the incidence of dystocia (Nix, Spitzer et al. 1998, Johanson and Berger 2003).

The Purdue Dairy Research and Education Center uses a five-point scoring: 1 = no assistance needed, 2 = easy pull (one person with minimal effort), 3 = moderate pull (one person with moderate effort), 4 = hard pull (one person with considerable effort or two people), and 5 = mechanical extraction or cesarean section. Regarding the numbering system, it is of the author's opinion that the five-point scale used at the Purdue dairy is sufficient but could be improved upon. The usage of a scoring system from 0 to 4 would be more intuitive with the allocation being: 0 = no assistance, 1 = easy

pull (requiring one person), 2 = moderate pull (requiring two persons), 3 = hard pull (or mechanical pull), and 4 = cesarean section or other surgical intervention.

Causes of dystocia

The classification of factors that cause dystocia in cattle is varied. One study (Mee 2008) used the following system: proximal (or immediate), intermediate, and ultimate. Another study (Zhang, Nakao et al. 1999) used the following factors: fetal, maternal, a combination of fetal and maternal, genetic, and environmental. A study done at Iowa State University (Johanson and Berger 2003) classified dystocia factors into effects common in field data, effects not common in field data, interactions of these effects, and quadratic effects of these effects. In order to formulate a clinical management plan, causes of dystocia have also been divided into maternal and fetal origin (Norman and Youngquist 2007). A classification system which divides the causes of dystocia into two groups, direct and indirect (Meijering 1984, Zaborski, Grzesiak et al. 2009), is preferred due to the ease of categorization and its ability to encompass all factors. The direct causes of dystocia consist of malpresentation and uterine torsion, and indirect effects are made up of phenotypic effects dependent on cow and calf, genetic effects, and non-genetic effect. Phenotypic effects encompassed oversized calves, small pelvic dimensions (both leading to fetopelvic disproportion), and gestation length, while genetic factors include influence of the calf, dam, and sire of dam effects. Non-genetic effects are age of cow, parity, calf sex, diet, and calving season. Other factors of dystocia that were not included are uterine inertia, vulval or cervical stenosis, birth canal undersize, hypocalcemia, hypomagnesemia, multiple fetuses, fetal abnormalities, history of dystocia, nutrition, exercise, and prolonged preceding calving interval (Fiedlerová, Řehák et al. 2008, Mee 2008).

In cattle, especially in primiparous where most dystocia is seen to occur (Nix, Spitzer et al. 1998, Zhang, Nakao et al. 1999, NAHMS 2009a, NAHMS 2009b), the most important causes of dystocia are fetopelvic disproportion, abnormal fetal presentation,

position or posture, uterine inertia, and incomplete dilatation of the vulva and cervix (Rice and Wiltbank 1972, Mee 2004).

Fetopelvic disproportion is the most common cause of dystocia, making up 50 to 55% of dystocia cases seen (Wright 1958, Rice and Wiltbank 1972), and is due to an oversized calf, a dam with below average pelvic dimensions for her body weight, or both. Fetopelvic disproportion is also the main reason cesarean sections are performed in cattle (Mee 2008). The odds for dystocia increase by 13% for every kg increase in birth weight (Johanson and Berger 2003). In addition, calf birth weights and maternal pelvic dimensions account for 50% and 10% of the phenotypic variance in dystocia respectively (Meijering 1984), and a linear relationship between birth weight and the incidence of difficult births and death rate has been seen (Rice and Wiltbank 1972). Calf birth weight, the most important predictor of calving difficulty (Colburn, Deutscher et al. 1997), is largely influenced by gestation length (Burris and Blunn 1952), parity (Kertz, Reutzel et al. 1997), fetal gender (Laster, Glimp et al. 1973, Kertz, Reutzel et al. 1997), sire or dam breed (Bar-Anan, Heiman et al. 1987), nutrition (Grunert 1979), climate (Colburn, Deutscher et al. 1997), and in vitro embryo culture (Kruip and Den Daas 1997).

Abnormal fetal presentation, position, and posture account for 1 to 16% of dystocias observed (Wright 1958, Holland, Speer et al. 1993, Nix, Spitzer et al. 1998). Some studies (Holland, Speer et al. 1993, Nix, Spitzer et al. 1998) use the term “malpresentation” to encompass abnormalities in fetal presentation, position, and posture. However, these three terms carry different meanings and should not be summed under malpresentation. Presentation is actually the relationship of the fetus’ spinal axis to that of the dam and malpresentations occur when the fetus is in caudal longitudinal presentation. The normal presentation is cranial longitudinal. Position is the relationship of the dorsum of the fetus to the quadrants of the dam’s pelvis and a malposition is when the fetus is in dorsopubic or dorsoileal position. The normal position for delivery is dorsosacral. Posture is the relationship of the fetal extremities to the fetal trunk. Malposture involves the flexion, extension or retention of the head, neck, or limbs (Norman and Youngquist 2007). Variations of malposture include elbow

flexion, hip flexion, hip extension, head retroflexed, and lateral retention of the head. Therefore, the normal presentation, position, and posture of a fetus for delivery is cranial longitudinal presentation, dorsosacral position, and forelimbs extended with the head between the forelimbs. Few causes have been related to the displacement of the fetus. However, increased myometrial activity and the filling of the uterus by the fetus may cause an increase in intrauterine pressure which brings about a fetal response to reposition itself (Rice and Wiltbank 1972).

Uterine inertia accounts for up to 21% of cattle dystocia cases particularly in multiparous cattle (Morten and Cox 1968, Williams 1968) and is caused by the inability of the myometrium to contract normally to bring the fetus to the cervical region (Norman and Youngquist 2007). Uterine inertia can be primary, attributed to debility, overstretching of uterus by multiple or abnormal fetuses, premature delivery, hypocalcemia, hypomagnesemia, old age, and lack of exercise (Morten and Cox 1968, Mee 2004, Norman and Youngquist 2007, Mee 2008), or secondary as a result of myometrial exhaustion from prolonged calving (Mee 2004, Norman and Youngquist 2007).

Incomplete dilatation of the vulva occurs more frequently in primiparous cattle (Williams 1968) while incomplete dilatation of the cervix (10% of dystocias) occurs more often in multiparous cattle (Morten and Cox 1968). In this condition, the genital tract does not soften and relax, and this relative inelasticity does not allow dilation to occur when pressure is given by the advancing fetus (Williams 1968). Confinement and periparturient environmental stress, hormonal asynchrony, preterm calving, and premature assistance are associated with failure of complete dilatations (Dufty 1981, Mee 2004).

Sequelae of dystocia

Dystocia is an economically important factor in dairy and beef production systems as it causes financial losses by impacting production (41% of costs), fertility (34%), and cow and calf morbidity and mortality (25%) without taking into account the

costs of increased culling, veterinary fees and other management costs. The average cost of dystocia was approximately \$29 for heifers and \$10 for cows (Dematawewa and Berger 1997).

In terms of production losses, dystocia decreases milk, fat, and protein yield (Dematawewa and Berger 1997, Berry, Lee et al. 2007) with the largest losses occurring in early lactation, in high producing animals, and in cattle with higher scores of dystocia (Rajala and Gröhn 1998, Lombard, Garry et al. 2003). As for fertility, dystocia causes delayed uterine involution (Morrow, Roberts et al. 1966), delayed onset of ovarian cyclicity post-partum (Dobson, Tebble et al. 2001), abnormal progesterone profiles (Dobson, Tebble et al. 2001), lower estrus detection rate (Laster, Glimp et al. 1973), lower conception rate (Laster, Glimp et al. 1973), more services per conception (Dematawewa and Berger 1997), increased calving interval (McClintock, Beard et al. 2005), affects the conception date of the second calf (Colburn, Deutscher et al. 1997), and cattle were significantly more likely to experience uterine related diseases such as metritis and retained placenta (Oltenacu, Frick et al. 1988, Lombard, Garry et al. 2003). In terms of cow and calf morbidity and mortality, dystocia increased the likelihood of cow and calf respiratory and digestive diseases (Lombard, Garry et al. 2003, Lombard, Garry et al. 2007), perinatal mortality (Nix, Spitzer et al. 1998), and mastitis (Oltenacu, Frick et al. 1988).

Other post-parturient complications associated with dystocia include injury to the vagina and cervix, uterine rupture, prolapse of the uterus or vagina, paraplegia, paresis, and peritonitis (Sloss 1974). Although severe dystocias caused the biggest losses, even mild ones negatively influenced calf health and survival (Garry 2004). The total cost of dystocia was four times greater than treatment costs alone when costs associated with sequelae of dystocia were taken into account (Oltenacu, Frick et al. 1988).

Prevention of dystocia

In order to prevent dystocia, there are five critical time periods (Mee 2004) when action can be taken:

a) Choices at the heifer's birth

Primiparous cattle that had a heavy birth weight (as a calf) experience more severe dystocia as a 2 year old due to them having heavier birth weight calves, which was probably genetically caused (Colburn, Deutscher et al. 1997).

b) Preservice period

Sire expected progeny differences (EPD) for low birth weights should be consulted in order to develop calves with smaller bone sizes and birth weights (Colburn, Deutscher et al. 1997), especially if the animals to be bred are primiparous cattle. Selecting for greater pelvic height, pelvic width, or pelvic area can also help to reduce dystocia (Green, Brinks et al. 1988, Murray, Cartwright et al. 1999). The use of internal pelvimetry measurements to remove heifers with small pelvic areas has also been advocated. However, pelvimetry performed at breeding or early stages of gestation is not capable of reliably predicting dystocia (Van Donkersgoed 1992, Basarab, Rutter et al. 1993, Van Donkersgoed, Ribble et al. 1993)

c) During pregnancy

Using sexed semen or determining the fetal gender via ultrasound at 55 to 65 days of conception can help to anticipate increased dystocia risks due to male fetuses (Mee 2004). Detection of twin fetuses will also compel farm personnel to pay closer attention to the dam at calving.

d) Precalving

Reducing environmental stress at the time of calving is beneficial especially for primiparous cattle and can be done by adapting them earlier to the maternity unit,

calving them separate from multiparous cattle, keeping them loose and not tethered at calving, and avoiding disturbances from farm tasks (Mee 2004).

e) During calving

Proper supervision at stage II of parturition with timely intervention can help prevent dystocia caused by prolonged calving and secondary uterine inertia (Mee 2004) as insufficient monitoring might prolong the calving process and increase the risk of perinatal mortality (Gundelach, Essmeyer et al. 2009). The choice to perform elective surgical interventions, such as cesarean section or episiotomy, should be considered if it will prevent unnecessary trauma that may endanger the dam or fetus (Norman and Youngquist 2007).

Management of dystocia

When presented with an animal experiencing dystocia, it is important for farm personnel to know whether or when to intervene, how to intervene, and when to seek for veterinary assistance (Mee 2004). When timely intervention is given to cattle that need assistance, the negative effects of dystocia on perinatal mortality may be reduced (Johanson and Berger 2003, Schuenemann, Nieto et al. 2011). Regardless of the dam's parity, it is suggested that personnel should assist cattle 70 minutes after the appearance of the amniotic sac or 65 minutes after the feet appear outside the vulva. However, it is imperative that earlier obstetric intervention be given when an abnormal position or posture is seen immediately after the amniotic sac appears (Schuenemann, Nieto et al. 2011).

Perinatal mortality

Perinatal mortality or stillbirth has been defined as the death of the neonate that occurs prior to, during or within 24 to 48 h of calving (Chassagne, Barnouin et al. 1999, Mee, Berry et al. 2008). A majority (57%) of calf deaths are reported to occur within the

first 24 h postpartum (Patterson, Bellows et al. 1987). For calf deaths that occur after 24 h, they could be unrelated to dystocia (due to infectious or digestive diseases like an *E. coli* infection). It is therefore preferred to limit the definition of perinatal mortality to within 24 h of birth (Philipsson, Foulley et al. 1979, Meijering 1984, Lombard, Garry et al. 2007, Gundelach, Essmeyer et al. 2009). The terms stillbirth and perinatal mortality have been used interchangeably but if looked at literally, stillbirth would refer to a fetus that is born dead and is included in the definition of perinatal mortality (Mee 1999). Saunder's Comprehensive Veterinary Dictionary defined stillbirth as the "delivery of a fully formed dead neonate" and stillborn as "born dead" (Blood, Studdert et al. 2007). Therefore, it is in the author's opinion that the term perinatal mortality (which covers death that occurs prepartum, at calving, and postpartum) be used in place of stillbirth to encompass the 24 h period after calving.

Perinatal mortality was 8.1% in dairy calves (NAHMS 2009a) and 4.0% in beef calves (APHIS 2010). Difficult and prolonged calvings are the most important causes of perinatal mortality (Nix, Spitzer et al. 1998), as they cause trauma, fetal hypoxia (which is a major cause of reduced neonatal vitality), and possibly premature separation of the placenta. Other than that, congenital bacterial infections (*Leptospira hardjo*) should also be considered as a cause of mortality (Mee 1999).

Risk factors associated with perinatal mortality are the sex of the calf (Woodward and Clark 1959, Collery, Bradley et al. 1996, Chassagne, Barnouin et al. 1999, Meyer, Berger et al. 2001, Mee, Berry et al. 2008), calf birth weight (Johanson and Berger 2003, Mee, Berry et al. 2008), dam parity (Johanson and Berger 2003, Mee, Berry et al. 2008), time of year at calving (Colburn, Deutscher et al. 1997, Mee, Berry et al. 2008), gestation length (Meyer, Berger et al. 2001), malpresentation (Woodward and Clark 1959), previous history of perinatal mortality in the dam (Mee, Berry et al. 2008), overconditioning of the dam (Arnett, Holland et al. 1971), age at calving (Ettema and Santos 2004), poor fetal viability (Mee, Berry et al. 2008), placental dysfunction (Mee, Berry et al. 2008), duration of the second stage of labor (Gundelach, Essmeyer et al. 2009), and whether the calf was a singleton or twin (Ettema and Santos 2004). A larger

proportion of perinatal mortality was seen with bull calves, twin calves, calves born to primiparous dams, and those born to dams that have experienced dystocia (Lombard, Garry et al. 2007) as well as heavier calves born in winter due to the increased uterine blood flow which supplied more nutrients to the fetus (Colburn, Deutscher et al. 1997). Deficiencies in trace elements like copper, iodine, and selenium, and congenital abnormalities that include intra-uterine growth retardation, are not considered to have a significant part in the deaths of calves (Collery, Bradley et al. 1996, Mee 2004). Lower perinatal mortality was linked to dams with good abdominal press, calves born in anterior presentation, dorsosacral position and normal posture, calves born spontaneously, and dams with pelvises that were longer, had a downward slope, and larger internal pelvic width (Gundelach, Essmeyer et al. 2009).

Perinatal mortality has been associated with reduced milk yield, increased average lactation somatic cell score (Berry, Lee et al. 2007), and is an important cause of economic loss in cattle production (Collery, Bradley et al. 1996) as it costs the dairy industry in the United States about \$125 million per year (Meyer, Berger et al. 2001). However, differences in defining perinatal mortality, method of data collection, and farm management has affected the validity to conduct detailed comparisons between studies (Mee 1999).

To improve calf viability, nursing care should be applied promptly to calves that had a difficult calving, such as warming, drying, providing extra colostrum, stimulation, shelter, providing oxygen, and extra mothering attention (Garry 2004).

Predicting parturition

Predicting the time of parturition in cattle is invaluable for producers and veterinarians in order to manage cattle with prepartal disorders and plan elective cesarean sections. Improved management, closer observation of periparturient cattle, and identification and correction of calving problems with the aid of parturition

prediction will also help prevent calf deaths and injury due to dystocia, the dam, or the surroundings (Bellows, Patterson et al. 1987, Shah, Nakao et al. 2006).

Predicting the time of parturition has been unreliable and dams may remain in maternity pens for a week or longer rather than the 1 to 2 days as expected (Cook and Nordlund 2004). In order to accurately predict parturition, the hormonal, biochemical, metabolic, morphometric, and behavioral signs and changes associated with calving need to be identified and understood. The impending signs of parturition that will be discussed are plasma progesterone concentration, plasma estrogen concentration, plasma cortisol concentration, circulating glucose concentration, sacrosciatic ligament relaxation, body temperature, feed intake, heart rate, respiratory rate, mean arterial pressure, hematocrit, and rumen contraction rate.

Progesterone

Progesterone (Δ^4 -pregnene-3,20-dione) is a steroid sex hormone which functions as the principal progestational hormone (Gomes and Erb 1965, Blood, Studdert et al. 2007). Other progestational compounds that are important quantitatively include 20 α -hydroxy- Δ^4 -pregnene-3-one (20 α -ol), 20 β -hydroxy- Δ^4 -pregnene-3-one (20 β -ol), and 17 α -hydroxy- Δ^4 -pregnene-3, 20-dione (17-hydroxyprogesterone).

During the estrous cycle, plasma progesterone is 0.1 to 0.4 ng/mL just before, during, and immediately after estrus. The progesterone concentration increases on the 4th to 6th day (day of estrus is considered day 1) and reaches a peak of 3 to 6 ng/mL on the 11th to 18th day before dropping quickly over a 24 to 48 h period to a basal value 24 to 72 h before the start of the next estrus cycle (Robertson 1972). Day 15 of estrus was the peak observed in another study with the progesterone concentration of 5.9 ± 0.9 ng/mL before dropping dramatically to 0.7 ± 0.2 ng/mL at 2 days before the next estrus (Edgerton and Hafs 1973).

At the start of pregnancy, progesterone concentrations increased from 0.3 ± 0.1 ng/ml at estrus to 7.3 ± 0.6 ng/ml at day 11 and continued to rise to 12.2 ± 2.1 ng/ml on day 20 of pregnancy. Comparatively, infertile cows had plasma progesterone

concentrations that reached a peak of 7.8 ± 0.6 ng/ml on day 15 and decreased thereafter to 3.4 ± 1.8 ng/ml on day 20. The discrepancy was related to the corpus luteum regressing in infertile cows (Edgerton and Hafs 1973). Robertson (1972) found that in early pregnancy (up till the 15th day), plasma progesterone concentration was 3 to 6 ng/mL which was similar to the maximum concentration during the luteal phase of the estrous cycle. Plasma progesterone concentration averages 9.4 ± 0.2 ng/mL until the third month of pregnancy before suffering a decline to 6.9 ± 0.8 ng/mL at the fourth month and remaining at 6.5 ng/mL until near term (Eissa and El-Belely 1990). A mean concentration of 4.6 ng/mL of plasma progesterone was observed from day 140 to 200 (Stabenfeldt, Osburn et al. 1970). Progesterone concentrations increased to 6.8 ng/mL by day 250 before declining to 4 ng/mL about 10 days before parturition (Gao, Short et al. 1988). From 4 to 9 months of pregnancy, plasma progesterone concentrations stayed reasonably constant (Eissa and El-Belely 1990). In bodily fluids like saliva, defatted milk, whole milk, and plasma, concentrations of progesterone were the lowest at estrus, and they were the highest during the mid-luteal phase and the first and second trimesters of gestation (Gao, Short et al. 1988).

The maternal plasma progesterone concentration gradually decreased during the last 20 days of pregnancy and averaged approximately 4 ng/mL during the final week of gestation before falling rapidly at approximately 2 to 3 days before parturition corresponding with the regression of the corpus luteum (Stabenfeldt, Osburn et al. 1970, Fairclough, Hunter et al. 1975, Thorburn, Challis et al. 1977, Kejela, Head et al. 1978, Fairclough, Hunter et al. 1981). Plasma progesterone concentrations in the dam correlate with the low levels of uterine activity until 2 to 4 days prepartum (Gillette 1966) and this supports the progesterone block hypothesis whereby the myometrium is unable to perform maximal tension due to blocking of the physiological mechanisms of excitation caused by progesterone (Csapo 1956). Uterine electromyogram also showed changes representative of impending parturition after the concentration of progesterone had decreased to levels of 1 ng/mL or less (Taverne, Van der Weyden et al. 1979).

At 24 h before parturition, plasma progesterone concentrations are < 2.0 ng/mL (Robertson 1972, Goff, Kimura et al. 2002) and can even drop to < 1.3 ng/mL at 24 to 12 h prior to parturition (Stabenfeldt, Osburn et al. 1970, Edgerton and Hafs 1973, Parker, Foulkes et al. 1988, Matsas, Nebel et al. 1992). Matsas et al. 1992 reported that more than 95% of cows calved within 24 h when plasma progesterone concentrations were < 1.3 ng/mL (Figure 2.1).

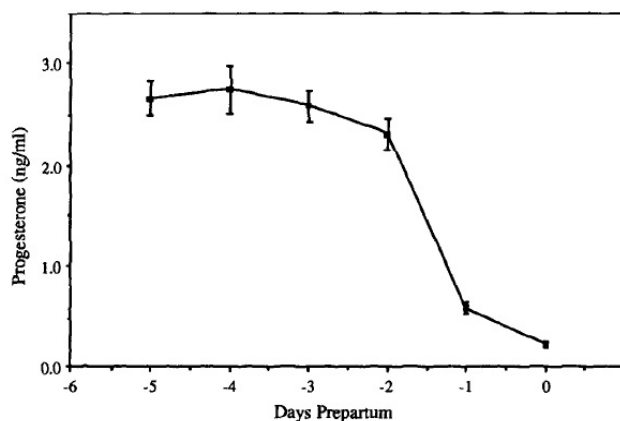


Figure 2.1 Mean \pm SEM for prepartum daily plasma progesterone concentrations in 45 cows with parturition occurring between Day -1 and Day 0 (Matsas et al. 1992).

Following parturition, plasma progesterone concentrations reach a nadir of 0.1 to 0.2 ng/mL within a day of calving (Goff, Kimura et al. 2002) and remain < 0.5 ng/mL until the first sign of resumption of the estrous cycle which ranged from 20 to > 60 days (Robertson 1972, Edgerton and Hafs 1973, Kejela, Head et al. 1978).

Throughout gestation, the corpus luteum and placenta synthesize and secrete progesterone. The maintenance of pregnancy relies on the progesterone as it supports uterine quiescence primarily via the hyperpolarization of myometrial cells (Wood 1999). Prior to days 165 to 180 of gestation, the corpus luteum is essential to maintain pregnancy. Thereafter, a viable fetus was sometimes maintained without this structure. In three cows that were ovariectomized at 101 to 123 days, pregnancy was sustained using a 30 day progesterone treatment period and was terminated 4 to 18 days after

the treatment ended. This indicates that abortion was due to the lack of progesterone in circulation following removal of the corpus luteum (Estergreen Jr, Frost et al. 1967). Ovariectomy in cattle on days 139 to 174 of gestation resulted in abortion 11 days later in seven out of eight cows while ovariectomy done on intervals of day 200 to 210, 226 to 237, and day 251 to 258 resulted in mean gestation lengths of 256, 264, and 264 days respectively (Estergreen Jr, Frost et al. 1967). An extraovarian source of progesterone (the placenta) contributes to progesterone production after day 200 of gestation and ensures that pregnancy is sustained to within 2 to 3 weeks of the normal expected calving date (Stabenfeldt, Osburn et al. 1970). However, many of the calves were born weak and died after delivery (Estergreen Jr, Frost et al. 1967). This shows that although the cow is able to carry on the pregnancy for some time, it still requires the continuous support of the corpus luteum, which is essentially the major producer of progesterone, to ensure a complete and normal gestation period (Stabenfeldt, Osburn et al. 1970, Thorburn, Challis et al. 1977, Kindahl, Kornmatitsuk et al. 2004).

After progesterone enters the blood circulation, it is subject to metabolism and is converted to a wide variety of metabolic products as it is an intermediate structure in the biosynthetic chain of steroid production from cholesterol (Loskutoff, Ott et al. 1983). Before being excreted in feces, progesterone is metabolized into groups of metabolites namely pregnanediones and mono and dihydroxylated pregnanes while intact and unmetabolized progesterone is hardly detectable in feces (Schwarzenberger, Son et al. 1996). In the urine, the predominant metabolite found in cows is pregnanediol-3-glucuronide (PdG) (Marker 1938, Klyne and Wright 1959, Feher, Orosz et al. 1975).

Assessments of matched urine and plasma for PdG and progesterone in the cow show that the PdG correlates with plasma progesterone concentration (Loskutoff, Ott et al. 1982, Yang, Wu et al. 2004) while in bison, PdG was a primary immunoreactive urinary metabolite and a valid indirect measurement of progesterone (Kirkpatrick, Kincy et al. 1991). Urinary PdG has the potential to be an excellent non-invasive and practical way to measure reproductive events (Loskutoff, Ott et al. 1982) as it accurately reflects

circulating progesterone concentrations and a functioning or non-functioning corpus luteum (Yang, Wu et al. 2004).

Other samples to measure progesterone concentrations include milk and saliva (Gao, Short et al. 1988, Kanchev, Marinova et al. 1988). Salivary progesterone concentration is linearly related with plasma progesterone concentration ($r = 0.85$, $P < 0.01$) but are present in much lower concentrations, amounting to 1% of plasma concentrations. Compared to plasma samples, saliva is able to serve as a non-invasive clinical indication of a cow's reproductive status and is relatively easy to collect via a method that involved the aspiration of saliva near the opening of the parotid gland's duct with a plastic tube attached to a plastic bottle. The saliva was then centrifuged to eliminate food particles and progesterone concentrations were determined via radioimmunoassay (Gao, Short et al. 1988). Another sampling method employed the use of cotton swabs placed in the buccal pouches of cattle. The animals were allowed to chew on them for 5 to 10 seconds until saturated before the swabs were stored in plastic vials and centrifuged to obtain the saliva (Grünberg, Morin et al. 2006). The only drawback that comes from using salivary samples is that an appropriately sensitive assay is needed to measure the low hormonal concentrations. When compared with milk, the turnover of saliva in the parotid gland is much faster than the turnover rate in milk which may be in the udder cisterns for some time. Therefore, salivary progesterone concentration provides a real time index of changes in plasma progesterone concentration. Additionally, progesterone concentrations in milk tend to be higher than in plasma which may imply that the mammary glands have the ability to concentrate progesterone while salivary samples likely show the free and biologically active concentrations of the hormone within the circulation (Gao, et al., 1988).

Estrogen

Estrogen is the naturally occurring female sex hormone formed in the adrenal cortex, ovary, and placenta (Mellin and Erb 1965, Blood, Studdert et al. 2007). It is responsible for the development of secondary female sex characteristics as well as acts

on female genitalia to establish a conducive environment for the fertilization, implantation, and nutrition of the early embryo (Blood, Studdert et al. 2007). There are several derivatives of estrogen and the key biologically active substances are estradiol (estradiol-17 α and estradiol-17 β being the two epimers), estrone, and estriol (Breuer 1962, Tsang, Hackett et al. 1975, Kindahl, Kornmatitsuk et al. 2004). Estradiol is the dominant estrogenic hormone in the non-pregnant animal and is produced by the mature ovarian follicle and adrenal cortex and is generally accountable for the sexual receptivity of the animal at estrus. Estrone is an oxidation product of estradiol and androstenedione, is less active than estradiol, and is produced in larger volumes in pregnant females (Blood, Studdert et al. 2007). Estrone sulphate is the conjugated form of estrone and is the major estrogen, produced by the placenta, present in the pregnant dam's circulation (Tsang, Hackett et al. 1975, Kindahl, Kornmatitsuk et al. 2004, Shah, Nakao et al. 2006). Estriol is relatively a weak estrogen as it is a metabolic product of estradiol and estrone found in the urine (Blood, Studdert et al. 2007).

During gestation, the placenta partially adopts the role of the ovaries to produce estrogen (Sloss and Dufty 1980) and this is demonstrated by the different concentrations of estrogen in the placental outflow when the uterine vein and umbilical vein are compared to the jugular vein and umbilical artery (Hoffmann, Schmidt et al. 1979). For the first three months of gestation, the concentration of total plasma estrogen was low (24.8 ± 3.1 pg/mL) before increasing progressively ($P < 0.05$) up to the sixth month (178.2 ± 20.0 pg/mL) and subsequently remained relatively constant (Eissa and El-Belely 1990). Concentrations of estrogen increased in the final three months of gestation and peaked just before or at parturition (Hoffmann, Schmidt et al. 1979).

During the period of 88 h prepartum, the mean plasma concentration of estrone sulfate was 13.4 ng/mL (equivalent to 10 ng estrone), compared to 1 ng/mL for estrone and for estradiol-17 β . At the time of parturition, at least 80% of the total plasma estrogen in the cow is in the form of estrone sulphate (Tsang, Hackett et al. 1975). During the final 6 days of gestation, total plasma estrogen concentrations increase progressively until the time of calving (Rexha, Grunert et al. 1993). Relative to

progesterone, the rate of production of estrogen is increased at this time and estrogen functions to produce a relative depolarization of the myometrial cells which augments its dormant activity (Wood 1999).

Total plasma estrogen concentrations start to increase rapidly ($P < 0.01$) from < 200 pg/mL on day 6.5 prepartum to $2,003 \pm 70$ pg/mL on day 5 prepartum. It continued to increase sharply and peaked on the day of calving at $4,604 \pm 26$ pg/mL (Eissa and El-Belely 1990). At 12 h postpartum, a quick decline in total plasma estrogen concentrations to 198 ± 17 pg/mL was seen (Eissa and El-Belely 1990). When the individual estrogen derivatives were observed, plasma estradiol concentrations increased in the final week of gestation and were seen to either peak on the day before parturition at 169 ± 23 pg/mL (Goff, Kimura et al. 2002) or on the day of parturition (4 to 12 h prepartum) at 340 ± 94 pg/mL (Kejela, Head et al. 1978). At day 1 postpartum (12 to 20 h postpartum) estradiol concentration was at 18 ± 2 pg/mL and 9 ± 2 pg/mL at 2 days postpartum (Kejela, Head et al. 1978). On the other hand, plasma estrone concentration was observed to peak just before parturition at 806 ± 63 pg/mL and drop abruptly at day 1 postpartum (Goff, Kimura et al. 2002). Overall, as gestation progressed the concentration of plasma estrone sulfate, estrone and estradiol-17 β increased and reached peak values around parturition (Shah, Nakao et al. 2006) before dropping rapidly within 8 h postpartum (Tsang, Hackett et al. 1975).

The estrogenic rise just before parturition may play a role in sensitizing the uterus to oxytocin, stimulate the release of prostaglandin F_{2 α} from the endometrium, and work with relaxin to soften the cervix and dilate the birth canal (Thorburn, Nicol et al. 1972, Kindahl, Kornmatitsuk et al. 2004).

In terms of periparturient problems, estrone sulphate was seen to be an important parameter as cows that gave birth to stillborn calves were found to have lower concentrations of the hormone (Kornmatitsuk, Dahl et al. 2004). Inadequate production of estrone sulphate also had an association with dystocia in dairy cattle (Zhang, Nakao et al. 1999). This indicates that the observation of estrone sulphate

concentration could be a part of fetal well-being monitoring (Kindahl, Kornmatitsuk et al. 2004).

Cortisol

In mammals under stress, glucocorticoids are secreted by the zona fasciculata cells of the adrenal cortex (Koper, Cordle et al. 1985) in response to the HPA axis being triggered by stressors or noxious stimuli. In ruminants, cortisol is the major circulating glucocorticoid (Sharpe, Buttery et al. 1986). An increase in plasma cortisol concentration serves as an adaptive mechanism to allow individuals to cope with stressors by mobilizing body reserves and regulate inflammatory responses to injury. Although fetal cortisol, not maternal cortisol, initiates parturition in ruminants (Hunter, Fairclough et al. 1977, Wood 1999), an increase in maternal circulating concentration occurs at the time of calving (Edgerton and Hafs 1973, Hudson, Mullford et al. 1976, Kejela, Head et al. 1978, Eissa and El-Belely 1990, Patel, Takahashi et al. 1996). A small amount of fetal cortisol crosses the placenta, but this makes up only less than 1% of the maternal circulating hormone (Dixon, Hyman et al. 1970), and does not account for all of the rise associated with parturition. Labor and delivery are traumatic, painful, and stressful experiences that likely elicit an increase in cortisol concentration (Hudson, Mullford et al. 1976, Hydbring, Madej et al. 1999). Cortisol also increased in cattle needing assistance at parturition which suggests that it is related with the amount of physical stress at calving (Hudson, Mullford et al. 1976)

Prepartum plasma cortisol concentrations are constant and range between 2 and 6 ng/mL (Hudson, Mullford et al. 1976, Kejela, Head et al. 1978, Patel, Takahashi et al. 1996). No relationship has been observed between the stage of gestation and/or the number of fetuses carried by the dam and the peripheral circulating cortisol concentrations (Patel, Takahashi et al. 1996) although twin bearing animals have been observed to have higher mean plasma cortisol concentrations on the day of parturition compared to singleton cows (Hudson, Mullford et al. 1976). Sharp rises in plasma cortisol concentration occur starting from the last 96 to 16 h before calving (Adams and

Wagner 1970, Hudson, Mullford et al. 1976, Patel, Takahashi et al. 1996, Kornmatitsuk, Konigsson et al. 2000, Goff, Kimura et al. 2002) and up to three fold increases from basal concentrations were observed (Edgerton and Hafs 1973). Cortisol concentration peaks of 14.8 ± 3.0 ng/mL (Kejela, Head et al. 1978) to 19.2 ng/mL (Hudson, Mullford et al. 1976) and even 19.4 ± 4.4 ng/mL (Goff, Kimura et al. 2002) were observed at the time of calving, followed by a return to basal concentrations by 1 to 3 days postpartum (Hudson, Mullford et al. 1976, Patel, Takahashi et al. 1996, Hydring, Madej et al. 1999). Comparatively, fetal plasma cortisol concentrations reached higher concentrations than their dams with reported concentrations of 5.0 ± 0.7 ng/mL at 20 days to 9.3 ± 3.0 ng/mL at 10 days before term, and up to 74 ng/mL at the time of parturition (Hunter, Fairclough et al. 1977). The increase in plasma cortisol concentration in primiparous cattle at parturition is strongly correlated with the phases of parturition (Hydring, Madej et al. 1999).

Cattle that delivered prematurely or experienced dystocia had higher plasma cortisol concentrations on the day of parturition (Patel, Takahashi et al. 1996) and this could be due to the added trauma and strain encountered. The elevation of cortisol concentration around parturition may be caused by the need for cortisol to initiate milk secretion (Martal and Djiane 1977), to accelerate mammary growth and lactation (Thorburn, Nicol et al. 1972), and the presence of estrogen that decreased the metabolic clearance rate of cortisol (Peterson, Nokes et al. 1960).

Glucose

Cortisol serves to both increase and sustain normal blood glucose concentrations by: a) stimulating gluconeogenesis (Radostits, Gay et al. 2007) which is the endogenous glucose production from non-carbohydrate substrates (Reilly and Black 1973, Danfær, Tetens et al. 1995); b) increasing utilization of amino acids from extrahepatic sources to serve as substrates for gluconeogenesis (Reilly and Black 1973); c) reducing the utilization of glucose by muscle and adipose tissues to conserve glucose (Bassett and Wallace 1966, Reilly and Black 1973); and d) stimulating lipolysis whereby the released

glycerol is used as a substrate for gluconeogenesis (Danfær, Tetens et al. 1995, Epperson 2005). Therefore along with cortisol, blood and plasma glucose concentrations also increase with stress response (Radostits, Gay et al. 2007).

Glucose provides energy for cells to maintain the fight or flight response (Landa 2011) and is easier to measure compared to cortisol, therefore it is able to serve as a proxy for cortisol concentrations. Prepartal blood glucose concentrations range between 45 to 70 mg/dL and show a definite and marked increase at the time of calving reaching concentrations of approximately 76 to 150 mg/dL before rapidly dropping to lower concentrations of approximately 34 to 70 mg/dL postpartum (Godden and Allcroft 1932, Schwalm and Schultz 1976, Jacob, Ramnath et al. 2001, Bionaz, Trevisi et al. 2007)

A point of care system that could be used cow-side would be ideal to monitor changes in glucose concentrations as it saves money and time due to less handling, transport, and laboratory analysis involved (Landa 2011). Whole blood, serum, and plasma could be used to measure glucose concentrations although values will be higher in serum and plasma compared to blood (Somogyi 1933, Goodwin 1956, D'Orazio, Burnett et al. 2005) due to glucose metabolism by red blood cells (Landa 2011). Also, in whole blood, glucose and water are distributed freely between erythrocytes and plasma, and the molality of glucose (amount of glucose per unit of water mass) is the same in primates but not in domestic animals. Whole blood glucose concentration relies on hematocrit which varies from animal to animal, and this variability serves as a confounder of the relationship between blood glucose and plasma glucose concentration.

A variety of portable blood glucose meters have been produced that allow the evaluation of blood glucose concentration using a drop of capillary blood. Most of these meters use quantification methods that are based on the enzymatic reaction between glucose in the sample and glucose oxidase. These meters are easily available, relatively cheap, and provide quick results with only a small quantity of blood (Cohn, McCaw et al. 2000). The portability and lightness of these meters makes it easy for farm personnel and veterinarians alike to carry them around. Point-of-care analyzers have also been

used to monitor glucose concentration but they typically require various cartridges to measure a number of biochemical parameters besides glucose concentrations. They are also more expensive than glucose meters and are designed more for use by health care professionals (Cohn, McCaw et al. 2000).

Glucose meters (glucometers) make measurements by using enzymatic reactions coupled to chromogen alterations that are detected via reflectance photometry and by electrochemical reactions whereby the electrical current is proportional to the glucose concentration (Cohn, McCaw et al. 2000). There is a plethora of glucometers available in the market and a number of them that have been used in animal studies (Cohn, McCaw et al. 2000, Galvão, Flaminio et al. 2010, Winkelman and Overton 2012) include the Glucometer 3 (Bayer Corp, Elkhart, IN), Glucometer Encore (Bayer Corp, Elkhart, IN), Accu-Chek® Easy (Roche Diagnostics, Indianapolis, IN), Accu-Chek® Active (Roche Diagnostics, Indianapolis, IN), ExacTech RSG (Medisense Inc, Waltham, MA), Glucometer Elite® (Bayer Corp, Elkhart, IN), and Precision Xtra® (Abbott Laboratories, Abbott Park, IL).

The Precision Xtra® glucose meter system consists of a handheld meter and electrochemical test strips. After the test strip is inserted into the meter, a 0.6 μL of blood sample is applied to the sensor. Via capillary action, the blood travels through the test strip and reacts with glucose oxidase to form gluconic acid. This in turn reacts with potassium ferricyanide to produce potassium ferrocyanide which reacts with the metal of the test strip electrodes creating electrical current. The current produced is directly proportional to the amount of glucose present in the blood sample. After 5 s, the glucose concentration (mmol/L or mg/dL) is displayed by the monitor. The Precision Xtra® is limited to the quantification of 1.1 to 27.8 mmol/L or 19.8 to 500.9 mg/dL (Wittrock, Duffield et al. 2013).

It should be noted that there are many potential sources of error when using glucose meters which include temperature, altitude, humidity, patient hematocrit, improper calibration, use of expired reagent strips, error in timing, inappropriate blood

droplet size or placement, and incorrect sample insertion (Fazel, Koutoubi et al. 1996, Gautier, Bigard et al. 1996, Cohn, McCaw et al. 2000, Tang, Lee et al. 2000).

Sacrosciatic ligament relaxation

The sacrosciatic ligament (SSL) is a broad sheet located in the pelvic girdle that is attached dorsally to the lateral border of the sacrum and transverse processes of the first and second coccygeal vertebrae (Sloss and Dufty 1980, Dyce, Sack et al. 2010). The ventral border is located between the supracotyloid ridge and tuber ischii. The greater and lesser sacrosciatic foramina are located cranial and caudal to the ligament respectively. The gluteal nerves and vessels as well as the sciatic nerve emerge from the greater sacrosciatic foramen. The caudal border of the ligament is free and traverses between the first or second coccygeal vertebrae and the tuber ischii (Sloss and Dufty 1980) and is palpable in cattle (Dyce, Sack et al. 2010). As parturition approaches, the SSL starts to soften and relax (Ewbank 1963, Mortimer 1997, Dyce, Sack et al. 2010) and the degree of relaxation increases significantly with increasing parity (Berglund and Philipsson 1987). Changes in the ligament proved to be reliable as they were easily identified and had a constant relationship with the start of dilatation of the cervix (Dufty 1971). The relaxation of the pelvic ligaments was also the best individual clinical predictor when measured in combination with various other parameters (Streyl, Sauter-Louis et al. 2011).

The relaxation of pelvic structures as calving approaches has been related to relaxin and estrogen. Relaxin causes the lysis of collagen that results in the softening of the cervix and relaxation of the SSL (Beagley, Whitman et al. 2010). However, intramuscular injections of porcine relaxin did not significantly alter periparturient attributes in beef heifers (Caldwell, Bellows et al. 1990) and this has led to the controversial and questionable role of relaxin in the relaxation of pelvic ligaments (Shah, Nakao et al. 2006). Placental estrogens like estrone sulphate and especially estradiol-17 β has been suggested to be the principal hormone that exerts an effect on the SSL as both these parameters corresponded well with each other (Figure 2.2) (Shah, Nakao et

al. 2006). The relaxation of pelvic ligaments in guinea pigs have also been induced with administration of estrogen (Emery and Lawton 1947).

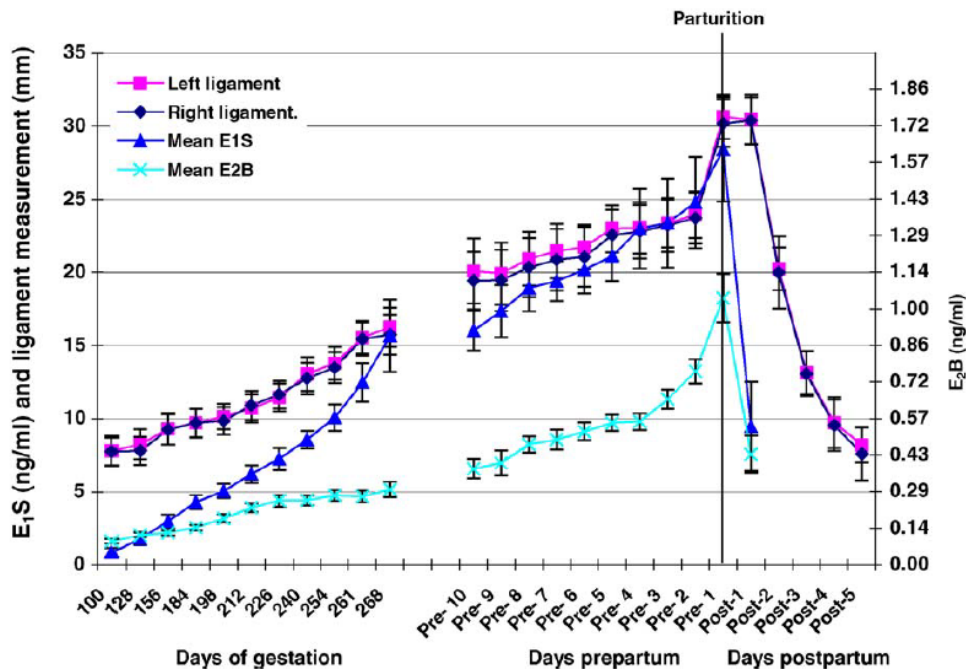


Figure 2.2 Plasma estrone sulphate (E_1S) and estradiol-17 β ($E_2\beta$) profiles in Holstein-Friesian cows from day 100 of gestation until day 1 postpartum and corresponding changes in the measurement of relaxation in the sacrosciatic ligaments (Shah et al., 2006).

The relaxation of the SSL can be observed visually as an insinking beside the tail head (Dyce, Sack et al. 2010). Various methods have been used to quantify the degree of SSL relaxation. By inserting one hand into the rectum and the other on the caudal border of the ligament externally, the displacement of the ligament can be assessed when pressure is provided against it from within the rectum (Mortimer 1997). This simultaneous external and rectal palpation was deemed a precise way to predict the onset of parturition in 82% of cattle studied (Dufty 1971). Semi-quantitative scoring systems have also been used (Dufty 1971, Kornmatitsuk, Konigsson et al. 2000, Streyl,

Sauter-Louis et al. 2011) with an example being: Negative = no relaxation (as in cow in the 4th month of lactation), 1 = slight relaxation (ligament “gives” when pressed with finger), 2 = relaxation (ligament feels slack), and 3 = complete relaxation (edge of hand can be placed between tuber ischia and coccyx) (Ewbank 1963). The length of the pelvic ligament from the point of origin to the point of insertion had also been done (Kornmatitsuk, Konigsson et al. 2000). A Japanese study used a more quantifiable method to measure the relaxation of the SSL using a two scale/ruler system (Shah, Nakao et al. 2006). One scale was placed exactly parallel/horizontal to the SSL between the sacrum and tuber ischia while the other was placed perpendicularly/vertically to the first scale. The bottom of the second scale is at a position where it touches the ligament while the graduated edge is touching the facing edge of the first scale. The depth that was measured was taken from the point that the second scale touched the ligament to where it touches the first scale (Shah, Nakao et al. 2006).

The relaxation of the SSL has been used to predict calving within 12 h (Berglund and Philipsson 1987, Kornmatitsuk, Konigsson et al. 2000). Consistent with changes in plasma estradiol-17 β concentrations, a slow increase in ligament relaxation was observed as gestation advanced from day 100 of gestation (8 ± 1 mm) until day 2 prepartum (24 ± 2 mm) and reached a peak value on the day before parturition (31 ± 2 mm). A significant increase ($P < 0.05$) was seen between measurements done on day 2 and day 1 prepartum with almost no difference between day 1 prepartum and day 1 postpartum. A marked decrease ($P < 0.05$) occurred after that until day 3 postpartum (10 ± 2 mm) while no significant difference was observed between days 3 and 4, and 4 and 5 postpartum. The increase in the relaxation of the ligament by ≥ 5 mm from the day before was the most effective to predict parturition within 24 h with the greatest accuracy (94%) in a high proportion of cows (31 of 37) in the herd.

Body temperature

Various methods have been employed to measure the body temperature of cattle which include using thermometers in the rectum (Ewbank 1963, Burfeind, Von

Keyserlingk et al. 2010, Burfeind, Suthar et al. 2011), microprocessor-controlled data loggers in the vagina (Aoki, Kimura et al. 2005, Vickers, Burfeind et al. 2010, Burfeind, Suthar et al. 2011), temperature boluses in the rumen (Bewley, Grott et al. 2008, Cooper-Prado, Long et al. 2011, Rose-Dye, Burciaga-Robles et al. 2011), transmitters implanted in the abdominal cavity, peritoneal cavity, udder, flank, or behind the rib cage (Bitman, Lefcourt et al. 1984, Lefcourt and Adams 1996, Lammoglia, Bellows et al. 1997, Brown-Brandt, Yanagi Jr et al. 2003), and infrared thermography or thermometry to measure surface temperature (Coppola, Collier et al. 2002, Dalton and Ayers 2012).

The rectal temperature, using mercury and digital thermometers, is a common and traditional way to measure body temperature (Ewbank 1963, Burfeind, Von Keyserlingk et al. 2010, Burfeind, Suthar et al. 2011). When measuring rectally, it is important that the thermometer remains in contact with the rectal wall for an adequate amount of time (Ewbank 1963) to obtain a stable and accurate corporeal reading. Compared to digital thermometers, analog or mercury thermometers break easily and the spilled mercury is hazardous.

Vaginal temperature has been measured via microprocessor-controlled data loggers attached to a modified vaginal controlled internal drug release insert or thermocouple sensor placed into the vaginal cavity which are able to measure the body temperature frequently and record diurnal variations (Aoki, Kimura et al. 2005, Vickers, Burfeind et al. 2010, Burfeind, Suthar et al. 2011). Measurements from vaginal loggers were found to closely correspond with readings from a liquid-in-glass thermometer that was calibrated in a water bath (gold standard) and with rectal temperatures which serve as the cow-side reference method (Vickers, Burfeind et al. 2010). The usage of data loggers is appropriate when continuous temperature readings need to be taken. However, acquiring a sufficient number of devices for the herd can be expensive and it needs to be attached to the animal which can prove troublesome. Additionally, the probe is placed in the dam's vagina which may interfere with the calving process.

Another method to measure body temperature is by the use of ruminal boluses and telemetry that are orally inserted into the rumen of the animal with a balling gun

(Cooper-Prado, Long et al. 2011). These boluses are able to transmit ruminal temperatures at a programmed time interval with minimal disturbances to the animal's behavior and temperature (Cooper-Prado, Long et al. 2011, Rose-Dye, Burciaga-Robles et al. 2011). Ruminal temperature was seen to have a high correlation ($r = 0.89$) with rectal temperature (Rose-Dye, Burciaga-Robles et al. 2011). A major setback of this method was that ruminal temperature decreased, sometimes as much as 8.5°C (15.3°F) in dairy cows, after the consumption of cold water (Bewley, Grott et al. 2008, Rose-Dye, Burciaga-Robles et al. 2011).

Transmitters implanted into the animal can be placed at various sites and allow for a continuous collection of data but are invasive as they need to be placed surgically (Lammoglia, Bellows et al. 1997). Surface temperatures are measured via infrared thermography or thermoscopy (Coppola, Collier et al. 2002, Dalton and Ayers 2012) and readings can be taken from various surfaces like the udder, side of animal, nose, eye, and third eyelid (Coppola, Collier et al. 2002, Dalton and Ayers 2012). The decrease in maternal body temperature is measurable from the skin surface, thereby reducing the need to handle the animal. However, surface temperatures of the side and udder were affected by breed, parity, air temperature, and solar radiation (Coppola, Collier et al. 2002). Other than that, infrared readings of the cornea, third eyelid, nose, and udder had poor correlations with rectal temperature due to variations in skin color that affected readings (Dalton and Ayers 2012).

The body temperature of cattle is known to decrease before parturition occurs (Porterfield and Olson 1957, Ewbank 1963, Kornmatitsuk, Konigsson et al. 2000) and it can be clinically used to highly predict the onset of parturition in many domestic animals (Weisz 1943).

Studies done on the timing of parturition based on rectal temperatures noted that about 4 weeks before parturition, the temperature of the dam reaches a physiological maximum of 103.1°F (Weisz 1943) before once again reaching average high temperatures of 103.0°F and 102.1°F on days 4 and 2 prepartum (Dufty 1971). The day before parturition, rectal temperatures were seen to drop quickly by about 0.5 to

1.6°F, which was able to predict birth occurring within a day (Weisz 1943, Strey, Sauter-Louis et al. 2011). The wide variation of the precalving temperature drop (0.2° to 1.9°F) observed starting between 33 to 74 h prior to parturition in another study (Ewbank 1963) limits its value in predicting the actual calving time. Rectal temperatures were useful in cows that showed external evidence of nearing parturition but had temperatures above 102°F as they were not likely to calve within the next 12 h. Temperatures reached normal limits again around 24 h postpartum (Weisz 1943).

Vaginal temperature measurements indicate that a pronounced decline in vaginal temperature of 1.0 to 1.6°F usually happen between 24 and 48 h before calving without any regards to the time of day or atmospheric temperature and this drop could predict calving times in over 50% of cows (Porterfield and Olson 1957). Decreases in vaginal temperature prior to parturition have been defined using two methods (Aoki, Kimura et al. 2005). The first was the “same hours method” that showed the difference of vaginal temperatures at a certain time of the day with the vaginal temperature at the same time but on the preceding day. When the difference was consistently ≥ 0.3 (0.54°F) or $\geq 0.5^\circ\text{C}$ (0.90°F) for more than 3 h, cows calved within 60 h. A second method was the “maximum-minimum” method whereby the decrease in temperature was deemed to have begun when the maximum and minimum values for the day went down by ≥ 0.3 or $\geq 0.5^\circ\text{C}$ from the preceding day’s readings. When this criterion was met, all cows calved within 72 h and 92% calved within 48 h. Additionally, pregnant cows bearing mixed-sex twin fetuses had lower vaginal temperatures when the weight of the weight of the female fetus was heavier while cows bearing single sex twins that had heavier total weights showed higher vaginal temperatures than those weighing lesser. This may be indicative of probable reasons for progesterone synthesis or estrogen disorders, or even other metabolic problems in freemartins which requires further research is required to determine the exact mechanism (Aoki, Kimura et al. 2005).

Ruminal temperatures decreased about 0.3°C (0.54°F) around 24 h before parturition (Cooper-Prado, Long et al. 2011) while implanted transmitters indicated that body temperatures decreased from 48 to 8 h prepartum (Lammoglia, Bellows et al.

1997). Surface temperatures of the eye, side of animal, and udder slowly increased from 10 days to 2 days before calving before decreasing. For the side measurement, the drop in temperature prior to parturition was up to 1.1°C (2.0°F) (Coppola, Collier et al. 2002).

It was interesting to note that in several studies, a decrease in body temperature was followed by an increase at 12 to 24 h before parturition (Porterfield and Olson 1957, Ewbank 1963, Birgel, Grunert et al. 1994, Lammoglia, Bellows et al. 1997, Burfeind, Suthar et al. 2011).

The mechanism and role of the prepartum temperature decrease remains unexplained (Aoki, Kimura et al. 2005). It is speculated that metabolic adaptation as well as endocrine and behavioral changes during the periparturient phase may contribute to the decline in body temperature before calving. Correlations between the concentration of plasma progesterone and body temperature (Birgel, Grunert et al. 1994) indicate the likelihood of the thermogenic effect of progesterone (Wrenn, Bitman et al. 1959) as vaginal temperature increased in ovariectomized cows treated with progestagens compared to untreated cows (Wrenn, Bitman et al. 1959). Higher vaginal temperatures during the luteal phase of the estrous cycle and lower temperatures pre-estrus in cows (Kyle, Kennedy et al. 1998) support the hypothesis of the thermogenic effect of progesterone. The increase in estradiol-17 β , which has a hypothermic effect, and the decrease in progesterone, which has a hyperthermic effect, may have an influence on the overall body temperature (Cagnacci, Melis et al. 1992). A close positive association was observed between the prepartum decrease in body temperature and progesterone concentration while a negative relationship was seen between the temperature and the estrogen/progesterone ratio. It was proposed that the estrogen/progesterone ratio may be a major factor that regulates body temperature during the prepartum period (Rexha, Grunert et al. 1993). The decrease in feed intake as parturition approaches could also lower the body temperature as metabolic rate corresponds with energy intake to correct for energy imbalances through the process of diet-induced thermogenesis as seen in humans (Stock 1999). Additionally, a fall in core body temperature of sheep was observed after prolonged food deprivation (Piccione, Caola et al. 2002).

Heart rate

In response to noxious stimuli, both the HPA axis and the autonomic nervous system (ANS) function to mediate the stress response and restore metabolic homeostasis (Stewart, Verkerk et al. 2010). Pain and fright activate the sympathetic division of the ANS to release adrenaline and noradrenaline from the adrenal medulla as part of the “flight or fight” response that prepares the body to cope with stressors by elevating the heart rate, blood pressure, and respiratory rate (Hydbring, Macdonald et al. 1997, Von Borell 2001, Stewart, Verkerk et al. 2010). Other parameters used to measure the sympathetic nervous system activity are heart rate variability, eye pupil diameter, peripheral blood flow, and plasma catecholamine concentration (Stewart, Verkerk et al. 2010). Calves that received an anti-inflammatory after dehorning had a lower heart rate and respiratory rate (Heinrich, Duffield et al. 2009) which further show that these parameters increase during periods of stress.

The heart rate and its beat to beat variability depend on the rate of discharge of the pacemaker, usually the sinoatrial node which is influenced by the two major divisions of the autonomic nerves namely the sympathetic and parasympathetic nervous system. Lower heart rates show predominant vagal activity while higher heart rates are caused by sympathetic activity (Hainsworth 2008). Heart rate provides a suitable parameter for studying animal responses to physiological or environmental challenges as it increases significantly with exposure to external stress or sickness (Pollard and Littlejohn 1995, Mohr, Langbein et al. 2002). In cattle, the normal heart rate is 73 ± 14 beats per minute (Radostits, Gay et al. 2007) and can be measured via auscultation, electrocardiography, or via a blood pressure monitor. In goats, heart rates increase at late parturition but did not show any further elevation close to parturition and during labor. Heart rates did peak at the moment the first kid was born (Hydbring, Macdonald et al. 1997) which was concomitant with the peak of plasma adrenaline concentration and this peak was also observed in primiparous cattle calving (Hydbring, Madej et al. 1999). A study done on German Holsteins found that at 24 h before parturition, the

heart rate of dams increased slightly with an evident elevation seen at 6 h before calving (Georg, Beintmann et al. 2008).

Respiratory rate

The resting respiratory rate in cattle is between 10 to 30 breaths per minute and should be examined from a distance, preferably when the animal is standing as recumbency can modify the rate substantially. It is important to note that rises in environmental temperature and humidity may double the normal respiratory rate (Radostits, Gay et al. 2007). Respiratory rates can be calculated by counting the movements of the flank, abdomen or thorax, or via auscultation if the animal is moving excessively or has a rapid shallow breath (Dufty 1971, Legates, Farthing et al. 1991, Radostits, Gay et al. 2007). For long term studies that require frequent measurements, the traditional methods of monitoring respiratory rate becomes tedious, labor intensive, and has a possibility of the observer influencing the animal. Automated monitors with data logging abilities that are attached to the animal can help increase measuring frequency for a more robust application of time series techniques and reduce labor requirements (Eigenberg, Hahn et al. 2000). A positive relationship was seen between respiratory rates and plasma cortisol concentrations (Tagawa, Okano et al. 1994) which may signify that respiration is tied to stress and could possibly be a parameter that could predict the time of calving.

Mean arterial blood pressure

Blood pressure typically refers to the pressure of the blood within arteries or arterial blood pressure and is determined by interrelated factors like the pumping action of the heart, the resistance of blood flow in arterioles, the elasticity of main arterial walls, blood volume and extracellular fluid volume, and the viscosity of blood (Blood, Studdert et al. 2007). Measurements of blood pressure can be made via the direct or indirect method. The direct method involves the catheterization of blood vessels and provides the most accurate measurements (Tagawa, Okano et al. 1994, Hydbring,

Macdonald et al. 1997, Aarnes, Hubbell et al. 2014). For routine use however, the indirect method is preferred as it does not require cannulation or needle puncture of the artery. This principle of the indirect method involves the occlusion of an artery via an inflatable cuff and the detection of blood flow, below or distal to the occlusion site, that returns as the occlusion pressure is lessened (Glen 1970). The various indirect methods of blood pressure measurement include the auscultatory technique (Glen 1970), the oscillometric technique (Brăslașu, Brăslașu et al. 2008, Aarnes, Hubbell et al. 2014), using a pulse monitor (Campbell, Lawson et al. 1964), and plethysmography (Byrom and Wilson 1938, Yamakoshi, Shimazu et al. 1979). When occlusion cuffs for indirect blood pressure measurement are used in cattle, they are typically applied to the tail at the intravertebral area. This is to allow the occlusion of the coccygeal blood vessels as the median coccygeal artery is protected by the ventral spinous processes (Glen 1970). The systolic, diastolic, and mean arterial blood pressure can be obtained from blood pressure readings (Hydbring, Macdonald et al. 1997). Blood pressure in goats increased on the day of parturition and reaches a peak value when the head of the first kid was visible (Hydbring, Macdonald et al. 1997) which indicates the possibility of using blood pressure measurements as an indicator of parturition.

Hematocrit

Hematocrit is the volume percentage (vol %) of erythrocytes that is present in whole blood and is obtained via the centrifugation of a blood sample to separate the cellular contents from the plasma (Blood, Studdert et al. 2007). The packed cell volume (PCV) that is obtained shows the ratio of cell volume to plasma volume and is expressed as a percentage. The size, functioning capacity, and amount of erythrocyte number can be obtained from the hematocrit when read together with other hematological tests. Hematocrit values increase due to splenic contraction or dehydration (Schaefer, Jones et al. 1997, Radostits, Gay et al. 2007). The activation of the sympathetic nervous system as a response to excitement or pain causes splenic contraction and the release of

erythrocytes into circulation (Fazio and Ferlazzo 2003). Dehydration can be caused by reduced water requirements as a result of a lowered feed intake (Winchester and Morris 1956) which typically occurs during the preparturient period.

Feed intake

The appetite and voluntary feed intake of cattle are controlled by various factors like environmental temperature (Bonsma, Scholtz et al. 1940), heat stress (Gorniak, Meyer et al. 2014), humidity (Gorniak, Meyer et al. 2014), wind speed (Grant and Albright 1995), solar radiation (Grant and Albright 1995), anabolic agents (Heitzman 1975), diseases (Fox 1993, Siivonen, Taponen et al. 2011), palatability (Baumont 1996), and pain (Fitzpatrick, Young et al. 1998). Dry matter intake (DMI) and feeding behavior are controlled by gut fill and chemostatic mechanisms, as well as modulated by the management of feeding, environment, health, and social interactions (Grant and Albright 1995).

Beginning 10 to 5 days prepartum, feed intake reduced by approximately 30% (Bertics, Grummer et al. 1992, Grant and Albright 1995, Greenfield, Cecava et al. 2000). Between days 7 and 2 prepartum, there was an average daily decrease of DMI at a rate of 0.15 kg/d (0.33 lb) with a sizeable drop on day 1 prepartum (relative to the previous day) by 33% (Huzzey, Veira et al. 2007). On the day of calving, there was a 55% decrease from the average DMI at 10 to 14 days prepartum seen in dams carrying twins (Goff, Kimura et al. 2002). Older multiparous cattle consumed less dry matter on the day of calving compared to primiparous and second calvers (Marquardt, Horst et al. 1977). With values at day 14 prepartum as the base, the DMI on day 1 prepartum and calving day for primiparous or 2nd calvers and multiparous cattle were depressed 14, 28%; and 35, 75% respectively. The DMI of cattle recovered on day 1 postpartum (Marquardt, Horst et al. 1977) with an improvement of 28% (Huzzey, Veira et al. 2007) coupled with an exponential increase that generally occurred in the post-calving period (Vazquez-Anon, Bertics et al. 1994). It was of particular note that an 11% decrease happened on day 1 postpartum (Huzzey, Veira et al. 2007).

Feeding times of cattle also decrease between days 7 and 2 prepartum at a rate of 2.6 minutes/day and dropped drastically by 33% on day 1 prepartum relative to day 2 prepartum (Huzzey, Veira et al. 2007). A significantly shorter total eating duration occurred at the final six h period before parturition (Miedema, Cockram et al. 2011).

The decrease in DMI of Holsteins during the prefresh transition period was fitted to an exponential function of $DMI(t) = a + pe^{(kt)}$, whereby $DMI(t)$ = DMI as percentage of body weight at time t , a = asymptotic intercept at time $-\infty$, p = change in intake (kg) from the asymptotic intercept till parturition, k = rate constant affecting the curve shape, and t = day relative to parturition shown as days pregnant – 280. The model was generated to help predict the DMI in order prepare balanced rations when actual on farm estimates were not taken. The proposed models for heifers and cows were $DMI(t) = 1.713 - 0.688e^{(0.344t)}$ ($R^2 = 0.96$) and $DMI(t) = 1.979 - 0.756e^{(0.154t)}$ ($R^2 = 0.97$) respectively (Hayirli, Grummer et al. 2003).

Estrogen had a significant depressing influence on DMI while progesterone did not affect DMI but was able to partially counteract the reduction in feed intake caused by estrogen (Muir, Hibbs et al. 1972). At parturition, progesterone and estrogen decrease and increase respectively and these changes play a role in reducing the DMI of the dam. Estradiol affects feed intake by acting on estrogen receptors within the brain and the direct stimulation of the ventromedial hypothalamus by estradiol significantly depressed feed intake (Wade and Zucker 1970). Reductions in feed intake could also be caused by pain due to a malpositioned fetus (Proudfoot, Huzzey et al. 2009) or large fetus that may reduce the amount of available space in the rumen (Stanley, Cochran et al. 1993).

Rumen contraction rate

The ruminant forestomach consists of the reticulum, rumen, and omasum that function as a multipurpose but well regulated fermentation vat that allows for symbiosis between the host and microorganisms (Kay 1983, Constable, Hoffsis et al. 1990). The reticulorumen in an adult cow takes up almost the whole left half of the abdominal

cavity and has a capacity of up to 90 kg (198 lb) of digesta. Due to its large size and ease of examination, rumen motility is regarded to represent digestive functions of a ruminant (Radostits, Gay et al. 2007).

There are four different contraction patterns in the ruminant forestomach namely the primary or mixing cycle, secondary or eructation cycle, rumination (associated with chewing of cud and the primary cycle), and the esophageal groove closure that is associated with milk suckling (Sellers and Stevens 1966, Radostits, Gay et al. 2007). The identification of ruminal contraction requires the auscultation and observation of the left paralumbar fossa (Constable, Hoffsis et al. 1990).

Rumen hypomotility is the reduction in the frequency or strength of contractions, or both, and is typically caused by the reduction of the excitatory drive to the gastric center or an elevation of inhibitory inputs (Constable, Hoffsis et al. 1990). The frequency of primary contractions in cows averages at 60 cycles per hour but reduces to 50 cycles per hour during rumination or even lower with the cow in recumbency. Feeding elevates the contractions to 105 cycles per hour (Sellers and Stevens 1966). Due to this variability, it is advisable to auscultate for a minimum of two minutes to determine contraction frequency (Constable, Hoffsis et al. 1990).

The four vital inhibitory inputs to the gastric center are pyrexia, pain, moderate to severe urinal distention, and increased concentrations of volatile fatty acids (Constable, Hoffsis et al. 1990). Painful stimuli act directly on the gastric center and together with the release of catecholamines changes the reticulorumen motility (Titchen 1958). The sympathetic nervous system also responds to pain and is capable of stimulating the splanchnic motor nerves and directly inhibit reticulorumen motility (Leek 1969). Besides that, a reduction in feed intake also reduces reticulorumen motility as it removes forestomach distention and chewing activity (Constable, Hoffsis et al. 1990).

Older multiparous cattle tend to have primary rumen contractions that were lesser and weaker than young cows on the day of parturition and for a few days postpartum. Following calving, the lowered plasma calcium concentration is speculated as the primary reason for the reduced rumen motility (Marquardt, Horst et al. 1977).

Pelvimetry

Pelvimetry is the “measurement of the capacity and diameter of the pelvis, either internally or externally or both, with hands or with a pelvimeter” (Blood, Studdert et al. 2007). In cattle, internal pelvimetry has been used to determine pelvic area and its association with calving difficulty (Rice and Wiltbank 1972, Deutscher 1991, Van Donkersgoed, Ribble et al. 1993, Coopman, de Smet et al. 2003).

Pelvimetry measurements

Pelvimetry measurements are comprised of external and internal pelvimetry. External pelvimetry is done to correlate pelvic dimensions with measurements taken outside of the animal like the distance between: the two tuber ischii (pin width), the two tuber coxae (hip or hook width), the anterior surface of the ilial wing and the posterior surface of the ischium (rump length), ilial wing to hip joint, and iliac crest to ischial tuberosity (hook to pin) (Craig 1912, Bellows, Gibson et al. 1971, Johnson, Deutscher et al. 1988, Coopman, de Smet et al. 2003). These distances were initially measured using straight pieces of wood and tape measure (Craig 1912) and later on with sliding calipers (Bellows, Gibson et al. 1971). There has been mixed responses on the value of external pelvimetry as a predictor for internal pelvic dimensions with one group noting significant correlations ($P < 0.001$) between the two (Murray, Cartwright et al. 2002) while another found that withers height and heart girth were better predictors (Kolkman, Hoflack et al. 2012). Internal pelvic height was reported to be 0.18 times the height of the animal at the withers and the pelvic width was 0.36 the distance of the external ilial angles (Saint-Cyr 1875) while a least square model that fitted data in an equation was proposed to be: Pelvic area = $- 122.2 + 23.2 \times (\text{Hook width}) + 24.3 (\text{Hook to pin length}) - 0.3 \times \text{Hook width} \times \text{Hook to pin length}$ (Murray, Cartwright et al. 2002). Internal pelvic dimensions consist of the pelvic height which was measured on the midline between the pubic symphysis and midsacrum, and pelvic width which was measured at the widest point between the shafts of the ilia (Rice and Wiltbank 1972).

Pelvic area is commonly calculated by multiplying the pelvic height with the width which results in a rectangular area (Wiltbank and LeFever 1961, Bellows, Gibson et al. 1971, Bellows, Short et al. 1971, Rice and Wiltbank 1972, Laster 1974, Morrison, Williamson et al. 1986, Green, Brinks et al. 1988, Johnson, Deutscher et al. 1988, Kolkman, Hoflack et al. 2009). Observations of the actual pelvic opening show that they resemble an ellipse more than a rectangle, and has been calculated as such whereby: Ellipsoidal area = $(\text{Width} + \text{Height})/2 \times \pi$ (Ben David 1960, Rice and Wiltbank 1972, Morrison, Williamson et al. 1986). When comparing these two methods to calculate pelvic area, the ellipsoidal equation was very representative of the actual pelvic opening area but had no advantage over the rectangular equation in predicting dystocia and was not different in ranking pelvic size (Rice and Wiltbank 1972). The ellipsoidal equation also did not affect variance components but simply multiplied the area obtained from the rectangular equation by a constant of $\pi/4$ which made the average ellipsoidal area lesser by about 21% (Morrison, Williamson et al. 1986).

Heritability of intrapelvic dimensions

Pelvic area has moderate to high heritability, ranging from 0.36 to 0.61, which suggests that it responds to selection (Benyshek and Little 1982, Morrison, Williamson et al. 1986, Nelsen, Short et al. 1986, Green, Brinks et al. 1988). Both pelvic height and width have moderate to high heritability estimates with pelvic width having higher values due to its more easily obtained measurements which leads to a higher repeatability (Benyshek and Little 1982, Morrison, Williamson et al. 1986), but the opposite is shown in Green et al., 1998. A useful correlation to examine would be the association between pelvic areas of bulls and the expected progeny differences (EPD) for daughters' calving ease which might give an indication if pelvic area measurements would be a good selection criteria for bulls (Van Donkersgoed 1992).

Pelvimetry and dystocia

Pelvic area has been seen as a reliable measurement influencing calving difficulty, as larger pelvic areas are associated with reduced calving difficulty (Bellows, Short et al. 1971, Murray, Cartwright et al. 1999) and is used to identify potential problem heifers with small pelvic sizes (Deutscher 1991, Micke, Sullivan et al. 2010) that may be at risk for dystocia at calving. In heifers, pelvic measurements are taken at the time of breeding or when pregnancy diagnoses are done, while in multiparous cows they are taken during pregnancy examinations (Ko and Ruble 1990). The average pelvic area grows at a rate of 0.27 cm² per day from yearling to 2 years of age and this fixed correction factor can be used to adjust the pelvic area of heifers to the standard 365 days of age (Smith 2005), whereby: 365 day pelvic area = Actual pelvic area (cm²) + [0.27 x (365 – age in days)].

Many producers cull cattle with the lowest 10 to 15 % pelvic area as it is deemed that heifers with small pelvic areas as yearlings usually have smallest pelvic areas at calving (Deutscher 1991). However, studies have shown that morphometric growth rates in cattle follow a curvilinear or logarithmic rather than a linear pattern, that extends past 24 months (Ragsdale 1934, Guilbert and Gregory 1952) and up to 6 years of age (Green, Brinks et al. 1988, West 1997), which makes it difficult to accurately predict the occurrence of dystocia when measurements are obtained as yearlings. Dystocia in 2 year old animals does not mean an unfavorable prognosis for calving ease in future births as pelvic dimensions change and the pelvic canal widens as they grow older (De Bruin 1901). It has also been reported that high variations in pelvic growth rate and the correlation of the pelvic area at any time before parturition to that at parturition is low. Even measurements obtained a month prior to calving only had moderate correlation with the pelvic area at calving (Gaines 1994). There is also a rapid increase in pelvic area just prior to calving due to dilation caused by hormonal changes like estrogen and relaxin (Bagna, Schwabe et al. 1991). Therefore, the clinical utility of using intrapelvic dimensions to predict dystocia is controversial as some studies deem it useful as a

predictor (Deutscher 1978, Johnson, Deutscher et al. 1988) while others find that it is not (Basarab, Rutter et al. 1993, Van Donkersgoed, Ribble et al. 1993).

A few alternative techniques of pelvimetry calculation have been proposed which include the measurements of ratio for Pelvic area:calf birth weight and Pelvic area:heifer body weight (Deutscher 1991, Basarab, Rutter et al. 1993). Also, a recent study ranked heifers based on their body weight adjusted pelvic area or lean body weight adjusted pelvic area using a regression coefficient (Holm, Webb et al. 2014). Additionally, there is also an equation to predict calving difficulty score using fetal hoof circumference at the coronary band, measured during Stage II of parturition, and pelvic dimensions (Ko and Ruble 1990), whereby Predicted calving difficulty score = $[(\text{Hoof circumference} - \text{Pelvic Height} + 3.5) + (\text{Hoof circumference} - \text{Pelvic Width} + 3.5)] \div 2$. The scores were then interpreted as follows: 0 to 4.00 = will calve unassisted, 4.01 to 5.50 = will require manual assistance, 5.51 to 6.50 = will require mechanical assistance (call puller), and ≥ 6.51 = will require cesarean section. These techniques however had poor positive predictive values and sensitivities (Van Donkersgoed, Ribble et al. 1993) and were not useful diagnostic tools to predict dystocia (Basarab, Rutter et al. 1993).

Pelvimeter

Internal pelvic dimensions were first estimated with fingers via rectal or vaginal examination (Saint-Cyr 1875, De Bruin 1901) by spanning the thumb to the other fingers with the distance between these previously measured. However, measurements done this way were always smaller than reality especially the pelvic height due to the rectovaginal pouch (Saint-Cyr 1875).

In the early 1960s, the usage of instruments to measure internal pelvimetry was reported. Studies that showcased a self-designed hemostat-like compass that had two 26 cm length arms and a 15 cm graduated metal arc at the end (Ben David 1960), and a pair of sliding calipers to measure pelvic area through the rectum (Wiltbank and LeFever 1961) were undertaken. Another self-designed compass was also reported (Menissier,

Vissac et al. 1971) and this instrument differed from the compass by Ben David as it had one fixed and one movable arm.

In more recent times, the Rice pelvimeter (Lane Manufacturing, Denver, CO), Krautmann-Litton bovine pelvic meter pelvimeter (Jorgensen Laboratories, Inc., Loveland, CO), and the Equibov pelvic clearance micrometer (Equibov, Ontario, Canada) have been more commonly used. These instruments are designed to be placed in the rectum of the cattle and measurements are read on a scale that is located outside of the animal (Deutscher 1991).

The Rice pelvimeter is made up of stainless steel tubing and molding epoxy. It works as a simple caliper that is placed per rectum with a calibrated scale on the other end in 0.25 cm graduations (Rice and Wiltbank 1972) and has readings from 3 to 20 cm. Although it is relatively straightforward to use with relatively moderate repeatability (Paputungan, Makarechian et al. 1993, Kolkman, Matthys et al. 2007), it requires regular calibration as it can be bent or sprung which results in inaccurate readings (Gaines 1994). The Krautmann-Litton pelvimeter is comprised of a recorder and a receiver hydraulic chamber that each has a piston and cylinder. These chambers are connected by a flexible cable and movements of one piston results in the movement of the other. The recorder has a measurement indicator, on a 0.25 cm graduated scale from 10.5 to 18.5 cm, which gives readings that are directly proportional to the receiver's piston extension (Krautmann 1975). This pelvimeter however can leak fluid which affects its readings (Gaines 1994) and when compared to the Rice pelvimeter, it had lower within operator repeatability (Van Donkersgoed, Ribble et al. 1993). The Equibov pelvic clearance micrometer is an electronic pelvimeter which uses a pistonlike sensor expanded by air compressed by an air pressure bulb (Wolverton, Perkins et al. 1991) that exerts a constant force at any extension and is touted to give more repeatable results (Equibov N.D.). Once the two measurements are obtained, the unit automatically calculates the pelvic area and shows the reading on the digital display. This digital recorder measures to the nearest 0.1 cm with a range from 10.5 to 18.0 cm (Wolverton, Perkins et al. 1991). Besides being small and light, it does not use hydraulic fluid,

therefore eliminating leakage and entrapment of air. However, the cost of this unit is much higher compared to the two former pelvimeters mentioned. In the pelvimetry study reported in this thesis, the Rice pelvimeter was chosen due to its ease of use, good repeatability, and low cost compared to the other pelvimeters.

Welfare

The issue of animal welfare when internal pelvimetry is conducted has been brought up due to it being an invasive procedure that has a risk of damaging rectal mucosa (Murray, Cartwright et al. 2002). Additionally, epidural anesthesia can be used to reduce arched backs and straining when measurements are taken but it requires special training whereas external pelvimetry needs neither specialized equipment nor training. In the author's opinion, there is an inherent risk for injury but internal pelvimetry done properly, gently, and with adequate lubrication can prevent damage to the rectal mucosa.

Cesarean section

Cesarean section is defined as the "delivery of a fetus by incision through the abdominal wall and uterus" (Blood, Studdert et al. 2007).

History in human medicine

The origin of the term "cesarean" is commonly believed to be derived from the surgical birth of Julius Caesar. However, this seems unlikely as at that time this procedure was only performed on a dead or dying mother and Aurelia, Julius Caesar's mother, is reputed to have lived to hear of her son's invasion of Britain. Other possible origins include the Latin verb "caedere" which means to cut and the term "caesones" that was applied to infants born by postmortem operations. Initially known as the cesarean operation, this term began to change following Jacques Guillimeau's 1598 publication on midwifery where he introduced the term "section" in place of "operation". Many of the earliest successful cesarean sections happened in rural and

remote areas that were lacking medical staff and facilities. They were performed on kitchen tables and beds (Sewell 1993).

With increased urbanization, the growth of hospitals and anatomy knowledge gave way to cesarean sections being performed routinely. New anesthetic products and antiseptics were developed which allowed surgeons to take the time to operate with precision and reduced shock in the patients. Over time, obstetricians were able to concentrate on improving their technique to control hemorrhage and prevent systemic infection (Sewell 1993).

History in bovine medicine

The first cesarean section to be performed in cattle was reported in 1813 by Morange to save a cow (Kolkman 2010). Following that report, various attempts at the procedure in different species have been done (Saint-Cyr 1875, De Bruin 1901). De Bruin in 1901 documented the recumbent approach in cattle and how cesarean sections were infrequently performed procedures. Now, cesarean sections are considered by many veterinarians and cattle producers as the primary solution for a dystocia (Dehghani 1982). In a study done in Victoria, Australia cesarean section was done in 4.7% of the dystocia cases that were attended by veterinary surgeons and the procedure was more frequently performed in beef cattle (8.8%) compared to dairy (3.8%) (Sloss 1974). The proportion of cattle that was operated on declined with the age of the dam whereby it was 12.5% in primiparous cattle to 2.8% in aged cows. In the same study, dairy practices generally handled dystocia using correction and traction while beef practices resorted to cesarean section and fetotomy.

Risk factors that are associated with cesarean section are first parity, single bull calf, long gestation period, extended interval between first service and conception, long dry period, sired by a double-muscle structured bull, less than 730 days of age at first calving, and previously having a cesarean section. Risk factors for dystocia also apply to cesarean section since cesarean section is one of the two extreme outcomes of dystocia with fetotomy being the other (Barkema, Schukken et al. 1992).

Indications for cesarean section

Cesarean section is recommended for cattle with dystocia when assisted vaginal delivery is ineffective or harmful towards the wellbeing of the calf or dam, and fetotomy is not a viable option due to inadequate room to place the fetotome or the presence of a live fetus (Norman and Youngquist 2007). The indications for a cesarean section are comprised of maternal and fetal factors (Campbell and Fubini 1990, Newman and Anderson 2005). Maternal factors include immature heifers, pelvic deformity, failure of cervical dilation, uncorrectable uterine torsion, uterine rupture, hydrops, prepartum paralysis, uterine torsion, and deformities of the birth canal while fetal factors are absolute fetal oversize, pathologic fetal oversize (emphysema), malposition, anasarca, schistosomus reflexus, hydrocephalus, conjoined twins, mummification, and prolonged gestation (Campbell and Fubini 1990, Cattell and Dobson 1990, Dawson and Murray 1992). In most animals, cesarean sections are performed as an emergency procedure as a last resort but it is elected when delivering an embryo transfer calf with high value (Campbell and Fubini 1990) or in double muscled breeds (such as the Belgian-Blue) that have an extremely high occurrence of dystocia due to extreme muscularity (Mijten 1998, Kolkman, De Vlieghe et al. 2007, Kolkman 2010). The decision to perform a cesarean section should be made as early as possible when approaching a dystocic case as dams that have undergone prolonged fetal manipulations or poor fetotomy attempts, and is systemically compromised are usually exhausted (Frazer and Perkins 1995) and are poor candidates for the surgery (Baird 2013).

Surgical approach

The surgeon's experience, nature of the surgical environment, and physical condition of the dam are crucial parameters to be considered when deciding on a surgical approach. The type and use of the animal (whether visible scarring is tolerated) as well as the individual variations (vascularity around the udder, obesity, and udder development) are also important as the incision size and healing are influenced (Campbell and Fubini 1990). Surgical approaches for cesarean section in bovine include

standing (left or right flank, lateral oblique), lateral recumbency (left or right flank, high, low ventral oblique), and dorsal recumbency (left or right paramedian, ventral midline) (Frazer and Perkins 1995, Parish, Tyler et al. 1995).

The standing left flank approach is one of the most common methods used (Sloss and Dufty 1977, Cattell and Dobson 1990, Dawson and Murray 1992, Mijten 1998, Kolkman, De Vliegher et al. 2007) as practitioners usually use this type of approach for most abdominal operations in cattle (Parish, Tyler et al. 1995). It is preferred over the right approach as the calf can typically be removed easily with no interference from small intestines that prolapse through the incision. Compared to the ventral midline, the standing flank approach avoids the problem of ligating large blood vessels (Straub and Kendrick 1965). The incision is made vertically in the middle of the paralumbar fossa starting from approximately 5 cm caudal to the 13th rib and 8 to 10 cm ventral to the transverse processes of the lumbar vertebrae and continues ventrally, enough for the removal of a calf, to about 20 to 40 cm (Straub and Kendrick 1965, Sloss and Dufty 1977, Dawson and Murray 1992, Kolkman, De Vliegher et al. 2007, Schultz, Tyler et al. 2008, Baird 2013).

A right sided approach is indicated when the rumen is markedly distended, a large fetus is in the right uterine horn, or an irreducible uterine torsion is present (Campbell and Fubini 1990, Frazer and Perkins 1995). A disadvantage of this approach is that intestinal loops can prolapse through the incision site with the resultant trauma and contamination predisposing the cow to peritonitis and ileus (Frazer and Perkins 1995).

The lateral oblique approach is useful when removing large calves or when the uterine contents are contaminated as the incision is larger and extends more cranioventrally compared to the traditional vertical incision. With this approach the apex of the gravid horn is easily maneuvered and the uterus is readily exteriorized. The incision starts 8 to 10 cm cranial and 8 to 10 cm ventral to the cranial aspect of the tuber coxae, and extends cranioventrally at a 45 degree angle, to end at 3 cm caudal to the last rib (Parish, Tyler et al. 1995, Newman 2008, Schultz, Tyler et al. 2008).

Drawbacks of a standing approach include relatively poor uterine exposure, potential for contamination of the abdomen with uterine fluids from a prolonged dystocia or emphysematous fetus, and the need to maintain the cow in standing position for the duration of the surgery (Frazer and Perkins 1995, Parish, Tyler et al. 1995). There is also chance that the animal may become recumbent during the surgery (Sloss and Dufty 1977, Hoeben, Mijten et al. 1997). More dairy and primiparous cattle were seen to become recumbent compared to their beef and multiparous counterparts respectively (Hoeben, Mijten et al. 1997).

The recumbent approach facilitates good exteriorization of the uterus especially when an oversized and dead fetus is presented and reduces the chances of contaminating the abdomen or peritoneum (Noorsdy 1979, Parish, Tyler et al. 1995).

For the animal that is placed on lateral recumbency, the high flank, the low flank (ventral oblique), and left or right flank approach can be done. The low ventral oblique or ventrolateral approach is a curvilinear incision that starts approximately 5 cm lateral to the umbilicus and extends caudodorsally toward the inguinal area. This approach easily allows the exteriorization of the uterus and is suitable for the removal of an emphysematous fetus (Schultz, Tyler et al. 2008).

The left or right flank approach is similar to the one done on standing animals except that the incision is made slightly more ventrally (Schultz, Tyler et al. 2008). It is indicated for dams with a viable oversized fetus, has marked ventral abdominal vascularity, or has a large udder. The left side is favored over the right, as in the standing procedure, as the rumen acts to prevent the prolapse of the intestinal tract. Compared with the standing animal, the incision is started more ventrally and care should be taken to avoid the subcutaneous abdominal vein. Disadvantages of this approach include problems with exteriorization of the uterus when the rumen is distended (Campbell and Fubini 1990) and incisional closure may be difficult due to increased tension on the muscle layers (Schultz, Tyler et al. 2008).

With the dam restrained in dorsal recumbency, the two approaches to be considered are the ventral paramedian (incision made between the ventral midline and

subcutaneous abdominal vein, extending from the umbilicus to the mammary gland) and ventral midline (starting 5 to 7 cm cranial to the umbilicus and extended caudally as needed) celiotomy. Both of these approaches are suitable for animals that require minimal postoperative scarring to ensure faster marketability and is advantageous in dams that have minimal vascularization.

The positioning of the animal is more at an oblique angle of 45 degrees which facilitates better exteriorization of the uterus. Disadvantages of the ventral paramedian approach include herniation and respiratory compromise due to a distended uterus exerting excessive pressure on the diaphragm (Campbell and Fubini 1990, Frazer and Perkins 1995, Schultz, Tyler et al. 2008). The ventral midline approach on the other hand is suitable for the delivery of an emphysematous fetus when fetotomy cannot be performed. The linea alba that is thick and fibrous serve as a secure anchor for holding sutures (Frazer and Perkins 1995) major disadvantage of the ventral approach is the need for extensive manual or pharmacological restraint compared to the standing approach (Parish, Tyler et al. 1995).

Approach to a dystocia case with a cesarean section outcome

At the Purdue University Veterinary Teaching Hospital, dams that are presented for dystocia are first restrained in a chute and prepared for a vaginal examination to determine if a vaginal delivery is practical. The perineal and vulval region is then prepared with a surgical scrub using a warm povidone-iodine solution. A vaginal examination is performed using a lubricated sterile obstetrical sleeve. If the animal strained excessively, 3 to 5 mL of 2% lidocaine was administered epidurally. During the examination, the vaginal wall, cervical dilatation, size of the pelvis in relation to the fetus, position and presentation of the fetus and fetal viability (retraction of limb or suckle reflex) are evaluated. Vaginal delivery is typically attempted unless an elective cesarean section is chosen or vaginal delivery has already been attempted by the Veterinary Teaching Hospital's ambulatory clinicians prior to presentation. If vaginal delivery was deemed not prudent, the dam was prepared for cesarean section.

In the teaching hospital setting, dams are mostly sent home within a week or two after surgery and this causes many complications such as wound infection, formation of seroma, and post-operative mortality to be missed as they may take several weeks to manifest (Mijten 1998).

Complications of cesarean section

Operative complications of cesarean section are bleeding of the abdominal wall, the uterus, the middle uterine artery, the omentum, or incision site, uterine tears, gastrointestinal trauma, and contamination of the peritoneal cavity (Dehghani 1982, Hoeben, Mijten et al. 1997). Complications after a cesarean section include wound infection, seroma, peritonitis, metritis, fever, vaginitis, vaginal or uterine prolapse, adhesions due to seepage caused by improper uterine closure, higher calf mortality rate, longer interval from first service to conception, lower milk production, and subcutaneous emphysema (Dehghani 1982, Clark 1987, Barkema, Schukken et al. 1992, Dawson and Murray 1992, Hoeben, Mijten et al. 1997, Mijten 1998). It was interesting to note that dams that underwent cesarean sections had a lower risk of retained placenta compared to dams that had spontaneous deliveries (Barkema, Schukken et al. 1992). Of the cows that returned to the farm after surgery, 64% managed to calve again (Bouchard, Daignault et al. 1994).

Bovine cesarean section is a major abdominal operation that is considered a clean-contaminated procedure and surgery contamination is inevitable (Mijten, Van den Bogaard et al. 1997, Mijten 1998). It is also sometimes performed in contaminated and unsuitable environments (Streyll, Sauter-Louis et al. 2011). The most frequent complications associated with cesarean sections are infectious in origin (Mijten 1998) and one of the most important sources of contamination is fetal fluid contaminated by endogenous vaginal flora from the start of calving (Mijten, Van den Bogaard et al. 1997). In double muscled cattle, cesarean section is seen as an elective surgery that is done in the early stages of parturition which leads to less contamination by fetal fluids. In other cattle, cesarean section is usually chosen when other methods have failed which may be

the reason that more infectious complications are seen in this group of animals (Mijten 1998).

Mortality in dams post-surgery was caused by peritonitis, wound infection, uterine tears, hemorrhage, and shock (Mijten 1998). From 159 cesarean section done on dairy cattle, the mortality risk was 24% following surgery and the risk if the dam had an emphysematous, dead, or live calf was 63%, 21%, and 14% respectively (Bouchard, Daignault et al. 1994). In another study, the maternal death rate was 18% following cesarean section which was higher than the mean of 6% for all dystocias. The percentage was 15% when the fetus was fresh and could reach 38% when there was purulent decomposition of the fetus (Sloss 1974).

Due to the complications that can arise from cesarean sections, it is sometimes seen as an undesirable choice by producers and veterinarians alike. This makes the early decision to perform the cesarean section, good technique, and adherence to a high quality and sterile surgical procedure crucial to the success of the operation and to reduce the chances of complications from occurring (Dawson and Murray 1992, Mijten 1998, Kolkman, De Vlieghe et al. 2007).

References

- Aarnes, T. K., J. A. Hubbell, P. Lerche and R. M. Bednarski (2014). "Comparison of invasive and oscillometric blood pressure measurement techniques in anesthetized sheep, goats, and cattle." *Veterinary Anaesthesia and Analgesia* **41**(2): 174-185.
- Adams, W. and W. Wagner (1970). "The role of corticoids in parturition." *Biology of Reproduction* **3**(2): 223-228.
- Aoki, M., K. Kimura and O. Suzuki (2005). "Predicting time of parturition from changing vaginal temperature measured by data-logging apparatus in beef cows with twin fetuses." *Animal Reproduction Science* **86**(1): 1-12.
- APHIS (2010). *Mortality of calves and cattle on US beef cow-calf operations*, US Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services, Centers for Epidemiology and Animal Health.
- Arnett, D. W., G. Holland and R. Totusek (1971). "Some effects of obesity in beef females." *Journal of Animal Science* **33**(5): 1129-1136.
- Bagna, B., C. Schwabe and L. Anderson (1991). "Effect of relaxin on facilitation of parturition in dairy heifers." *Journal of Reproduction and Fertility* **91**(2): 605-615.
- Baird, A. (2013). *Bovine Gastrointestinal Surgery*. *Turner and Mcllwraith's Techniques in Large Animal Surgery*, John Wiley & Sons, Inc.: 211-233.
- Baird, A. (2013). *Bovine Urogenital Surgery*. *Turner and Mcllwraith's Techniques in Large Animal Surgery*, John Wiley & Sons, Inc.: 235-271.
- Bar-Anan, R., M. Heiman, M. Ron and J. Weller (1987). "Comparison of proven sires from five Holstein-Friesian strains in high-yield Israeli dairy herds." *Livestock Production Science* **17**: 305-322.
- Barkema, H., Y. Schukken, C. Guard, A. Brand and G. Van der Weyden (1992). "Cesarean section in dairy cattle: A study of risk factors." *Theriogenology* **37**(2): 489-506.
- Barkema, H., Y. Schukken, C. Guard, A. Brand and G. Van der Weyden (1992). "Fertility, production and culling following cesarean section in dairy cattle." *Theriogenology* **38**(4): 589-599.
- Basarab, J., L. Rutter and P. Day (1993). "The efficacy of predicting dystocia in yearling beef heifers: I. Using ratios of pelvic area to birth weight or pelvic area to heifer weight." *Journal of Animal Science* **71**(6): 1359-1371.

Bassett, J. and A. Wallace (1966). "Short-term effects of ovine growth hormone on plasma glucose, free fatty acids and ketones in sheep." Metabolism **15**(10): 933-944.

Baumont, R. (1996). "Palatability and feeding behaviour in ruminants. A review." Annales de Zootechnie **45**(5): 385-400.

Beagley, J., K. Whitman, K. E. Baptiste and J. Scherzer (2010). "Physiology and treatment of retained fetal membranes in cattle." Journal of Veterinary Internal Medicine **24**(2): 261-268.

Bellows, R., R. Gibson, D. Anderson and R. Short (1971). "Precalving body size and pelvic area relationships in Hereford heifers." Journal of Animal Science **33**(2): 455-457.

Bellows, R. and M. Lammoglia (2000). "Effects of severity of dystocia on cold tolerance and serum concentrations of glucose and cortisol in neonatal beef calves." Theriogenology **53**(3): 803-813.

Bellows, R., D. Patterson, P. Burfening and D. Phelps (1987). "Occurrence of neonatal and postnatal mortality in range beef cattle. II. Factors contributing to calf death." Theriogenology **28**(5): 573-586.

Bellows, R., R. Short, D. Anderson, B. Knapp and O. Pahnish (1971). "Cause and effect relationships associated with calving difficulty and calf birth weight." Journal of Animal Science **33**(2): 407-415.

Ben David, B. (1960). "Sulla distocia causata da un feto relativamente grande, nella vacca frisona israeliana." La Clinica Veterinaria **83**: 412-419.

Benyshek, L. and D. Little (1982). "Estimates of genetic and phenotypic parameters associated with pelvic area in Simmental cattle." Journal of Animal Science **54**(2): 258-263.

Berglund, B. and J. Philipsson (1987). "External signs of preparation for calving and course of parturition in Swedish dairy cattle breeds." Animal Reproduction Science **15**(1): 61-79.

Berry, D., J. Lee, K. Macdonald and J. Roche (2007). "Body condition score and body weight effects on dystocia and stillbirths and consequent effects on postcalving performance." Journal of Dairy Science **90**(9): 4201-4211.

Bertics, S. J., R. R. Grummer, C. Cadorniga-Valino and E. E. Stoddard (1992). "Effect of prepartum dry matter intake on liver triglyceride concentration and early lactation." Journal of Dairy Science **75**(7): 1914-1922.

- Bewley, J., M. Grott, M. Einstein and M. Schutz (2008). "Impact of intake water temperatures on reticular temperatures of lactating dairy cows." Journal of Dairy Science **91**(10): 3880-3887.
- Bionaz, M., E. Trevisi, L. Calamari, F. Librandi, A. Ferrari and G. Bertoni (2007). "Plasma paraoxonase, health, inflammatory conditions, and liver function in transition dairy cows." **90**(4): 1740–1750.
- Birgel, E., E. Grunert and J. Soares (1994). "The preparatory phase of delivery in cattle, under consideration of the external signs of delivery and changes in progesterone to predicting the calving time." Deutsche Tierärztliche Wochenschrift **101**(9): 355-359.
- Bitman, J., A. Lefcourt, D. Wood and B. Stroud (1984). "Circadian and ultradian temperature rhythms of lactating dairy cows." Journal of Dairy Science **67**(5): 1014-1023.
- Blood, D. C., V. P. Studdert and C. C. Gay (2007). Saunders Comprehensive Veterinary Dictionary, Elsevier Ltd.
- Bonsma, J. C., G. Scholtz and F. Badenhorst (1940). "The influence of climate on cattle. Fertility and hardiness of certain breeds." Farming **15**: 7-12; 16.
- Bouchard, E., D. Daignault, D. Belanger and Y. Couture (1994). "Cesarienne chez la vache laitière: 159 cas." The Canadian Veterinary Journal **35**(12): 770-774.
- Brakel, W., D. Rife and S. Salisbury (1952). "Factors associated with the duration of gestation in dairy cattle." Journal of Dairy Science **35**(3): 179-194.
- Brăslășu, D., M. Brăslășu, S. Joița, M. Ghiță and S. Ionescu (2008). "Indirect oscillometric blood pressure in conscious calves." Bulletin of University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca. Veterinary Medicine **65**(2): 4-8.
- Breuer, H. (1962). "The metabolism of the natural estrogens." Vitamins and Hormones **20**: 285-335.
- Broom, D. M. and K. Johnson (1993). Stress and animal welfare, Chapman and Hall.
- Brown-Brandt, T. M., T. Yanagi Jr, H. Xin, R. S. Gates, R. A. Bucklin and G. S. Ross (2003). "A new telemetry system for measuring core body temperature in livestock and poultry." Applied Engineering in Agriculture **19**(5): 583-589.
- Burfeind, O., V. Suthar, R. Voigtsberger, S. Bonk and W. Heuwieser (2011). "Validity of prepartum changes in vaginal and rectal temperature to predict calving in dairy cows." Journal of Dairy Science **94**(10): 5053-5061.

Burfeind, O., M. Von Keyserlingk, D. Weary, D. Veira and W. Heuwieser (2010). "Short communication: Repeatability of measures of rectal temperature in dairy cows." Journal of Dairy Science **93**(2): 624-627.

Burris, M. J. and C. T. Blunn (1952). "Some factors affecting gestation length and birth weight of beef cattle." Journal of Animal Science **11**(1): 34-41.

Byrom, F. and C. Wilson (1938). "A plethysmographic method for measuring systolic blood pressure in the intact rat." The Journal of Physiology **93**(3): 301-304.

Cagnacci, A., G. Melis, R. Soldani, A. Paoletti and P. Fioretti (1992). "Effect of sex steroids on body temperature in postmenopausal women. Role of endogenous opioids." Life Sciences **50**(7): 515-521.

Caldwell, R., R. Bellows, J. Hall and R. Anthony (1990). "Administration of pig relaxin to beef heifers 4 or 7 days pre partum." Journal of Reproduction and Fertility **90**(1): 165-174.

Campbell, J., D. Lawson and J. Sanford (1964). "The use of pulse monitors in dogs and cats." Journal of Small Animal Practice **5**(3): 255-257.

Campbell, M. and S. Fubini (1990). "Indications and surgical approaches for cesarean section in cattle." The Compendium on continuing education for the practicing veterinarian (USA) **12**(2): 285-291.

Cattell, J. and H. Dobson (1990). "A survey of caesarean operations on cattle in general veterinary practice." The Veterinary Record **127**(16): 395-399.

Chassagne, M., J. Barnouin and J. Chacornac (1999). "Risk factors for stillbirth in Holstein heifers under field conditions in France: a prospective survey." Theriogenology **51**(8): 1477-1488.

Clark, W. A. (1987). "Bovine caesarian section." The Veterinary Record **120**: 443.

Cohn, L. A., D. L. McCaw, D. J. Tate and J. C. Johnson (2000). "Assessment of five portable blood glucose meters, a point-of-care analyzer, and color test strips for measuring blood glucose concentration in dogs." Journal of the American Veterinary Medical Association **216**(2): 198-202.

Colburn, D., G. H. Deutscher, M. K. Nielsen and D. C. Adams (1997). "Effects of sire, dam traits, calf traits, and environment on dystocia and subsequent reproduction of two-year-old heifers." Journal of Animal Science **75**(6): 1452-1460.

- Collery, P., J. Bradley, J. Fagan, P. Jones, E. Redehan and E. Weavers (1996). "Causes of perinatal calf mortality in the Republic of Ireland." Irish Veterinary Journal **49**(8): 491-496.
- Comline, R., L. Hall, R. Lavelle, P. Nathanielsz and M. Silver (1974). "Parturition in the cow: endocrine changes in animals with chronically implanted catheters in the foetal and maternal circulations." Journal of Endocrinology **63**(3): 451-472.
- Constable, P., G. Hoffsis and D. Rings (1990). "The reticulorumen: Normal and abnormal motor function. Part I. Primary contraction cycle." Compendium on Continuing Education for the Practicing Veterinarian **12**(7): 1008-1014.
- Cook, N. B. and K. V. Nordlund (2004). "Behavioral needs of the transition cow and considerations for special needs facility design." Veterinary Clinics of North America: Food Animal Practice **20**(3): 495-520.
- Cooper-Prado, M., N. Long, E. Wright, C. Goad and R. Wettemann (2011). "Relationship of ruminal temperature with parturition and estrus of beef cows." Journal of Animal Science **89**(4): 1020-1027.
- Coopman, F., S. de Smet, N. Gengler, A. Haegeman, K. Jacobs, M. van Poucke, H. Laevens, A. van Zeveren and A. Groen (2003). "Estimating internal pelvic sizes using external body measurements in the double-muscled Belgian Blue beef breed." Animal Science **76**(Part 2): 229-235.
- Coppola, C., R. Collier and R. Enns (2002). Using body surface temperature to predict calving. Proceedings-American Society of Animal Science Western Section.
- Craig, J. (1912). Obstetrical anatomy. Fleming's Veterinary Obstetrics. London, Baillière, Tindall and Cox: 1-49.
- Csapo, A. (1956). "Progesterone "block"." American Journal of Anatomy **98**(2): 273-291.
- Dalton, N. and M. Ayers (2012). "Correlation of rectal temperatures with infrared non-contact temperatures of the eye, third eyelid, nose and udder in Holstein dairy cattle." World Buiatrics Congress 2012.
- Danfær, A., V. Tetens and N. Agergaard (1995). "Review and an experimental study on the physiological and quantitative aspects of gluconeogenesis in lactating ruminants." Comparative Biochemistry and Physiology Part B: Biochemistry and Molecular Biology **111**(2): 201-210.
- Dawson, J. and R. Murray (1992). "Caesarean sections in cattle attended by a practice in Cheshire." Veterinary Record **131**(23): 525-527.

- De Bruin, M. (1901). Caesarean section. Bovine Obstetrics (Wyman, WEA Trans.), William R Jenkins: 217-221.
- De Bruin, M. (1901). The pelvic canal. Bovine Obstetrics (Wyman, WEA Trans.), William R Jenkins: 46-56.
- DeFries, J., R. Touchberry and R. Hays (1959). "Heritability of the length of the gestation period in dairy cattle." Journal of Dairy Science **42**(4): 598-606.
- Dehghani, S. (1982). "Cesarean section in cattle: Complications." Compendium On Continuing Education For The Practicing Veterinarian **4**(9): S387-S392.
- Dematawewa, C. and P. Berger (1997). "Effect of dystocia on yield, fertility, and cow losses and an economic evaluation of dystocia scores for Holsteins." Journal of Dairy Science **80**(4): 754-761.
- Dessouky, F. and A. Rakha (1961). "Studies on the gestation period and post-partum heat of Friesian cattle in Egypt." The Journal of Agricultural Science **57**(3): 325-327.
- Deutscher, G. (1978). "Factors influencing dystocia and pelvic area in beef heifers." Journal of Animal Science **47**(Suppl 1): 8.
- Deutscher, G. H. (1991). Pelvic measurements for reducing calving difficulty Rev. ed. Beef Cattle Handbook, Cooperative Extension, Institute of Agriculture and Natural Resources, University of Nebraska-Lincoln.
- Dixon, R., A. Hyman, E. Gursipde, I. Dyrenfurth, H. Cohen, E. Bowe, T. Engel, S. Daniel, S. James and R. Vande Wiele (1970). "Feto-maternal transfer and production of cortisol in the sheep." Steroids **16**: 771-789.
- Dobson, H., J. Tebble, R. Smith and W. Ward (2001). "Is stress really all that important?" Theriogenology **55**(1): 65-73.
- Drost, M. and L. Holm (1968). "Prolonged gestation in ewes after foetal adrenalectomy." Journal of Endocrinology **40**(3): 293-296.
- Dufty, J. (1971). "Determination of the onset of parturition in Hereford cattle." Australian veterinary journal **47**(3): 77-82.
- Dufty, J. (1981). "The influence of various degrees of confinement and supervision on the incidence of dystokia and stillbirths in Hereford heifers." New Zealand Veterinary Journal **29**(4): 44-48.
- Dyce, K. M., W. O. Sack and C. J. G. Wensing (2010). Chapter 2: The locomotor apparatus. Textbook of veterinary anatomy. St Louis, MO, Saunders Elsevier: 32-99.

- Dyce, K. M., W. O. Sack and C. J. G. Wensing (2010). Chapter 29 The pelvis and reproductive organs of the ruminant. Textbook of veterinary anatomy. St Louis, MO, Saunders Elsevier: 698-727.
- D’Orazio, P., R. W. Burnett, N. Fogh-Andersen, E. Jacobs, K. Kuwa, W. R. Külpmann, L. Larsson, A. Lewenstam, A. H. Maas and G. Mager (2005). "Approved IFCC recommendation on reporting results for blood glucose (abbreviated)." Clinical Chemistry **51**(9): 1573-1576.
- Edgerton, L. and H. Hafs (1973). "Serum luteinizing hormone, prolactin, glucocorticoid, and progesterin in dairy cows from calving to gestation." Journal of Dairy Science **56**(4): 451-458.
- Eigenberg, R., G. Hahn, J. Nienaber, T. Brown-Brandl and D. Spiers (2000). "Development of a new respiration rate monitor for cattle." Transactions of the ASAE - American Society of Agricultural Engineers **43**(3): 723-728.
- Eissa, H. and M. El-Belely (1990). "Sequential changes in plasma progesterone, total oestrogens and corticosteroids in the cow throughout pregnancy and around parturition." British Veterinary Journal **146**(1): 24-29.
- Emery, F. E. and A. H. Lawton (1947). "Relaxation of the pelvic ligaments in guinea-pigs by estrogens and prostigmine." American Journal of Physiology **151**(1): 134-137.
- Epperson, W. B. (2005). Risk factors for metabolic disease. Tri-State Dairy Nutrition Conference.
- Equibov (N.D.). Pelvimetry can be this easy... [Pamphlet], N.P.
- Estergreen Jr, V. L., O. L. Frost, W. R. Gomes, R. E. Erb and J. F. Bullard (1967). "Effect of ovariectomy on pregnancy maintenance and parturition in dairy cows." Journal of Dairy Science **50**(8): 1293-1295.
- Ettema, J. and J. Santos (2004). "Impact of age at calving on lactation, reproduction, health, and income in first-parity Holsteins on commercial farms." Journal of Dairy Science **87**(8): 2730-2742.
- Ewbank, R. (1963). "Predicting the time of parturition in the normal cow: a study of the precalving drop in body temperature in relation to the external signs of imminent calving." Vet. Rec **75**: 367-371.

Fairclough, R., J. Hunter, A. Peterson and R. Welch (1981). "Plasma concentrations of progesterone, oestrogens and prostaglandin F in maternal blood and corticosteroids and oestrogens in foetal blood of cows during dexamethasone-induced deliveries." Acta Endocrinologica **96**(3): 406-412.

Fairclough, R., J. Hunter and R. Welch (1975). "Peripheral plasma progesterone and utero-ovarian prostaglandin F concentrations in the cow around parturition." Prostaglandins **9**(6): 901-914.

Fazel, A., Z. Koutoubi, T. B. Sorg and B. Mehrotra (1996). "Influence of sample temperature on reflectance photometry and electrochemical glucometer measurements." Diabetes Care **19**(7): 771-774.

Fazio, E. and A. Ferlazzo (2003). "Evaluation of stress during transport." Veterinary Research Communications **27**(Suppl. 1): 519-524.

Feher, T., F. Orosz, L. Bodrogi and J. Haraszti (1975). "Gas chromatographic evidence of pregnanediols in non-pregnant cow's urine." Acta Veterinaria Academiae Scientiarum Hungaricae **25**(2-3): 241-244.

Fiedlerová, M., D. Řehák, M. Vacek, J. Volek, J. Fiedler, P. Šimeček, O. Mašata and F. Jílek (2008). "Analysis of non-genetic factors affecting calving difficulty in the Czech Holstein population." Czech Journal of Animal Science **53**(7): 284-291.

Fitzpatrick, J. L., F. J. Young, D. Eckersall, D. Logue, C. Knight and A. Nolan (1998). Recognising and controlling pain and inflammation in mastitis. Proceedings of the British Mastitis Conference, Axient/Institute for Animal Health, Milk Development Council/NovartisAnimal Health.

Fourichon, C., F. Beaudeau, N. Bareille and H. Seegers (2001). "Incidence of health disorders in dairy farming systems in western France." Livestock Production Science **68**(2): 157-170.

Fox, M. (1993). "Pathophysiology of infection with *Ostertagia ostertagi* in cattle." Veterinary parasitology **46**(1): 143-158.

Frazer, G. S. and N. R. Perkins (1995). "Cesarean section." Veterinary Clinics of North America: Food Animal Practice **11**(1): 19-35.

Gaines, J. D. (1994). Pelvic area and dystocia in cattle: strategies for improving performance. DVM Newsmagazine: 6A-17A.

Galvão, K., M. Flaminio, S. Brittin, R. Sper, M. Fraga, L. Caixeta, A. Ricci, C. Guard, W. Butler and R. Gilbert (2010). "Association between uterine disease and indicators of neutrophil and systemic energy status in lactating Holstein cows." Journal of Dairy Science **93**(7): 2926-2937.

Gao, Y., R. Short and T. Fletcher (1988). "Progesterone concentrations in plasma, saliva and milk of cows in different reproductive states." British Veterinary Journal **144**(3): 262-268.

Garry, F. (2004). "An overview of animal welfare in the US dairy industry." The Bovine Practitioner **38**: 1-23.

Gautier, J.-F., A. X. Bigard, P. Douce, A. Duvallet and G. Cathelineau (1996). "Influence of simulated altitude on the performance of five blood glucose meters." Diabetes Care **19**(12): 1430-1433.

Georg, H., S. Beintmann, A. Schwalm and G. Ude (2008). "Evaluation of heart rate, laying behaviour and activity measurement to predict calving of dairy cows." AgEng Knossos 2008 : International Conference on Agricultural Engineering: 7.

Gillette, D. D. (1966). "Placental influence on uterine activity in the cow." American Journal of Physiology **211**: 1095-1098.

Glen, J. B. (1970). "Indirect blood pressure measurement in anaesthetised animals." Veterinary Anaesthesia and Analgesia **1**(1): 25-37.

Godden, W. and W. M. Allcroft (1932). "Changes in the composition of cow's blood at the time of calving and a comparison of the blood of the calf with that of its dam." Biochemical Journal **26**(5): 1640-1646.

Goff, J. P., K. Kimura and R. L. Horst (2002). "Effect of Mastectomy on Milk Fever, Energy, and Vitamins A, E, and β -Carotene Status at Parturition." Journal of Dairy Science **85**(6): 1427-1436.

Gomes, W. and R. Erb (1965). "Progesterone in bovine reproduction: A review." Journal of Dairy Science **48**(3): 314-330.

Goodwin, R. (1956). "The distribution of sugar between red cells and plasma: variations associated with age and species." The Journal of Physiology **134**(1): 88-101.

Gorniak, T., U. Meyer, K.-H. Südekum and S. Dänicke (2014). "Impact of mild heat stress on dry matter intake, milk yield and milk composition in mid-lactation Holstein dairy cows in a temperate climate." Archives of Animal Nutrition **68**(5): 358-369.

Grant, R. and J. Albright (1995). "Feeding behavior and management factors during the transition period in dairy cattle." Journal of Animal Science **73**(9): 2791-2803.

Green, R., J. Brinks and D. LeFever (1988). "Genetic characterization of pelvic measures in beef cattle: Heritabilities, genetic correlations and breed differences." Journal of Animal Science **66**(11): 2842-2850.

Greenfield, R., M. Cecava, T. Johnson and S. Donkin (2000). "Impact of dietary protein amount and rumen undegradability on intake, peripartum liver triglyceride, plasma metabolites, and milk production in transition dairy cattle." Journal of Dairy Science **83**(4): 703-710.

Grunert, E. (1979). Clinical aspects of the nutritional status of the dam and parturition. Calving Problems and Early Viability of the Calf, Springer. **4**: 468-477.

Grünberg, W., D. E. Morin, J. K. Drackley and P. D. Constable (2006). "Effect of rapid intravenous administration of 50% dextrose solution on phosphorus homeostasis in postparturient dairy cows." Journal of Veterinary Internal Medicine **20**(6): 1471-1478.

Guilbert, H. and P. Gregory (1952). "Some features of growth and development of Hereford cattle." Journal of Animal Science **11**(1): 3-16.

Gundelach, Y., K. Essmeyer, M. Teltscher and M. Hoedemaker (2009). "Risk factors for perinatal mortality in dairy cattle: cow and foetal factors, calving process." Theriogenology **71**(6): 901-909.

Hainsworth, R. (2008). "Physiological background of heart rate variability." Dynamic Electrocardiography: 3-12.

Hansen, M., M. S. Lund, J. Pedersen and L. Christensen (2004). "Gestation length in Danish Holsteins has weak genetic associations with stillbirth, calving difficulty, and calf size." Livestock Production Science **91**(1): 23-33.

Hayirli, A., R. Grummer, E. Nordheim and P. Crump (2003). "Models for predicting dry matter intake of Holsteins during the prefresh transition period." Journal of Dairy Science **86**(5): 1771-1779.

Heinrich, A., T. Duffield, K. Lissemore, E. Squires and S. Millman (2009). "The impact of meloxicam on postsurgical stress associated with cautery dehorning." Journal of Dairy Science **92**(2): 540-547.

Heitzman, R. (1975). "The effectiveness of anabolic agents in increasing rate of growth in farm animals; report on experiments in cattle." Environmental Quality and Safety Supplement(5): 89-98.

Hoeben, D., P. Mijten and A. de Kruif (1997). "Factors influencing complications during caesarean section on the standing cow." Veterinary Quarterly **19**(2): 88-92.

Hoffmann, B., J. Schmidt and E. Schallenberger (1979). Hormonal mechanisms involved in control of parturition in the cow. Calving Problems and Early Viability of the Calf. B. Hoffman, I. Mason and J. Schmidt, Springer. **4**: 263-281.

Holland, M., N. Speer, D. LeFever, R. Taylor, T. Field and K. Odde (1993). "Factors contributing to dystocia due to fetal malpresentation in beef cattle." Theriogenology **39**(4): 899-908.

Holm, D., E. Webb and P. Thompson (2014). "A new application of pelvis area data as culling tool to aid in the management of dystocia in heifers." Journal of Animal Science **92**(5): 2296-2303.

Holm, L., H. Parker and S. Galligan (1961). "Adrenal insufficiency in postmature Holstein calves." American journal of obstetrics and gynecology **81**(5): 1000-1008.

Hudson, S., M. Mullford, W. Whittlestone and E. Payne (1976). "Bovine plasma corticoids during parturition." Journal of Dairy Science **59**(4): 744-746.

Hunter, J., R. Fairclough, A. Peterson and R. Welch (1977). "Foetal and maternal hormonal changes preceding normal bovine parturition." Acta Endocrinologica **84**(3): 653-662.

Huzzey, J., D. Veira, D. Weary and M. Von Keyserlingk (2007). "Prepartum behavior and dry matter intake identify dairy cows at risk for metritis." Journal of Dairy Science **90**(7): 3220-3233.

Hydbring, E., E. Macdonald and K. Olsson (1997). "Radiotelemetrically recorded blood pressure and heart rate changes in relation to plasma catecholamine levels during parturition in the conscious, unrestrained goat." Acta Physiologica Scandinavica **161**(3): 295-302.

Hydbring, E., A. Madej, E. MacDonald, G. Drugge-Boholm, B. Berglund and K. Olsson (1999). "Hormonal changes during parturition in heifers and goats are related to the phases and severity of labour." Journal of Endocrinology **160**(1): 75-85.

Jacob, S., V. Ramnath, P. Philomina, K. Raghunandhan and A. Kannan (2001). "Assessment of physiological stress in periparturient cows and neonatal calves." Indian Journal of Physiology and Pharmacology **45**(2): 233-238.

Jacobsen, H., M. Schmidt, P. Holm, P. Sangild, T. Greve and H. Callesen (2000). "Ease of calving, blood chemistry, insulin and bovine growth hormone of newborn calves derived from embryos produced in vitro in culture systems with serum and co-culture or with PVA." Theriogenology **54**(1): 147-158.

Janowski, T., S. Zduńczyk, J. Małecki-Tepicht, W. Barański and A. Raś (2002). "Mammary secretion of oestrogens in the cow." Domestic Animal Endocrinology **23**(1): 125-137.

Johanson, J. and P. Berger (2003). "Birth weight as a predictor of calving ease and perinatal mortality in Holstein cattle." Journal of Dairy Science **86**(11): 3745-3755.

Johnson, S., G. Deutscher and A. Parkhurst (1988). "Relationships of Pelvic Structure, Body Measurements, Pelvic." Journal of Animal Science **66**: 1081-1088.

Kanchev, L., C. P. Marinova and B. Stankov (1988). "Bovine salivary progesterone: Application to the assessment of ovarian function and early pregnancy diagnosis." Animal Reproduction Science **17**(1): 1-8.

Kay, R. (1983). "Rumen function and physiology." The Veterinary Record **113**(1): 6-9.

Kejela, G., H. Head, C. Wilcox and W. Thatcher (1978). "Adrenal responsiveness in pre- and postpartum dairy cows." Journal of Dairy Science **61**(12): 1736-1741.

Kertz, A., L. Reutzel, B. Barton and R. Ely (1997). "Body weight, body condition score, and wither height of prepartum Holstein cows and birth weight and sex of calves by parity: A database and summary." Journal of Dairy Science **80**(3): 525-529.

Kindahl, H., B. Kornmatitsuk and H. Gustafsson (2004). "The cow in endocrine focus before and after calving." Reproduction in Domestic Animals **39**(4): 217-221.

Kirkpatrick, J., V. Kincy, K. Bancroft, S. Shideler and B. Lasley (1991). "Oestrous cycle of the North American bison (*Bison bison*) characterized by urinary pregnanediol-3-glucuronide." Journal of Reproduction and Fertility **93**(2): 541-547.

Klyne, W. and A. Wright (1959). "Steroids and other lipids of pregnant cow's urine." Journal of Endocrinology **18**(1): 32-45.

Knott, J. (1932). "A study of the gestation period of Holstein-Friesian cows." Journal of Dairy Science **15**(2): 87-98.

Ko, J. and M. Ruble (1990). "Using maternal pelvis size and fetal hoof circumference to predict calving difficulty in beef cattle." Veterinary Medicine (USA): 1030-1036.

Kolkman, I. (2010). Calving problems and calving ability in the phenotypically double muscled Belgian Blue breed, Ghent University.

Kolkman, I., S. De Vliegher, G. Hoflack, M. Van Aert, J. Laureyns, D. Lips, A. De Kruif and G. Opsomer (2007). "Protocol of the caesarean section as performed in daily bovine practice in Belgium." Reproduction in Domestic Animals **42**(6): 583-589.

Kolkman, I., G. Hoflack, S. Aerts, H. Laevens, D. Lips and G. Opsomer (2012). "Pelvic dimensions in phenotypically double-musled Belgian Blue cows." Reproduction in Domestic Animals **47**(3): 365-371.

Kolkman, I., G. Hoflack, S. Aerts, R. Murray, G. Opsomer and D. Lips (2009). "Evaluation of the Rice pelvimeter for measuring pelvic area in double musled Belgian Blue cows." Livestock Science **121**(2): 259-266.

Kolkman, I., K. Matthys, G. Hoflack, L. Fiems, D. Lips, A. De Kruif and G. Opsomer (2007). "The agreement of pelvic measurements obtained in Belgian Blue cows with a Rice pelvimeter and the differences between these measurements around parturition." Vlaams Diergeneeskundig Tijdschrift **76**(6): 431-437.

Koper, W. J., S. R. Cordle and S. J. Yeaman (1985). "Effect of high and low density lipoproteins on corticotropin-mediated cortisol synthesis by bovine zona fasciculata cells." Journal of Steroid Biochemistry **23**(3): 369-371.

Kornmatitsuk, B., E. Dahl, E. Ropstad, J. F. Beckers, H. Gustafsson and H. Kindahl (2004). "Endocrine profiles, haematology and pregnancy outcomes of late pregnant Holstein dairy heifers sired by bulls giving a high or low incidence of stillbirth." Acta Veterinaria Scandinavica **45**: 47-68.

Kornmatitsuk, B., K. Konigsson, H. Kindahl, H. Gustafsson, M. Forsberg and A. Madej (2000). "Clinical signs and hormonal changes in dairy heifers after induction of parturition with prostaglandin F2 alpha." Journal of Veterinary Medicine. A, Physiology, Pathology, Clinical Medicine **47**(7): 395-409.

Krautmann, E. J. (1975). Measuring device having remote indicating means US 3918164 A.

Kruip, T. A. and J. Den Daas (1997). "In vitro produced and cloned embryos: effects on pregnancy, parturition and offspring." Theriogenology **47**(1): 43-52.

Kyle, B., A. Kennedy and J. Small (1998). "Measurement of vaginal temperature by radiotelemetry for the prediction of estrus in beef cows." Theriogenology **49**(8): 1437-1449.

Lammoglia, M., R. Bellows, R. Short, S. Bellows, E. Bighorn, J. Stevenson and R. Randel (1997). "Body temperature and endocrine interactions before and after calving in beef cows." Journal of Animal Science **75**(9): 2526-2534.

- Landa, C. E. (2011). Evaluation of weaning stress in beef calves, Virginia Polytechnic Institute and State University.
- Laster, D. B. (1974). "Factors affecting pelvic size and dystocia in beef cattle." Journal of Animal Science **38**(3): 496-503.
- Laster, D. B., H. A. Glimp, L. V. Cundiff and K. E. Gregory (1973). "Factors affecting dystocia and the effects of dystocia on subsequent reproduction in beef cattle." Journal of Animal Science **36**(4): 695-705.
- Leek, B. (1969). "Reticulo-ruminal function and dysfunction." The Veterinary Record **84**(10): 238-243.
- Lefcourt, A. M. and W. Adams (1996). "Radiotelemetry measurement of body temperatures of feedlot steers during summer." Journal of Animal Science **74**(11): 2633-2640.
- Legates, J., B. Farthing, R. Casady and M. Barrada (1991). "Body temperature and respiratory rate of lactating dairy cattle under field and chamber conditions." Journal of Dairy Science **74**(8): 2491-2500.
- Lombard, J., F. Garry, S. Tomlinson and L. Garber (2003). "Relationship of dystocia to dairy cow health and productivity." Journal of Dairy Science **86**(Suppl 1): 32.
- Lombard, J., F. Garry, S. Tomlinson and L. Garber (2007). "Impacts of dystocia on health and survival of dairy calves." Journal of Dairy Science **90**(4): 1751-1760.
- Lopez de Maturana, E., A. Legarra and E. Ugarte (2006). Effects of calving ease on fertility in the Basque Holstein population using recursive models. Proceedings of the 8th World Congress on Genetics Applied to Livestock Production, August 13-18, Belo Horizonte, MG, Brazil.
- Loskutoff, N., J. Ott and B. Lasley (1983). "Strategies for assessing ovarian function in exotic species." The Journal of Zoo Animal Medicine: 3-12.
- Loskutoff, N. M., J. Ott and B. Lasley (1982). "Urinary steroid evaluations to monitor ovarian function in exotic ungulates: I. Pregnanediol-3-glucuronide immunoreactivity in the okapi (*Okapia johnstoni*)." Zoo Biology **1**(1): 45-53.
- Marker, R. E. (1938). "Sterols. XLVI. The Steroid Content of Cows' Pregnancy Urine." Journal of the American Chemical Society **60**(10): 2442-2444.
- Marquardt, J., R. Horst and N. Jorgensen (1977). "Effect of parity on dry matter intake at parturition in dairy cattle." Journal of Dairy Science **60**(6): 929-934.

- Martal, J. and J. Djiane (1977). "Mammotrophic and growth promoting activities of a placental hormone in sheep." Journal of Steroid Biochemistry **8**(5): 415-417.
- Matsas, D. J., R. L. Nebel and K. D. Pelzer (1992). "Evaluation of an on-farm blood progesterone test for predicting the day of parturition in cattle." Theriogenology **37**(4): 859-868.
- McClintock, S., K. Beard, M. Goddard and D. Johnston (2005). Hidden costs of dystocia: fertility and long term survival in dairy cows. Proceedings of the 16th Conference of the Association for the Advancement of Animal Breeding and Genetics, Noosa Lakes, Queensland, Australia, Association for the Advancement of Animal Breeding and Genetics.
- McDougall, S. (2001). "Effects of periparturient diseases and conditions on the reproductive performance of New Zealand dairy cows." New Zealand Veterinary Journal **49**(2): 60-67.
- Mee, J. (1999). "Stillbirths -what can you do?" Cattle Practice **7**: 277-281.
- Mee, J. (2004). "The role of micronutrients in bovine periparturient problems." Cattle Practice **12**(2): 95-108.
- Mee, J. (2008). "Prevalence and risk factors for dystocia in dairy cattle: A review." The Veterinary Journal **176**(1): 93-101.
- Mee, J., D. Berry and A. Cromie (2011). "Risk factors for calving assistance and dystocia in pasture-based Holstein–Friesian heifers and cows in Ireland." The Veterinary Journal **187**(2): 189-194.
- Mee, J. F. (2004). "Managing the dairy cow at calving time." Veterinary Clinics of North America: Food Animal Practice **20**(3): 521-546.
- Mee, J. F., D. P. Berry and A. R. Cromie (2008). "Prevalence of, and risk factors associated with, perinatal calf mortality in pasture-based Holstein-Friesian cows." Animal **2**(4): 613-620.
- Meijering, A. (1984). "Dystocia and stillbirth in cattle—A review of causes, relations and implications." Livestock Production Science **11**(2): 143-177.
- Mellin, T. and R. Erb (1965). "Estrogens in the bovine - a review." Journal of Dairy Science **48**(6): 687-700.
- Menissier, F., B. Vissac, B. Perreau and P. Moine (1971). Possibilités d'amélioration des conditions de vêlage par sélection I.-Technique de mesure de l'ouverture pelvienne des bovins. Annales de génétique et de sélection animale, EDP Sciences.

Meyer, C., P. Berger and K. Koehler (2000). "Interactions among factors affecting stillbirths in Holstein cattle in the United States." Journal of Dairy Science **83**(11): 2657-2663.

Meyer, C. L., P. J. Berger, K. J. Koehler, J. R. Thompson and C. G. Sattler (2001). "Phenotypic trends in incidence of stillbirth for Holsteins in the United States." J Dairy Sci **84**(2): 515-523.

Micke, G., T. Sullivan, P. Rolls, B. Hasell, R. Greer, S. Norman and V. Perry (2010). "Dystocia in 3-year-old beef heifers; Relationship to maternal nutrient intake during early-and mid-gestation, pelvic area and hormonal indicators of placental function." Animal Reproduction Science **118**(2): 163-170.

Miedema, H. M., M. S. Cockram, C. M. Dwyer and A. I. Macrae (2011). "Changes in the behaviour of dairy cows during the 24h before normal calving compared with behaviour during late pregnancy." Applied Animal Behaviour Science **131**(1): 8-14.

Mijten, P. (1998). "Puerperal complications after cesarean section in dairy cows and in double-muscled cows." Reproduction in Domestic Animals **33**(3-4): 175-179.

Mijten, P., A. Van den Bogaard, M. Hazen and A. de Kruif (1997). "Bacterial contamination of fetal fluids at the time of cesarean section in the cow." Theriogenology **48**(3): 513-521.

Mohr, E., J. Langbein and G. Nürnberg (2002). "Heart rate variability a noninvasive approach to measure stress in calves and cows." Physiology & Behavior **75**(1): 251-259.

Morrison, D., W. Williamson and P. Humes (1986). "Estimates of heritabilities and correlations of traits associated with pelvic area in beef cattle." Journal of Animal Science **63**(2): 432-437.

Morrow, D., S. Roberts, K. McEntee and H. Gray (1966). Postpartum ovarian activity and uterine involution in dairy cattle. Journal of the American Veterinary Medical Association, AMER VETERINARY MEDICAL ASSOC 1931 N MEACHAM RD SUITE 100, SCHAUMBURG, IL 60173-4360.

Morten, D. and J. Cox (1968). "Bovine dystocia - a survey of 200 cases met with in general practice." The Veterinary Record **82**: 530-537.

Mortimer, R. G. (1997). Calving Difficulty. Proceedings The Range Beef Cow Symposium XV, Rapid City, South Dakota.

- Muir, L., J. Hibbs, H. Conrad and K. Smith (1972). "Effect of estrogen and progesterone on feed intake and hydroxyproline excretion following induced hypocalcemia in dairy cows." Journal of Dairy Science **55**(11): 1613-1620.
- Murray, R., T. Cartwright, D. Downham and M. Murray (1999). "Some maternal factors associated with dystocia in Belgian Blue cattle." Animal Science **69**(1): 105-113.
- Murray, R., T. Cartwright, D. Downham, M. Murray and A. De Kruif (2002). "Comparison of external and internal pelvic measurements of Belgian Blue cattle from sample herds in Belgium and the United Kingdom." Reproduction in Domestic Animals **37**(1): 1-7.
- Musah, A., C. Schwabe, R. Willham and L. Anderson (1988). "Dystocia, pelvic and cervical dilatation in beef heifers after induction of parturition with relaxin combined with cloprostenol or dexamethasone." Animal Reproduction Science **16**(3): 237-248.
- NAHMS (2009a). Dairy 2007: Part IV Reference of dairy cattle health and management practices in the United States, 2007, US Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services, National Animal Health Monitoring System.
- NAHMS (2009b). Beef 2007-08 Part III: Changes in the U.S. Beef Cow-calf Industry, 1993-2008, US Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services, National Animal Health Monitoring System. **3**.
- Nelsen, T., R. Short, J. Urick and W. Reynolds (1986). "Heritabilities and genetic correlations of growth and reproductive measurements in Hereford bulls." Journal of Animal Science **63**(2): 409-417.
- Newman, K. D. (2008). "Bovine cesarean section in the field." Veterinary Clinics of North America: Food Animal Practice **24**(2): 273-293.
- Newman, K. D. and D. E. Anderson (2005). "Cesarean section in cows." Veterinary Clinics of North America: Food Animal Practice **21**(1): 73-100.
- Nix, J., J. Spitzer, L. Grimes, G. Burns and B. Plyler (1998). "A retrospective analysis of factors contributing to calf mortality and dystocia in beef cattle." Theriogenology **49**(8): 1515-1523.
- Noorsdy, J. (1979). "Selection of an incision site for cesarean section in the cow." Veterinary Medicine Small Animal Clinician **74**(4): 530-537.
- Norman, H., J. Wright, M. Kuhn, S. Hubbard, J. Cole and P. VanRaden (2009). "Genetic and environmental factors that affect gestation length in dairy cattle." Journal of Dairy Science **92**(5): 2259-2269.

- Norman, S. and R. S. Youngquist (2007). Parturition and Dystocia. Current Therapy in Large Animal Theriogenology 2, Saunders Elsevier: 310-335.
- Oltenucu, P., A. Frick and B. Lindhe (1988). "Use of a statistical modelling and decision analysis to estimate financial losses due to dystocia and other diseases in Swedish cattle." Acta Veterinaria Scandinavica: Proceedings of the 5th International Symposium on Veterinary Epidemiology and Economics Supl 84: 353-355.
- Paputungan, U., M. Makarechian and M. Liu (1993). "Repeatability estimates of pelvic diameters measured by Rice pelvimeter in beef heifers." Canadian Journal of Animal Science 73(4): 977-980.
- Parish, S., J. Tyler and J. Ginsky (1995). "Left oblique celiotomy approach for cesarean section in standing cows." Journal of the American Veterinary Medical Association 207(6): 751-752.
- Parker, B., J. Foulkes, P. Jones, I. Dexter and H. Stephens (1988). "Prediction of calving times from plasma progesterone concentration." The Veterinary Record 122(4): 88-89.
- Patel, O., T. Takahashi, N. Takenouchi, M. Hirako, N. Sasaki and I. Domekis (1996). "Peripheral cortisol levels throughout gestation in the cow: Effect of stage of gestation and foetal number." British Veterinary Journal 152(4): 425-432.
- Patterson, D., R. Bellows, P. Burfening and J. Carr (1987). "Occurrence of neonatal and postnatal mortality in range beef cattle. I. Calf loss incidence from birth to weaning, backward and breech presentations and effects of calf loss on subsequent pregnancy rate of dams." Theriogenology 28(5): 557-571.
- Peterson, R. E., G. Nokes, P. S. Chen Jr and R. L. Black (1960). "Estrogens and adrenocortical function in man." The Journal of Clinical Endocrinology and Metabolism 20(4): 495-514.
- Philipsson, J., J. Foulley, J. Lederer, T. Liboriussen and A. Osinga (1979). "Sire evaluation standards and breeding strategies for limiting dystocia and stillbirth. Report of an EEC/EAAP working group." Livestock Production Science 6(2): 111-127.
- Phocas, F. and D. Laloë (2004). "Genetic parameters for birth and weaning traits in French specialized beef cattle breeds." Livestock Production Science 89(2): 121-128.
- Piccione, G., G. Caola and R. Refinetti (2002). "Circadian modulation of starvation-induced hypothermia in sheep and goats." Chronobiology International 19(3): 531-541.
- Pollard, J. and R. Littlejohn (1995). "Effects of social isolation and restraint on heart rate and behaviour of alpacas." Applied Animal Behaviour Science 45(1): 165-174.

- Porterfield, I. and N. Olson (1957). "Vaginal temperature of dairy cows before and after calving." Journal of the American Veterinary Medical Association **131**(8): 381.
- Proudfoot, K., J. Huzzey and M. Von Keyserlingk (2009). "The effect of dystocia on the dry matter intake and behavior of Holstein cows." Journal of Dairy Science **92**(10): 4937-4944.
- Radostits, O., C. Gay, K. Hinchcliff and P. Constable (2007). Clinical examination and making a diagnosis. Veterinary medicine: a text book of the diseases of cattle, horses, sheep, pigs and goats: 3-38.
- Radostits, O., C. Gay, K. Hinchcliff and P. Constable (2007). Diseases of the alimentary tract I. Veterinary medicine: a textbook of the diseases of cattle, horses, sheep, pigs and goats. Philadelphia, Saunders
- Radostits, O., C. Gay, K. Hinchcliff and P. Constable (2007). Diseases of the alimentary tract II. Veterinary medicine: a textbook of the diseases of cattle, horses, sheep, pigs and goats. **10th**: 293-382.
- Radostits, O., C. Gay, K. Hinchcliff and P. Constable (2007). Diseases of the cardiovascular system. Veterinary medicine: a text book of the diseases of cattle, horses, sheep, pigs and goats. **10**: 399-438.
- Radostits, O., C. Gay, K. Hinchcliff and P. Constable (2007). General systemic states. Veterinary medicine: a textbook of the diseases of cattle, horses, sheep, pigs and goats, Saunders Elsevier, Philadelphia.: 39-124.
- Ragsdale, A. C. (1934). Growth standards for dairy cattle, University of Missouri, College of Agriculture, Agricultural Experiment Station.
- Rajala, P. and Y. Gröhn (1998). "Effects of dystocia, retained placenta, and metritis on milk yield in dairy cows." Journal of Dairy Science **81**(12): 3172-3181.
- Reilly, P. and A. Black (1973). "Early effects of cortisol on glucose and alanine metabolism in adrenalectomized sheep." American Journal of Physiology **225**(3): 689-695.
- Rexha, S., E. Grunert and P. Saratsis (1993). "Relationships between the steroid hormone profiles and prodromal external signs of calving." Tierärztliche Umschau **48**(7): 431-436.
- Rice, L. and J. Wiltbank (1972). "Factors affecting dystocia in beef heifers." Journal of the American Veterinary Medical Association **161**(11): 1348-1358.

Robertson, H. (1972). "Sequential changes in plasma progesterone in the cow during the estrous cycle, pregnancy, at parturition, and post-partum." Canadian Journal of Animal Science **52**(4): 645-658.

Rose-Dye, T., L. Burciaga-Robles, C. Krehbiel, D. Step, R. Fulton, A. Confer and C. Richards (2011). "Rumen temperature change monitored with remote rumen temperature boluses after challenges with bovine viral diarrhoea virus and Mannheimia haemolytica." Journal of Animal Science **89**(4): 1193-1200.

Rumph, J. and M. Faust (2006). Genetic analysis of calving ease in Holsteins in the UK based on data from heifers and cows. Proceedings of the 8th World Congress on Genetics Applied to Livestock Production, August 13-18, Belo Horizonte, MG, Brazil.

Saint-Cyr, F. (1875). De l'operation césarienne. Traité d'obstétrique Vétérinaire, Asselin P, Paris: 566-580.

Saint-Cyr, F. (1875). Pelvimétrie. Traité d'obstétrique vétérinaire, Asselin P, Paris: 1-26.

Schaefer, A., S. Jones and R. Stanley (1997). "The use of electrolyte solutions for reducing transport stress." Journal of Animal Science **75**(1): 258-265.

Schuenemann, G., I. Nieto, S. Bas, K. Galvão and J. Workman (2011). "Assessment of calving progress and reference times for obstetric intervention during dystocia in Holstein dairy cows." Journal of Dairy Science **94**(11): 5494-5501.

Schultz, L. G., J. W. Tyler, H. D. Moll and G. M. Constantinescu (2008). "Surgical approaches for cesarean section in cattle." The Canadian Veterinary Journal **49**(6): 565.

Schwalm, J. and L. Schultz (1976). "Relationship of insulin concentration to blood metabolites in the dairy cow." Journal of Dairy Science **59**(2): 255-261.

Schwarzenberger, F., C. Son, R. Pretting and K. Arbeiter (1996). "Use of group-specific antibodies to detect fecal progesterone metabolites during the estrous cycle of cows." Theriogenology **46**(1): 23-32.

Sellers, A. and C. Stevens (1966). "Motor functions of the ruminant forestomach." Physiological Reviews **46**: 634-661.

Senger, P. (2003). Placentation, the endocrinology of gestation and parturition. Pathways to pregnancy and parturition, Current Conceptions, Inc. **2**: 304-325.

Sewell, J. E. (1993). "Cesarean section-a brief history." A brochure to accompany an exhibition on the history of cesarean section at the National Library of Medicine for the American College of Obstetricians and Gynecologists **30**.

Shah, K. D., T. Nakao and H. Kubota (2006). "Plasma estrone sulphate (E_1S) and estradiol-17beta ($E_2\beta$) profiles during pregnancy and their relationship with the relaxation of sacrosciatic ligament, and prediction of calving time in Holstein-Friesian cattle." Anim Reprod Sci **95**(1-2): 38-53.

Sharpe, P., P. Buttery and N. Haynes (1986). "The effect of manipulating growth in sheep by diet or anabolic agents on plasma cortisol and muscle glucocorticoid receptors." British Journal of Nutrition **56**(1): 289-304.

Siivonen, J., S. Taponen, M. Hovinen, M. Pastell, B. Lensink, S. Pyörälä and L. Hänninen (2011). "Impact of acute clinical mastitis on cow behaviour." Applied Animal Behaviour Science **132**(3): 101-106.

Silva, H., C. Wilcox, W. Thatcher, R. Becker and D. Morse (1992). "Factors affecting days open, gestation length, and calving interval in Florida dairy cattle." Journal of Dairy Science **75**(1): 288-293.

Sloss, V. (1974). "A clinical study of dystocia in cattle 1. Treatment." Australian Veterinary Journal **50**(7): 290-293.

Sloss, V. (1974). "A clinical study of dystocia in cattle 2. Complications." Australian Veterinary Journal **50**(7): 294-297.

Sloss, V. and J. Dufty (1977). "Elective caesarean operation in Hereford cattle." Australian Veterinary Journal **53**(9): 420-424.

Sloss, V. and J. Dufty (1980). Gross anatomy. Handbook of Bovine Obstetrics. Baltimore, MD, Williams & Wilkins: 17-27.

Sloss, V. and J. Dufty (1980). Pregnancy and gestation. Handbook of Bovine Obstetrics. Baltimore, MD, Williams and Wilkins: 30-68.

Smith, J. W. (2005). Correlation of pelvic shape and birth weight EPDs in reducing dystocia in beef cattle. Master of Science, Univ. of Tennessee at Martin.

Somogyi, M. (1933). "The distribution of sugar and rate of glycolysis in the blood of some mammals." Journal of Biological Chemistry **103**(2): 665-670.

Stabenfeldt, G., B. Osburn and L. Ewing (1970). "Peripheral plasma progesterone levels in the cow during pregnancy and parturition." American Journal of Physiology **218**: 571-575.

Stanley, T., R. Cochran, E. Vanzant, D. Harmon and L. Corah (1993). "Periparturient changes in intake, ruminal capacity, and digestive characteristics in beef cows consuming alfalfa hay." Journal of Animal Science **71**(3): 788-795.

- Stewart, M., G. Verkerk, K. Stafford, A. Schaefer and J. Webster (2010). "Noninvasive assessment of autonomic activity for evaluation of pain in calves, using surgical castration as a model." Journal of Dairy Science **93**(8): 3602-3609.
- Stock, M. J. (1999). "Gluttony and thermogenesis revisited." International journal of obesity and related metabolic disorders: journal of the International Association for the Study of Obesity **23**(11): 1105-1117.
- Straub, O. and J. Kendrick (1965). "Standing left flank cesarean section in the cow." Journal of the American Veterinary Medical Association **147**(4): 377-380.
- Streyl, D. (2011). Establishment of a standard operating procedure for predicting the time of calving in cattle. DVM, Ludwig Maximilian University of Munich.
- Streyl, D., C. Sauter-Louis, A. Braunert, D. Lange, F. Weber and H. Zerbe (2011). "Establishment of a standard operating procedure for predicting the time of calving in cattle." Journal of Veterinary Science **12**(2): 177-185.
- Tagawa, M., S. Okano, T. Sako, H. Orima and E. P. Steffey (1994). "Effect of change in body position on cardiopulmonary function and plasma cortisol in cattle." The Journal of Veterinary Medical Science **56**(1): 131-134.
- Tang, Z., J. H. Lee, R. F. Louie and G. J. Kost (2000). "Effects of different hematocrit levels on glucose measurements with handheld meters for point-of-care testing." Archives of Pathology & Laboratory Medicine **124**(8): 1135-1140.
- Taverne, M., V. Breeveld-Dwarkasing, F. van Dissel-Emiliani, M. Bevers, R. De Jong and G. Van der Weijden (2002). "Between parturition luteolysis and onset of expulsion." Domestic Animal Endocrinology **23**(1): 329-337.
- Taverne, M., G. Van der Weyden and P. Fontijne (1979). Preliminary observations on myometrial electrical activity before, during and after parturition in the cow. Calving Problems and Early Viability of the Calf, Springer: 297-311.
- Thorburn, G., D. H. Nicol, J. Bassett, D. Shutt and R. Cox (1972). "Parturition in the goat and sheep: changes in corticosteroids, progesterone, oestrogens and prostaglandin F." Journal of Reproduction and Fertility. Supplement **16**: 61-84.
- Thorburn, G. D., J. R. Challis and W. B. Currie (1977). "Control of parturition in domestic animals." Biology of Reproduction **16**(1): 18-27.
- Titchen, D. (1958). "Reflex stimulation and inhibition of reticulum contractions in the ruminant stomach." The Journal of Physiology **141**(1): 1-21.

- Tsang, C., A. Hackett and E. Turner Jr (1975). "Plasma levels of estrone sulfate, estrone and estradiol-17 β in the cow around parturition." Canadian Journal of Animal Science **55**(4): 509-512.
- Van Donkersgoed, J. (1992). "A critical analysis of pelvic measurements and dystocia in beef heifers." The Compendium on Continuing Education for the Practicing Veterinarian (USA) **14**(3): 405-408.
- Van Donkersgoed, J., C. S. Ribble, C. W. Booker, D. McCartney and E. D. Janzen (1993). "The predictive value of pelvimetry in beef cattle." Canadian Journal of Veterinary Research **57**(3): 170-175.
- Van Werven, T., Y. Schukken, J. Lloyd, A. Brand, H. T. Heeringa and M. Shea (1992). "The effects of duration of retained placenta on reproduction, milk production, postpartum disease and culling rate." Theriogenology **37**(6): 1191-1203.
- Vazquez-Anon, M., S. Bertics, M. Luck, R. Grummer and J. Pinheiro (1994). "Peripartum liver triglyceride and plasma metabolites in dairy cows." Journal of Dairy Science **77**(6): 1521-1528.
- Vickers, L., O. Burfeind, M. Von Keyserlingk, D. Veira, D. Weary and W. Heuwieser (2010). "Technical note: Comparison of rectal and vaginal temperatures in lactating dairy cows." Journal of Dairy Science **93**(11): 5246-5251.
- Von Borell, E. (2001). "The biology of stress and its application to livestock housing and transportation assessment." Journal of Animal Science **79**(E-Suppl): E260-E267.
- Wade, G. N. and I. Zucker (1970). "Modulation of food intake and locomotor activity in female rats by diencephalic hormone implants." Journal of Comparative and Physiological Psychology **72**(2): 328-336.
- Weisz, L. (1943). "The temperature phenomenon before parturition and its clinical importance." Journal of the American Veterinary Medical Association **102**: 123.
- West, H. (1997). "Dimensions and weight of Belgian Blue and crossbred calves and the pelvic size of the dam." The Veterinary Journal **153**(2): 225-228.
- Whittle, W., A. Holloway, S. Lye, W. Gibb and J. Challis (2000). "Prostaglandin Production at the Onset of Ovine Parturition Is Regulated by Both Estrogen-Independent and Estrogen-Dependent Pathways." Endocrinology **141**(10): 3783-3791.
- Williams, K. (1968). "A study of dystocia in the heifer (Primipara)." The Veterinary Record **83**(4): 87-97.

- Winchester, C. and M. Morris (1956). "Water intake rates of cattle." Journal of Animal Science **15**(3): 722-740.
- Wiltbank, J. and D. LeFever (1961). "Save more calves at birth." Nebraska Experiment Station Quarterly (Summer Edition): 19.
- Winkelman, L. and T. Overton (2012). "The effects of increasing doses of 2 preparations of long-acting insulin on short-term plasma profiles of glucose and insulin in lactating dairy cows." Journal of Dairy Science **95**(12): 6974-6982.
- Wittrock, J., T. Duffield and S. LeBlanc (2013). "Short communication: Validation of a point-of-care glucometer for use in dairy cows." Journal of Dairy Science **96**(7): 4514-4518.
- Wolverton, D., N. Perkins and G. Hoffsis (1991). "Veterinary application of pelvimetry in beef cattle." The Compendium on Continuing Education for the Practicing Veterinarian **13**: 1315-1320.
- Wood, C. (1999). "Control of parturition in ruminants." Journal of Reproduction and Fertility Supplement **54**: 115-126.
- Woodward, R. and R. Clark (1959). "A study of stillbirths in a herd of range cattle." Journal of Animal Science **18**(1): 85-90.
- Wrenn, R. T., J. Bitman and J. F. Sykes (1959). "The thermogenic influence of progesterone in ovariectomized cows." Endocrinology **65**(2): 317-321.
- Wright, J. (1958). "Bovine dystocia." The Veterinary Record **70**: 347-356.
- Yamakoshi, K., H. Shimazu and T. Togawa (1979). "Indirect measurement of instantaneous arterial blood pressure in the rat." American Journal of Physiology **237**(5): H632-H637.
- Yang, C., L. Wu, S. Liu and J. Lin (2004). "Monitoring the reproductive status of dairy cows by urinary pregnanediol glucuronide." Asian Australasian Journal Of Animal Sciences **17**(4): 460-466.
- Zaborski, D., W. Grzesiak, I. Szatkowska, A. Dybus, M. Muszynska and M. Jedrzejczak (2009). "Factors affecting dystocia in cattle." Reproduction in Domestic Animals **44**(3): 540-551.

Zhang, W., T. Nakao, M. Moriyoshi, K. Nakada, A. Ribadu, T. Ohtaki and Y. Tanaka (1999). "Relationship of maternal plasma progesterone and estrone sulfate to dystocia in Holstein-Friesian heifers and cows." The Journal of Veterinary Medical Science **61**(8): 909-913.

CHAPTER 3. CLINICAL UTILITY OF CALF FRONT HOOF CIRCUMFERENCE AND MATERNAL INTRAPELVIC AREA IN PREDICTING DYSTOCIA IN 103 LATE GESTATION HOLSTEIN-FRIESIAN HEIFERS AND COWS

Abstract

Dystocia is a major problem in the dairy industry as it increases cow and calf mortality and morbidity. Fetopelvic disproportion is a major cause of dystocia and is frequently seen in primiparous cattle due to their smaller stature and late maturation of pelvic dimensions. The objective of this study was to determine the clinical utility of measuring calf front hoof circumference, maternal intrapelvic area, and selected morphometric values in predicting dystocia in dairy cattle. An observational study using a convenience sample of 103 late gestation Holstein-Friesian heifers and cows was done. Intrapelvic height and width of the dam were measured using a pelvimeter and the intrapelvic area was calculated. Calf front hoof circumference and birth weight were also measured. Data was analyzed using Spearman's correlation coefficient (r_s), Mann-Whitney U test, and binary or ordered logistic regression; $P < 0.05$ was significant. Calving difficulty score (1 to 5) was greater in heifers (median, 3.0) than cows (median, 1.0). Median intrapelvic area immediately before parturition was smaller in heifers (268 cm²) than cows (332 cm²). Front hoof circumference and birth weight of the calf were similar in both groups. Calving difficulty score was positively associated with calf birth weight in heifers ($r_s = 0.39$) and cows ($r_s = 0.24$), as well as front hoof circumference in heifers ($r_s = 0.35$). Calving difficulty score was not associated with intrapelvic area in heifers or cows. Binary logistic regression using dam and calf data indicated that the ratio of front hoof circumference of the calf to the maternal intrapelvic area provided the best predictor of dystocia (calving difficulty score = 4 or 5), with $Se = 0.50$

and $Sp = 0.93$ at the optimal cutpoint for the ratio ($> 0.068 \text{ cm/cm}^2$). Determining the ratio of calf front hoof circumference to maternal intrapelvic area has clinical utility in predicting calving difficulty score in Holstein-Friesian cattle.

Introduction

Dystocia remains a major problem in the dairy industry as it increases cow and calf mortality (Dematawewa and Berger, 1997; Barrier et al., 2013), decreases milk yield (Rajala and Grohn, 1998), delays uterine involution (Morrow et al., 1966), and decreases reproductive performance (Gaafar et al., 2011), ultimately resulting in substantial financial loss. Fetopelvic disproportion is the most common cause of dystocia in dairy cattle (Mee, 2008). Primiparous animals have a higher incidence of fetopelvic disparity and dystocia than multiparous dairy cattle because of their smaller stature (Meyer et al., 2001; Johanson and Berger, 2003; Zaborski et al., 2009; Gaafar et al., 2011) and late maturation of pelvic dimensions (West, 1997). Other causes of dystocia in dairy and beef cattle include uterine inertia (10%; Sloss and Dufty, 1980), uterine torsion (5-10%; Frazer et al., 1996; Laven and Howe, 2005), and fetal malpresentation (0.9%, Nix et al., 1998; 20-30%; Philipsson, 1976). Accurate prediction of dystocia allows early and appropriate intervention, thereby decreasing morbidity and mortality of the dam and fetus, improving animal welfare, and reducing economic losses.

Calf birth weight, particularly from first-calving heifers, as well as morphologic measurements of the dam such as thoracic circumference, height at the withers, and body weight are positively associated with the incidence of dystocia in dairy cattle, (Sieber et al., 1989; Nogalski, 2003; Linden et al., 2009). Calf birth weight is also positively associated with morphologic measurements of the calf, including thoracic circumference, height at the withers or sacrococcygeal region (Heinrichs et al., 1992), front hoof circumference (Ko and Ruble, 1990; Tozer et al., 2002), and circumference of the carpus, tarsus, or fetlock (Hindson, 1978; West, 1997). Of these calf morphologic

measurements, front hoof circumference is easily measured during stage II of parturition and consequently has the greatest clinical potential to predict calf birth weight and therefore the likelihood of dystocia. Linear equations have been developed for beef calves relating calf birth weight (kg) to the circumference of the front hoof at the coronary band (cm), such that: $\text{weight} = 4.96 \times \text{circumference} - 51.4$ for heifer calves (Ruble, 1987; Ko and Ruble, 1990; Thomas, 1996); and $\text{weight} = 3.63 \times \text{circumference} - 29.4$ (Tozer et al., 2002). These equations vary numerically and were developed for beef cattle, but predict similar calf body weights for front hoof circumferences of 16 to 18 cm. A commercially available tape measure, calibrated using the first equation, accurately predicted body weight in Holstein-Friesian and Jersey calves weighing between 31 and 45 kg (Long et al., 2012). However, the clinical utility of front hoof circumference in predicting the likelihood of dystocia in Holstein-Friesian cattle is unknown.

The clinical utility of using maternal intrapelvic dimensions to predict dystocia remains controversial in beef cattle and has been minimally investigated in dairy cattle with the exception of a study published more than 30 years ago (Thomson and Wiltbank, 1983). Intrapelvic dimensions are most commonly measured in beef heifers before the start of the breeding season or during the first and second trimester when palpation per rectum is used for pregnancy diagnosis. Heifers with exceptionally small intrapelvic dimensions for their body weight or abnormal intrapelvic shape are culled or mated to “easy-calving” bulls because of their increased risk of dystocia. The ability of intrapelvic measurements measured at breeding time or early in gestation to accurately predict dystocia in beef heifers is questionable (Van Donkersgoed, 1992; Van Donkersgoed et al., 1993; Basarab et al., 1993). This is because extrapolation of intrapelvic dimensions obtained during first service or the first or second trimester leads to unacceptably high 95% confidence intervals for the predicted intrapelvic dimensions at parturition (Van Donkersgoed et al., 1993) and do not accurately predict dystocia in primiparous beef cattle (Basarab et al., 1993). A second area of concern is that a strong positive genetic association exists between intrapelvic area and calf birth weight

(Benyshek and Little, 1982). The selection that is done based on intrapelvic dimensions is not likely to impact the incidence of dystocia caused by fetopelvic disproportion because such a strategy also selects for higher calf birth weights (Laster, 1974; Sieber et al., 1989; Basarab et al., 2003). As a consequence, the predictive ability of intrapelvic dimensions is improved when they are indexed to the dam's body weight (Short et al., 1979). Thirdly, increased plasma estradiol and relaxin concentrations at parturition (Bagna et al., 1991; Shah et al., 2006), and abdominal straining during fetal expulsion may transiently increase intrapelvic dimensions (Rice and Wiltbank, 1972; Meijering, 1984; Tsousis et al., 2010), particularly the intrapelvic height (Kolkman et al., 2007). A fourth area of concern in using maternal intrapelvic dimensions to predict dystocia is whether the measures have adequate intra- and inter-observer repeatability (Rice and Wiltbank, 1970; Menissier and Vissac, 1971; Meijering, 1984; Van Donkersoed et al., 1993; Kolkman et al., 2007; Bureš et al., 2008). Despite these concerns, measurement of intrapelvic dimensions is believed to be of value in predicting dystocia in dairy cattle (Thomson and Wiltbank, 1983; Johanson and Berger, 2003). A preliminary recommendation is that the prepartum pelvic area should be $> 270 \text{ cm}^2$ in Holstein-Friesian heifers in order to minimize the incidence of dystocia (Philipsson, 1976; Hoffman, 1997). Selected external measurements, such as heart girth, height at the withers, and horizontal distance between the tuber coxae and horizontal distance between tuber ischia (inter-ischial distance or pin width) could potentially be used in adult cattle as proxies for intrapelvic dimensions (Nelsen et al., 1986; Weiher et al., 1992; Coopman, 2003; Kolkman et al., 2012). However, these measurements appear to be weakly associated with calving difficulty score (Meijering and Postma, 1984).

Based on the above, we hypothesized that the measurement of calf front hoof circumference, maternal intrapelvic and selected morphologic dimensions in late gestation, and an estimate of the dam's body weight would be predictive of calving difficulty score in dairy cattle as previously documented for primiparous beef cattle (Short et al., 1979). We also hypothesized that the ratio of calf front hoof circumference to maternal intrapelvic area or width has clinical utility to predict dystocia in dairy cattle,

as these ratios directly reflect the magnitude of fetopelvic disproportion which is the most common cause of dystocia in cattle (Philipsson, 1976; Meijering, 1984; Mee, 2008). Support for our hypothesis is provided by studies conducted in beef and dairy cattle that demonstrate the ratio of calf birth weight to maternal intrapelvic area or body weight was positively associated with calving difficulty score (Rice and Wiltbank, 1970; Philipsson, 1976; Deutscher, 1988; Naazie et al., 1989; Basarab et al., 1993; Nogalski, 2003; Nogalski and Mordas, 2012). We also hypothesized that the ratio of maternal intrapelvic area to body weight would be negatively associated with calving difficulty score in dairy cattle. Therefore the objectives of this study were to: 1) determine the repeatability of measuring intrapelvic width, height, and area in late gestation dairy cattle, and front hoof circumference in calves; 2) determine the clinical utility of measuring intrapelvic dimensions, selected morphometric measurements, age, and calculated body weight in late gestation dairy cattle, and front hoof circumference of calves to predict dystocia; and 3) determine whether the ratio of calf front hoof circumference to maternal intrapelvic area and the ratio of maternal intrapelvic area to calculated body weight would be negatively associated with calving difficulty score in dairy cattle.

Materials and methods

All methods were approved by the Purdue University Institutional Animal Care and Use Committee.

Animals, housing, and feeding

An observational study using a convenience sample of 103 late gestation non-lactating Holstein-Friesian cattle (34 primiparous, 69 multiparous) from the Purdue University Dairy Research and Education Center was performed over a 10 month period between May 29, 2012 and March 29, 2013. Cattle were housed outside in a dry lot and fed an acidogenic total mixed ration (dietary cation-anion difference {DCAD} = -10

mEq/100 g of dry matter {DM}, where DCAD = $([Na^+] + [K^+]) - ([Cl^-] + [S^{2-}])$; Lean et al., 2006) based on formulations recommended by the National Research Council (NRC, 2001) for close up cows. Primiparous and multiparous cattle were fed an acidogenic close up ration starting six and three weeks before parturition, respectively. The ration was fed once daily between 08:00 and 09:30 and consisted predominantly of grass hay, alfalfa haylage and corn silage. Water was available *ad libitum*.

Cattle were moved from an outside dry lot to a temperature-controlled building that contained individual box stalls four days before the estimated parturition date based on breeding records and pregnancy diagnosis at approximately 40 days after insemination. All animals were deemed healthy based on daily routine physical examinations in the box stalls. Feeding and access to water were similar to that in the dry lot.

Experimental methods

Physical examinations were performed daily between 08:00 and 10:00 while cattle were gently restrained in a headlock. Intrapelvic height and width measurements were obtained using the Rice pelvimeter (Lane Manufacturing, Denver, CO) to the nearest 0.25 cm. Feces were manually evacuated from the rectum by the investigator, the pelvimeter was lubricated using an aqueous based lubricant containing sodium carboxymethylcellulose (Equi-Phar Vedlube, VEDCO Inc, St Joseph, MO) and then carefully introduced into the rectum in a closed position by the left hand and arm that was protected using a disposable obstetrical sleeve (Ag-Tek® Polysleeve®, Neogen Corporation, Lexington, KY). The pelvimeter was slowly advanced inside the rectum and carefully opened in a vertical plane to enable measurement of the narrowest vertical distance between the ventral aspect of the sacrum and the dorsal aspect of the pubic symphysis (intrapelvic height). The pelvimeter was then closed, gently rotated 90° and expanded to measure the widest horizontal distance between the left and right shafts of the ilium (intrapelvic width). The pelvimeter was then closed and slowly retracted from the rectum. A limitation of the Rice pelvimeter was that it has a maximum reading

of 20 cm and up to 25% of multiparous cattle had pelvic width measurements that exceeded 20 cm. Consequently, all intrapelvic width measurements > 20 cm were assigned a value of 20.5 cm. Intrapelvic area (cm^2) was calculated as the area of rectangle by multiplying intrapelvic height (h) by the corresponding intrapelvic width (w) (Laster, 1974; Green et al., 1988; Weiher et al., 1992; Gaines et al., 1993; Ramin et al., 1995; Nogalski and Mordas, 2012). Intrapelvic areas have also been measured as an ellipse with the area = $h \times w \times \pi / 4$ (Ben David, 1960; Morrison et al., 1986). We elected to calculate intrapelvic area as a rectangle due to its ease of calculation (Rice and Wiltbank, 1972), to assist in comparison with other studies, and because statistical analysis provides identical outcomes when intrapelvic area is modelled as a rectangle or ellipse because they differ by a fixed factor of $\pi/4$. Pelvimetry was repeated the next day by the same or different investigator in order to obtain an estimate of intra- and inter-observer variability.

Selected maternal morphologic measurements were obtained once before parturition with the animal standing on level ground and its weight evenly distributed. The measurements were: 1) thoracic circumference (heart girth) in a vertical plane immediately caudal to the scapula; 2) height at the withers; 3) height at the highest point of the tail head (sacrococcygeal region); and 4) inter-ischial distance (pin width; the horizontal distance between the most caudal aspect of each tuber ischii as described by Hindson, 1978 and Wittek et al., 2007). Body condition score (on a 1 to 5 scale) was measured at the same time as morphometric measurements using an established scoring system (Ferguson et al., 1994; Elanco Animal Health, 1996). Body weight was calculated from thoracic circumference (heart girth) using a quadratic equation developed from Holstein-Friesian heifers 1 to 821 days of age (Heinrichs et al., 1992).

Animals were kept under frequent observation in order to detect the start of parturition (stage I). Cattle were individually examined by the herdsman whenever 30 minutes had elapsed following rupture of the amniotic sac or progress was deemed to be slow. The time of calving (i.e. the hour corresponding to the end of stage II of parturition) was recorded by the herdsman and was defined as the time when the four

legs and head of the calf were on the ground. Calving difficulty scores were assigned by the herdsman based on a scale of 1 to 5 whereby: 1 = no assistance needed; 2 = easy pull (one person with minimal effort); 3 = moderate pull (one person with moderate effort); 4 = hard pull (one person with considerable effort or two people); and 5 = mechanical extraction or cesarean section. We elected to use the term calving difficulty score instead of calving ease score because the focus of our analysis was on identifying cattle with a high likelihood of dystocia, rather than identifying cattle with a high likelihood of unassisted delivery. The scoring system was similar to the calving ease scoring system used by the Holstein Association USA and the National Association of Animal Breeders (NAAB, Columbia, MO) that scored dystocia as 1 = no assistance, 2 = slight problem, 3 = needed assistance, 4 = considerable force and 5 = extreme difficulty. The calving ease scores for the sire of the dam (daughter calving ease score) and the sire of the calf (service sire calving ease score) were recorded in order to evaluate their association with dystocia. Both calving ease scores reflect the expected percentage of difficult births (calving difficulty score 4 or 5) in primiparous cattle (Weigel, 2002).

Calves were separated from their dam as soon as possible after birth (almost all within 1 h). Dairy staff measured birth weight by placing the calf into a moveable cart that was wheeled to a weighing scale (Rice Lake floor scale with IQ Plus 355 Weight Indicator, Rice Lake Weighing Systems, WI). The combined weight of the calf and cart was measured and the weight of the cart subtracted to obtain the calf's birth weight. Dairy staff estimated that body weight was recorded in at least 75% of the calves before colostrum was administered; however, the timing of weighing relative to colostrum administration was not recorded.

Calves were encouraged to suckle first milking colostrum that was usually obtained from another dam while calves that failed to suckle their allotted volume within 10 minutes were oroesophageally intubated and a total of 3.8 L (4 quarts) of colostrum was administered. Calves were ear-tagged and their umbilicus was dipped with 7% tincture iodine (Animal and Fields Products, MN). Heifer calves were vaccinated

intramuscularly with 2 mL of a core-antigen vaccine (ENDOVAC-Dairy[®] with Immune Plus[®], IMMVAC, Columbia, MO).

Forelimb and hindlimb hoof circumference were measured within 24 h of birth using a flexible calibrated tape (Calfscale[®] Birthweight Tape; Nasco, Fort Atkinson, WI). The tape was placed firmly around the coronary band of the left or right forelimb and the circumference measured twice in cm by the same observer. Thoracic circumference (chest girth) of the calf was measured once using a non-stretch fiberglass calibrated tape immediately caudal to the scapula (Loops & Threads Tape Measure, Michaels Stores Inc., Irving TX). Body weight was calculated from chest girth using the same equation as for their dams.

Statistical analysis

Data was expressed as mean \pm SD (standard deviation) or median and range (in parentheses) and $P < 0.05$ was considered significant. Calvings where the calf was in abnormal presentation, position, or posture were retained in the analysis because the goal of the study was to predict dystocia, including those cases of dystocia not due to fetopelvic disproportion. Perinatal mortality was defined as calves born dead or died within 24 h of calving. Proportion data were expressed as percentages with 95% confidence intervals calculated using the binomial theorem. The distribution of perinatal mortality and calving difficulty scores, and calving difficulty scores for primiparous and multiparous cattle, were compared using Fisher's exact test.

Intrapelvic height and external morphologic dimensions of primiparous and multiparous cows were compared using the Mann-Whitney U test. Intrapelvic width and area were compared using a maximum likelihood regression method (PROC LIFEREG, SAS Inc) that was suitable for analysis of right-censored data. This was required because some multiparous cattle had intrapelvic width dimensions > 20 cm. The intrapelvic area measured by the two investigators was compared using difference plots with bias as the mean percentage difference and the 95% limits of agreements as the interval defined from observed bias plus or minus $1.96 \times SD$. The limits of agreement reflects the range

of differences that contains 95% of future measurements. The percentage bias value was regarded as providing the best estimate of bias between the two investigators because SD was proportional to the mean value (Bland and Altman, 2003).

An exponential equation was used to characterize the maternal relationships between intrapelvic dimensions and age, and between selected morphometric measurements and age. The function $y = A \times (1 - e^{-k \times t})$ was used to model the relationship between the morphometric measurement and time (in years); A is the asymptotic value for the dimension at infinite age and k is an estimate of the earliness of maturing, such that a smaller value for k represents late maturation. This equation was modified from that of Brody (Brown et al., 1972) and ignores the influence of weight changes in young animals (< 18 months) because we did not have data for cattle < 22 months of age.

Linear regression was used to characterize the relationship between calf birth weight and hoof circumference while the presence of curvilinearity was assessed by evaluating whether the coefficient for a quadratic term was significant and by visual examination of residuals. Spearman's rho (r_s) was used to characterize the association between calving difficulty score and calf birth weight, front hoof circumference, gestation length, dam age, body condition score, intrapelvic dimensions, thoracic circumference, height at the withers, height at the highest point of the tail head, and inter-ischial distance. The intrapelvic width and height values were averaged and the value subtracted from the value for the front hoof circumference of the calf (Thomas, 1996). The association between the resultant value (called the dystocia index) and calving difficulty score was evaluated using Spearman's rho. A dystocia index < 0.4 = no assistance required, 0.4 to 1.9 = some assistance may be required, 2.0 to 3.0 = mechanical assistance is required, > 3.0 = extremely difficult delivery or cesarean section was required (Thomas, 1996).

The five categories of calving difficulty score were collapsed into two categories: dystocia = 0 (calving difficulty score = 1, 2, or 3) and dystocia = 1 (calving difficulty score = 4 or 5) for binary logistic regression analysis (logit analysis) using the descending option and maximum likelihood method. This cutpoint for dystocia was selected based

on a study that quantified the maximum force required to deliver a calf (Meijering and Postma, 1984); the results of that study indicated that the difference between scores 2 and 3 were more influenced by subjectivity or chance, compared to the difference between scores 3 and 4. The selected cutpoint was also consistent with differences in the magnitude of force measured by a dynamometer during traction (Hindson, 1978). Forward stepwise logistic regression was used to characterize the relationship between dystocia and variables of interest that had a probability < 0.20 for association with calving difficulty score. For the prediction of dystocia, adjusted odds ratios and 95% confidence intervals were estimated simultaneously for all predictors in the binary logistic regression equation, with P values calculated using the Wald chi-square values.

Ordered logistic regression analysis using the proportional odds model (cumulative logit model) was then used for the significant predictor variables identified in forward stepwise logistic regression in order to further characterize the association between calving difficulty score (5 outcome levels) and identified predictors, as well as between the occurrence of perinatal mortality and identified predictors. The adequacy of the final binary and ordered logistic regression model fits were evaluated using the Hosmer-Lemeshow goodness-of-fit statistic and plots of deviance influence statistics against the predicted values. Receiver operating characteristic (ROC) curves were constructed for the final logistic regression models.

Results

Animals

Multiparous cattle produced 4 sets of twins, for a total of 107 calves from 103 cattle. The twinning rate was therefore 3.9% (95% confidence interval, 1.0 to 9.5%). Six calves were in posterior presentation (5.6%) and 5 calves (4.7%) had abnormal posture, manifested as a leg flexed backwards ($n = 4$) or a head bent backwards ($n = 1$). Thirteen of the 107 calves had perinatal mortality (12.1%, 95% confidence interval, 6.5 to 19.5%), with the incidence in primiparous cattle (24%, 8/34) being more than 3 times the

incidence in multiparous cattle (7%, 5/69; $P = 0.024$). Perinatal mortality incidence was strongly associated ($P = 0.0012$) with calving difficulty score, with deaths occurring in 0% of score 1 ($n = 43$), 20% of score 2 ($n = 30$), 11% of score 3 ($n = 18$), 25% of score 4 ($n = 8$), and 38% of score 5 ($n = 8$) calvings.

Accurate gestation length information was unavailable for the heifers, but mean gestation length of multiparous cattle was 281 days.

Pelvimetry

Pelvimetry was performed a median of 2.8 days before the day of parturition. The median coefficient of variation (CV) for intrapelvic width was 1.8% (range, 0 to 6.0%; $n = 44$) for observer 1 and 1.0% (range, 0 to 2.2%; $n = 13$) for observer 2. Median CV for intrapelvic height was 2.2% (range, 0 to 11.6%; $n = 43$) for observer 1 and 0% (range, 0 to 4.2%, $n = 13$) for observer 2. Median CV for intrapelvic area was 3.6% (range, 0 to 14.5%; $n = 43$) for observer 1 and 2.0% (range, 0 to 4.4%; $n = 13$) for observer 2. Median inter-observer CV for intrapelvic width was 2.0% (range, 0 to 12.9%; $n = 31$), for intrapelvic height was 3.8% (range, 0 to 17.1%, $n = 31$), and for intrapelvic area was 4.7% (range, 0 to 19.3%; $n = 33$). In order to obtain the most repeatable estimates, intrapelvic width, height, and area were calculated using the median values measured by observer 2 for width and height when 2 measurements were available ($n = 13$). For 31 animals, intrapelvic width, height, and area were calculated using the median values for width and height measured by observer 1 and 2 ($n = 31$). For the remaining 59 animals where observer 2 measurements were not available, intrapelvic width, height, and area were calculated using measurements obtained by observer 1.

All intrapelvic height measurements were 20 cm or less. Twenty-six of the 103 cattle (1 primiparous, 25 multiparous) had intrapelvic width measurements exceeding 20 cm. Intrapelvic width, height, and area measurements are presented in Table 3.1 and Figure 3.1. A difference plot indicated a significant bias of -5.8% between the two investigators in measuring intrapelvic area on different days before parturition ($P = 0.0028$, Figure 3.2). The limits of agreement were -25.4 % to +13.7 %.

Intrapelvic width and area were the latest maturing traits, as estimated by the value for k (Table 3.2). The estimated values for A were higher, and for k were lower, than the true value for both intrapelvic width and area because intrapelvic width could not be accurately measured beyond 20.0 cm in 26 cattle (25%; Figure 3.1). In comparison, height at the withers was the earliest maturing external morphologic dimension, based on the estimated value for k (Figure 3.3).

Calving difficulty scores

Calving difficulty score was greater in primiparous cattle than multiparous cattle (Table 3.1). Percentages of calving difficulty scores for primiparous cattle were 8.8% (score of 1), 23.5% (2), 32.3% (3), 17.7% (4), and 17.7% (5). As expected, the distribution of scores for primiparous cattle was different ($P < 0.0001$) to that of multiparous cattle; percentages for calving difficulty scores for the latter group were 56.5% (1), 29.0% (2), 8.7% (3), 2.9% (4), and 2.9% (5). Dystocia (defined as a calving difficulty score of 4 or 5) therefore occurred at a much higher incidence ($P < 0.0001$) in primiparous cattle (35%) than multiparous cattle (6%).

Calving difficulty score was positively associated with dystocia index ($r_s = 0.44$) and negatively associated with intrapelvic area ($r_s = -0.43$), age ($r_s = -0.42$), body weight of the dam as calculated from thoracic circumference ($r_s = -0.42$), intrapelvic width ($r_s = -0.40$), the ratio of intrapelvic area to body weight ($r_s = -0.44$), height at the withers ($r_s = -0.37$), intrapelvic height ($r_s = -0.32$), and distance between the pins ($r_s = -0.25$), but was not associated with gestation length, the body condition score and tail head height of the dam, or the chest girth or front hoof circumference of the calf.

Calf birth weight

Calf birth weights were similar for primiparous and multiparous cattle (Table 3.1). For all cattle, calf birth weight was not associated with calving difficulty score. However, calf birth weight was associated with calving difficulty score when analyzed separately for primiparous ($r_s = 0.36$, $P = 0.04$) and multiparous cattle ($r_s = 0.28$, $P =$

0.02). Calving difficulty score was positively associated with the ratio of calf birth weight to maternal intrapelvic area ($r_s = 0.44$). The median value for calf birth weight as a percent of dam body weight was 6.5% (range, 4.2 to 8.0%).

Calf front hoof circumference

Median CV for front and hind hoof circumferences were 0.4% (range, 0 to 1.1%; $n = 29$) for observer 1 (CV not estimated for observer 2). The first measurement for front hoof circumference was therefore used for analysis due to the precision of the estimate.

Calf front hoof circumference was positively associated with calf birth weight ($r_s = 0.59$, $P < 0.0001$; Figure 3.4). A linear equation was developed for dairy calves relating birth weight in kg to the circumference of the front hoof at the coronary band in cm, such that: $\text{weight} = 3.18 \times \text{circumference} - 12.4$ ($R^2 = 0.41$). Interestingly, front hoof circumference was not associated with calving difficulty score ($r_s = 0.17$, $P = 0.09$), the age of the dam ($r_s = 0.04$, $P = 0.68$), or the heart girth of the dam ($r_s = 0.18$, $P = 0.08$).

Ratio of front hoof circumference to pelvic area, thoracic circumference and pin distance

The ratio of calf front hoof circumference to the pelvic area of the dam was higher for primiparous cattle than multiparous cattle and was positively associated with calving difficulty score ($r_s = 0.46$, $P < 0.0001$). However, the ratio of front hoof circumference to thoracic circumference and pin distance for primiparous and multiparous cattle were not significantly different.

Logistic regression analysis of dystocia and perinatal mortality

Variables examined using binary logistic regression to predict dystocia and perinatal mortality included maternal intrapelvic width, height, and area, heart girth, withers height and pin width (for dam factors), front hoof circumference, heart girth, and sex (for analysis of calf factors), and the cow factors, calf factors, and the ratio of

calf front hoof circumference to maternal intrapelvic width, height, and area (for combined analysis of cow and calf factors).

Binary logistic regression analysis indicated that intrapelvic area provided the best predictor of dystocia from cow data (area under ROC = 0.81). At the optimal cutpoint of $< 270 \text{ cm}^2$ to predict dystocia, the Se = 0.56 and the Sp = 0.89 (Figure 3.5). There was no significant predictor of dystocia derived solely from the calf data.

Binary logistic regression using both dam and calf data indicated that the ratio of front hoof circumference of the calf to the maternal intrapelvic area provided the best predictor of dystocia (area under ROC = 0.78). At the optimal cutpoint for the ratio ($> 0.068 \text{ cm/cm}^2$), the Se = 0.50 and the Sp = 0.93 (Figure 3.6). Ordered logistic regression revealed a score dependent effect of the probability of dystocia score of 2, 3, 4 or 5 (Figure 3.7).

Binary logistic regression using both dam and calf data indicated that a smaller thoracic circumference of the calf and the presence of dystocia (calving difficulty score 4 or 5) provided the best predictors of the occurrence of perinatal mortality (area under ROC = 0.88; Table 3.3).

Discussion

The major findings of the study reported here were that: 1) measurements of maternal intrapelvic width, height, and area in late gestation dairy cattle, and front hoof circumference measurements in calves are highly repeatable, as demonstrated by inter-observer CV $< 2.0\%$ and intra-observer CV $< 1.4\%$, but can differ by 5.8% between two investigators; 2) intrapelvic width and area are late maturing morphometric characteristics of dairy cows, whereas height at the withers is an early maturing morphometric characteristic; 3) calving difficulty score was negatively associated with age ($r_s = -0.42$), body weight of the dam as calculated from thoracic circumference ($r_s = -0.42$), and intrapelvic area ($r_s = -0.41$), but was not associated with body weight or front hoof circumference of the calf; and 4) the ratio of calf front hoof circumference to

maternal intrapelvic area ($r_s = 0.46$) provided the most accurate method for predicting dystocia in primiparous and multiparous dairy cattle. In other words, when evaluating the likelihood of dystocia in late gestation dairy cattle, the focus should be on direct measurement of the intrapelvic area if the calf is not in the birth canal, or if the calf is in the birth canal, measurement of front hoof circumference and estimating the intrapelvic area from the dam's age or thoracic circumference. The latter two variables are predictive of calving difficulty score because of the positive association between maternal intrapelvic area and age ($r_s = 0.70$) and between maternal intrapelvic area and thoracic circumference ($r_s = 0.63$).

Excellent repeatability is a desirable property of any diagnostic test. Initial reports from France using a custom-designed pelvimeter indicated that intrapelvic height and width measurements had a CV of 3.4% and 3.7%, respectively (Menissier and Vissac, 1971). The Rice pelvimeter is reported to have CV of < 1.5% and < 5.0% for intra-observer and inter-observer, respectively in Belgian Blue cows (Kolkman et al., 2007), similar to the values reported in the study reported here. Mean differences in Belgian Blue cows for Rice pelvimeter measurements in live animals and after slaughter were - 0.2 cm for intrapelvic width and 1.2 cm for pelvic height (Kolkman et al., 2009). The Rice pelvimeter provides an estimate for intrapelvic area that was 9 cm² less than that produced by the brass Krautman pelvic meter (Wolverton et al., 1991). Measurement of intrapelvic dimensions using the Rice pelvimeter is more repeatable than use of computed tomography, with reported values of 7.6% (intrapelvic height), 8.2% (intrapelvic width), and 12.0% (intrapelvic area) for German Holstein-Friesian cattle aged 2 to 9 years (Tsousis et al., 2010).

The rate of maturation has been extensively investigated in cattle but few studies have attempted to relate this information to the development of clinically useful predictors of calving difficulty score. Important findings of our study were that intrapelvic width and area are very late to mature, and thoracic circumference and pin width are late to mature, whereas withers height is early to mature in dairy cattle. We also found that intrapelvic area immediately before parturition was more strongly

associated with thoracic circumference (heart girth) than pin width or height at the withers. These findings suggest that breeding recommendations for dairy heifers should be based on thoracic circumference rather than withers height, as thoracic circumference provides a more accurate predictor of intrapelvic dimensions than does withers height.

The primiparous dairy cattle in our study had similar intrapelvic width measurements but smaller intrapelvic height measurements than studies of dairy cattle conducted in The Netherlands (Meijering and Postma, 1984), Poland (Nogalski and Mordas, 2012), and Brazil (de Oliveira and Gheller, 2009). The shape of the pelvic inlet of primiparous cattle in our study therefore differed from that of dairy cattle in other countries, suggesting the presence of genetic differences. In the present study, intrapelvic width had a greater influence on intrapelvic area ($r_s = 0.85$) than intrapelvic height ($r_s = 0.73$). This is because intrapelvic width is slower to mature in cattle than intrapelvic height (Green et al., 1988).

We observed that primiparous cattle had smaller intrapelvic areas and the ratio of calf front hoof circumference to maternal intrapelvic area than did multiparous cattle. Previous studies in beef cattle (Deutscher, 1988; Basarab et al., 1992) and dairy cattle (Nogalski, 2003; Nogalski and Mordas, 2012) have measured the ratio of maternal intrapelvic area to calf birth weight as an index of dystocia but this is not helpful in decision making at parturition because the calf birth weight is unknown. The results of the present study here indicated that the ratio of calf front hoof circumference to maternal intrapelvic area was the best predictor of calving difficulty score, based on individual association ($r_s = 0.46$, $P < 0.0001$) and the results of binary logistic regression. However, it should be noted that the association with calving difficulty score was not appreciably greater than that obtained by measuring intrapelvic area alone ($r_s = -0.41$) or thoracic circumference of the dam ($r_s = -0.42$), or knowledge of the dam's age ($r_s = -0.42$). If only maternal factors for predicting dystocia in late gestation dairy cattle are available, then intrapelvic area, age, or thoracic circumference (heart girth) would appear to be the parameters of choice.

The median front hoof circumference of calves in our study was 17.8 cm which was greater than that reported previously in beef calves (16.9 ± 0.8 cm; Tozer et al., 2002) and in Holstein-Friesian calves in Poland (16.7 to 17.1 cm; Nogalski, 2003). We found that calf hoof circumference did not correspond with measurements of calf birth weight as indicated on the Calfscale® birthweight tape; as such our results are different from those reported by Long et al., 2012 in a study that involved 872 Holstein-Friesian calves. We cannot offer a satisfactory reason for the disparity in results. The regression equation for the relationship between calf birth weight and calf forelimb hoof circumference in this study (Figure 3.4) presented higher values compared to those from Tozer et al., 2002 and Thomas, 1996; which showed that direct comparison between Holstein-Friesian and beef breeds was not accurate. The diameter of the calf front fetlock is also well correlated with calf weight (Hindson, 1978; West, 1997), whereas metacarpal circumference and length are poorly correlated with calf weight (Nugent et al., 1991).

The mean birth weight of a calf ranges from 5 to 10% of the dam's weight (Holland and Odde, 1992) while the mean birth weight of a Holstein-Friesian calf has been reported to be 7.3% of the dam weight (Nogalski, 2003). This was slightly higher than the calculated value of 6.5% in the present study, and 7.2% represents the minimum risk of perinatal mortality in Holstein-Friesian calves (Johanson and Berger, 2003). The Holstein-Friesian breed has the highest calf birth weight to dam body weight ratio in dairy cattle, and this high ratio is thought to be responsible for the higher incidence of dystocia in Holstein-Friesian cattle (Murray and Leslie, 2013). An interesting finding of our study is the similarity in calf birth weights between primiparous and multiparous cattle as primiparous Holstein-Friesian cattle typically produce calves that weigh 2 to 3 kg less than multiparous cattle in the United States (Olson et al., 2009; Dhakal et al., 2013).

Calf birth weights and calf front hoof circumference were not associated with calving difficulty score in this study; similar findings were reported previously in Gascon cattle that had a similarly large range in age (Bureš et al., 2008). In contrast, other

studies reported that increased calving difficulty was associated with increasing body weight and selected morphometric measurements of calves (Tozer et al., 2002; Nogalski, 2003). Also evident in our study and many others, dystocia is more commonly observed in primiparous cattle (Johanson and Berger, 2003; Berger et al., 1992; Fiedlerova et al., 2008; Olson et al., 2009; Gaafar et al., 2011), and age, independent of intrapelvic area, is an important predictor of dystocia (Basarab et al., 1993; Kolkman et al., 2012).

There is no commonly accepted scoring system to categorize calving difficulty (Mee, 2008) with scoring systems using a range of categories from two (Johanson and Berger, 2003) to seven (McClintock, 2004). The calving scoring system employed by the Purdue Dairy Research and Education Center emphasizes fetopelvic disproportion and is similar to the one used by Tozer et al., 2002 and Lombard et al., 2007 that assigned 1 = no assistance, 2 = assistance by one person, 3 = assistance by two or more people, 4 = mechanical extraction and 5 = surgical procedures were done. Development of a standardized scoring system that reflects the application of force and the likelihood of delivery-related trauma to the dam and calf would be very helpful. Of interest is that the observed percentage of difficult births was 35%, which exceeded the reported range of 5 to 15% for artificial insemination dairy bulls in North America (Weigel, 2002).

Perinatal mortality in the study reported here was associated with the presence of dystocia and a smaller calf thoracic circumference. We believe that this is the first study to identify a negative association between calf thoracic circumference and the incidence of perinatal mortality. Our findings should be regarded as preliminary as they are based on a small number of perinatal mortality. Moreover, a smaller thoracic circumference could also be a proxy for a primiparous dam as these dams produced calves that had a smaller thoracic circumference than that in calves born to multiparous animals.

There were some limitations in this study. First, our study was conducted on one farm and additional studies are indicated to determine the external validity of the results. We believe the results of our study can be generalized to North American

Holstein-Friesian cattle. The genetic background of Holstein-Friesian cattle on the study farm is diverse and believed to be representative of the US Holstein-Friesian breed. The 95% confidence interval for the stillborn rate (6.5 to 19.5%) included the estimated stillborn rate of 8.1% in the US (USDA, 2007). Likewise, the 95% confidence interval for the twinning rate (1.0 to 9.5%) included the estimated range of 2.5 to 5.8% for Holstein-Friesian cattle (Fricke, 2001; Johanson et al., 2001; Del Río et al., 2007) with twins occurring much more often in multiparous cattle, similar to the findings of other studies (Johanson et al., 2001; Del Río et al., 2007). Second, the Rice pelvimeter, although a useful tool, has a drawback in its inability to measure dimensions greater than 20 cm. We therefore had to assign a maximum value of 20.5 cm to pelvimetry measurements and this requirement dictated the use of statistical methods for analysis that could accommodate right censored data. Finally, given that dystocia occurs more frequently in heifers, it would be helpful to confine future studies to larger numbers of primiparous cattle.

Conclusion

In conclusion, our finding that calving difficulty score is negatively associated with intrapelvic dimensions suggests that preparturient pelvimetry of primiparous cattle may be useful in identifying the small percentage of heifers that have a small intrapelvic area and are therefore at an increased risk for dystocia. This association, coupled with recent emphasis on calving Holstein-Friesian heifers at 22 to 24 months of age in North America, suggests that insufficient body development at calving may provide a partial explanation for the relatively high incidence of perinatal mortality in Holstein-Friesian heifers in North America. This speculation needs to be confirmed by measurement of intrapelvic dimensions in a much larger population of primiparous late gestation Holstein-Friesians. Although fetopelvic disproportion is the most common cause of dystocia, it must be kept in mind that calf presentation, position, posture, and sex, dam body condition score, gestation length, and environmental factors including season,

nutrition and overall general management are also important factors that influence the occurrence of dystocia (Laster, 1974; Meijering, 1984; Mee, 2008; Fiedlerova et al., 2008; Zaborski et al., 2009). An accurate test for dystocia in cattle will therefore be challenging to develop because of the large number of factors that can result in dystocia.

References

- Bagna B, Schwabe C, Anderson LL. Effect of relaxin on facilitation of parturition in dairy heifers. *J Reprod and Fertility*, 1991;91(2):605-615.
- Barrier AC, Haskell MJ, Birch S et al. The impact of dystocia on dairy calf health, welfare, performance and survival. *Vet J* 2013; 195:86-90.
- Basarab JA, Rutter LM, Day PA. The efficacy of predicting dystocia in yearling beef heifers: I. Using ratios of pelvic area to birth weight or pelvic area to heifer weight. *J Anim Sci* 1993;71(6):1359-1371.
- Ben David B. Contributi ed osservazioni pratiche sulla distocia causata de un feto relativamente grande, nella vacca frisona israeliana. *La Clinica Veterinaria* 1960;83:412-419
- Benyshek LL, Little DE. Estimates of genetic and phenotypic parameters associated with pelvic area in Simmental cattle. *J Anim Sci* 1982; 54:258-XX
- Berger PJ, Cubas AC, Koehler KJ, et al. Factors affecting dystocia and early calf mortality in Angus cows and heifers. *J Anim Sci* 1992;70(6):1775-1786.
- Bland JM, Altman DG. Applying the right statistics: analysis of measurement studies. *Ultrasound Obstet Gynecol* 2003;22:85-93.
- Brown JE, Brown CJ, Butts WT. A discussion of the genetic aspects of weight, mature weight and rate of maturing in Hereford and Angus cattle. *J Anim Sci* 1972; 34:525-537.
- Bureš D, Bartoň L, Zahrádková R, et al. Calving difficulty as related to body weights and measurements of cows and calves in a herd of Gascon breed. *Czech J Anim Sci* 2008;53:187-194.
- Coopman F, de Smet S, Gengler N, et al. Estimating internal pelvic sizes using external body measurements in the double-muscled Belgian Blue beef breed. *Brit Society Anim Sci* 2003;76:229-235.
- De Oliveira LF, Gheller VA. Avaliação de medidas pélvicas internas de vacas holandesas do estado de minas gerais, Brasil. *Ciência Animal Brasileira* 2009;1:802-807.
- Del Río NS, Stewart S, Rapnicki P, et al. An observational analysis of twin births, calf sex ratio, and calf mortality in Holstein dairy cattle. *J Dairy Sci* 2007;90(3):1255-1264.

Dematawewa CMB, Berger PJ. Effect of dystocia on yield, fertility, and cow losses and an economic evaluation of dystocia scores for Holsteins. *J Dairy Sci* 1997;80(4):754-761.

Deutscher GH. *Pelvic measurements for reducing calving difficulty*. Cooperative Extension, Institute of Agriculture and Natural Resources, University of Nebraska--Lincoln. 1988.

Dhakal K, Maltecca C, Cassady JP, et al. Calf birth weight, gestation length, calving ease, and neonatal calf mortality in Holstein, Jersey, and crossbred cows in a pasture system. *J Dairy Sci* 2013;96:690-698.

Elanco Animal Health. Body Condition Scoring. Bulletin AI 8478 (Rev. 9/96). Elanco Animal Health, Indianapolis, IN. 1996.

Ferguson JD, Galligan DT, Thomsen N. Principal descriptors of body condition score in Holstein cows. *J Dairy Sci* 1994;77(9):2695-2703.

Fiedlerova M, Rehak D, Vacek M et al. Analysis of non-genetic factors affecting calving difficulty in the Czech Holstein population. *Czech J Anim Sci* 2008; 53:284-291.

Frazer GS, Perkins NR, Constable PD. Bovine uterine torsion: 164 hospital referral cases. *Theriogenology* 1996;46(5):739-758.

Fricke PM. Review: Twinning in dairy cattle. *The Professional Animal Scientist*, 2001;17(2):61-67.

Gaafar HMA, Shamiah SM, El-Hamd MA, et al. Dystocia in Friesian cows and its effects on postpartum reproductive performance and milk production. *Trop Anim Health and Prod* 2011;43(1):229-234.

Gaines JD, Peschel D, Kauffman RG, et al. Pelvic growth, calf birth weight and dystocia in Holstein × Hereford heifers. *Theriogenology* 1993;40(1):33-41.

Green RD, Brinks JS, LeFever DG. Genetic characterization of pelvic measures in beef cattle: Heritabilities, genetic correlations and breed differences. *J Anim Sci* 1988;66(11):2842-2850.

Heinrichs AJ, Rogers GW, Cooper JB. Predicting body weight and wither height in Holstein heifers using body measurements. *J Dairy Sci* 1992;75(12):3576-3581.

Hindson JC. Quantification of obstetric traction. *Vet Record* 1978;102(15):327-332.

Hoffman PC. Optimum body size of Holstein replacement heifers. *J Anim Sci* 1997; 75:836-845.

Holland MD, Odde KG. Factors affecting calf birth weight: a review. *Theriogenology* 1992;38(5):769-798.

Johanson JM, Berger PJ. Birth weight as a predictor of calving ease and perinatal mortality in Holstein cattle. *J Dairy Sci* 2003;86(11):3745-3755.

Johanson JM, Berger PJ, Kirkpatrick BW, et al. Twinning rates for North American Holstein sires. *J Dairy Sci* 2001;84(9):2081-2088.

Ko JCH, Ruble MV. Using maternal pelvis size and fetal hoof circumference to predict calving difficulty in beef cattle. *Vet Med* 1990;85:1030-1036.

Kolkman I, Matthys K, Hoflack G, et al. The agreement of pelvic measurements obtained in Belgian Blue cows with a Rice pelvimeter and the differences between these measurements around parturition. *Vlaams diergeneeskundig tijdschrift* 2007;76(6):431-437.

Kolkman I, Hoflack G, Aerts S, et al. Evaluation of the Rice pelvimeter for measuring pelvic area in double muscled Belgian Blue cows. *Livestock Science*. 2009;121(2):259-266.

Kolkman I, Hoflack G, Aerts S, et al. Pelvic dimensions in phenotypically double-muscled Belgian Blue cows. *Reprod Dom Anim* 2012;47(3):365-371.

Laster DB. Factors affecting pelvic size and dystocia in beef cattle. *J Anim Sci* 1974;38(3):496-503.

Laven R, Howe M. Uterine torsion in cattle in the UK. *Vet Rec* 2005;157(3):96-96.

Lean IJ, PJ DeGaris, DM McNeil, et al. Hypocalcemia in dairy cows: Meta-analysis and dietary cation anion difference theory revisited. *J Dairy Sci* 2006;89:669-684.

Linden TC, Bicalho RC, Nydam DV. Calf birth weight and its association with calf and cow survivability, disease incidence, reproductive performance, and milk production. *J Dairy Sci* 2009; 92:2580-2588.

Lombard JE, Garry FB, Tomlinson SM, et al. Impacts of dystocia on health and survival of dairy calves. *J Dairy Sci* 2007;90(4):1751-1760.

- Long NM, Collier RJ, Smith JF. Short communication: Comparison of 2 methods of assessing calf birth weights in dairy calves. *J Dairy Sci* 2012; 95:7206-7209.
- McClintock SE. A genetic evaluation of dystocia in Australian Holstein-Friesian cattle. Ph.D., University of Melbourne. 2004.
- Mee JF. Prevalence and risk factors for dystocia in dairy cattle: A review. *Vet J* 2008;176:93-101.
- Meijering A. Dystocia and stillbirth in cattle—A review of causes, relations and implications. *Livestock Prod Sci* 1984;11(2):143-177.
- Meijering A, Postma A. Morphologic aspects of dystocia in dairy and dual purpose heifers. *Can J Anim Sci* 1984; 64:551-562.
- Menissier F, Vissac B. Possibilités d'amélioration des conditions de vêlage par sélection: i. Technique de mesure de l'ouverture pelvienne des bovins. *Ann Genet Sel Anim* 1971;3(2):207-214
- Meyer CL, Berger PJ, Koehler KJ, et al. Phenotypic trends in incidence of stillbirth for Holsteins in the United States. *J Dairy Sci* 2001;84(2):515-523.
- Morrison DG, Williamson WD, Humes PE. Estimates of heritabilities and correlations of traits associated with pelvic area in beef cattle. *J Anim Sci* 1986;63(2):432-437.
- Morrow DA, Roberts SJ, McKentee K, Gray HG. Postpartum ovarian activity and uterine involution in dairy cattle. *J Amer Vet Med Assoc* 1966;149:1596-1609.
- Murray CF, Leslie KE. Newborn calf vitality: Risk factors, characteristics, assessment, resulting outcomes and strategies for improvement. *The Vet J*, 2013;198(2):322-328.
- Naazie A, Makarechian M, Berg RT. Factors influencing calving difficulty in beef heifers. *J Anim Sci* 1989; 67:3243-3249.
- Nelsen TC, Short RE, Urick JJ, et al. Heritabilities and genetic correlations of growth and reproductive measurements in Hereford bulls. *J Anim Sci* 1986;63(2):409.
- Nix JM, Spitzer JC, Grimes LW, Burns GL, Plyler BB. A retrospective analysis of factors contributing to calf mortality and dystocia in beef cattle. *Theriogenology* 1998;49:151-1523.

- Nugent RA, Notter DR, Beal WE. Body measurements of newborn calves and relationship of calf shape to sire breeding values for birth weight and calving ease. *J Anim Sci* 1991;69(6):2413-2421.
- Nogalski Z. Relations between the course of parturition, body weights and measurements of Holstein-Friesian calves. *Czech J Anim Sci*, 2003;48(2):51-60.
- Nogalski Z, Mordas W. Pelvic parameters in Holstein-Friesian and Jersey heifers in relation to their calving. *Pak Vet J* 2012;32(4):507-510.
- Olson KM, Cassell BG, McAllister AJ, et al. Dystocia, stillbirth, gestation length, and birth weight in Holstein, Jersey, and reciprocal crosses from a planned experiment. *J Dairy Sci* 2009;92(12):6167-6175.
- Philipsson, J. Studies on Calving Difficulty, Stillbirth and Associated Factors in Swedish Cattle Breeds: I. General Introduction and Breed Averages. *Acta Agriculturae Scandinavica* 1976;26(2), 151-164.
- Ramin AG, Daniel RCW, Fenwick DC, et al. Pelvic parameters, growth rate, puberty, and their interrelationships in young dairy heifers. *Reprod Dom Anim* 1995;30(3):117-123.
- Rajala PJ, Gröhn YT. Effects of dystocia, retained placenta, and metritis on milk yield in dairy cows. *J Dairy Sci* 1998;81(12):3172-3181.
- Rice LE, Wiltbank JN. Dystocia in beef heifers. *J Anim Sci* 1970;30:1043.
- Rice LE, Wiltbank JN. Factors affecting dystocia in beef heifers. *J Am Vet Med Assoc* 1972;161(11):1348-1358.
- Ruble MV. *U.S. Patent No. 4,688,653*. Washington, DC: U.S. Patent and Trademark Office. 1987.
- Shah KD, Nakao T, Kubota H. Plasma estrone sulphate (E₁S) and estradiol-17 β (E₂ β) profiles during pregnancy and their relationship with the relaxation of sacrosciatic ligament, and prediction of calving time in Holstein–Friesian cattle. *Anim Repro Sci* 2006;95(1):38-53.
- Short RE, Bellows RA, Staigmiller RB, Carr JB. Multiple linear and nonlinear regression analyses of factors causing calving difficulty. *Theriogenology* 1979; 12:121-130.
- Sieber M, Freeman AE, Kelley DH. Effects of body measurements and weight on calf size and calving difficulty of Holsteins. *J Dairy Sci* 1989; 72:2402-2410.

Sloss V, Dufty JH. Handbook of Bovine Obstetrics. Williams & Wilkins. Baltimore/London 1980;98.

Thomas HS. A hoof tells the story. Beef. 1996 January 77-78.

Thomson DB, Wiltbank JN. Dystocia in relationship to size and shape of pelvic opening in Holstein heifers. *Theriogenology* 1983; 20:683-692.

Tozer PR, Scollard DL, Marsh TL, et al. Recursive systems model of fetal birth weight and calving difficulty in beef heifers. *Can J Anim Sci* 2002;82(1):19-27.

Tsousis G, Heun C, Becker M, et al. Application of computed tomography for the evaluation of obstetrically relevant pelvic parameters in German Holstein-Friesian cows. *Theriogenology* 2010;73(3):309-315.

USDA. Dairy. Part IV: Reference of Dairy Cattle Health and Management Practices in the United States. Fort Collins, Colo: USDA-APHIS-Veterinary Services, 2007;1-185.

Van Donkersgoed J. A critical analysis of pelvic measurements and dystocia in beef heifers. *The Comp Cont Edu Prac Vet* 1992;14(3):405-408.

Van Donkersgoed J, Ribble CS, Booker CW, et al. The predictive value of pelvimetry in beef cattle. *Can J Vet Res* 1993;57(3):170.

Weigel K. Daughter and service sire calving ease. There's new help to avoid calving problems. *Breeders Journal* 2002; September, 8-9.

Weiher VO, Hoffman G, Sass D. Investigations into relationships between internal and external pelvic measurements in Frisian cows. *Dtsch tierarztl Wschr* 1992; 99:452-454.

West, H. J. Dimensions and weight of Belgian Blue and crossbred calves and the pelvic size of the dam. *Vet J* 1997;153(2):225-228.

Wittek T, Sen I, Constable PD. Changes in abdominal dimensions during late gestation and early lactation in Holstein-Friesian heifers and cows and their relationship to left displaced abomasum. *Vet Rec*. 2007;161(5):155-161.

Wolverton DJ, Bishop MD, Day ML et al. Repeatability of measurements on two instruments used in pelvimetry of beef cattle. *Ohio Beef Cattle Res Ind Rep* Mar 1991;91-2:54-64.

Zaborski D, Grzesiak W, Szatkowska I, et al. Factors affecting dystocia in cattle. *Reprod Dom Anim* 2009;44(3):540-551.

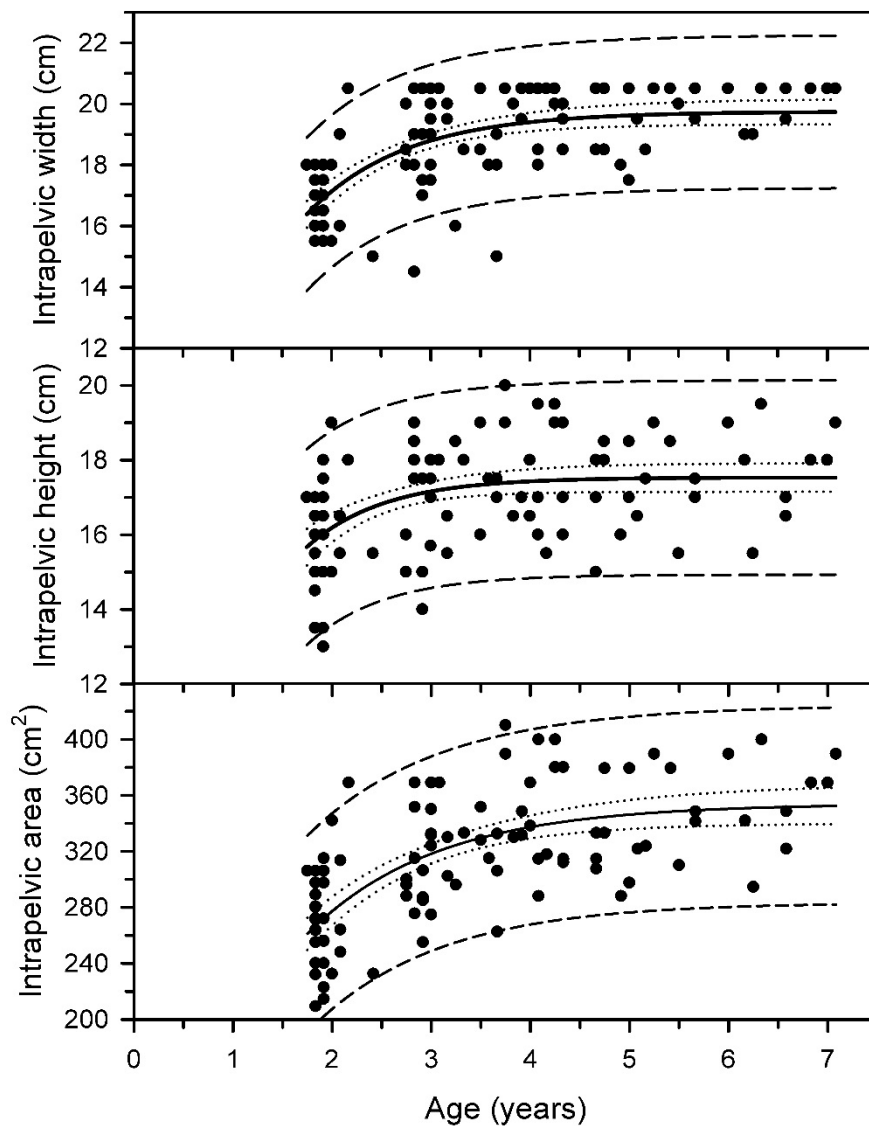


Figure 3.1 Scatterplot of the relationship between intrapelvic width (top panel), intrapelvic height (middle panel) and intrapelvic area (bottom panel) versus age for primiparous ($n = 34$) and multiparous ($n = 69$) Holstein-Friesian cattle in late gestation. Intrapelvic width dimensions > 20 cm were assigned a value of 20.5 cm. The thick curvilinear line represents an exponential equation relating the respective intrapelvic dimension to age (the function $y = A \times (1 - e^{-kx})$ was used to model the relationship between the measurement and time in years; A is the asymptotic value for the dimension at infinite age and k is an estimate of the earliness of maturation). The dotted lines are the 95% confidence interval for the line, and the dashed lines are the 95% confidence interval for prediction.

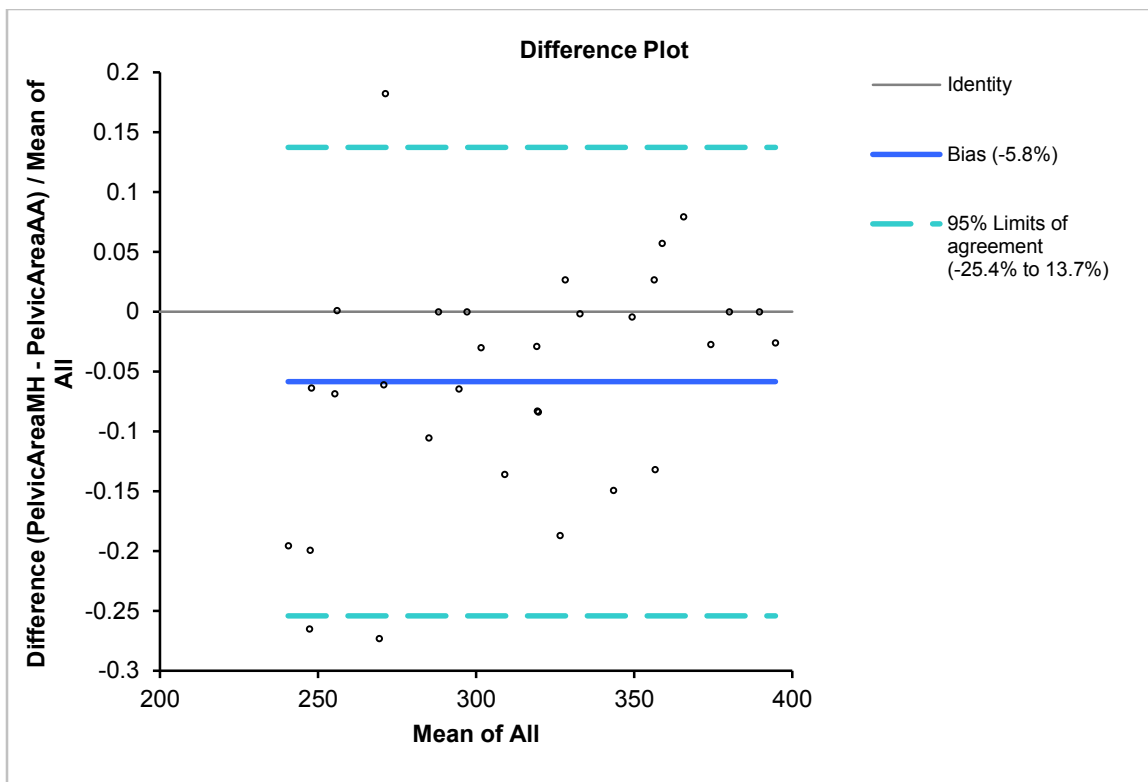


Figure 3.2 Difference plot (Bland and Altman plot) of the difference in intrapelvic area (cm^2) as measured by two investigators expressed as a percentage of the mean value for 31 cattle, against the mean value for measured area. The horizontal solid line of the difference plot identifies the mean percentage bias between the two investigators (-5.8%), and the horizontal dashed lines reflect the limits of agreement (mean percentage bias $\pm 1.96 \times \text{SD} = -25.4\%$ to $+13.7\%$) which is equivalent to the range of differences that contains 95% of future measurements.

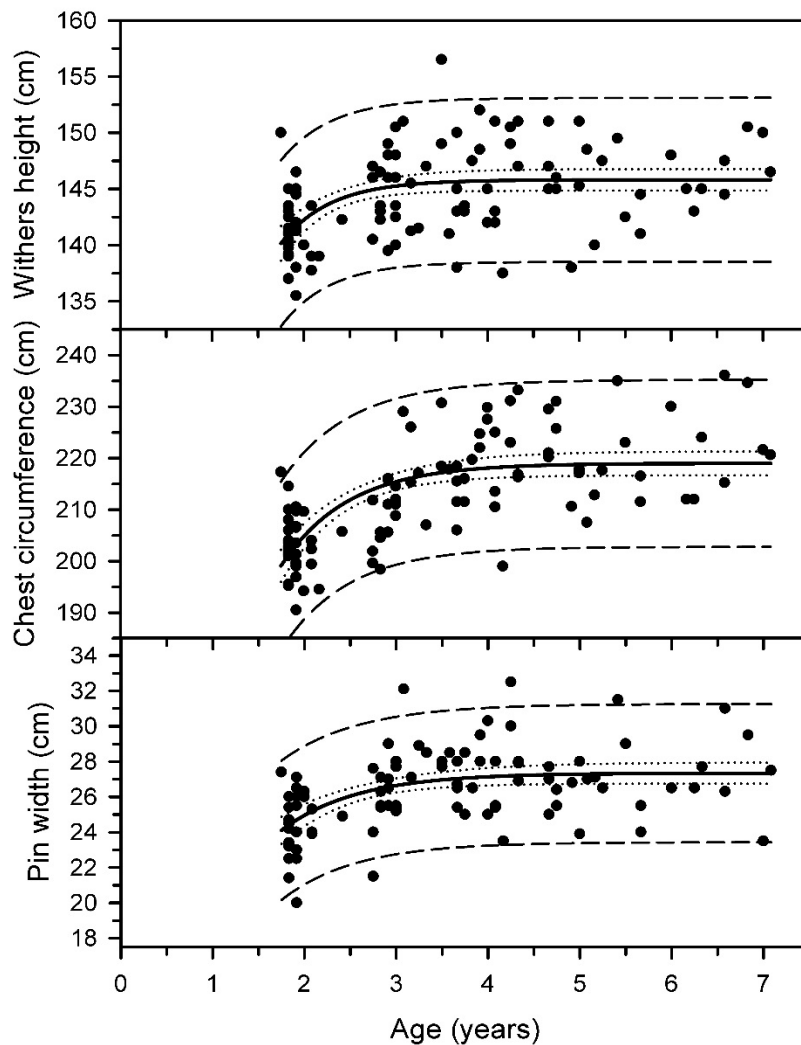


Figure 3.3 Scatterplot of the relationship between height at the withers (top panel), heart girth (thoracic or chest circumference; middle panel) and width of the pins (bottom panel) versus age for primiparous ($n = 34$) and multiparous ($n = 69$) Holstein-Friesian cattle in late gestation. The thick curvilinear line represents an exponential equation relating the respective measurement to age (the function $y = A \times (1 - e^{-k \times t})$ was used to model the relationship between the measurement and time in years; A is the asymptotic value for the dimension at infinite age and k is an estimate of the earliness of maturation). The dotted lines are the 95% confidence interval for the line, and the dashed lines are the 95% confidence interval for prediction.

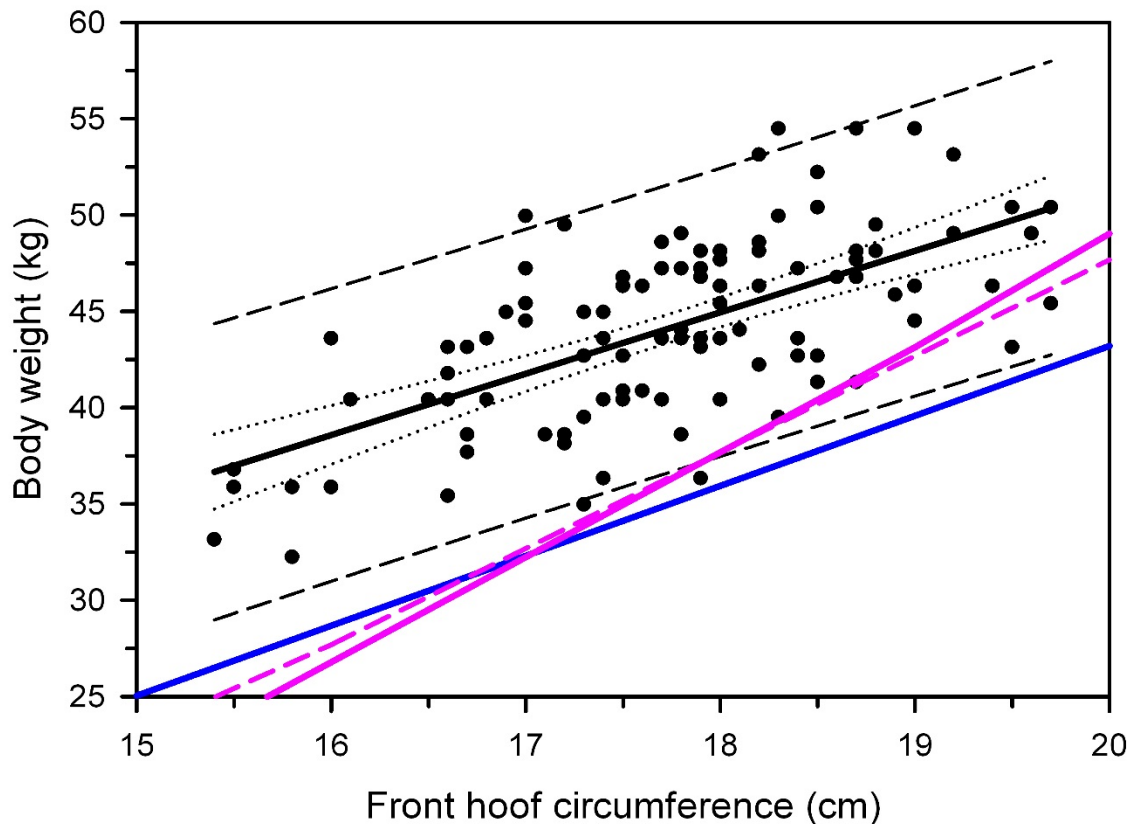


Figure 3.4 Scatterplot plot of the relationship between calf birth weight (kg) and calf forelimb hoof circumference (cm). Data was obtained from 101 Holstein-Friesian calves instead of 107 due to missing values for hoof circumference or body weight. The thick solid black line is the regression line ($y = 3.18 \times \text{circumference} - 12.4$, $R^2 = 0.41$), the dotted lines are the 95% confidence interval for the line, and the dashed lines are the 95% confidence interval for prediction. The blue solid line is the regression equation developed by Tozer et al., 2002 for beef calves ($y = 3.63 \times \text{circumference} - 29.4$). The pink solid line is the regression equation developed by Ruble for beef bull calves ($y = 5.55 \times \text{circumference} - 62.1$). The pink dashed line is the regression equation developed by Ruble for beef heifer calves ($y = 4.96 \times \text{circumference} - 51.4$) (Thomas, 1996).

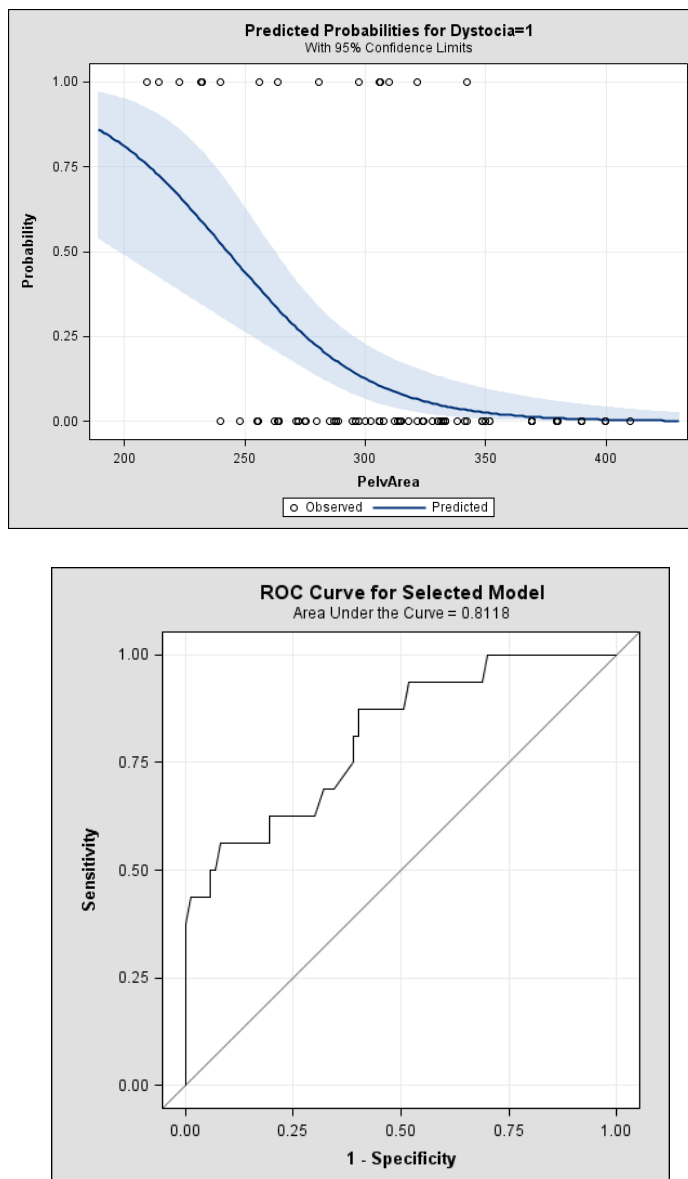


Figure 3.5 Binary logistic regression plot (top panel) of the relationship between probability of dystocia and maternal intrapelvic area (cm^2) in 103 primiparous and multiparous late gestation Holstein-Friesian cattle. The thick solid line is the logistic regression line and the gray shaded area blue area represents the 95% confidence interval for the predicted probability. The open circles represent the intrapelvic areas for cattle with ($P = 1.00$) or without ($P = 0.00$) dystocia. The right panel represents the receiver-operating characteristic curve for maternal intrapelvic area used to predict dystocia in Holstein-Friesian cattle. The diagonal thin line is the line of chance (no predictive ability). The optimal cutpoint for prediction of dystocia occurred at $< 270 \text{ cm}^2$ (area under the ROC curve = 0.81; Se = 0.56; Sp = 0.89).

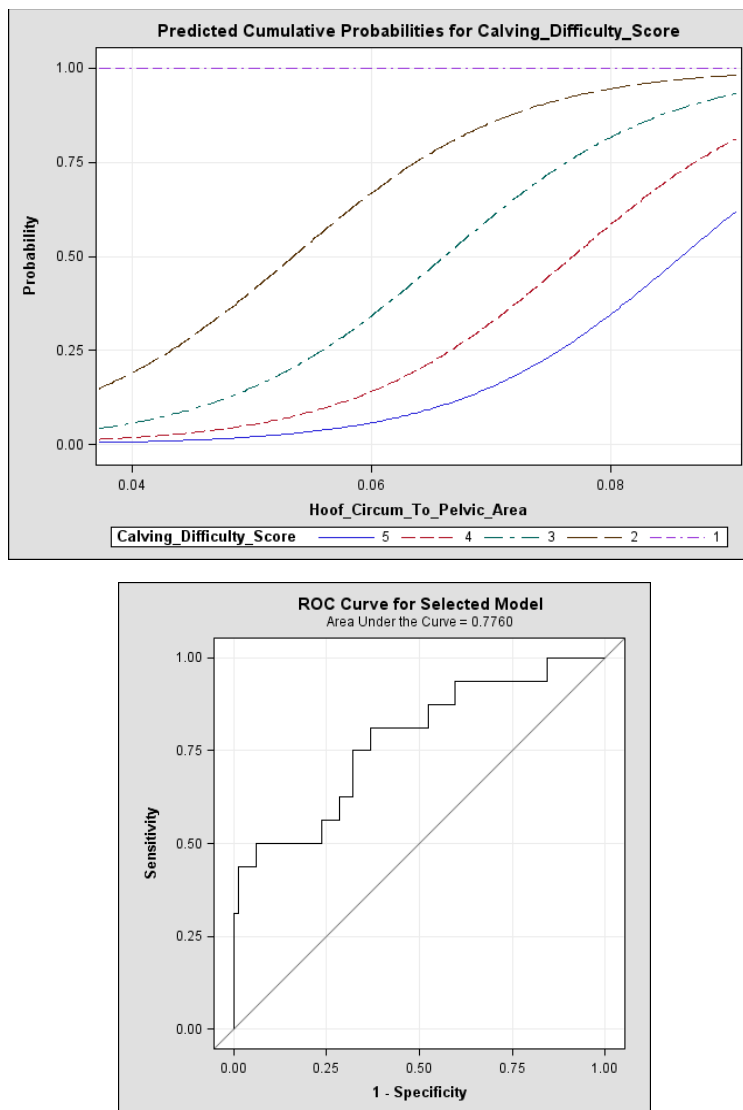


Figure 3.6 Ordered logistic regression plot (top panel) of the ratio of calf front hoof circumference (cm) to maternal intrapelvic area (cm^2) as a predicted cumulative probability for calving difficulty score in 103 primiparous and multiparous late gestation Holstein-Friesian cattle. Calving difficulty score was categorized on a five point scale whereby: 1 = no assistance needed; 2 = easy pull (one person with minimal effort); 3 = moderate pull (one person with moderate effort); 4 = hard pull (one person with considerable effort or two people); and 5 = mechanical extraction or cesarean section. The right panel represents the receiver-operating characteristic curve for the ratio of calf front hoof circumference to maternal intrapelvic area used to predict dystocia (calving difficulty score of 4 or 5) in Holstein-Friesian cattle. The diagonal thin line is the line of chance (no predictive ability). The optimal cutpoint for prediction of calving difficulty score occurred at $> 0.068 \text{ cm/cm}^2$ (area under the ROC curve = 0.78; Se = 0.50; Sp = 0.93).

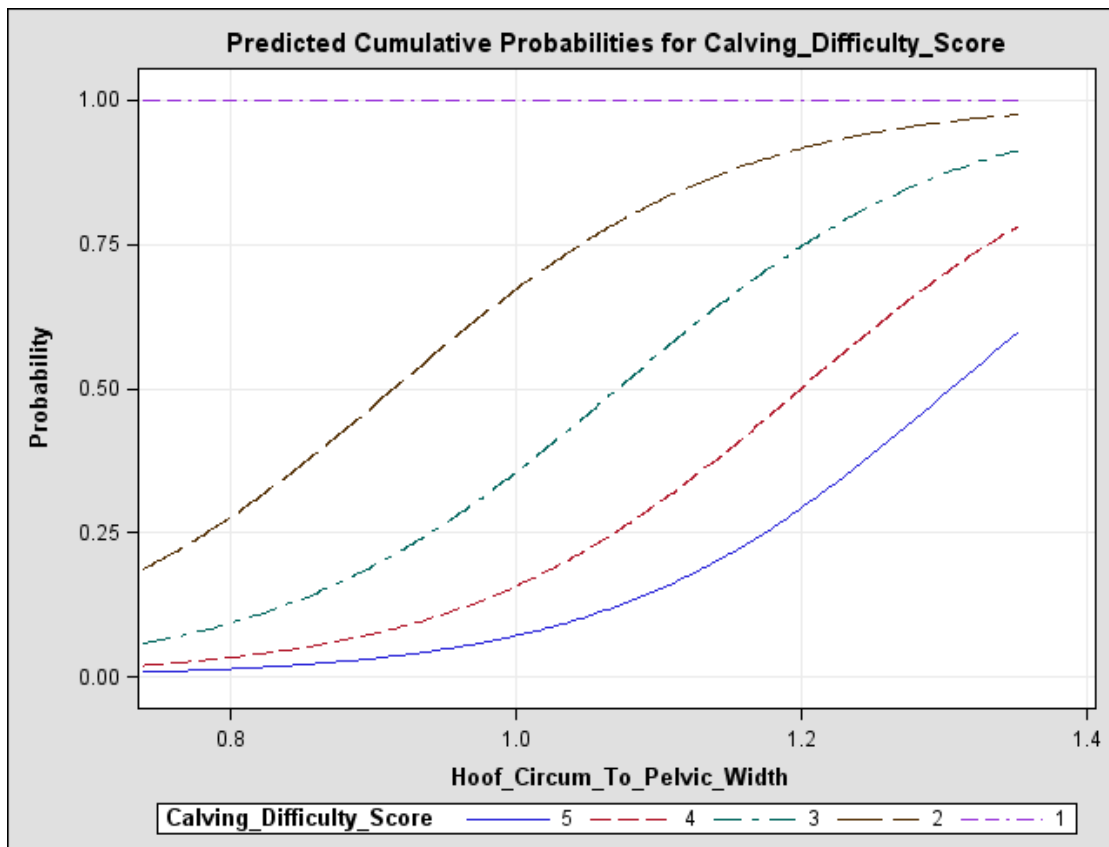


Figure 3.7 Ordered logistic regression plot of the ratio of calf front hoof circumference (cm) to maternal intrapelvic width (cm) as a predicted cumulative probability for calving difficulty score in 103 primiparous and multiparous late gestation Holstein-Friesian cattle. Calving difficulty score was categorized on a five point scale whereby: 1 = no assistance needed; 2 = easy pull (one person with minimal effort); 3 = moderate pull (one person with moderate effort); 4 = hard pull (one person with considerable effort or two people); and 5 = mechanical extraction or cesarean section.

Table 3.1 Comparison of mean \pm SD or median and range (in parentheses) values for selected variables in primiparous (n = 34) and multiparous (n = 69) Holstein-Friesian cattle in late gestation. The P value is derived by using a t-test or Mann-Whitney U test. ND = not determined.

Variable	Primiparous	Multiparous	P value
<u>Cow factors</u>			
Age at calving (months)	23 (21 – 29)		ND
Gestation length (days)	ND	281 \pm 3	ND
Thoracic circumference (cm)	204 \pm 6	217 \pm 9	< 0.0001
Height at withers (cm)	141 \pm 3	146 \pm 4	< 0.0001
Height at tail base (cm)	150 \pm 3	151 \pm 4	0.25
Interischial distance (cm)	24.6 \pm 1.7	27.0 \pm 2.1	< 0.0001
Body condition score (1-5)	3.5 \pm 0.4	3.2 \pm 0.2	0.0009
Calculated body weight (kg)	619 \pm 48	731 \pm 81	< 0.0001
Daughter calving ease score	8.1 \pm 2.4	7.8 \pm 1.6	0.48
Service sire calving ease score	6.7 \pm 1.2	7.5 \pm 1.6	0.011
Calving difficulty score (1-5)	3.0 (1.0 – 5.0)	1.0 (1.0 – 5.0)	< 0.0001
Intrapelvic width (cm)	17.0 (15.0 – 20.5)	19.5 (14.5 – 20.5)	< 0.0001
Intrapelvic height (cm)	16.1 \pm 1.3	17.3 \pm 1.3	< 0.0001
Intrapelvic area (cm ²)	268 (209 - 369)	332 (255 – 410)	< 0.0001
<u>Calf factors</u>			
Calf body weight (kg)	43.8 \pm 4.2	45.1 \pm 4.6	0.17
Calf body weight as a percent of dam body weight (%)	7.1 \pm 0.8	6.2 \pm 0.9	< 0.0001
Calf thoracic circumference (cm)	82.8 \pm 3.7	85.4 \pm 3.5	0.0010

Table 3.2 Estimated values for selected mature dimensions (A) at infinite age and rate of maturation (k) for selected intrapelvic and morphometric dimensions in primiparous (n = 34) and multiparous (n = 69) Holstein-Friesian cattle in late gestation. The numbers in parentheses represents the SE for the estimated value. The estimated mean value for A was higher and k was lower than the true value for both intrapelvic width and area because intrapelvic width could not be accurately measured beyond 20.0 cm in 26 multiparous cattle.

Factor	A (cm)	k (year⁻¹)	R²
Height at withers (cm)	145.8 (0.5)	1.86 (0.10)	0.22
Thoracic circumference (cm)	219.0 (1.2)	1.37 (0.06)	0.42
Intrapelvic height (cm)	17.5 (0.2)	1.28 (0.11)	0.45
Inter-ischial distance (cm)	27.4 (0.3)	1.22 (0.09)	0.26
Intrapelvic width (cm)	> 19.7 (0.2)	< 1.01 (0.06)	0.47
Intrapelvic area (cm ²)	> 354 (7)	< 0.76 (0.06)	0.45

Table 3.3 Binary logistic regression models for dystocia and perinatal mortality in primiparous (n = 34) and multiparous (n = 69) dairy cattle. NA = not applicable.

Variable	Coefficient (SE)	Probability	Odds ratio	95% confidence interval
Dystocia: Cow model (n = 103 cows)				
Intercept	8.23 (2.49)	0.0010	NA	NA
Intrapelvic area (cm ²)	-0.034 (0.009)	< 0.0001	0.967	0.950 to 0.984
Hosmer-Lemeshow goodness of fit test, P = 0.22				
Dystocia: Cow and calf model (n = 100 cows)				
Intercept	-9.6 (2.2)	< 0.0001	NA	NA
Front hoof circumference to intrapelvic area (cm/cm ²)	129.2 (34.0)	< 0.0001	>999	>999 to >999
Hosmer-Lemeshow goodness of fit test, P = 0.50				
Perinatal mortality: Cow and calf model (n = 101 cows)				
Intercept	37.8 (12.1)	0.0019	NA	NA
Calf thoracic circumference	-0.49 (0.15)	0.0011	0.61	0.45 to 0.82
Dystocia	2.34 (0.97)	0.016	10.4	1.6 to 69.3
Hosmer-Lemeshow goodness of fit test, P = 0.38				

CHAPTER 4. ABILITY OF CHANGES IN PLASMA PROGESTERONE CONCENTRATION,
RECTAL TEMPERATURE, SACROSCIATIC LIGAMENT RELAXATION, AND FEED INTAKE
TO PREDICT PARTURITION IN HOLSTEIN-FRIESIAN CATTLE

Abstract

Accurate prediction of parturition permits more frequent observation of periparturient dairy cattle and minimizes dystocia related injuries that lead to animal pain and suffering. The objective of this study was to evaluate the predictive ability of changes in plasma progesterone concentration, rectal temperature, sacrosciatic ligament relaxation, and feed intake as indicators of parturition within 24 hours in 34 primiparous and 72 multiparous Holstein-Friesians. Measurements and samples were obtained daily between 8 and 10am. Data was analyzed using repeated measures ANOVA and logistic regression with generalized estimating equations and $P < 0.05$ was significant. Mean plasma progesterone concentrations in primiparous and multiparous cattle at 24 hours before parturition decreased by 2.9 ng/mL and 2.5 ng/mL respectively, compared to values 24 hours previously (6.1 ± 0.8 ng/mL and 5.8 ± 1.3 ng/mL). Mean rectal temperature in primiparous and multiparous cattle at 24 hours before parturition declined by 0.6°F and 0.5°F respectively, compared to values 24 hours previously ($101.7 \pm 0.9^\circ\text{F}$ and $101.6 \pm 0.7^\circ\text{F}$). Mean sacrosciatic ligament relaxation in primiparous and multiparous cattle at 24 hours before parturition increased by 4.5 mm and 3.7 mm respectively, compared to values 24 hours previously (21.8 ± 7.7 mm and 32.5 ± 9.7 mm). Mean feed intake values for cattle declined by 2.0 lb at 24 hours before parturition compared to values 24 hours previously (48.1 ± 16.1 lb and 50.1 ± 14.7 lb). All four parameters have clinical utility as predictors of parturition in dairy cattle.

Predictive utility can be increased by using logistic regression but this decreases the practicality of using a single index to predict parturition within 24 hours.

Introduction

A practical, inexpensive, and accurate method to predict parturition in primiparous cattle is needed in the cattle industry. Primiparous cattle have a smaller intrapelvic area and associated increased incidence of fetopelvic disparity and dystocia compared to multiparous cattle (Zaborski, Grzesiak et al. 2009, Gaafar, Shamiah et al. 2011). Predicting the time of parturition will permit more frequent observations of late gestation cattle and minimize dystocia related injuries that lead to animal pain, morbidity, and mortality. Additionally, prediction of parturition can optimize the assignment of personnel on the farm to facilitate the observation of parturition in high-risk animals that may require intervention.

Multiple physiological parameters, including plasma progesterone concentration ([progesterone]), rectal temperature, and sacrosciatic ligament relaxation have been used to predict parturition with variable outcomes. Plasma progesterone concentrations during pregnancy remain stable in cattle for much of the last trimester (Sloss and Dufty 1980); but decrease rapidly below 1.3 or 1.0 ng/mL 12 to 36 h before calving (Stabenfeldt, Osburn et al. 1970, Symons 1973, Corah, Quealy et al. 1974, Erb, Chew et al. 1977, Matsas, Nebel et al. 1992, Birgel, Grunert et al. 1994, Streyll, Sauter-Louis et al. 2011). Rectal, vaginal, and core temperatures decrease by approximately 1°F before parturition in cattle (Weisz 1943, Porterfield and Olson 1957, Ewbank 1963, Aoki, Kimura et al. 2006). A reduction in rectal temperature of more than 0.5°F indicates that parturition will occur within 24 h, provided that the decrease could be differentiated from normal diurnal variations (Dufty 1971). Major challenges with using rectal or vaginal temperature to predict parturition is the influence of ambient temperature on core body temperature, particularly in summer, and the impact of concurrent disease.

As parturition approaches, the sacrosciatic ligament progressively relaxes (Shah, Nakao et al. 2006, Strey, Sauter-Louis et al. 2011) and the posterior border of the ligament becomes more easily displaced by moderate pressure (Dufty 1971). This change occurs reliably, is readily detected in dairy cattle, shows a reasonably constant time relationship with the start of cervical dilatation, and is least influenced by external factors (Dufty 1971). Quantifying the magnitude of sacrosciatic ligament relaxation may have clinical utility in predicting parturition, and has been recently evaluated as one component of a predictive index of calving in cattle (Strey, Sauter-Louis et al. 2011).

Starting from 10 to 5 days prepartum, feed intake is reduced by approximately 30% in dairy cattle (Bertics, Grummer et al. 1992, Grant and Albright 1995, Greenfield, Cecava et al. 2000). Daily feed intake continues to decrease from day 5 and 2 prepartum, with a sizeable decrease of 33% occurring at day 1 prepartum (Huzzey, Veira et al. 2007). On the day of parturition, a 33 and 75% depression in feed intake, compared to values at 14 days prepartum, occurs in primiparous and multiparous cattle, respectively (Marquardt, Horst et al. 1977). Monitoring feed intake may therefore have clinical utility as a predictor of parturition.

The majority of studies identifying useful predictors of parturition in cattle have evaluated individual factors and none have specifically evaluated differences that may occur between primiparous and multiparous dairy cattle. We hypothesized that changes in plasma [progesterone], rectal temperature, sacrosciatic ligament relaxation, and feed intake have clinical utility in predicting parturition in late gestation Holstein-Friesian cattle, and that there would be no difference in the predictive ability of these factors between primiparous and multiparous animals. Therefore, the major objectives of this study were to determine and compare the predictive ability of changes in plasma [progesterone], rectal temperature, sacrosciatic ligament relaxation, and feed intake as indicators of parturition within 24 h in primiparous and multiparous dairy cattle.

Materials and methods

All methods were approved by the Purdue University Institutional Animal Care and Use Committee.

Animals, housing, and feeding

An observational study using a convenience sample of 106 late gestation non-lactating Holstein-Friesian cattle (34 primiparous, 72 multiparous) from the Purdue University Dairy Research and Education Center was performed over a 10 month period between May 29 2012 and March 29 2013. Cattle were housed outdoors in a dry lot and fed an acidogenic total mixed ration (dietary cation-anion difference, DCAD = -10 mEq/100 g of dry matter (DM), where $DCAD = ([Na^+] + [K^+]) - ([Cl^-] + [S^{2-}])$; Lean et al., 2006) based on formulations recommended by the National Research Council (NRC, 2001) for close up cows. Primiparous and multiparous cattle were fed acidogenic close up rations starting six and three weeks before parturition, respectively. The ration was fed once daily between 08:00 and 09:30 and consisted predominantly of grass hay, alfalfa haylage, and corn silage. Water was available *ad libitum*. Amounts of total mixed ration fed and refused, on a wet weight basis, were recorded daily during the study period. Feed samples were collected weekly to determine the dry matter content with an oven (Research Specialties Co., Richmond, CA).

Cattle were moved from the dry lot to a temperature-controlled building that contained individual box stalls four days before the estimated parturition date, based on breeding records and pregnancy diagnosis at approximately 40 days after insemination. All animals were deemed healthy based on daily routine physical examinations in the box stalls. Feeding and access to water were similar to that in the dry lot.

Experimental methods

Physical examinations were performed daily between 08:00 and 10:00 with cattle gently restrained in a headlock. Rectal temperature, sacrosciatic ligament

relaxation depth, and wet weight intake were obtained from day -4, -3, -2, -1, 0, 1, 2, and 3 relative to the day of parturition, while plasma [progesterone] measurements were obtained from day -3, -2, -1, and 0 relative to the day of parturition.

Rectal temperature was obtained with a standard GLA M700 digital thermometer (GLA Agricultural Electronics, San Luis Obispo, CA) that had an angle probe of 42°. The thermometer was lubricated with an aqueous based lubricant (Equi-Phar Vedlube, VEDCO Inc, St Joseph, MO) and slowly inserted into the rectum of the animal until the angle of the probe, located 11.5 cm from the tip, and kept in contact with the rectal mucosa. Once the reading on the unit stabilized, the measurement was taken and the probe was gently removed from the rectum.

Two rulers were used to measure the depth of sacrosciatic ligament relaxation (mm). The first ruler was placed such that it traversed the point of the tuber ischii and the shallowest point of the sacrum while being parallel with the sacrosciatic ligament. The second ruler was then placed perpendicularly to the first ruler with its base in contact with the ligament and the graduation edge touching the first ruler. The depth that was measured was the reading taken from the second ruler, from the point where it touched the ligament to the point where it was in contact with the first ruler (Figure 4.1) (Shah, Nakao et al. 2006).

Blood samples for determination of plasma [progesterone] were collected from the coccygeal vein or artery with 20 G vacutainer needles, vacutainer holders, and 10 mL lithium heparin blood tubes, after clearing the proposed puncture site at the ventrum of the tail of debris and feces and swabbing the site with gauze containing 70% isopropyl alcohol. The heparinized blood samples were centrifuged for 5 min at 1300 x *g* within 30 minutes of collection using PowerSpin™ C856 Model LX Centrifuge (UNICO, Dayton, NJ). The resulting plasma was transferred into polypropylene vials within 1 h of centrifugation and stored at -20°C until further analysis. The Ovucheck® Plasma ELISA kit (Biovet Inc., QC, Canada) was used to determine the concentration (ng/mL) of progesterone in the plasma samples of 30 cattle (11 primiparous and 19 multiparous). This immunoenzymatic test is based on the competitive binding of unlabeled

progesterone present in the sample or standard and a predetermined quantity of alkaline phosphatase labeled progesterone, to binding sites available on a fixed amount of specific progesterone antibodies. The wells of the kit are pre-coated with antibodies and serve as a solid medium for the separation of bound and free progesterone in the sample. After incubation and washing, only components bound to the plate wells remain. The number of bound alkaline phosphatase labeled progesterone left in the wells is inversely proportional to the concentration of unlabeled progesterone in the sample. This bound and labeled progesterone is then measured by allowing alkaline phosphatase to react with its substrate during a second incubation. The yellow color that was produced at the end of the test was measured spectrophotometrically with a microplate reader (Molecular Devices, LLC) at a wavelength of 405 nm.

Amounts of total mixed ration fed and refused (orts), on a wet weight basis, were recorded daily each morning during the study period with the wet weight intake (lb) = (weight of ration fed) – (weight of ration refused). Feed samples were collected weekly to determine the dry matter content by drying the samples to constant weight for 48 h in an oven (Research Specialties Co., Richmond, CA) at 60°C. To calculate the dry matter, an empty container was first weighed with a scale and the weight recorded (A). The feed sample was then placed in the container and reweighed (B). The weight of the wet feed sample (C) was B-A. After the feed was dried, the combined weight of the dried sample and container was measured (D). The weight of the dry feed alone (E) was D-A. The weight of the dried feed (E) was then divided by the wet feed (C) and multiplied by 100 in order to calculate the dry matter percentage.

Statistical Analysis

Data was expressed as mean \pm SD with $P < 0.05$ considered significant. Repeated measures ANOVA (PROC MIXED, SAS 9.3, SAS Inc, Cary NC) was used to determine the main effects of parity (2 levels), time, and the interaction between parity and time, with cow nested within parity. When indicated by a significant F-test, Bonferroni-adjusted

post tests were conducted between primiparous and multiparous cattle at a specific time, and between days within a parity group.

The sensitivity and specificity of selected factors to predict calving within 12 and 24 h were calculated using logistic regression and generalized estimating equations (GEE). This approach was used because the dataset contained longitudinal data with repeated measurements for individual cattle. Logistic regression models were calculated using PROC GENMOD (SAS 9.3, SAS Inc, Cary NC) with a repeated statement, binomial distribution for the response variable, a logit link function, and an autoregressive(1) covariance structure that was selected based on the lowest QIC (Quasilikelihood under the Independence model Criterion). Receiver Operating Characteristic (ROC) curves and Youden's index were used to identify the optimal cutpoint for each factor, and the sensitivity and specificity calculated at that point. The Hosmer and Lemeshow Goodness-Of-Fit test P value was calculated in order to assess overall model fit. The area under the ROC curve was calculated to assist comparison of different tests in predicting parturition.

Results

Plasma progesterone

A total of 93 data points from 30 cattle were available to evaluate the clinical utility of using plasma [progesterone] to predict parturition within 12 h or 24 h. Of the 93 data points, 9 were from cattle that calved within 12 h and 30 were from cattle that calved within 24 h.

A decline in plasma progesterone concentration started on day -1.5 (Figure 4.2). Plasma progesterone concentrations differed from the previous 24 h value on days -1.5, -1.0, and -0.5 relative to parturition.

Binary logistic regression was run separately to predict parturition within 12 h and 24 h. Parity (primiparous or multiparous) was not a significant factor when plasma [progesterone] was evaluated as a predictor for parturition within 12 h ($P = 0.59$) or 24 h

($P = 0.21$). Plasma [progesterone] was a significant predictor of parturition within 12 h ($P < 0.0001$) or 24 h ($P < 0.0001$). The estimated probability (P) for predicting calving within 12 h from the plasma [progesterone] in ng/mL was: $P = \frac{e^{(-1.61 \times [\text{progesterone}] + 3.19)}}{1 + e^{(-1.61 \times [\text{progesterone}] + 3.19)}}$. The optimal cutpoint for predicting parturition within 12 h was plasma [progesterone] < 4.0 ng/mL (area under the ROC curve = 0.93; Se = 0.89; Sp = 0.81; Hosmer and Lemeshow Goodness-of-Fit test P value = 0.31), equivalent to an estimated probability of 0.04 (Figure 4.3). For comparison, the estimated probability (P) for predicting calving within 24 h from the plasma [progesterone] in ng/mL was: $P = \frac{e^{(-1.36 \times [\text{progesterone}] + 5.54)}}{1 + e^{(-1.36 \times [\text{progesterone}] + 5.54)}}$. The optimal cutpoint for predicting parturition within 24 h was plasma [progesterone] < 4.6 ng/mL (area under the ROC curve = 0.93; Se = 0.87; Sp = 0.92; Hosmer and Lemeshow Goodness-of-Fit test P value = 0.76), equivalent to an estimated probability of 0.32 (Figure 4.3).

Rectal temperature

A total of 312 data points were available from 106 cattle to evaluate the clinical utility of rectal temperature and sacrosciatic ligament relaxation to predict parturition within 12 h or 24 h. Of the 312 data points, 41 were from cattle that calved within 12 h and 106 were from cattle that calved within 24 h.

A decline in rectal temperature started to occur on day -1.5 (Figure 4.4). Rectal temperature differed from the previous 24 h value on days -1.5, -1.0, 0, and 0.5 relative to parturition.

Binary logistic regression was run separately to predict parturition within 12 h and 24 h. Parity (primiparous or multiparous) was not a significant factor when rectal temperature was evaluated as a predictor for parturition within 12 h ($P = 0.86$) or 24 h ($P = 0.86$). Rectal temperature was a significant predictor of parturition within 12 h ($P = 0.0003$) or 24 h ($P < 0.0001$). The estimated probability (P) for predicting calving within 12 h from the rectal temperature in $^{\circ}\text{F}$ was: $P = \frac{e^{(-1.42 \times [\text{temperature}] + 141.5)}}{1 + e^{(-1.42 \times [\text{temperature}] + 141.5)}}$. The optimal cutpoint for predicting parturition within 12 h was rectal temperature < 101.1 $^{\circ}\text{F}$ (area under the ROC curve = 0.74; Se = 0.81; Sp = 0.64;

Hosmer and Lemeshow Goodness-of-Fit test P value = 0.044 which indicated a poor model fit), equivalent to an estimated probability of 0.12 (Figure 4.5). For comparison, the estimated probability (P) for predicting calving within 24 h from the rectal temperature in °F was: $P = e^{(-1.42 \times [\text{temperature}] + 143.4)} / \{1 + e^{(-1.42 \times [\text{temperature}] + 143.4)}\}$. The optimal cutpoint for predicting parturition within 24 h was rectal temperature < 101.4 °F (area under the ROC curve = 0.74; Se = 0.69; Sp = 0.72; Hosmer and Lemeshow Goodness-of-Fit test P value = 0.11), equivalent to an estimated probability of 0.35 (Figure 4.5).

Sacrosciatic ligament relaxation

An increase in the extent of sacrosciatic ligament relaxation was present on day -0.5 in primiparous and multiparous cattle with the extent of relaxation rapidly declining after parturition (Figure 4.6). Primiparous animals reached a maximum relaxation at 12 h before parturition with a depth of 25 mm while multiparous animals reached a maximum relaxation at the time of parturition with a depth of 36 mm.

Binary logistic regression was run separately to predict parturition within 12 h and 24 h. Parity (primiparous or multiparous) was a significant factor when sacrosciatic ligament relaxation was evaluated as a predictor for parturition within 12 h (P = 0.0002) or 24 h (P < 0.0001).

For primiparous cattle, sacrosciatic ligament relaxation was a significant predictor of parturition within 12 h (P = 0.0003) and 24 h (P < 0.0001). The estimated probability (P) for predicting calving within 12 h from the sacrosciatic ligament relaxation in mm was: $P = e^{(0.151 \times [\text{relaxation}] - 4.89)} / \{1 + e^{(0.151 \times [\text{relaxation}] - 4.89)}\}$. The optimal cutpoint for predicting parturition within 12 h was sacrosciatic ligament relaxation > 20 mm (area under the ROC curve = 0.77; Se = 0.64; Sp = 0.80; Hosmer and Lemeshow Goodness-of-Fit test P value = 0.35), equivalent to an estimated probability of 0.14 (Figure 4.7). For comparison, the estimated probability (P) for predicting calving within 24 h from the sacrosciatic ligament relaxation in mm was: $P = e^{(0.093 \times [\text{relaxation}] - 2.39)} / \{1 + e^{(0.093 \times [\text{relaxation}] - 2.39)}\}$. The optimal cutpoint for predicting parturition within 24 h was

sacrosciatic ligament relaxation > 23 mm (area under the ROC curve = 0.68; Se = 0.50; Sp = 0.85; Hosmer and Lemeshow Goodness-of-Fit test P value = 0.18), equivalent to an estimated probability of 0.44 (Figure 4.7).

For multiparous cattle, sacrosciatic ligament relaxation was a significant predictor of parturition within 12 h ($P = 0.0003$) or 24 h ($P < 0.0001$). The estimated probability (P) for predicting calving within 12 h from the sacrosciatic ligament relaxation in mm was: $P = e^{(0.094 \times [\text{relaxation}] - 5.01)} / \{1 + e^{(0.094 \times [\text{relaxation}] - 5.01)}\}$. The optimal cutpoint for predicting parturition within 12 h was sacrosciatic ligament relaxation > 34 mm (area under the ROC curve = 0.73; Se = 0.56; Sp = 0.83; Hosmer and Lemeshow Goodness-of-Fit test P value = 0.50), equivalent to an estimated probability of 0.14 (Figure 4.8). For comparison, the estimated probability (P) for predicting calving within 24 h from the sacrosciatic ligament relaxation in mm was: $P = e^{(0.047 \times [\text{relaxation}] - 2.22)} / \{1 + e^{(0.047 \times [\text{relaxation}] - 2.22)}\}$. The optimal cutpoint for predicting parturition within 24 h was sacrosciatic ligament relaxation > 30 mm (area under the ROC curve = 0.63; Se = 0.68; Sp = 0.54; Hosmer and Lemeshow Goodness-of-Fit test P value = 0.80), equivalent to an estimated probability of 0.31 (Figure 4.8).

Feed intake

A total of 292 data points were available from 98 cattle (32 primiparous and 66 multiparous) to evaluate the clinical utility of feed intake (wet weight basis) to predict parturition within 12 h or 24 h. Of the 292 data points, 39 were from cattle that calved within 12 h and 98 were from cattle that calved within 24 h.

Wet weight intake differed from the previous 24 h value on day 1 relative to parturition (Figure 4.9).

Binary logistic regression was run to predict parturition within 24 h because feed intake represented intakes over the previous 24 h period. Parity (primiparous or multiparous) was not a significant factor when feed intake was evaluated as a predictor for parturition within 24 h ($P = 0.87$). Feed intake was a significant predictor of parturition within 24 h ($P = 0.0092$). The estimated probability (P) for predicting calving

within 24 h from the feed intake data was not calculated because the area under the ROC curve (0.053) was not significantly different from 0.05 (Figure 4.10).

Discussion

By predicting the time of parturition, improved management, closer observation of periparturient cattle, and the timely identification and correction of calving problems can be carried out. This will help prevent and minimize dystocia related damage and injuries to the calf and dam that may lead to animal pain, suffering, and mortality (Bellows, Patterson et al. 1987, Shah, Nakao et al. 2006).

The process of parturition is initiated by the fetus and is dependent on the activation of the fetal hypothalamus-pituitary-adrenal (HPA) axis (Hunter, Fairclough et al. 1977, Wood 1999) which releases corticotrophin releasing factor (by the hypothalamus) which in turn stimulates the anterior pituitary gland to produce adrenocorticotrophic hormone. This peptide hormone is produced in response to stress and its release causes the fetal adrenal cortex to produce cortisol (Broom and Johnson 1993, Wood 1999). Fetal cortisol promotes the production and activation of 17 α -hydroxylase, 17-20 desmolase, and aromatase that convert and aromatize progesterone (that has high concentrations at the placental interface) to 17 α -hydroxyprogesterone, androstenedione, and ultimately estradiol. This conversion accounts in part for the decrease in progesterone and increase in estradiol concentrations one to two days before parturition (Senger 2003, Kindahl, Kornmatitsuk et al. 2004). Therefore, a decline in maternal plasma [progesterone], which is the principal progestational hormone (Gomes and Erb 1965, Blood, Studdert et al. 2007), leading up to parturition has been used often to predict the time of parturition.

The concentration of plasma progesterone gradually decreases during the last 20 days of pregnancy and averages approximately 4 ng/mL during the final week before falling rapidly at 2 to 3 days before parturition which corresponds with the regression of the corpus luteum (Stabenfeldt, Osburn et al. 1970, Fairclough, Hunter et al. 1975,

Thorburn, Challis et al. 1977, Kejela, Head et al. 1978, Fairclough, Hunter et al. 1981). Progesterone concentration correlates with low levels of uterine myoelectrical activity (Gillette 1966) and this supports the progesterone block hypothesis whereby the myometrium is unable to perform maximal tension due to blocking of the physiological mechanisms of excitation by progesterone (Csapo 1956). At 24 h before parturition, plasma progesterone concentrations are < 2.0 ng/mL (Robertson 1972, Goff, Kimura et al. 2002) and can even drop to < 1.3 ng/mL (Stabenfeldt, Osburn et al. 1970, Edgerton and Hafs 1973, Parker, Foulkes et al. 1988, Matsas, Nebel et al. 1992). Matsas et al. 1992 reported that more than 95% of cows calved within 24 h when plasma progesterone concentrations were < 1.3 ng/mL. In the present study, plasma progesterone concentration started to decline at 2 days prepartum but values at 24 h prepartum were not lower than 2 ng/mL. This result is probably due to differences in the method of analysis (ELISA) used compared to other studies, which typically utilized a radio-immunoassay method.

The predicted probability curve of parturition incidence in 24 h using plasma progesterone concentration (Figure 4.3) did show that when concentrations were ≤ 2.0 ng/mL or ≤ 1.3 ng/mL the probability that calving would occur within 24 h was approximately 0.90 and 0.98, respectively, which is consistent with the aforementioned findings. The area under the curve (AUC) for the progesterone ROC curve was higher than that for other investigated factors; AUC values for ROC curves > 0.9 typically indicate a highly accurate test, whereas AUC values of 0.7 – 0.9 indicates moderate accuracy, 0.5 – 0.7 low accuracy, and 0.5 a chance result (Swets 1988, Fischer, Bachmann et al. 2003).

Mean rectal temperature of primiparous and multiparous cattle at 24 h before parturition in this study declined by 0.6°F and 0.5°F respectively, compared to values taken during the previous 24 h. This was consistent with previous studies whereby rectal temperatures dropped quickly by 0.5 to 1.6°F on the day before parturition, and this decline has been used to predict parturition (Weisz 1943, Streyll 2011, Streyll, Sauter-Louis et al. 2011). However, the wide variability in the precalving temperature drop (0.2°

to 1.9°F) observed starting between 33 to 74 h before parturition (Ewbank 1963) indicates its limitations in accurately predicting the calving time. Rectal temperatures were shown useful in cows that had external signs of nearing parturition but with temperatures above 102°F – these animals were not likely to calve within the next 12 h. Vaginal temperature measurements on the other hand have indicated that a pronounced decline of 1.0 to 1.6°F usually happened between 24 and 48 h before calving, without regards to the time of day or atmospheric temperature, and this drop could predict calving times in over 50% of cows (Porterfield and Olson 1957). In the present study, the AUC of the rectal temperature ROC curve was 0.74 which indicates this test has moderate accuracy.

The mechanism and role of the prepartum temperature decrease remains unexplained (Aoki, Kimura et al. 2005) but it is speculated that metabolic adaptation as well as endocrine and behavioral changes during the periparturient phase may contribute to the decline in temperature before calving. Positive correlations between plasma progesterone concentration and body temperature (Birgel, Grunert et al. 1994) indicate the likelihood that progesterone has a thermogenic effect (Wrenn, Bitman et al. 1959). In humans, estradiol-17 β (E₂ β) has a hypothermic effect while progesterone has a hyperthermic effect and they play a role in influencing the overall body temperature (Cagnacci, Melis et al. 1992). In the present study, the decline in progesterone and body temperature as parturition approached could very well support the fact that progesterone has hyperthermic qualities. Additionally, a study done on German black pied cows revealed a close positive association between the prepartum decrease in body temperature and progesterone concentration and a negative relationship between temperature and the estrogen/progesterone ratio (Rexha, Grunert et al. 1993). It was proposed that the estrogen/progesterone ratio may be a predominant factor that regulates body temperature during the prepartum period.

The body's metabolic rate corresponds with the energy intake to correct for energy imbalances through the process of diet-induced thermogenesis as has been seen in humans (Stock 1999). In sheep, falls in core body temperature were observed after

prolonged food deprivation (Piccione, Caola et al. 2002). In the present study feed intake decreased with body temperature as the time of parturition drew nearer and this supports the idea of diet-induced thermogenesis.

The sacrosciatic ligament is a broad sheet located in the pelvic girdle that is attached dorsally to the lateral border of the sacrum and transverse processes of the first and second coccygeal vertebrae while the ventral border is located between the supracotyloid ridge and tuber ischii (Sloss and Dufty 1980, Dyce, Sack et al. 2010). The caudal border of the ligament is free and traverses between the first or second coccygeal vertebrae and the tuber ischii (Sloss and Dufty 1980) and is palpable in cattle (Dyce, Sack et al. 2010). As parturition approaches, the ligament softens and relaxes (Ewbank 1963, Mortimer 1997, Dyce, Sack et al. 2010) and this can be observed visually by the insinking beside the tail head (Dyce, Sack et al. 2010). Changes in the ligament have proved to be reliable as they were easily identified and had a constant relationship with the start of cervical dilatation (Dufty 1971).

Hormones like relaxin and estrogen have been related to the relaxation of pelvic structures. Relaxin lyses collagen and this causes the softening of the cervix and relaxation of the sacrosciatic ligament (Beagley, Whitman et al. 2010). However, intramuscular injections of porcine relaxin did not significantly alter periparturient attributes in beef heifers (Caldwell, Bellows et al. 1990) and this has led to the controversial and questionable role of relaxin in the relaxation of pelvic ligaments (Shah, Nakao et al. 2006). Placental estrogens especially $E_2\beta$ was suggested as the principal hormone that exerts an effect on the sacrosciatic ligament as they both corresponded well with each other (Shah, Nakao et al. 2006). The relaxation of pelvic ligaments in guinea pigs has also been induced with administration of estrogen (Emery and Lawton 1947).

Relaxation of the sacrosciatic ligament has been used to predict calving within 12 h (Berglund and Philipsson 1987, Kornmatitsuk, Konigsson et al. 2000). Consistent with $E_2\beta$ concentrations, a slow increase in ligament relaxation was observed as gestation advanced from day 100 of gestation (8 ± 1 mm) until day 2 prepartum (24 ± 2 mm) and

reached a peak value on the day before parturition (31 ± 2 mm) (Shah, Nakao et al. 2006). In the same study, there was a significant increase ($P < 0.05$) between measurements on day 2 and day 1 prepartum with almost no difference between day 1 prepartum and day 1 postpartum. A marked decrease ($P < 0.05$) occurred after that until day 3 postpartum (10 ± 2 mm) while no significant difference was observed between days 3 and 4, and 4 and 5 postpartum. The increase in the relaxation of the ligament by ≥ 5 mm from the day before was deemed the most effective to predict parturition within 24 h with the greatest accuracy (94%) in a high proportions of cows (31 of 37) in the herd. In the present study, increases in the relaxation of the ligament for both primiparous and multiparous cattle at 24 h before parturition were less than 5 mm. However, significant differences were seen in the relaxation depth for both the groups at 12 h compared to 24 h before parturition. This indicates that sacrosciatic ligaments could be a better predictor of parturition within 12 h instead of 24 h. Overall, the relaxation of the ligament in multiparous cattle was greater than those seen in primiparus cattle which was in agreement with a study that noted that relaxation increased with increasing parity (Berglund and Philipsson 1987). Ligaments are essentially bands of fibrous tissue (Blood, Studdert et al. 2007) and they could be likened to rubber bands whereby repeated stretching can cause it to lose its initial elasticity. Multiparous cattle could therefore potentially have maximally stretched their sacrosciatic ligaments which causes them to have greater relaxation depths when measured at subsequent calvings. Despite being an easily measurable parameter and touted as the best individual clinical predictor when measured in combination with other parameters (Strey, Sauter-Louis et al. 2011), the AUC of sacrosciatic ligament was only 0.68 and 0.63 for primiparous and multiparous cattle which showed low accuracy.

A study to predict parturition within 22 h found that the time of birth could be predicted in 91% of animals using reductions in plasma progesterone concentration, 53% using relaxation of the broad pelvic ligaments, and 44% based on a decrease in rectal temperature (Birgel, Grunert et al. 1994). When pelvic ligament relaxation and rectal temperature were considered together, prediction of parturition time increased

to 65%; however, this remains much lower than that provided by plasma [progesterone].

Appetite and voluntary feed intake in cattle are controlled by various factors like environmental temperature (Bonsma, Scholtz et al. 1940), heat stress (Gorniak, Meyer et al. 2014), humidity (Gorniak, Meyer et al. 2014), wind speed (Grant and Albright 1995), solar radiation (Grant and Albright 1995), anabolic agents (Heitzman 1975), diseases (Fox 1993, Siivonen, Taponen et al. 2011), palatability (Baumont 1996), and gut fill as well as modulated by the management of feeding, environment, health, and social interactions (Grant and Albright 1995).

In the present study, there was a fluctuating trend in feed intake in the days leading to parturition, with a non-significant decrease in intake at 12 h prepartum. Compared to day -4 prepartum, the intake of animals on the day of calving was reduced by 15%. Previous studies have observed drops in the dry matter intake of 14 to 75% (Marquardt, Horst et al. 1977, Goff, Kimura et al. 2002, Huzzey, Veira et al. 2007) which is a wide range. The feed intake of cattle in the present study recovered on day 1 postpartum (Marquardt, Horst et al. 1977) with an improvement of 34% which is higher than 28% which was previously reported (Huzzey, Veira et al. 2007). With an AUC of 0.57, wet weight intake as a predictor of parturition had only a low accuracy.

Although not measured in the present study, feeding times of cattle are decreased between days 7 and 2 prepartum at a rate of 2.6 min/day and dropped drastically by 33% on day 1 prepartum relative to day 2 prepartum (Huzzey, Veira et al. 2007). A significantly shorter total eating duration was also observed at the final six h period before parturition (Miedema, Cockram et al. 2011).

At parturition, plasma progesterone and estrogen concentrations decrease and increase respectively and these changes play a role in reducing the feed intake of the dam. Estrogen has a significant depressing influence on the dry matter intake (DMI) while progesterone does not affect DMI but it is able to partially counteract the reduction in feed intake caused by estrogen (Muir, Hibbs et al. 1972). In rats, estradiol affects feed intake by acting on estrogen receptors within the brain and the direct

stimulation of the ventromedial hypothalamus by estradiol significantly depressed feed intake (Wade and Zucker 1970). Reductions in feed intake could also be caused by pain (Fitzpatrick, Young et al. 1998) due to a malpositioned fetus (Proudfoot, Huzzey et al. 2009) or the presence of a large fetus that may reduce the amount of available space in the rumen (Stanley, Cochran et al. 1993).

Conclusion

Plasma [progesterone], rectal temperature, and feed intake decrease as the time of parturition approaches. On the other hand, the relaxation of the sacrosciatic ligament increases near term. In order of decreasing accuracy according to the AUC, the best individual predictors for parturition within 24 h were plasma progesterone concentration followed by rectal temperature, sacrosciatic ligament relaxation, and feed intake. In terms of practicality, the relaxation of the sacrosciatic ligament and rectal temperature were the easiest and most economical signs to monitor in the field condition. However, if all four of these parameters were considered together, there is a better chance of predicting the time of parturition more accurately than the separate application of each factor.

References

- Aoki, M., et al. (2005). "Predicting time of parturition from changing vaginal temperature measured by data-logging apparatus in beef cows with twin fetuses." Animal Reproduction Science **86**(1): 1-12.
- Aoki, M., et al. (2006). "Influence of feeding regime on timing of parturition in beef cattle and the relationship of vaginal temperature to parturition." Animal Science Journal **77**(3): 290-299.
- Baumont, R. (1996). "Palatability and feeding behaviour in ruminants. A review." Annales de Zootechnie **45**(5): 385-400.
- Beagley, J., et al. (2010). "Physiology and treatment of retained fetal membranes in cattle." Journal of Veterinary Internal Medicine **24**(2): 261-268.
- Bellows, R., et al. (1987). "Occurrence of neonatal and postnatal mortality in range beef cattle. II. Factors contributing to calf death." Theriogenology **28**(5): 573-586.
- Berglund, B. and J. Philipsson (1987). "External signs of preparation for calving and course of parturition in Swedish dairy cattle breeds." Animal Reproduction Science **15**(1): 61-79.
- Bertics, S. J., et al. (1992). "Effect of prepartum dry matter intake on liver triglyceride concentration and early lactation." Journal of Dairy Science **75**(7): 1914-1922.
- Birgel, E., et al. (1994). "The preparatory phase of delivery in cattle, under consideration of the external signs of delivery and changes in progesterone to predicting the calving time." Deutsche Tierärztliche Wochenschrift **101**(9): 355-359.
- Blood, D. C., et al. (2007). Saunders Comprehensive Veterinary Dictionary, Elsevier Ltd.
- Bonsma, J. C., et al. (1940). "The influence of climate on cattle. Fertility and hardiness of certain breeds." Farming **15**: 7-12; 16.
- Broom, D. M. and K. Johnson (1993). Stress and animal welfare, Chapman and Hall.
- Cagnacci, A., et al. (1992). "Effect of sex steroids on body temperature in postmenopausal women. Role of endogenous opioids." Life Sciences **50**(7): 515-521.
- Caldwell, R., et al. (1990). "Administration of pig relaxin to beef heifers 4 or 7 days pre partum." Journal of Reproduction and Fertility **90**(1): 165-174.
- Corah, L., et al. (1974). "Prepartum and postpartum levels of progesterone and estradiol in beef heifers fed two levels of energy." Journal of Animal Science **39**(2): 380-385.

- Csapo, A. (1956). "Progesterone "block". " American Journal of Anatomy **98**(2): 273-291.
- Dufty, J. (1971). "Determination of the onset of parturition in Hereford cattle." Australian Veterinary Journal **47**(3): 77-82.
- Dyce, K. M., et al. (2010). Chapter 2: The locomotor apparatus. Textbook of veterinary anatomy. St Louis, MO, Saunders Elsevier: 32-99.
- Dyce, K. M., et al. (2010). Chapter 29 The pelvis and reproductive organs of the ruminant. Textbook of veterinary anatomy. St Louis, MO, Saunders Elsevier: 698-727.
- Edgerton, L. and H. Hafs (1973). "Serum luteinizing hormone, prolactin, glucocorticoid, and progesterin in dairy cows from calving to gestation." Journal of Dairy Science **56**(4): 451-458.
- Emery, F. E. and A. H. Lawton (1947). "Relaxation of the pelvic ligaments in guinea-pigs by estrogens and prostigmine." American Journal of Physiology **151**(1): 134-137.
- Erb, R., et al. (1977). "Relative concentrations of estrogen and progesterone in milk and blood, and excretion of estrogen in urine." Journal of Animal Science **45**(3): 617-626.
- Ewbank, R. (1963). "Predicting the time of parturition in the normal cow: a study of the precalving drop in body temperature in relation to the external signs of imminent calving." The Veterinary Record **75**(14): 367-371.
- Fairclough, R., et al. (1981). "Plasma concentrations of progesterone, oestrogens and prostaglandin F in maternal blood and corticosteroids and oestrogens in foetal blood of cows during dexamethasone-induced deliveries." Acta Endocrinologica **96**(3): 406-412.
- Fairclough, R., et al. (1975). "Peripheral plasma progesterone and utero-ovarian prostaglandin F concentrations in the cow around parturition." Prostaglandins **9**(6): 901-914.
- Fischer, J. E., et al. (2003). "A readers' guide to the interpretation of diagnostic test properties: clinical example of sepsis." Intensive Care Medicine **29**(7): 1043-1051.
- Fitzpatrick, J. L., et al. (1998). Recognising and controlling pain and inflammation in mastitis. Proceedings of the British Mastitis Conference, Axient/Institute for Animal Health, Milk Development Council/Novartis Animal Health.
- Fox, M. (1993). "Pathophysiology of infection with *Ostertagia ostertagi* in cattle." Veterinary Parasitology **46**(1): 143-158.

Gaafar, H., et al. (2011). "Dystocia in Friesian cows and its effects on postpartum reproductive performance and milk production." Tropical Animal Health and Production **43**(1): 229-234.

Gillette, D. D. (1966). "Placental influence on uterine activity in the cow." American Journal of Physiology **211**: 1095-1098.

Goff, J. P., et al. (2002). "Effect of Mastectomy on Milk Fever, Energy, and Vitamins A, E, and β -Carotene Status at Parturition." Journal of Dairy Science **85**(6): 1427-1436.

Gomes, W. and R. Erb (1965). "Progesterone in bovine reproduction: A review." Journal of Dairy Science **48**(3): 314-330.

Gorniak, T., et al. (2014). "Impact of mild heat stress on dry matter intake, milk yield and milk composition in mid-lactation Holstein dairy cows in a temperate climate." Archives of Animal Nutrition **68**(5): 358-369.

Grant, R. and J. Albright (1995). "Feeding behavior and management factors during the transition period in dairy cattle." Journal of Animal Science **73**(9): 2791-2803.

Greenfield, R., et al. (2000). "Impact of dietary protein amount and rumen undegradability on intake, peripartum liver triglyceride, plasma metabolites, and milk production in transition dairy cattle." Journal of Dairy Science **83**(4): 703-710.

Heitzman, R. (1975). "The effectiveness of anabolic agents in increasing rate of growth in farm animals; report on experiments in cattle." Environmental Quality and Safety. Supplement(5): 89-98.

Hunter, J., et al. (1977). "Foetal and maternal hormonal changes preceding normal bovine parturition." Acta Endocrinologica **84**(3): 653-662.

Huzzey, J., et al. (2007). "Prepartum behavior and dry matter intake identify dairy cows at risk for metritis." Journal of Dairy Science **90**(7): 3220-3233.

Kejela, G., et al. (1978). "Adrenal responsiveness in pre-and postpartum dairy cows." Journal of Dairy Science **61**(12): 1736-1741.

Kindahl, H., et al. (2004). "The cow in endocrine focus before and after calving." Reproduction in Domestic Animals **39**(4): 217-221.

Kornmatitsuk, B., et al. (2000). "Clinical signs and hormonal changes in dairy heifers after induction of parturition with prostaglandin F2 alpha." Journal of Veterinary Medicine. A, Physiology, Pathology, Clinical Medicine **47**(7): 395-409.

Marquardt, J., et al. (1977). "Effect of parity on dry matter intake at parturition in dairy cattle." Journal of Dairy Science **60**(6): 929-934.

Matsas, D. J., et al. (1992). "Evaluation of an on-farm blood progesterone test for predicting the day of parturition in cattle." Theriogenology **37**(4): 859-868.

Miedema, H. M., et al. (2011). "Changes in the behaviour of dairy cows during the 24h before normal calving compared with behaviour during late pregnancy." Applied Animal Behaviour Science **131**(1): 8-14.

Mortimer, R. G. (1997). Calving Difficulty. Proceedings The Range Beef Cow Symposium XV, Rapid City, South Dakota.

Muir, L., et al. (1972). "Effect of estrogen and progesterone on feed intake and hydroxyproline excretion following induced hypocalcemia in dairy cows." Journal of Dairy Science **55**(11): 1613-1620.

Parker, B., et al. (1988). "Prediction of calving times from plasma progesterone concentration." The Veterinary Record **122**(4): 88-89.

Piccione, G., et al. (2002). "Circadian modulation of starvation-induced hypothermia in sheep and goats." Chronobiology International **19**(3): 531-541.

Porterfield, I. and N. Olson (1957). "Vaginal temperature of dairy cows before and after calving." Journal of the American Veterinary Medical Association **131**(8): 381-383.

Porterfield, I. and N. Olson (1957). "Vaginal temperature of dairy cows before and after calving." Journal of the American Veterinary Medical Association **131**(8): 381.

Proudfoot, K., et al. (2009). "The effect of dystocia on the dry matter intake and behavior of Holstein cows." Journal of Dairy Science **92**(10): 4937-4944.

Rexha, S., et al. (1993). "Relationships between the steroid hormone profiles and prodromal external signs of calving." Tierarztliche Umschau **48**(7): 431-436.

Robertson, H. (1972). "Sequential changes in plasma progesterone in the cow during the estrous cycle, pregnancy, at parturition, and post-partum." Canadian Journal of Animal Science **52**(4): 645-658.

Senger, P. (2003). Placentation, the endocrinology of gestation and parturition. Pathways to pregnancy and parturition, Current Conceptions, Inc. **2**: 304-325.

Shah, K. D., et al. (2006). "Plasma estrone sulphate (E₁S) and estradiol-17 β (E₂ β) profiles during pregnancy and their relationship with the relaxation of sacrosciatic ligament, and prediction of calving time in Holstein-Friesian cattle." Animal Reproduction Science **95**: 38-53.

Siivonen, J., et al. (2011). "Impact of acute clinical mastitis on cow behaviour." Applied Animal Behaviour Science **132**(3): 101-106.

Sloss, V. and J. Dufty (1980). Gross anatomy. Handbook of Bovine Obstetrics. Baltimore, MD, Williams & Wilkins: 17-27.

Sloss, V. and J. Dufty (1980). "Handbook of Bovine Obstetrics." Baltimore/London: 54, 69.

Stabenfeldt, G., et al. (1970). "Peripheral plasma progesterone levels in the cow during pregnancy and parturition." American Journal of Physiology **218**: 571-575.

Stanley, T., et al. (1993). "Periparturient changes in intake, ruminal capacity, and digestive characteristics in beef cows consuming alfalfa hay." Journal of Animal Science **71**(3): 788-795.

Stock, M. J. (1999). "Gluttony and thermogenesis revisited." International Journal of Obesity **23**(11): 1105-1117.

Streyl, D. (2011). Establishment of a standard operating procedure for predicting the time of calving in cattle. Veterinary Faculty. Germany, Ludwig Maximilian University of Munich. DVM: 1-35.

Streyl, D., et al. (2011). "Establishment of a standard operating procedure for predicting the time of calving in cattle." Journal of Veterinary Science **12**(2): 177-185.

Swets, J. A. (1988). "Measuring the accuracy of diagnostic systems." Science **240**(4857): 1285-1293.

Symons, A. (1973). "Levels of oestrogen and progesterone in the plasma of the cow during the last month of pregnancy." Journal of Endocrinology **56**(2): 327-328.

Thorburn, G. D., et al. (1977). "Control of parturition in domestic animals." Biology of Reproduction **16**(1): 18-27.

Wade, G. N. and I. Zucker (1970). "Modulation of food intake and locomotor activity in female rats by diencephalic hormone implants." Journal of Comparative and Physiological Psychology **72**(2): 328-336.

Weisz, L. (1943). "The temperature phenomenon before parturition and its clinical importance." Journal of the American Veterinary Medical Association **102**: 123.

Wood, C. (1999). "Control of parturition in ruminants." Journal of Reproduction and Fertility Supplement **54**: 115-126.

Wrenn, R. T., et al. (1959). "The thermogenic influence of progesterone in ovariectomized cows." Endocrinology **65**(2): 317-321.

Zaborski, D., et al. (2009). "Factors affecting dystocia in cattle." Reproduction in Domestic Animals **44**(3): 540-551.

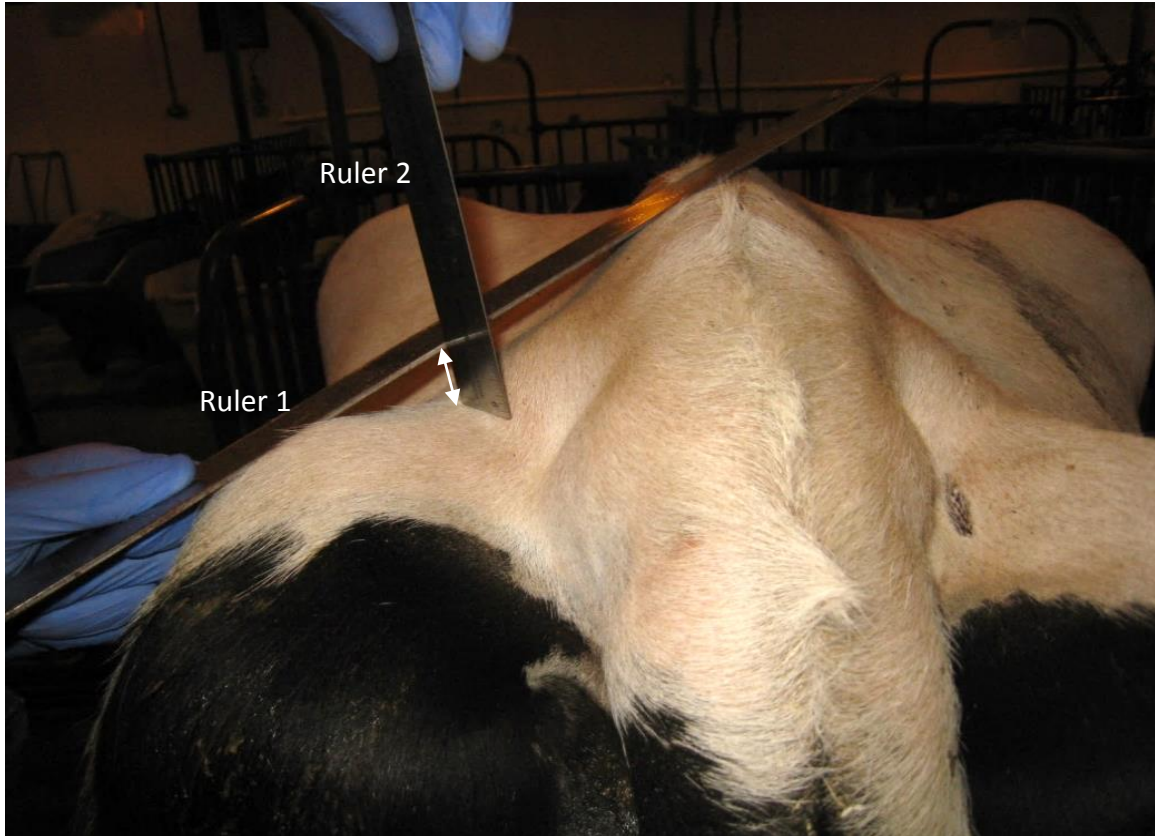


Figure 4.1 The measurement of the depth of relaxation of the sacrosciatic ligament (mm) in a late gestation Holstein-Friesian using two rulers perpendicularly placed to each other according to the method by Shah et al., 2006. The white line with arrowheads indicate the measurement that was taken.

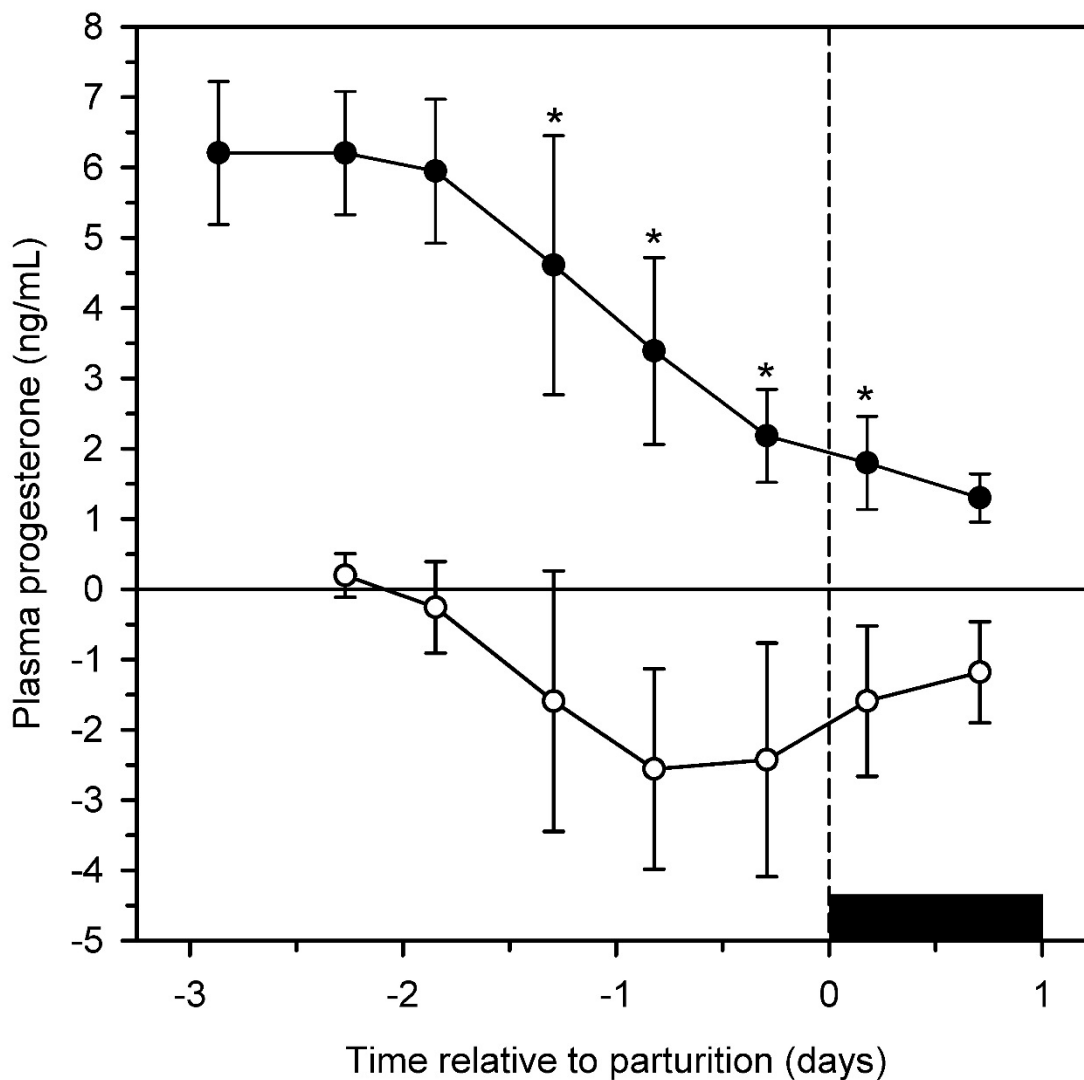


Figure 4.2 Plot of the relationship between time relative to parturition (days) and plasma progesterone concentrations (ng/mL) in 11 primiparous and 19 multiparous late gestation Holstein-Friesian cattle. Closed circles denote the mean plasma progesterone concentrations for the corresponding day while open circles denote the change in the last 24 h. Time is expressed as the geometric mean value which represents the time that data was recorded for each 12 h interval. The black rectangle is the 24 h period during which all cows calved. Data is presented as mean \pm SD. * $P < 0.0083$ (Bonferroni adjusted) compared to the value obtained 24 h previously.

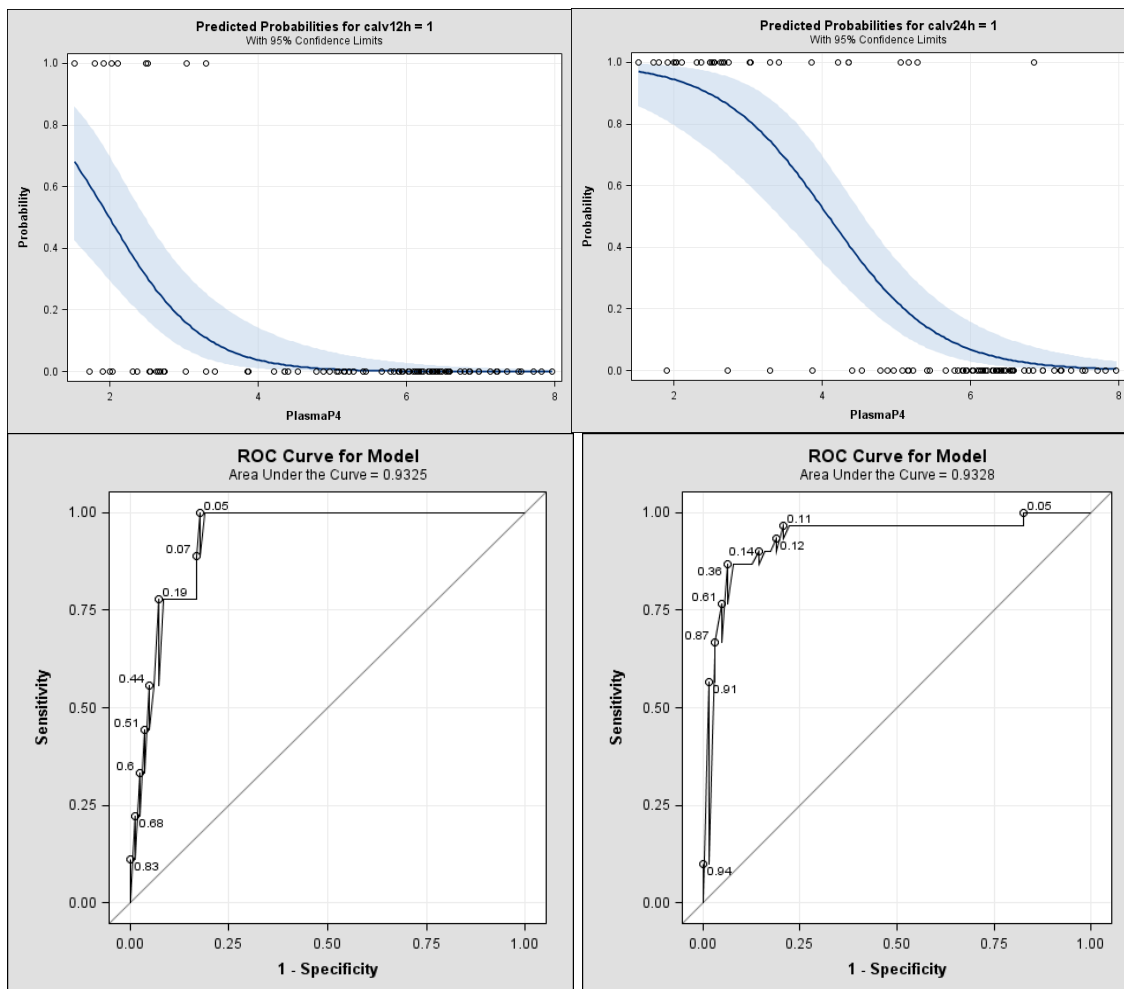


Figure 4.3 Binary logistic regression plot (top panel) of the relationship between the probability of parturition within 12 h (top left panel) or 24 h (top right panel) and plasma progesterone concentration (ng/mL) in 11 primiparous and 19 multiparous late gestation Holstein-Friesian cattle. The thick solid line is the logistic regression line and the shaded area represents the 95% confidence interval for the predicted probability. The open circles represent the plasma progesterone concentration for cattle that calved ($P = 1.00$) or did not calve ($P = 0.00$) within 12 h or 24 h. The bottom panels represent the receiver-operating characteristic (ROC) curves for plasma progesterone concentration as a predictor of parturition within 12 h (bottom left panel) or 24 h (bottom right panel). The diagonal thin line is the line of chance (no predictive ability). The optimal cutpoint for predicting parturition within 12 h was plasma progesterone concentration < 4.0 ng/mL (area under the ROC curve = 0.93; Se = 0.89; Sp = 0.81), equivalent to $P = 0.04$ for the logistic regression equation. The optimal cutpoint for predicting parturition within 24 h was plasma progesterone concentration < 4.6 ng/mL (area under the ROC curve = 0.93; Se = 0.87; Sp = 0.92), equivalent to $P = 0.32$ for the logistic regression equation.

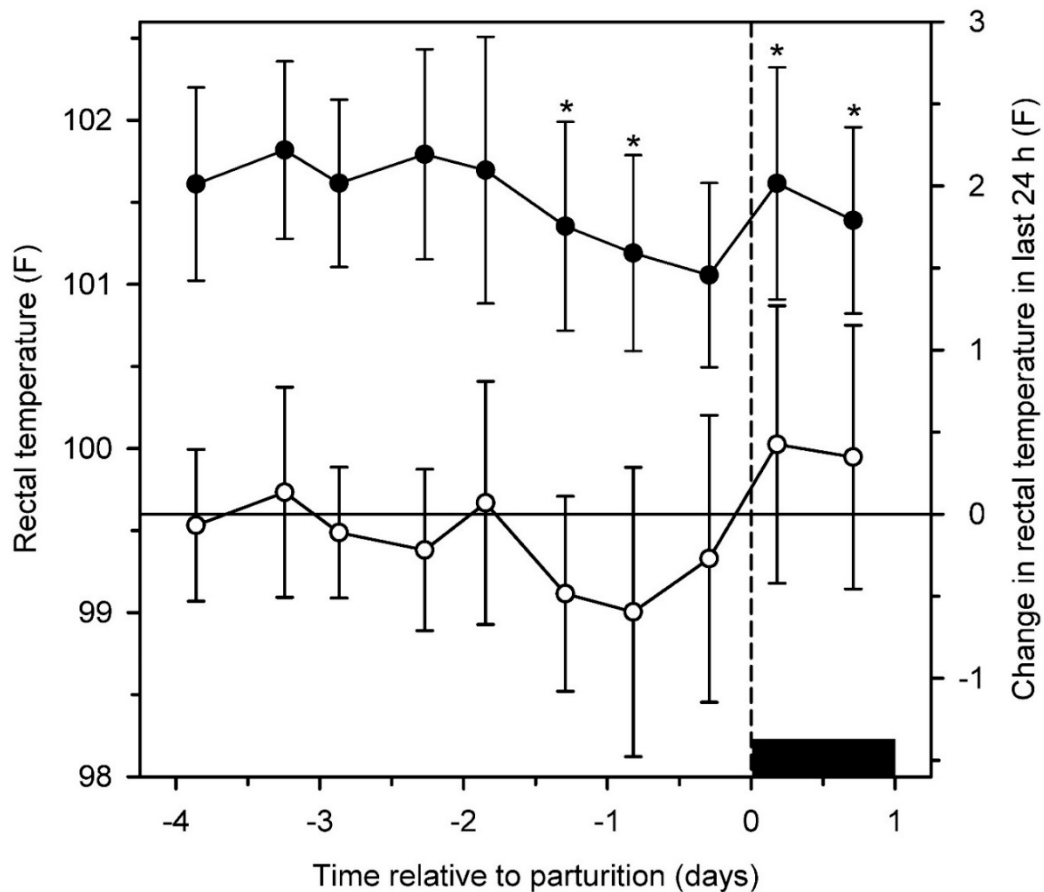


Figure 4.4 Plot of the relationship between time relative to parturition (days) and rectal temperature ($^{\circ}\text{F}$) in 34 primiparous and 72 multiparous late gestation Holstein-Friesian cattle. Closed circles denote the mean temperatures for the corresponding day while open circles denote the change in temperature in the last 24 h. Time is expressed as the geometric mean value which represents the time that data was recorded for each 12 h interval. The black rectangle is the 24 h period during which all cows calved. Data is presented as mean \pm SD. * $P < 0.0063$ (Bonferroni adjusted) compared to the value obtained 24 h previously.

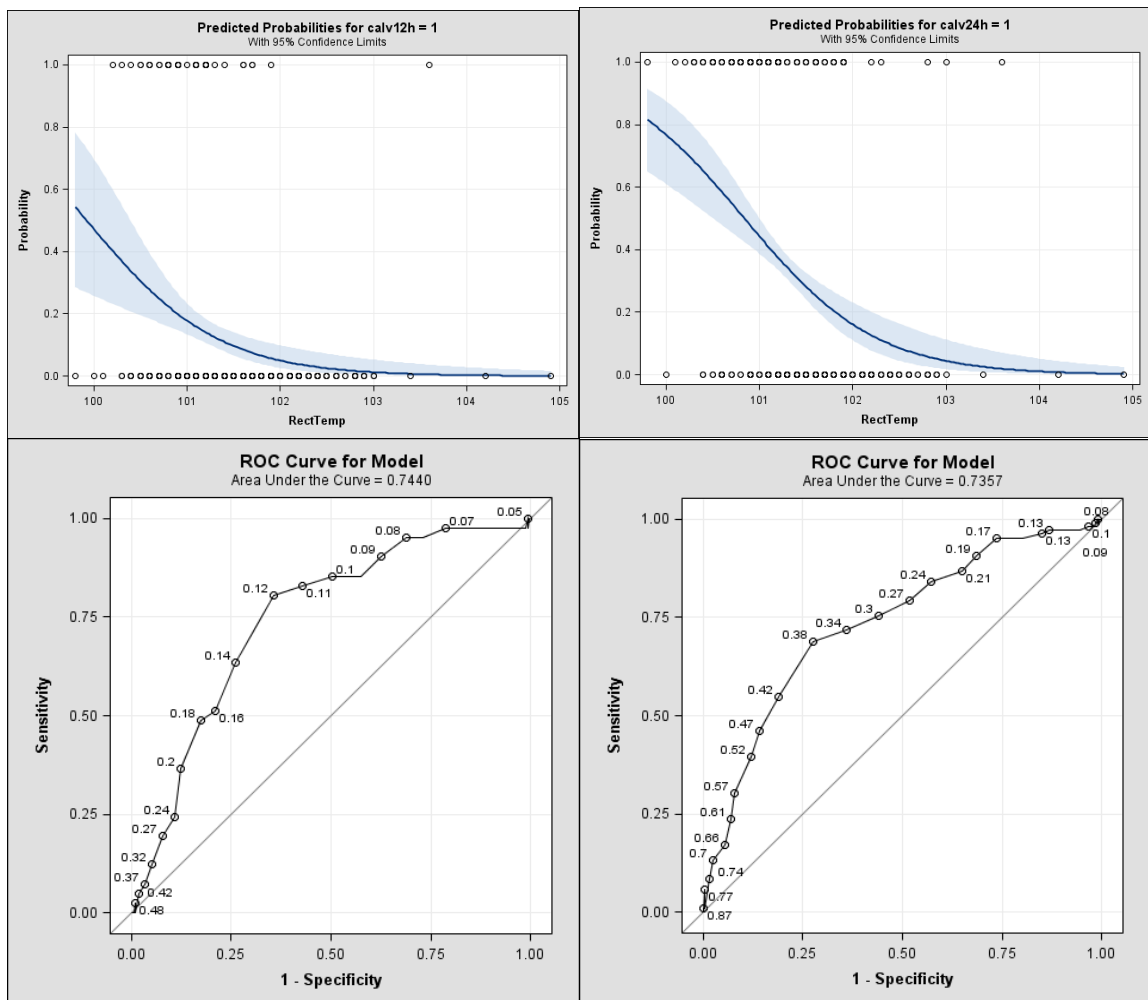


Figure 4.5 Binary logistic regression plots of the relationship between the probability of parturition within 12 h (top left panel) or 24 h (top right panel) and rectal temperature (°F) in 34 primiparous and 72 multiparous late gestation Holstein-Friesian cattle. The thick solid line is the logistic regression line and the shaded area represents the 95% confidence interval for the predicted probability. The open circles represent the rectal temperature for cattle that calved ($P = 1.00$) or did not calve ($P = 0.00$) within 12 h or 24 h. The bottom panels represent the receiver-operating characteristic (ROC) curves for rectal temperature as a predictor of parturition within 12 h (bottom left panel) or 24 h (bottom right panel). The diagonal thin line is the line of chance (no predictive ability). The optimal cutpoint for predicting parturition within 12 h was rectal temperature < 101.1 °F (area under the ROC curve = 0.74; Se = 0.81; Sp = 0.64), equivalent to $P = 0.12$ for the logistic regression equation. The optimal cutpoint for predicting parturition within 24 h was rectal temperature < 101.4 °F (area under the ROC curve = 0.74; Se = 0.69; Sp = 0.72), equivalent to $P = 0.35$ for the logistic regression equation.

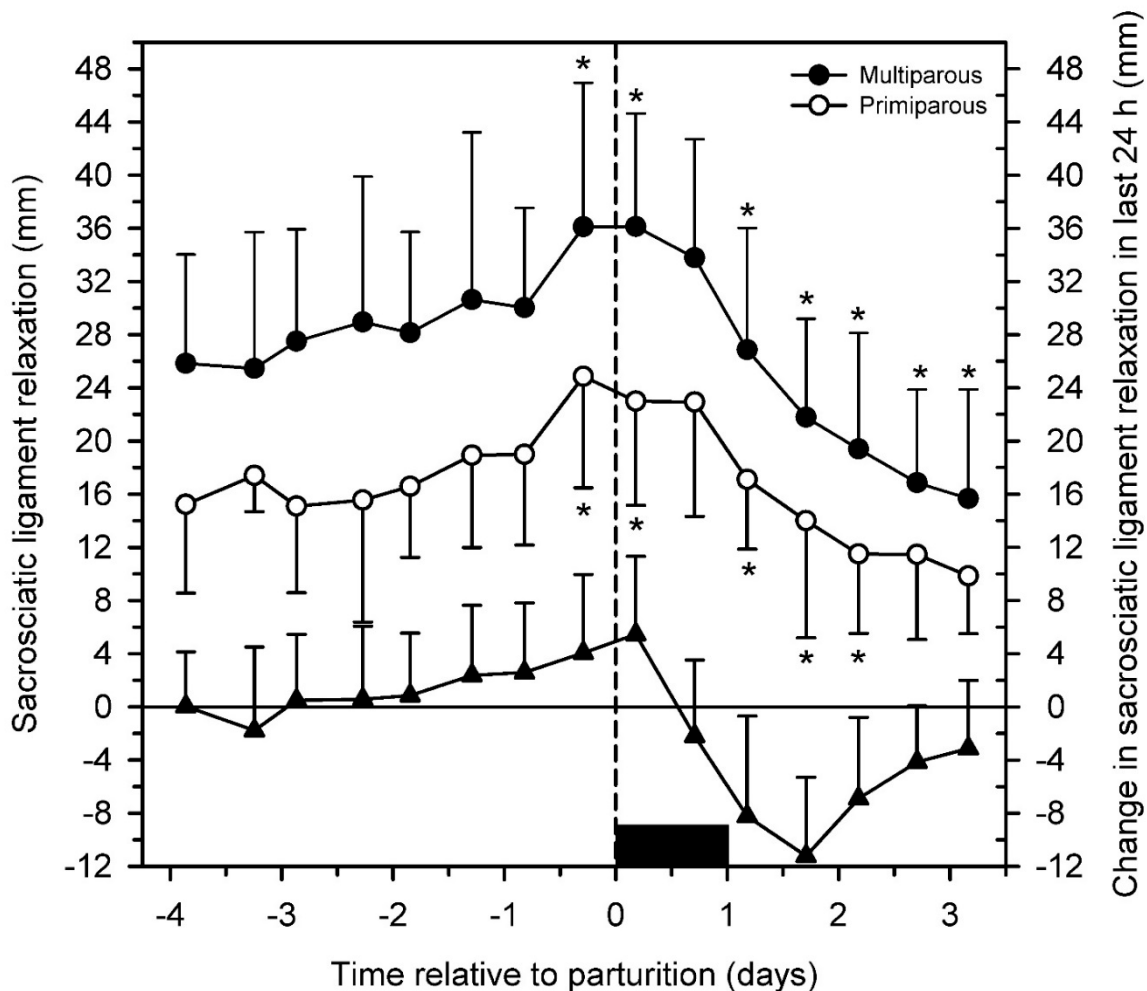


Figure 4.6 Plot of the relationship between time relative to parturition (days) and sacrosciatic ligament relaxation (mm) in 34 primiparous and 72 multiparous late gestation Holstein-Friesian cattle. Closed and open circles denote the mean sacrosciatic ligament relaxation for multiparous and primiparous cattle respectively for the corresponding day while triangles denote the change in the last 24 h. Time is expressed as the geometric mean value which represents the time that data was recorded for each 12 h interval. The black rectangle is the 24 h period during which all cows calved. Data is presented as mean \pm SD. * $P < 0.0038$ (Bonferroni adjusted) compared to the value obtained 24 h previously.

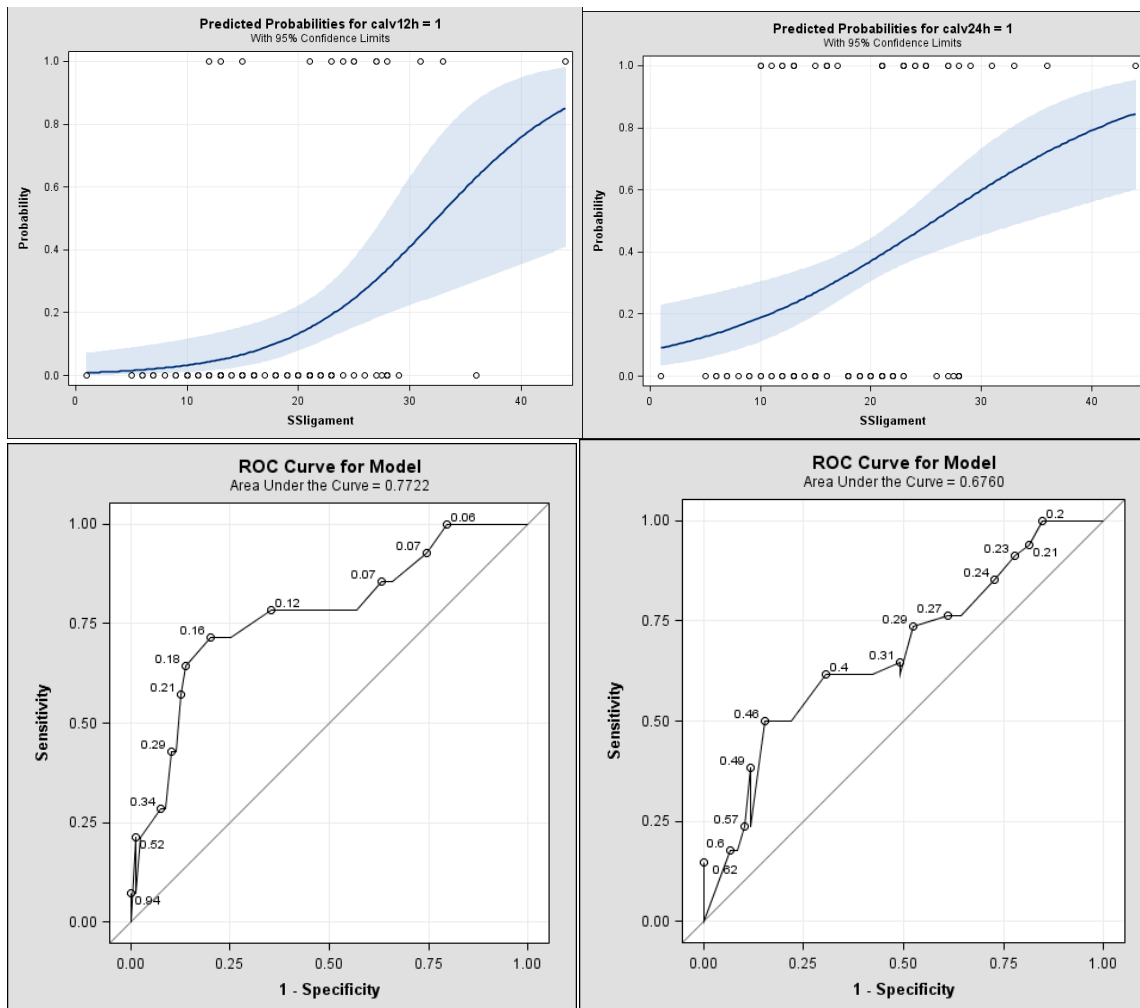


Figure 4.7 Binary logistic regression plots of the relationship between the probability of parturition within 12 h (top left panel) or 24 h (top right panel) and the extent of sacrosciatic ligament relaxation (mm) in 34 primiparous late gestation Holstein-Friesian cattle. The thick solid line is the logistic regression line and the shaded area represents the 95% confidence interval for the predicted probability. The open circles represent the degree of sacrosciatic ligament relaxation for cattle that calved ($P = 1.00$) or did not calve ($P = 0.00$) within 12 h or 24 h. The bottom panels represent the receiver-operating characteristic (ROC) curves for sacrosciatic ligament relaxation as a predictor of parturition within 12 h (bottom left panel) or 24 h (bottom right panel). The diagonal thin line is the line of chance (no predictive ability). The optimal cutpoint for predicting parturition within 12 h was sacrosciatic ligament relaxation > 20 mm (area under the ROC curve = 0.77; Se = 0.64; Sp = 0.80), equivalent to $P = 0.14$ for the logistic regression equation. The optimal cutpoint for predicting parturition within 24 h was sacrosciatic ligament relaxation > 23 mm (area under the ROC curve = 0.68; Se = 0.50; Sp = 0.85), equivalent to $P = 0.44$ for the logistic regression equation.

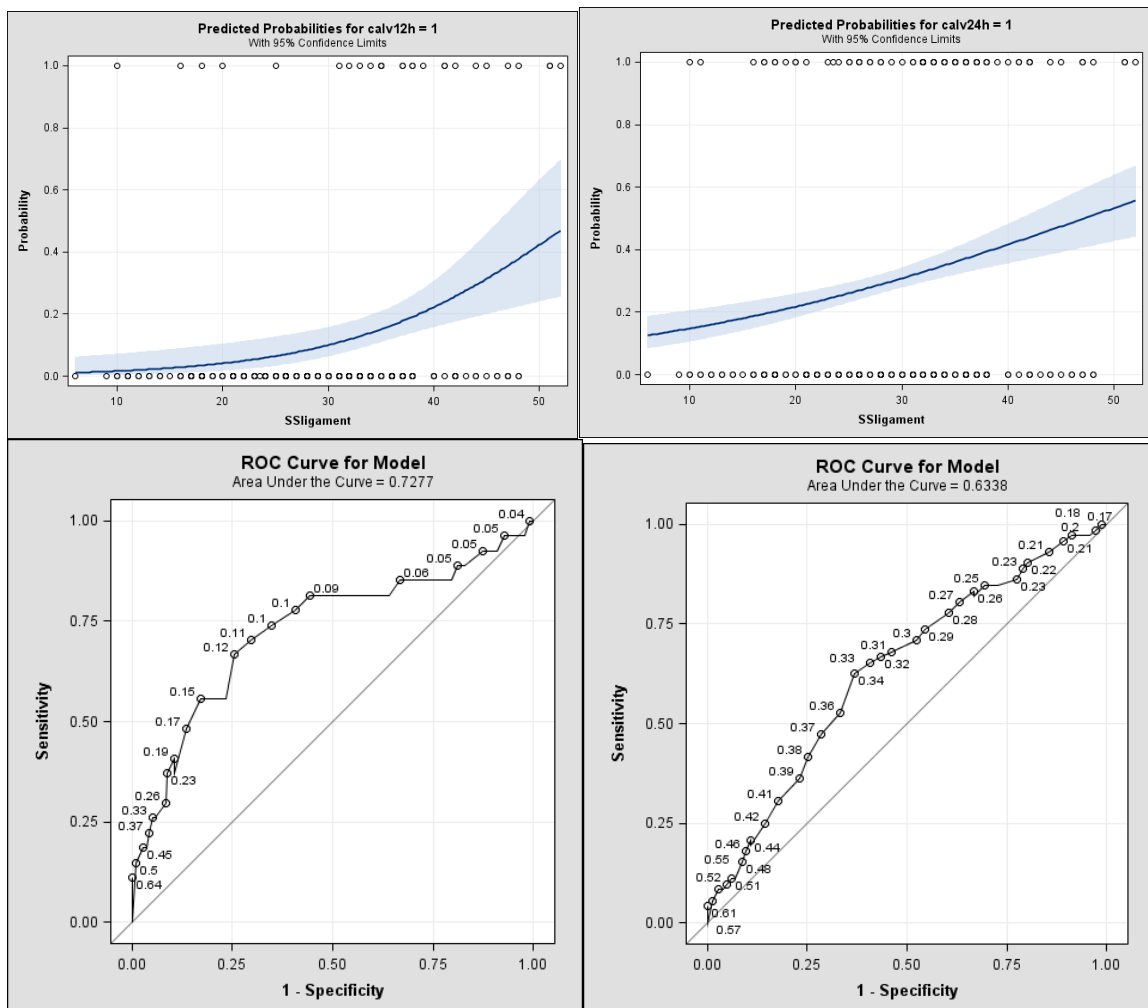


Figure 4.8 Binary logistic regression plots of the relationship between the probability of parturition within 12 h (top left panel) or 24 h (top right panel) and the extent of sacrosciatic ligament relaxation (mm) in 72 multiparous late gestation Holstein-Friesian cattle. The thick solid line is the logistic regression line and the shaded area represents the 95% confidence interval for the predicted probability. The open circles represent the degree of sacrosciatic ligament relaxation for cattle that calved ($P = 1.00$) or did not calve ($P = 0.00$) within 12 h or 24 h. The bottom panels represent the receiver-operating characteristic (ROC) curves for sacrosciatic ligament relaxation as a predictor of parturition within 12 h (bottom left panel) or 24 h (bottom right panel). The diagonal thin line is the line of chance (no predictive ability). The optimal cutpoint for predicting parturition within 12 h was sacrosciatic ligament relaxation > 34 mm (area under the ROC curve = 0.73; Se = 0.56; Sp = 0.83), equivalent to $P = 0.14$ for the logistic regression equation. The optimal cutpoint for predicting parturition within 24 h was sacrosciatic ligament relaxation > 30 mm (area under the ROC curve = 0.63; Se = 0.68; Sp = 0.54), equivalent to $P = 0.31$ for the logistic regression equation.

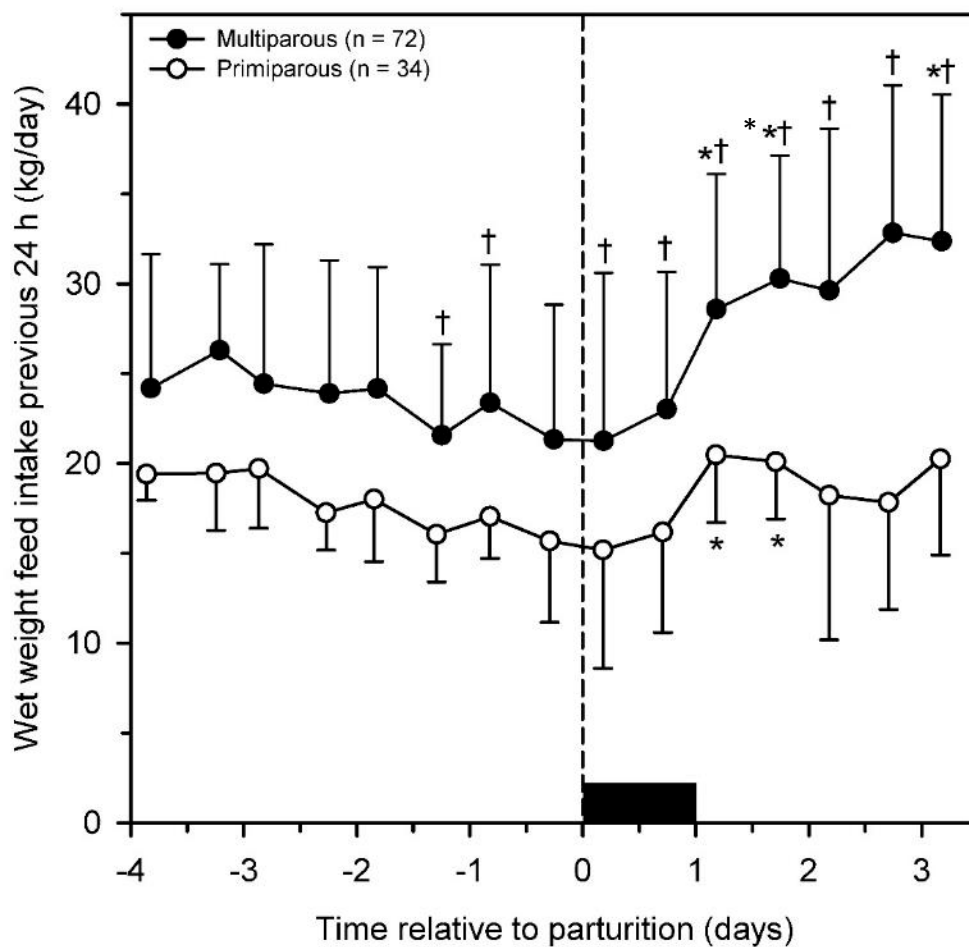


Figure 4.9 Plot of the relationship between time relative to parturition (days) and mean wet weight intake (lb/day) in 98 late gestation Holstein-Friesian cattle. Data is presented as mean \pm SD. * $P < 0.05$ compared to the value obtained 24 h previously. † $P < 0.0033$ (Bonferroni adjusted) compared to the value for multiparous cattle at the same time.

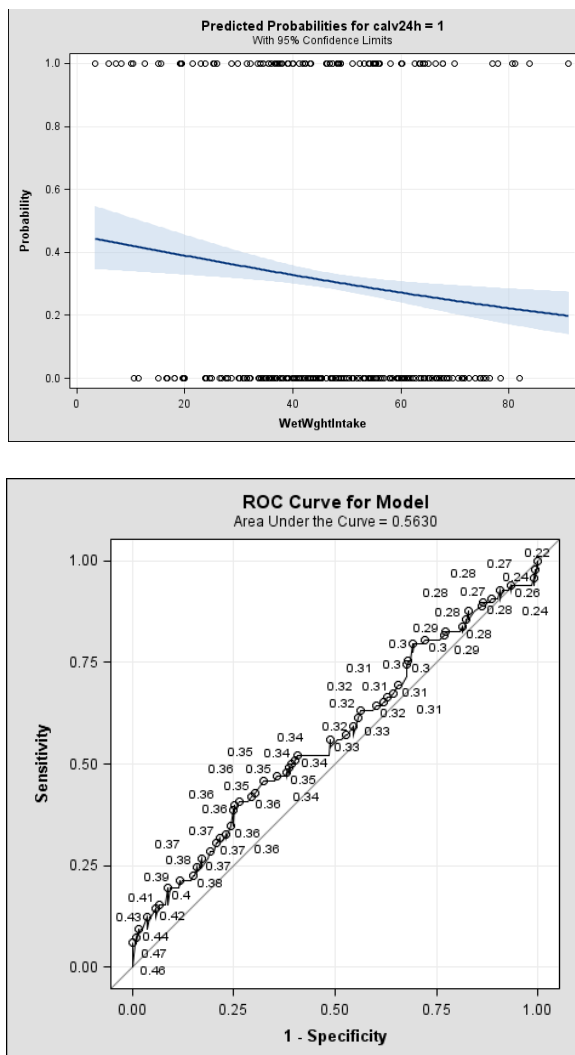


Figure 4.10 Binary logistic regression plot of the relationship between the probability of parturition within 24 h (top panel) and daily feed intake (wet weight basis, lb/day) in 32 primiparous and 66 multiparous late gestation Holstein-Friesian cattle. The thick solid line is the logistic regression line and the shaded area represents the 95% confidence interval for the predicted probability. The open circles represent the feed intake for cattle that calved ($P = 1.00$) or did not calve ($P = 0.00$) within 24 h. The bottom panel represents the receiver-operating characteristic (ROC) curves for feed intake as a predictor of parturition within 24 h. The diagonal thin line is the line of chance (no predictive ability). The area under the ROC curve was 0.56, which was not significantly different from 0.05 ($P = 0.053$).

CHAPTER 5. THE CLINICAL UTILITY OF BLOOD AND PLASMA GLUCOSE
CONCENTRATIONS IN PREDICTING PARTURITION IN HOLSTEIN-FRIESIAN CATTLE

Abstract

The prediction of parturition in dairy cattle is important especially in primiparous cattle as they are prone to dystocia. An improved monitoring of prepartum cattle will help reduce the morbidity and mortality of the dam and calf that are caused by dystocia. This study evaluated the use of blood and plasma glucose concentration to predict the time of parturition in 106 late gestation Holstein-Friesian cattle, as well as the relationship between glucose concentration and plasma cortisol concentration as well as with sympathetic nervous system activation which included heart rate, mean arterial blood pressure, hematocrit, respiratory rate, and rumen contraction rate. The mean blood glucose concentration peaked at the time of calving for both primiparous and multiparous cattle. Heart rate and hematocrit were increased while rumen contraction rate was decreased on the day of parturition. Mean arterial pressure and respiratory rate did not show any trends in regards to the time of parturition. These changes suggest the role of stress and the activation of the hypothalamus-pituitary-adrenal (HPA) axis and sympathetic nervous system at parturition. Measurement of blood glucose concentration is a promising new test for predicting parturition in cattle due to its accuracy, practicality, and cost effectiveness.

Introduction

The accurate prediction of parturition in dairy cattle is especially important in primiparous cattle as they are prone to dystocia (Cattell and Dobson 1990, Meyer, Berger et al. 2001) which remains a major welfare and economic problem in the dairy industry (Dematawewa and Berger 1997, Barrier, Haskell et al. 2013). Predicting the time of parturition will allow better monitoring of prepartum cattle and reduce morbidity and mortality to the dam and calf related to dystocia (Streyll, Sauter-Louis et al. 2011).

Plasma cortisol concentration starts to increase 25 to 32 h before parturition in cattle, peaks immediately at the time of delivery, and rapidly decreases within 1 hour after parturition (Hudson, Mullford et al. 1976, Patel, Takahashi et al. 1996). Although a marked increase in fetal plasma cortisol concentration appears to play a central role in initiating parturition in ruminants (Hunter, Fairclough et al. 1977), the primary mechanism for the periparturient increase in maternal plasma cortisol concentration remains unclear. It is likely that maternal stress during stage I of parturition and decreased feed intake in the late prepartum period (Vazquez-Anon, Bertics et al. 1994, Goff, Kimura et al. 2002) are responsible for most of the periparturient increase in plasma cortisol concentration in the dam, with fetal hypercortisolemia providing a minimal contribution to maternal hypercortisolemia in late gestation (Patel, Takahashi et al. 1996). Cattle that are carrying twins have higher plasma cortisol concentrations on the day of calving than those carrying a single calf (Patel, Takahashi et al. 1996), cattle requiring assistance at parturition due to dystocia have higher plasma cortisol concentrations than cattle with unassisted deliveries (Hudson, Mullford et al. 1976), and periparturient cattle with clinical signs of hypocalcemia have higher plasma cortisol concentrations than periparturient cattle with subclinical hypocalcemia (Horst and Jorgensen 1982). These findings all support the concept that parturition is a stressful event in dairy cattle.

Increased plasma cortisol concentrations results in hyperglycemia due to increased gluconeogenesis and decreased glucose utilization (Radostits, Gay et al. 2007) which provide an energy source for cells to maintain the fight or flight response (Landa 2011). The results of a number of studies in cattle have indicated that plasma glucose concentrations are increased on the day of parturition (Godden and Allcroft 1932, Schwalm and Schultz 1976, Bionaz, Trevisi et al. 2007), presumably in response to increased plasma cortisol concentration. Although plasma and serum glucose concentrations increase at the time of parturition, we are not aware of any studies that have documented the clinical utility of using an increase in blood or plasma glucose concentration to predict parturition in cattle. This issue is relevant because glucose concentrations can be easily and rapidly measured cow-side at low cost using whole blood, serum, or plasma and a point of care device; with glucose concentrations being higher in serum and plasma than blood (Somogyi 1933, Goodwin 1956, D’Orazio, Burnett et al. 2005).

Based on the above, we hypothesized that blood and plasma glucose concentrations are increased in the 12 to 24 h period before parturition, that blood and plasma glucose concentrations are positively associated with plasma cortisol concentration, and that an increase in blood or plasma glucose concentration was predictive of parturition. The primary objective of this study was therefore to determine the ability of blood and plasma glucose concentration to predict parturition in late gestation Holstein-Friesian cattle. A secondary objective was to explore associations of blood and plasma glucose concentration with plasma cortisol concentration and indices of sympathetic nervous system activation, including heart rate, mean arterial pressure, hematocrit, respiratory rate, and rumen contraction rate. We anticipated that the identification of significant associations would generate hypotheses for subsequent studies to determine the mechanism for increased blood and plasma glucose concentrations in late gestation dairy cattle.

Materials and methods

All methods were approved by the Purdue University Institutional Animal Care and Use Committee.

Animals, housing, and feeding

A convenience sample of 106 late gestation non-lactating Holstein-Friesian cattle (34 primiparous and 72 multiparous) from the Purdue University Dairy Research and Education Center were enrolled into the study between May 29 2012 and March 29 2013. Two hundred and forty animals calved during the course of the study; 134 of these animals were not enrolled in the study due to workload constraints. Enrolled cattle were moved from the outdoor dry lot to temperature controlled individual box stalls (10' x 10') located indoors at four days before the estimated parturition date. All animals were deemed healthy based on a routine physical examination. They were fed an acidogenic total mixed ration (TMR) based on formulations by the National Research Council (NRC, 2001) that was suitable for dry cows. The ration was fed once daily between 08:00 and 09:30. Daily amounts of TMR that were fed and refused (orts) were recorded throughout the study. Cattle were given *ad libitum* access to water at all times.

Experimental study

Physical examination and sampling were done daily between 08:00 and 10:00 with the animal gently restrained in a headlock. Respiratory rate was obtained via visual inspection of thoracic excursions for 30 seconds. Heart rate and mean arterial blood pressure was obtained from the proximal portion of the tail using a blood pressure cuff (Dura-Cuf® Ref 2781 12-19 cm, Critikon Inc., Tampa, FL) attached to a blood pressure monitor (Dinamap™ Adult/Pediatric and Neonatal Vital Signs Monitor 1846, Critikon Inc., Tampa, FL). The sensor was situated ventrally over the coccygeal artery. Five readings were taken for each animal each day and the mean of the readings was used. Respiratory rate was obtained via visual observation of thoracic excursions for 30

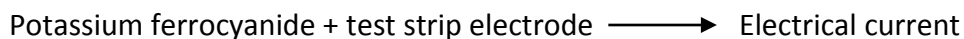
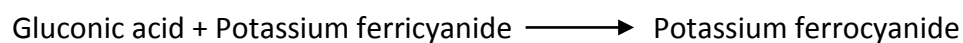
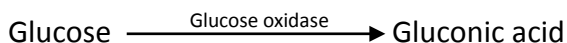
seconds. Rumen contraction rate was determined by auscultation of the left paralumbar fossa for 3 minutes. The calf and dam were separated within a few hours of calving. The time of calving was recorded to the nearest hour and data collected was then categorized into 12 h intervals relative to the time of calving.

Blood samples were obtained daily at approximately 09:00 from the coccygeal vein or artery on days -4, -3, -2, -1, 0, 1, 2, and 3 relative to calving (day 0) with 20G vacutainer needles, vacutainer holders and 10 mL lithium heparin blood collection tubes (BD Diagnostics, NJ).

Analytical methods

Blood glucose concentration ($[\text{glucose}]_b$) was determined with a handheld electronic glucose meter (Precision Xtra[®] Blood Glucose and Ketone Monitoring System, Abbott Diabetes Care Inc., CA) previously validated to measure $[\text{glucose}]_b$ in dairy cows (Wittrock, Duffield et al. 2013). Immediately after blood collection, a drop of non-heparinized blood from the tip of the vacutainer needle was applied to the sensor of a glucose test strip that was then inserted into the meter.

The glucose meter employs the following methods to measure the glucose concentration in blood or plasma:



The electrical current generated is proportional to the concentration of glucose in the plasma water component of blood or plasma. The overall reaction is assumed to reach equilibrium within 5 seconds, at which time the unit uses a proprietary algorithm to calculate the glucose concentration in mg/dL.

Hematocrit was measured in triplicate using the heparinized blood samples and plain capillary tubes (Jorgensen Labs Inc., CO) that were centrifuged for 5 minutes at 14,800 x g using an LWS-M24 Hematocrit Centrifuge (LW Scientific, Inc., GA). Following determination of hematocrit, the heparinized blood samples were then centrifuged

within 30 minutes of collection with a PowerSpin™ C856 Model LX Centrifuge (United Products & Instruments Inc., Cary, NJ) for 5 minutes at 1400 x *g* in order to separate plasma from cells and minimize glucose metabolism.

Plasma glucose concentration ($[\text{glucose}]_p$) was then measured using the same method as that described above for $[\text{glucose}]_b$. The $[\text{glucose}]_p$ in mg/dL was calculated from the measured concentration using the following validated equation: $[\text{glucose}]_p = 0.65 \times [\text{glucose}]_{p\text{-PrecisionXtra}} + 14$ (Abdelhamed, Hiew et al. 2014). The time interval between blood and plasma glucose concentration readings was no longer than 90 minutes.

Plasma cortisol concentrations on the day before parturition were analyzed at the Animal Health Diagnostic Center, Cornell University using the Coat-A-Count Cortisol (Siemens, Los Angeles, CA). This day was selected for analysis instead of the day of parturition because plasma cortisol concentration is significantly increased 24 h before parturition and rapidly decreases within 1 h after parturition (Hudson, Mullford et al. 1976) and because plasma glucose concentration in dairy cattle peaks 6 to 9 hours after a peak in plasma cortisol concentration (Kim, Yamagishi et al. 2012). The Coat-A-Count kit employs a solid-phase radioimmunoassay whereby ^{125}I -labeled cortisol competes at a fixed time with cortisol in samples for antibody sites that are immobilized to the wall of a polypropylene tube. The supernatant is decanted and this is sufficient to end the competition and to isolate the antibody-bound fraction of the radiolabeled cortisol. The tube is then counted in a gamma counter (LKB Model 1277, LKB Instruments, MD) and produces a number that is converted via a calibration curve to the concentration of cortisol present in the sample (Coat-A-Count(R) 2012).

Statistical analysis

Data was expressed as mean \pm SD (standard deviation) with $P < 0.05$ considered significant. Repeated measures ANOVA (PROC MIXED, SAS 9.3, SAS Inc, Cary NC PROC MIXED) was used to determine the main effects of parity (2 levels), time, and the interaction between parity and time, with cow nested within parity. When indicated by

a significant F-test, post tests were conducted between primiparous and multiparous cattle at a specific time, and with the previous 24 h value within a parity group.

The sensitivity and specificity for $[\text{glucose}]_b$ and $[\text{glucose}]_p$ to predict calving within 12 and 24 h were calculated using logistic regression and generalized estimating equations (GEE) because the dataset contained longitudinal data with repeated measurements for individual cattle. Logistic regression models were calculated using PROC GENMOD (SAS 9.3, SAS Inc, Cary NC) with a repeated statement, binomial distribution for the response variable, a logit link function, and an autoregressive(1) covariance structure, which was selected based on the lowest QIC (Quasilikelihood under the Independence model Criterion). Receiver Operating Characteristic (ROC) curves and Youden's index were used to identify the calculated probability at the optimal cutpoint, and the sensitivity and specificity calculated at the optimal cutpoint. The Hosmer and Lemeshow Goodness-of-Fit test P value was calculated in order to assess model fit. The area under the curve was calculated to assist comparison of different tests in predicting parturition.

Associations of plasma cortisol concentration in the 24 h period before calving with indices of sympathetic nervous system activation (heart rate, mean arterial pressure, hematocrit, and respiratory rate) during the same time period were evaluated using Spearman's rho (r_s) and linear regression. Unpaired t-tests were used to determine the effects of parity (primiparous, multiparous), fetal number (single, twin), stillbirth (yes, no; defined as cattle that delivered a dead calf or a calf that died within 24 h after parturition), dystocia (yes, no; defined as calving difficulty score 4 or 5 in chapter III), or retained placenta (yes, no; defined as the failure to expel all of the fetal membranes within 24 h after parturition) on \log_{10} (plasma cortisol concentration) in the 24 h period before parturition. Plasma cortisol concentration was log transformed for these analyses in order to approximate a normal distribution, based on the Shapiro-Wilk test, and summarized as geometric mean and 95% confidence interval for the range.

Results

A total of 312 data points were available to evaluate the clinical utility of selected factors to predict parturition within 12 or 24 hours. Of the 312 data points, 41 were from cattle that calved within 12 hours and 106 were from cattle that calved within 24 h.

Glucose

Blood and plasma glucose concentrations at 12 h intervals from -4 days prepartum to 3 days postpartum for primiparous and multiparous cattle are shown in Figures 5.1 and 5.2. Blood glucose concentration differed from the previous 24 h value in primiparous cattle on days 0 and 1.0 relative to parturition (Figure 5.1). In comparison, [glucose]_b differed from the previous 24 h value in multiparous cattle on days -0.5, 0, 0.5, and 1.0 relative to parturition. Primiparous cattle had higher [glucose]_b than multiparous cattle on days 0.5 and 1.0 relative to parturition.

Plasma glucose concentration differed from the previous 24 h value in primiparous cattle on days -0.5, 0, 1.0, 1.5, 2.0 relative to parturition (Figure 5.2). In comparison, [glucose]_p differed from the previous 24 h value in multiparous cattle on days -0.5, 0, 0.5, and 1.0 relative to parturition. Primiparous cattle had higher [glucose]_p than multiparous cattle on days -2.0, -1.0, and 0.5 to 3.0 relative to parturition.

Binary logistic regression was run separately to predict parturition within 12 and 24 h. Parity (primiparous or multiparous) was not a significant factor when [blood glucose] was evaluated as a predictor for parturition within 12 (P = 0.29) or 24 h (P = 0.23). The estimated probability (P) for predicting calving within 12 h from the [glucose]_b in mg/dL was: $P = e^{(0.081 \times [\text{glucose}]_b - 7.56)} / \{1 + e^{(0.081 \times [\text{glucose}]_b - 7.56)}\}$. The optimal cutpoint for predicting parturition within 12 h was [glucose]_b > 73 mg/dL (area under the ROC curve = 0.77; Se = 0.54; Sp = 0.92; Hosmer and Lemeshow Goodness-of-Fit test P value = 0.68), equivalent to an estimated probability of 0.16 (Figure 5.3). For comparison, the estimated probability (P) for predicting calving within 24 h from the [glucose]_b in mg/dL was: $P = e^{(0.045 \times [\text{glucose}]_b - 3.69)} / \{1 + e^{(0.045 \times [\text{glucose}]_b - 3.69)}\}$. The optimal cutpoint for predicting

parturition within 24 h was $[\text{glucose}]_b > 80 \text{ mg/dL}$ (area under the ROC curve = 0.65; Se = 0.30; Sp = 0.94; Hosmer and Lemeshow Goodness-of-Fit test P value = 0.21), equivalent to an estimated probability of 0.48 (Figure 5.3).

Parity (primiparous or multiparous) was a significant factor when $[\text{glucose}]_p$ was evaluated as a predictor for parturition within 12 (P = 0.033) or 24 h (P = 0.012). The estimated probability (P) for predicting calving in primiparous cattle within 12 h using the measured $[\text{glucose}]_p$ in mg/dL was: $P = e^{(0.098 \times [\text{glucose}]_p - 9.82)} / \{1 + e^{(0.098 \times [\text{glucose}]_p - 9.82)}\}$. The optimal cutpoint for predicting parturition within 12 h in primiparous cattle was $[\text{glucose}]_p > 82 \text{ mg/dL}$ (area under the ROC curve = 0.82; Se = 0.71; Sp = 0.84; Hosmer and Lemeshow Goodness-of-Fit test P value = 0.10), equivalent to an estimated probability of 0.14 (Figure 5.4). For comparison, the estimated probability (P) for predicting calving in multiparous cattle within 12 h using $[\text{glucose}]_p$ in mg/dL was: $P = e^{(0.135 \times [\text{glucose}]_p - 11.88)} / \{1 + e^{(0.135 \times [\text{glucose}]_p - 11.88)}\}$. The optimal cutpoint for predicting parturition within 12 h in multiparous cattle was $[\text{glucose}]_p > 72 \text{ mg/dL}$ (area under the ROC curve = 0.83; Se = 0.74; Sp = 0.89; Hosmer and Lemeshow Goodness-of-Fit test P value = 0.54), equivalent to an estimated probability of 0.10 (Figure 5.4).

The estimated probability (P) for predicting calving in primiparous cattle within 24 h from the $[\text{glucose}]_p$ in mg/dL was: $P = e^{(0.091 \times [\text{glucose}]_p - 7.82)} / \{1 + e^{(0.091 \times [\text{glucose}]_p - 7.82)}\}$. The optimal cutpoint for predicting parturition within 24 h in primiparous cattle was $[\text{glucose}]_p > 81 \text{ mg/dL}$ (area under the ROC curve = 0.78; Se = 0.62; Sp = 0.86; Hosmer and Lemeshow Goodness-of-Fit test P value = 0.61), equivalent to an estimated probability of 0.38 (Figure 5.5). For comparison, the estimated probability (P) for predicting calving in multiparous cattle within 24 h using $[\text{glucose}]_p$ in mg/dL was: $P = e^{(0.070 \times [\text{glucose}]_p - 5.67)} / \{1 + e^{(0.070 \times [\text{glucose}]_p - 5.67)}\}$. The optimal cutpoint for predicting parturition within 24 h in multiparous cattle was $[\text{glucose}]_p > 75 \text{ mg/dL}$ (area under the ROC curve = 0.66; Se = 0.40; Sp = 0.89; Hosmer and Lemeshow Goodness-of-Fit test P value = 0.14), equivalent to an estimated probability of 0.40 (Figure 5.5).

Heart rate

The mean heart rate (HR) for primiparous and multiparous cattle at 12 h intervals from -4 days prepartum to 3 days postpartum is shown in Figure 5.6. Heart rate differed from the previous 24 h value in primiparous cattle on days 0, 1.0, and 2.0 relative to parturition (Figure 5.6). In comparison, HR differed from the previous 24 h value in multiparous cattle on days -0.5, 1.0, 1.5, and 2.5 relative to parturition. Primiparous cattle had a higher HR than multiparous cattle for all studied days except days -3.5 and -0.5 relative to parturition.

Parity (primiparous or multiparous) was not a significant factor when HR was evaluated as a predictor for parturition within 12 h ($P = 0.47$) or 24 h ($P = 0.26$). The estimated probability (P) for predicting calving in primiparous cattle within 12 h using HR in beats/min was: $P = e^{(0.054 \times \text{HR} - 6.98)} / \{1 + e^{(0.054 \times \text{HR} - 6.98)}\}$. The optimal cutpoint for predicting parturition within 12 h in primiparous cattle was HR > 96 beats/min (area under the ROC curve = 0.66; Se = 0.55; Sp = 0.73; Hosmer and Lemeshow Goodness-of-Fit test P value = 0.50), equivalent to an estimated probability of 0.14 (Figure 5.7). For comparison, the estimated probability (P) for predicting calving within 24 h using HR was: $P = e^{(0.033 \times \text{HR} - 3.81)} / \{1 + e^{(0.033 \times \text{HR} - 3.81)}\}$. The optimal cutpoint for predicting parturition within 24 h was HR > 95 beats/min (area under the ROC curve = 0.60; Se = 0.48; Sp = 0.67; Hosmer and Lemeshow Goodness-of-Fit test P value = 0.73), equivalent to an estimated probability of 0.34 (Figure 5.7).

Mean arterial pressure

The mean arterial pressure (MAP) for primiparous and multiparous cattle at 12 h intervals from -4 days prepartum to 3 days postpartum is shown in Figure 5.8. Mean arterial pressure did not differ from the previous 24 h value in primiparous or multiparous cattle. Primiparous cattle had a higher MAP than multiparous cattle on days 0.5 and 1.0 relative to parturition.

Parity (primiparous or multiparous) was not a significant factor when MAP was evaluated as a predictor for parturition within 12 h ($P = 0.66$) or 24 h ($P = 0.43$). Mean

arterial pressure was not a significant predictor of parturition within 12 (P = 0.091) or 24 h (P = 0.10).

Hematocrit

The hematocrit (Hct) for primiparous and multiparous cattle at 12 h intervals from -4 days prepartum to 3 days postpartum is shown in Figure 5.9. Hematocrit differed from the previous 24 h value in primiparous cattle on days 0 and 1.0 relative to parturition. In comparison, Hct differed from the previous 24 h value in multiparous cattle on days -0.5, 0, and 1.0 relative to parturition. Parity (primiparous or multiparous) was not a significant factor when Hct was evaluated as a predictor for parturition within 12 (P = 0.46) or 24 h (P = 0.20).

Hematocrit was a significant predictor of parturition within 12 (P = 0.0005) or 24 h (P < 0.0001). The estimated probability (P) for predicting calving within 12 h using Hct in volume (vol) % was: $P = e^{(0.323 \times \text{Hct} - 12.94)} / \{1 + e^{(0.323 \times \text{Hct} - 12.94)}\}$. The optimal cutpoint for predicting parturition within 12 h in primiparous cattle was hematocrit > 34 vol % (area under the ROC curve = 0.72; Se = 0.63; Sp = 0.77; Hosmer and Lemeshow Goodness-of-Fit test P value = 0.25), equivalent to an estimated probability of 0.13 (Figure 5.10). For comparison, the estimated probability (P) for predicting calving within 24 h using hematocrit was: $P = e^{(0.231 \times \text{Hct} - 8.60)} / \{1 + e^{(0.231 \times \text{Hct} - 8.60)}\}$. The optimal cutpoint for predicting parturition within 24 h was hematocrit > 35 vol % (area under the ROC curve = 0.65; Se = 0.45; Sp = 0.82; Hosmer and Lemeshow Goodness-of-Fit test P value = 0.37), equivalent to an estimated probability of 0.36 (Figure 5.10).

Respiratory rate

The respiratory rate (RR) for primiparous and multiparous cattle at 12 h intervals from -4 days prepartum to 3 days postpartum is shown in Figure 5.11. Respiratory rate did not differ from the previous 24 h value in primiparous or multiparous cattle. Primiparous cattle had a significantly higher RR than multiparous cattle on days -4.0, -2.0, and 0 relative to parturition.

Parity (primiparous or multiparous) was not a significant factor when RR was evaluated as a predictor for parturition within 12 ($P = 0.44$) or 24 h ($P = 0.77$). Respiratory rate was not a significant predictor of parturition within 12 h ($P = 0.70$), but was a weak predictor of parturition within 24 h ($P = 0.049$; Figure 5.12). An optimal cutpoint for predicting parturition within 24 h could not be determined for respiratory rate because the area under the ROC curve (0.56) was not significantly greater than 0.50 ($P = 0.083$).

Rumen contraction rate

The average rumen contraction rate over 3 minutes for the cattle in the study started to decline from day -1.5 and reached a nadir on the day of parturition at 3.6 ± 1.3 contractions (Figure 5.13). The contraction rate increased within 12 h of calving. Analysis at 12 h intervals showed significant differences between day -0.5 and 0 ($P = 0.0040$) and 0 and 0.5 ($P = 0.0007$) while at 24 h intervals significant differences were present between days -1 and 0 ($P < 0.0001$), and 0 and 1 ($P < 0.0001$). At 12 h, the area under the ROC = 0.56, with an optimal cutpoint for predicting parturition of < 4.3 contractions, $Se = 0.54$, and $Sp = 0.55$. For 24 h, the area under the ROC = 0.56, with the optimal cutpoint for predicting parturition of < 4.2 contractions, $Se = 0.54$, and $Sp = 0.58$ (Figure 5.14).

Cortisol

Plasma cortisol concentrations were determined for 32 primiparous and 67 multiparous cattle. The plasma cortisol concentration on the day before parturition was greater ($P = 0.028$) for primiparous cattle (geometric mean, 10.3 ng/mL; 95% confidence interval for range, 2.8 to 37.4 ng/mL) than multiparous cattle (geometric mean, 7.7 ng/mL; 95% confidence interval for range, 2.5 to 24.0 ng/mL).

Plasma cortisol concentration was positively associated with $[glucose]_p$ ($r_s = 0.24$; $P = 0.019$) and hematocrit ($r_s = 0.21$, $P = 0.037$), but was not associated with $[glucose]_b$, heart rate, mean arterial pressure, or respiratory rate. Plasma glucose concentration

was weakly but linearly associated with \log_{10} (plasma cortisol concentration) (Figure 5.15) such that $y = 11.5 \times (\log_{10}(\text{plasma [cortisol]}) + 66$; $R^2 = 0.052$, $P = 0.023$.

Discussion

Parturition is a process initiated by the fetus and is dependent on the hypothalamus-pituitary-adrenal (HPA) axis (Hunter, Fairclough et al. 1977, Wood 1999). As parturition approaches, fetal stress activates the HPA axis and corticotrophin releasing factor (CRF) is secreted by the hypothalamus. Adrenocorticotrophic hormone (ACTH) is then released from the anterior pituitary gland which in turn causes the release of cortisol from the cortical region of the fetal adrenal glands (Broom and Johnson 1993, Wood 1999). Fetal plasma cortisol concentrations rapidly increased at the time of parturition to a mean of 74 ng/mL (Hunter, Fairclough et al. 1977). Fetal hypercortisolemia is followed by an increase in plasma cortisol concentration in the dam (Edgerton and Hafs 1973, Hudson, Mullford et al. 1976, Kejela, Head et al. 1978, Eissa and El-Belely 1990, Patel, Takahashi et al. 1996) due to the activation of the HPA axis of the dam in response to the pain and stress of stage I and II of parturition. Although plasma fetal cortisol concentration is high immediately before parturition, only a very small amount of fetal cortisol crosses over into the maternal circulation where it makes up less than 1% of the plasma cortisol concentration in the periparurient ewe (Dixon, Hyman et al. 1970).

In this study, plasma cortisol concentrations on the day before parturition were similar to those observed in previous studies (Hudson, Mullford et al. 1976, Kejela, Head et al. 1978). An important finding of this study was that plasma [glucose]_p was positively and linearly associated with \log_{10} (plasma cortisol concentration). A second important finding was that plasma cortisol concentration was higher in primiparous cattle than multiparous cattle on the day before parturition. The physiological reason for this difference remains to be determined, but we speculate that increased stress in primiparous cattle contributed to their higher plasma cortisol concentration. This is

consistent with the higher heart rate and hematocrit in primiparous cattle in the days immediately before parturition.

The increase in the dam's plasma cortisol concentration leads to an increase in plasma glucose concentration due to the process of gluconeogenesis. The mean plasma glucose concentration at the time of calving for primiparous and multiparous cattle was approximately 100 mg/dL and within the range of 76 to 150 mg/dL reported in previous studies (Schwalm and Schultz 1976, Jacob, Ramnath et al. 2001, Bionaz, Trevisi et al. 2007). Primiparous cattle had higher $[\text{glucose}]_p$ than multiparous cattle at many time points, with a clear exception being within a few hours of parturition. Collectively, the data supports the hypothesis that higher prepartum $[\text{glucose}]_p$ in primiparous cattle reflects a higher level of stress as these cattle were housed, fed, watered, and handled similarly to multiparous cattle. According to the numerical ranking of the area under the ROC curves, $[\text{glucose}]_p > 82$ mg/dL (primiparous cattle) and $[\text{glucose}]_p > 72$ mg/dL (multiparous cattle) provided the best overall prediction of parturition within 12 h, based on equal weighting to optimizing sensitivity and specificity. The probability plots in Figure 5.4 should prove useful in predicting parturition as the veterinarian or producer is able to set the probability of parturition that is preferred for each situation. For example, if a veterinarian wants to estimate the 0.50 probability that a primiparous dam will calve in the next 12 h, a blood sample is obtained and plasma is harvested and analyzed using the glucometer. The measured value is then corrected using the validated equation stated in the materials and methods section. Whenever the $[\text{glucose}]_p > 100$ mg/dL, the veterinarian will know that the animal has a probability of 0.5 or higher of calving within the next 12 h. A simpler and more practical but less accurate method is to directly place a drop of blood on the reagent strip and measure the blood sample using the glucometer. The probability plot in Figure 5.3 (upper left panel) indicates that the veterinarian will know that the animal has a probability of 0.5 or higher of calving within the next 12 h if $[\text{glucose}]_b > 93$ mg/dL.

The Precision Xtra[®] glucometer used in this study was easy to use, provided quick results, and had minimal cost (the glucometer cost USD\$27 and glucose strips

were USD\$0.30 each). The small size of the meter enhanced its portability and it is a good and easy addition to prepartum animal checks. Additionally, the Precision Xtra[®] meter also has the capability of measuring blood β -hydroxybutyrate (ketone) concentrations. Blood draws done from the coccygeal vessels were relatively quick once the animal was restrained in the headlock and the authors believe that for monitoring purposes, a needle with a hub would be adequate to acquire a drop of blood to run the meter. However, some producers might not be supportive of frequent blood draws from the coccygeal vessels. As an alternative, pin pricks to the tail or ear to obtain capillary blood could be performed although no studies on this method for glucose evaluation appear to have been completed in cattle.

Besides activating the HPA axis, stress also stimulates the sympathetic nervous system and leads to the secretion of adrenaline and noradrenaline from the adrenal medulla. This is characteristic of the flight or fight response that prepares the body to cope with stressors by elevating the heart rate, mean arterial pressure, and respiratory rate (Hydbring, Macdonald et al. 1997, Von Borell 2001, Stewart, Verkerk et al. 2010).

In this study, heart rate was consistently higher in primiparous than multiparous cattle, which was consistent with increased [glucose]_p in primiparous cattle. Heart rate increased transiently immediately before parturition in multiparous animals, and immediately after parturition in primiparous animals, presumably due to discomfort and pain experienced by the dam that stimulates the sympathetic nervous system and induces the release of adrenaline. In goats, the heart rate increased in late gestation and did not further increase immediately before parturition and during labor. However, heart rate peaked at the moment when the first kid was delivered (Hydbring, Macdonald et al. 1997) which was concomitant with the peak of plasma adrenaline concentration. Similar results have been reported in primiparous cattle undergoing parturition (Hydbring, Madej et al. 1999). Similar to our findings, a study completed on 44 Hereford cattle in Australia did not find any value in the heart rate as a predictor of parturition as that study only observed minimal changes (Dufty 1971).

Mean arterial pressure was approximately 10 beats/min higher in primiparous than multiparous cattle for the first 24 h after parturition. In goats, MAP increased on the day of parturition and reached a maximal value when the head of the first kid was visible (Hydbring, Macdonald et al. 1997). This may be similar in cattle but blood pressure readings were not taken at any time during the calving process. Mean arterial pressure was not predictive of parturition in the dairy cattle in this study.

Starting from day -2 relative to parturition, an increase in the Hct of both primiparous and multiparous cattle groups were seen and the Hct peaked on the day of parturition. The activation of the sympathetic nervous system in response to pain causes splenic contraction and the release of erythrocytes into circulation (Fazio and Ferlazzo 2003). Hematocrit values increase when there is a higher ratio of cell volume to plasma volume. This coupled with the potential for reduced water intake as a result of preparturient feed depression (Winchester and Morris 1956) can account for the increase in the hematocrit vol % on the day of parturition.

Respiratory rate has minimal clinical utility in predicting parturition in dairy. Healthy cattle housed in the thermoneutral zone typically have a respiratory rate between 10 to 30 breaths per minute. Increased environmental temperature and humidity increase respiratory rate in cattle, making it difficult to detect an association between increased respiratory rate and increased likelihood of parturition (Radostits, Gay et al. 2007). A positive association between respiratory rate and plasma cortisol concentration has been observed in cattle (Tagawa, Okano et al. 1994), although this study is confounded by positional changes which were likely to induce hypercortisolemia. Changes in respiratory rate due to environmental effects impede the use of this parameter as a predictor of parturition predictor, and any changes in respiratory rate associated with parturition are small and are easily masked by diurnal variations (Dufty 1971).

There was a gradual decrease in rumen contraction rate in the days leading to parturition and on the day of calving a transient decrease in the rumen contraction rate was observed. The frequency of primary contractions in cows averages at 60 cycles/h

but decreases to 50 cycles/h during rumination or even lower with the cow in recumbency. The act of feeding elevates the contractions to 105 cycles/h (Sellers and Stevens 1966). Rumen hypomotility is typically caused by the reduction of the excitatory drive to the gastric center or an elevation of inhibitory inputs (Constable, Hoffsis et al. 1990). Painful stimuli, such as those associated with labor and delivery, acts as an inhibitory input to the gastric center and together with the release of catecholamines, the reticulorumen motility is changed (Titchen 1958, Constable, Hoffsis et al. 1990). The sympathetic nervous system also responds to pain and is capable of stimulating the splanchnic motor nerves and directly inhibit reticulorumen motility (Leek 1969). Besides that, a reduction in feed intake, which is seen in cattle prepartum (Marquardt, Horst et al. 1977, Goff, Kimura et al. 2002, Huzzey, Veira et al. 2007), also reduces reticulorumen motility as it removes forestomach distention and chewing activity (Constable, Hoffsis et al. 1990).

Increases in plasma cortisol and glucose concentration, heart rate, and hematocrit, and lowered rumen contraction rate can also result from excitement and stress during handling. The animals in this study were moved into individual box stalls at approximately four days before calving and it is likely that acclimatization to handling, study personnel, and environment had occurred by the time of parturition, thereby minimizing stressors. Dairy cattle moved into new groups experience a period of social disruption of 2 to 3 days (Cook and Nordlund 2004) and exhibit agonistic interaction and dramatic changes in behavior that last for 48 h before stabilizing (Kondo and Hurnik 1990). However, there is no competition for feed, water and space when cattle are housed in individual box stalls, and little to no hierarchical interaction with herd mates. Therefore, it is likely that individually housed cows suffer less stress compared to animals moved into a group pen and findings associated with group pen movements may not be applicable to cows housed in individual calving pens. Animals that are used to frequent handling and close contact with humans are less stressed by restraint and handling compared to animals that seldom see people (Grandin 1997). Additionally, plasma cortisol concentrations increase from baseline in cattle approximately 6 to 27

minutes after manipulation (Alam and Dobson 1986, Lay, Friend et al. 1992). Venipuncture in this study was done almost immediately after the animal was restrained in headlocks and almost certainly within the 6 minute time frame. Besides that, the adrenal cortex is able to adapt and cease responding to stimuli that is repeated frequently (Broom and Johnson 1993). With these factors in mind, it is likely that handling and restraint had minimal impact on the increases of some studies factors at the time of parturition.

When blood pressure is measured, some animals are disturbed by the blood pressure cuff as indicated by higher heart rates and mean arterial pressures (Bazil, Krulan et al. 1993). Telemetric devices have been used in animals to continuously measure heart rate and blood pressure without the need for restraint to obtain undisturbed responses (Bazil, Krulan et al. 1993, Von Borell 2001, Huetteman and Bogie 2009). However, this method requires the implantation of the device into the animal (Huetteman and Bogie 2009) which is invasive, incurs additional cost, requires surgical expertise, and is only suitable for a laboratory setting. Non-invasive heart rate monitors that are strapped to the body could also be used to measure heart rate changes in the periparturient period without having to approach the animal (Hopster and Blokhuis 1994).

Handheld glucometer systems are susceptible to errors caused by temperature, altitude, humidity, patient hematocrit, improper calibration, use of expired reagent strips, error in timing, inappropriate blood droplet size or placement, and incorrect sample insertion (Fazel, Koutoubi et al. 1996, Gautier, Bigard et al. 1996, Cohn, McCaw et al. 2000, Tang, Lee et al. 2000). A problem that the authors faced while conducting this study was using the glucometer during the winter. As the Precision Xtra® has an optimum operating temperature of 10 to 50°C (Landa 2011), the glucometer would stop working in very cold temperatures and had to be brought indoors to be warmed up which was time consuming.

Besides increasing $[glucose]_b$ and $[glucose]_p$, cortisol disrupts phosphorus homeostasis and suppresses bone metabolism, as demonstrated by a decrease in

biochemical bone resorption markers tartrate-resistant acid phosphatase 5b, hydroxyproline and bone specific alkaline phosphatase. Cortisol also suppresses bone formation and osteoblast activity (Kim, Yamagishi et al. 2012). Plasma calcium and phosphorus concentrations are also negatively correlated with plasma cortisol concentrations (Horst and Jorgensen 1982). These parameters could be looked at in future studies to determine their effectiveness in predicting the time of parturition. Other than heart rate, heart rate variability (HRV) analysis could also be investigated as this is an additional parameter that indicates the sympatho-vagal balance in the animal and is measured by looking at the constantly changing temporal distance between two heartbeats at the R – R interval (Mohr, Langbein et al. 2002). Heart rate variability allows a more accurate and detailed information of the functional regulatory characteristic of the autonomic nervous system (von Borell, Langbein et al. 2007). Low HRV values indicate that an individual is stressed (Mohr, Langbein et al. 2002).

Conclusion

The stress of parturition causes the stimulation of the maternal HPA axis and cortisol is released which in turn causes the increase in circulating glucose concentrations. Stress also stimulates the sympathetic nervous system to release adrenaline and the effects of this can be seen in elevated heart rate, blood pressure, and respiratory rate while rumen contraction rates are reduced. Point of care testing to determine blood glucose concentration in periparturient dairy cattle appears to provide the best method for predicting parturition within 12 and 24 h due to its practicality, low cost, and reasonable accuracy.

References

- Abdelhamed, A., M. W. Hiew, J. R. Townsend and P. D. Constable (2014). "Evaluation of the Precision Xtra® hand-held meter for the rapid point of care measurement of blood and plasma glucose concentration in periparturient dairy cattle." Unpublished manuscript.
- Alam, M. and H. Dobson (1986). "Effect of various veterinary procedures on plasma concentrations of cortisol, luteinising hormone and prostaglandin F2 alpha metabolite in the cow." The Veterinary Record **118**(1): 7-10.
- Barrier, A., M. Haskell, S. Birch, A. Bagnall, D. Bell, J. Dickinson, A. Macrae and C. Dwyer (2013). "The impact of dystocia on dairy calf health, welfare, performance and survival." The Veterinary Journal **195**(1): 86-90.
- Bazil, M. K., C. Krulan and R. L. Webb (1993). "Telemetric monitoring of cardiovascular parameters in conscious spontaneously hypertensive rats." Journal of Cardiovascular Pharmacology **22**(6): 897-905.
- Bionaz, M., E. Trevisi, L. Calamari, F. Librandi, A. Ferrari and G. Bertoni (2007). "Plasma paraoxonase, health, inflammatory conditions, and liver function in transition dairy cows." Journal of Dairy Science **90**(4): 1740-1750.
- Broom, D. M. and K. Johnson (1993). Stress and animal welfare, Chapman and Hall.
- Cattell, J. and H. Dobson (1990). "A survey of caesarean operations on cattle in general veterinary practice." The Veterinary Record **127**(16): 395-399.
- Coat-A-Count(R) (2012). Cortisol. [package insert] Siemens Healthcare Diagnostics Inc, Tarrytown, New York.
- Cohn, L. A., D. L. McCaw, D. J. Tate and J. C. Johnson (2000). "Assessment of five portable blood glucose meters, a point-of-care analyzer, and color test strips for measuring blood glucose concentration in dogs." Journal of the American Veterinary Medical Association **216**(2): 198-202.
- Constable, P., G. Hoffsis and D. Rings (1990). "The reticulorumen: Normal and abnormal motor function. Part I. Primary contraction cycle." Compendium on Continuing Education for the Practicing Veterinarian **12**(7): 1008-1014.
- Cook, N. B. and K. V. Nordlund (2004). "Behavioral needs of the transition cow and considerations for special needs facility design." Veterinary Clinics of North America: Food Animal Practice **20**(3): 495-520.

Dematawewa, C. and P. Berger (1997). "Effect of dystocia on yield, fertility, and cow losses and an economic evaluation of dystocia scores for Holsteins." Journal of Dairy Science **80**(4): 754-761.

Dixon, R., A. Hyman, E. Gurpide, I. Dyrenfurth, H. Cohen, E. Bowe, T. Engel, S. Daniel, S. James and R. Vande Wiele (1970). "Feto-maternal transfer and production of cortisol in the sheep." Steroids **16**: 771-789.

Dufty, J. (1971). "Determination of the onset of parturition in Hereford cattle." Australian Veterinary Journal **47**(3): 77-82.

D'Orazio, P., R. W. Burnett, N. Fogh-Andersen, E. Jacobs, K. Kuwa, W. R. K lpmann, L. Larsson, A. Lewenstam, A. H. Maas and G. Mager (2005). "Approved IFCC recommendation on reporting results for blood glucose (abbreviated)." Clinical Chemistry **51**(9): 1573-1576.

Edgerton, L. and H. Hafs (1973). "Serum luteinizing hormone, prolactin, glucocorticoid, and progesterin in dairy cows from calving to gestation." Journal of Dairy Science **56**(4): 451-458.

Eissa, H. and M. El-Belely (1990). "Sequential changes in plasma progesterone, total oestrogens and corticosteroids in the cow throughout pregnancy and around parturition." British Veterinary Journal **146**(1): 24-29.

Fazel, A., Z. Koutoubi, T. B. Sorg and B. Mehrotra (1996). "Influence of sample temperature on reflectance photometry and electrochemical glucometer measurements." Diabetes Care **19**(7): 771-774.

Fazio, E. and A. Ferlazzo (2003). "Evaluation of stress during transport." Veterinary Research Communications **27**(Suppl. 1): 519-524.

Gautier, J.-F., A. X. Bigard, P. Douce, A. Duvallet and G. Cathelineau (1996). "Influence of simulated altitude on the performance of five blood glucose meters." Diabetes Care **19**(12): 1430-1433.

Godden, W. and W. M. Allcroft (1932). "Changes in the composition of cow's blood at the time of calving and a comparison of the blood of the calf with that of its dam." Biochemical Journal **26**(5): 1640-1646.

Goff, J. P., K. Kimura and R. L. Horst (2002). "Effect of Mastectomy on Milk Fever, Energy, and Vitamins A, E, and β -Carotene Status at Parturition." Journal of Dairy Science **85**(6): 1427-1436.

Goodwin, R. (1956). "The distribution of sugar between red cells and plasma: variations associated with age and species." The Journal of Physiology **134**(1): 88-101.

Grandin, T. (1997). "Assessment of stress during handling and transport." Journal of Animal Science **75**(1): 249-257.

Hopster, H. and H. J. Blokhuis (1994). "Validation of a heart-rate monitor for measuring a stress response in dairy cows." Canadian Journal of Animal Science **74**(3): 465-474.

Horst, R. and N. Jorgensen (1982). "Elevated plasma cortisol during induced and spontaneous hypocalcemia in ruminants." Journal of Dairy Science **65**(12): 2332-2337.

Hudson, S., M. Mullford, W. Whittlestone and E. Payne (1976). "Bovine plasma corticoids during parturition." Journal of Dairy Science **59**(4): 744-746.

Huetteman, D. A. and H. Bogie (2009). Direct blood pressure monitoring in laboratory rodents via implantable radio telemetry. Cardiovascular Genomics, Springer: 57-73.

Hunter, J., R. Fairclough, A. Peterson and R. Welch (1977). "Foetal and maternal hormonal changes preceding normal bovine parturition." Acta Endocrinologica **84**(3): 653-662.

Huzzey, J., D. Veira, D. Weary and M. Von Keyserlingk (2007). "Prepartum behavior and dry matter intake identify dairy cows at risk for metritis." Journal of Dairy Science **90**(7): 3220-3233.

Hydbring, E., E. Macdonald and K. Olsson (1997). "Radiotelemetrically recorded blood pressure and heart rate changes in relation to plasma catecholamine levels during parturition in the conscious, unrestrained goat." Acta Physiologica Scandinavica **161**(3): 295-302.

Hydbring, E., A. Madej, E. MacDonald, G. Drugge-Boholm, B. Berglund and K. Olsson (1999). "Hormonal changes during parturition in heifers and goats are related to the phases and severity of labour." Journal of Endocrinology **160**(1): 75-85.

Jacob, S., V. Ramnath, P. Philomina, K. Raghunandhan and A. Kannan (2001). "Assessment of physiological stress in periparturient cows and neonatal calves." Indian Journal of Physiology and Pharmacology **45**(2): 233-238.

Kejela, G., H. Head, C. Wilcox and W. Thatcher (1978). "Adrenal responsiveness in pre- and postpartum dairy cows." Journal of Dairy Science **61**(12): 1736-1741.

Kim, D., N. Yamagishi, B. Devkota and K. Furuhashi (2012). "Effects of cortisol secreted via a 12-h infusion of adrenocorticotrophic hormone on mineral homeostasis and bone metabolism in ovariectomized cows." Domestic Animal Endocrinology **43**(3): 264-269.

- Kondo, S. and J. Hurnik (1990). "Stabilization of social hierarchy in dairy cows." Applied Animal Behaviour Science **27**(4): 287-297.
- Landa, C. E. (2011). Evaluation of weaning stress in beef calves, Virginia Polytechnic Institute and State University.
- Lay, D., T. Friend, C. Bowers, K. Grissom and O. Jenkins (1992). "A comparative physiological and behavioral study of freeze and hot-iron branding using dairy cows." Journal of Animal Science **70**(4): 1121-1125.
- Leek, B. (1969). "Reticulo-ruminal mechanoreceptors in sheep." The Journal of Physiology **202**(3): 585-609.
- Marquardt, J., R. Horst and N. Jorgensen (1977). "Effect of parity on dry matter intake at parturition in dairy cattle." Journal of Dairy Science **60**(6): 929-934.
- Meyer, C. L., P. J. Berger, K. J. Koehler, J. R. Thompson and C. G. Sattler (2001). "Phenotypic trends in incidence of stillbirth for Holsteins in the United States." J Dairy Sci **84**(2): 515-523.
- Mohr, E., J. Langbein and G. Nürnberg (2002). "Heart rate variability a noninvasive approach to measure stress in calves and cows." Physiology & Behavior **75**(1): 251-259.
- Patel, O., T. Takahashi, N. Takenouchi, M. Hirako, N. Sasaki and I. Domekis (1996). "Peripheral cortisol levels throughout gestation in the cow: Effect of stage of gestation and foetal number." British Veterinary Journal **152**(4): 425-432.
- Radostits, O., C. Gay, K. Hinchcliff and P. Constable (2007). Clinical examination and making a diagnosis. Veterinary medicine: a text book of the diseases of cattle, horses, sheep, pigs and goats: 3-38.
- Radostits, O., C. Gay, K. Hinchcliff and P. Constable (2007). General systemic states. Veterinary medicine: a textbook of the diseases of cattle, horses, sheep, pigs and goats, Saunders Elsevier, Philadelphia.: 39-124.
- Schwalm, J. and L. Schultz (1976). "Relationship of insulin concentration to blood metabolites in the dairy cow." Journal of Dairy Science **59**(2): 255-261.
- Sellers, A. and C. Stevens (1966). "Motor functions of the ruminant forestomach." Physiological Reviews **46**: 634-661.
- Somogyi, M. (1933). "The distribution of sugar and rate of glycolysis in the blood of some mammals." Journal of Biological Chemistry **103**(2): 665-670.

- Stewart, M., G. Verkerk, K. Stafford, A. Schaefer and J. Webster (2010). "Noninvasive assessment of autonomic activity for evaluation of pain in calves, using surgical castration as a model." Journal of Dairy Science **93**(8): 3602-3609.
- Streyl, D., C. Sauter-Louis, A. Braunert, D. Lange, F. Weber and H. Zerbe (2011). "Establishment of a standard operating procedure for predicting the time of calving in cattle." Journal of Veterinary Science **12**(2): 177-185.
- Tagawa, M., S. Okano, T. Sako, H. Orima and E. P. Steffey (1994). "Effect of change in body position on cardiopulmonary function and plasma cortisol in cattle." The Journal of Veterinary Medical Science **56**(1): 131-134.
- Tang, Z., J. H. Lee, R. F. Louie and G. J. Kost (2000). "Effects of different hematocrit levels on glucose measurements with handheld meters for point-of-care testing." Archives of Pathology & Laboratory Medicine **124**(8): 1135-1140.
- Titchen, D. (1958). "Reflex stimulation and inhibition of reticulum contractions in the ruminant stomach." The Journal of Physiology **141**(1): 1-21.
- Vazquez-Anon, M., S. Bertics, M. Luck, R. Grummer and J. Pinheiro (1994). "Peripartum liver triglyceride and plasma metabolites in dairy cows." Journal of Dairy Science **77**(6): 1521-1528.
- Von Borell, E. (2001). "The biology of stress and its application to livestock housing and transportation assessment." Journal of Animal Science **79**(E-Suppl): E260-E267.
- Von Borell, E., J. Langbein, G. Després, S. Hansen, C. Leterrier, J. Marchant-Forde, R. Marchant-Forde, M. Minero, E. Mohr, A. Prunier, D. Valance and I. Veissier (2007). "Heart rate variability as a measure of autonomic regulation of cardiac activity for assessing stress and welfare in farm animals—a review." Physiology & Behavior **92**(3): 293-316.
- Winchester, C. and M. Morris (1956). "Water intake rates of cattle." Journal of Animal Science **15**(3): 722-740.
- Wittrock, J., T. Duffield and S. LeBlanc (2013). "Short communication: Validation of a point-of-care glucometer for use in dairy cows." Journal of Dairy Science **96**(7): 4514-4518.
- Wood, C. (1999). "Control of parturition in ruminants." Journal of Reproduction and Fertility Supplement **54**: 115-126.

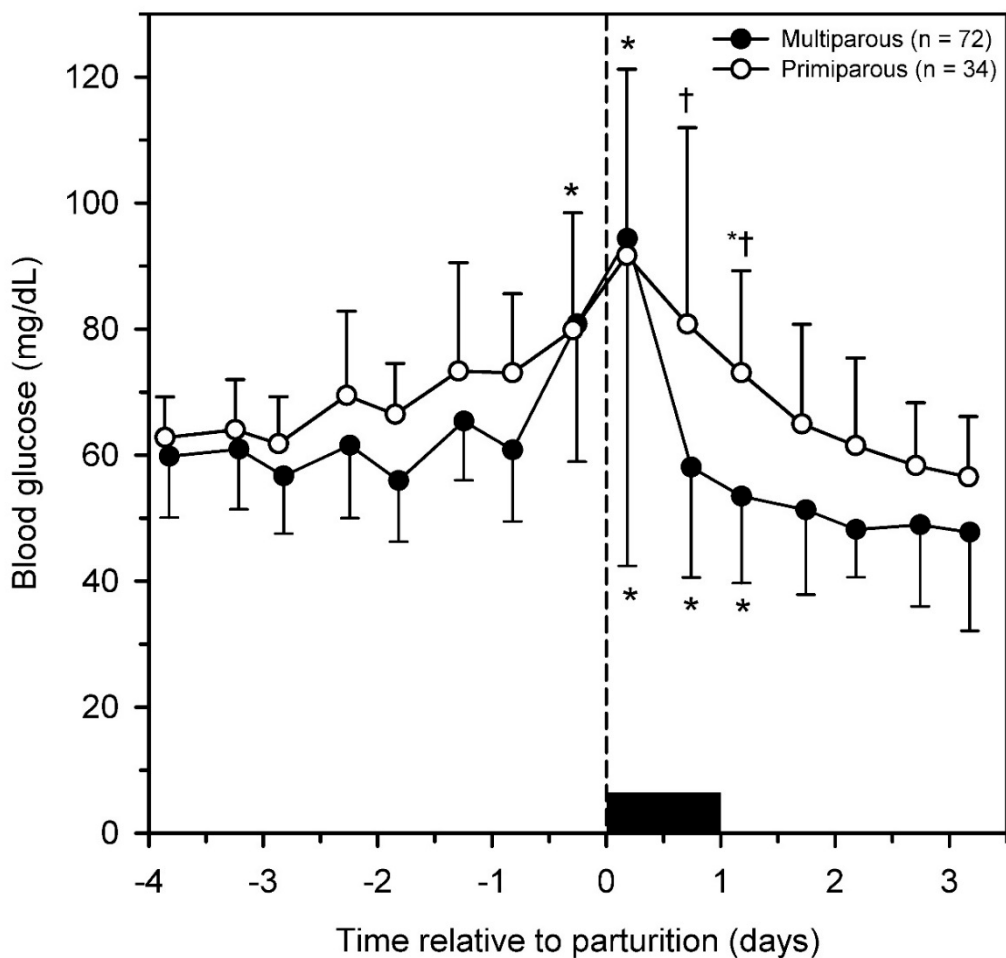


Figure 5.1 Blood glucose concentrations (mg/dL) for primiparous (open circles) and multiparous (filled circles) Holstein-Friesian cattle at 12 h intervals from 4 days prepartum to 3 days postpartum. Time is expressed as the geometric mean value which represents the time that data was recorded for each 12 h interval. The black rectangle is the 24 h period during which all cows calved. Data is presented as mean \pm SD. *P < 0.0038 (Bonferroni adjusted) compared to the value obtained 24 h previously. †P < 0.0033 (Bonferroni adjusted) compared to the value for multiparous cattle at the same time.

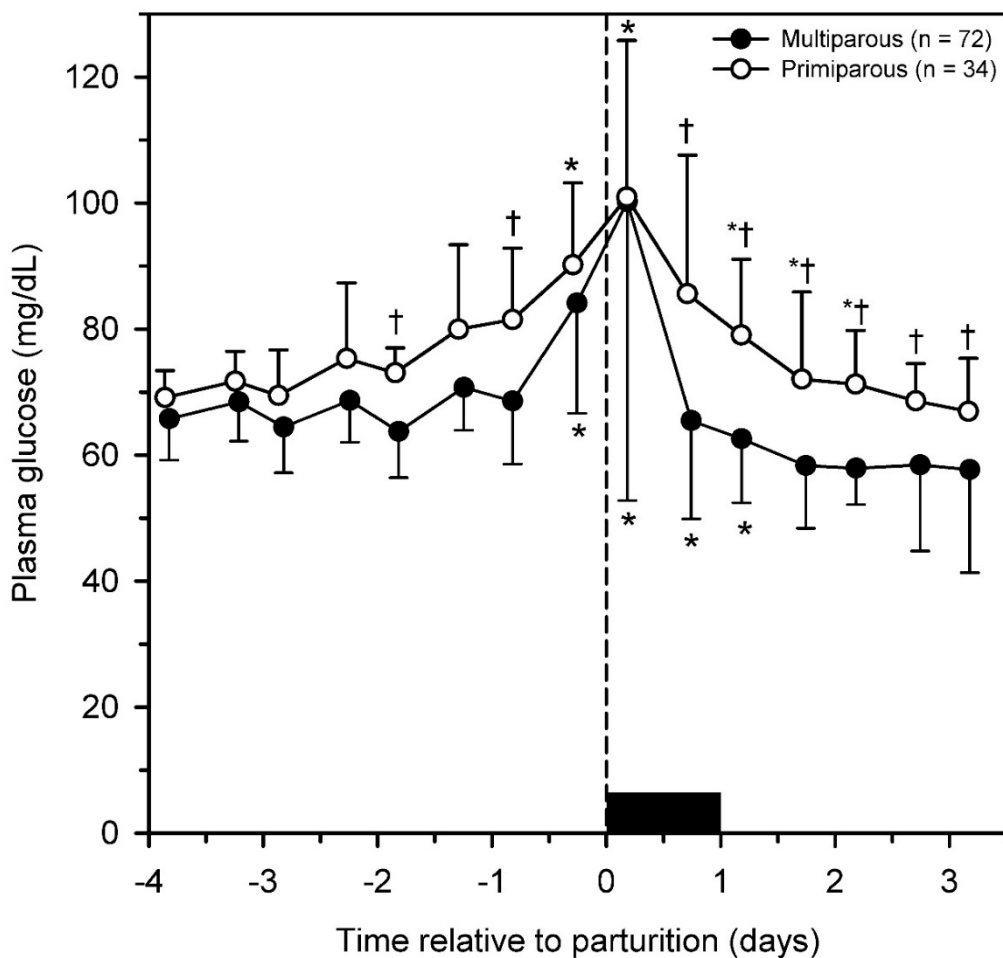


Figure 5.2 Plasma glucose concentrations (mg/dL) for primiparous (open circles) and multiparous (filled circles) Holstein-Friesian cattle at 12 h intervals from 4 days prepartum to 3 days postpartum. Time is expressed as the geometric mean value which represents the time that data was recorded for each 12 h interval. The black rectangle is the 24 h period during which all cows calved. Data is presented as mean \pm SD. *P < 0.0038 (Bonferroni adjusted) compared to the value obtained 24 h previously. †P < 0.0033 (Bonferroni adjusted) compared to the value for multiparous cattle at the same time.

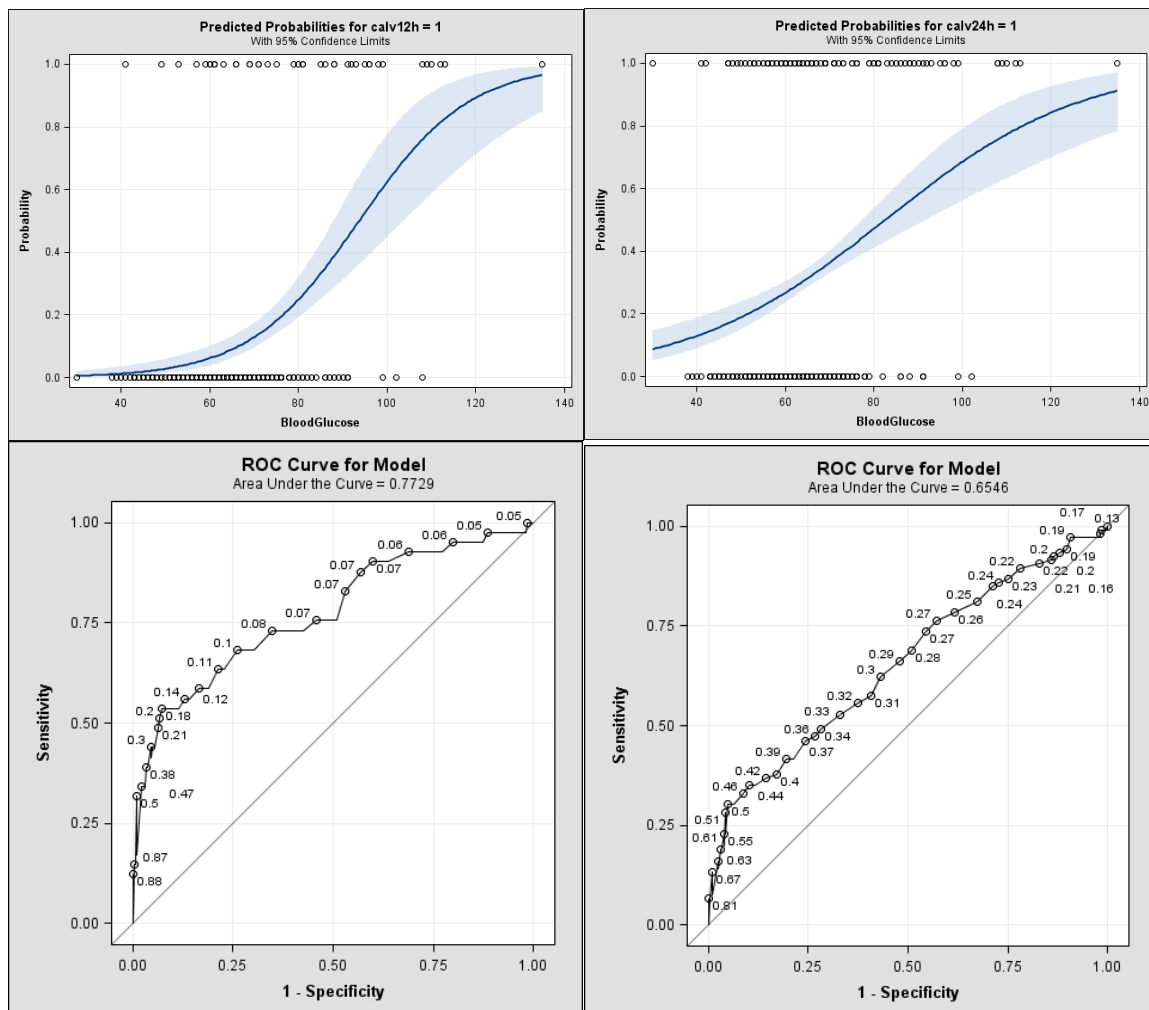


Figure 5.3 Binary logistic regression plot (top panel) of the relationship between the probability of parturition within 12 h (top left panel) or 24 h (top right panel) and blood glucose concentration (mg/dL) in 34 primiparous and 72 multiparous late gestation Holstein-Friesian cattle. The thick solid line is the logistic regression line and the shaded area represents the 95% confidence interval for the predicted probability. The open circles represent the blood glucose concentration for cattle that calved ($P = 1.00$) or did not calve ($P = 0.00$) within 12 h or 24 h. The bottom panels represent the receiver-operating characteristic (ROC) curves for blood glucose concentration as a predictor of parturition within 12 h (bottom left panel) or 24 h (bottom right panel). The diagonal thin line is the line of chance (no predictive ability). The optimal cutpoint for predicting parturition within 12 h was blood glucose concentration > 73 mg/dL (area under the ROC curve = 0.77; Se = 0.54; Sp = 0.92), equivalent to $P = 0.16$ for the logistic regression equation. The optimal cutpoint for predicting parturition within 24 h was blood glucose concentration > 80 mg/dL (area under the ROC curve = 0.65; Se = 0.30; Sp = 0.94), equivalent to $P = 0.48$ for the logistic regression equation.

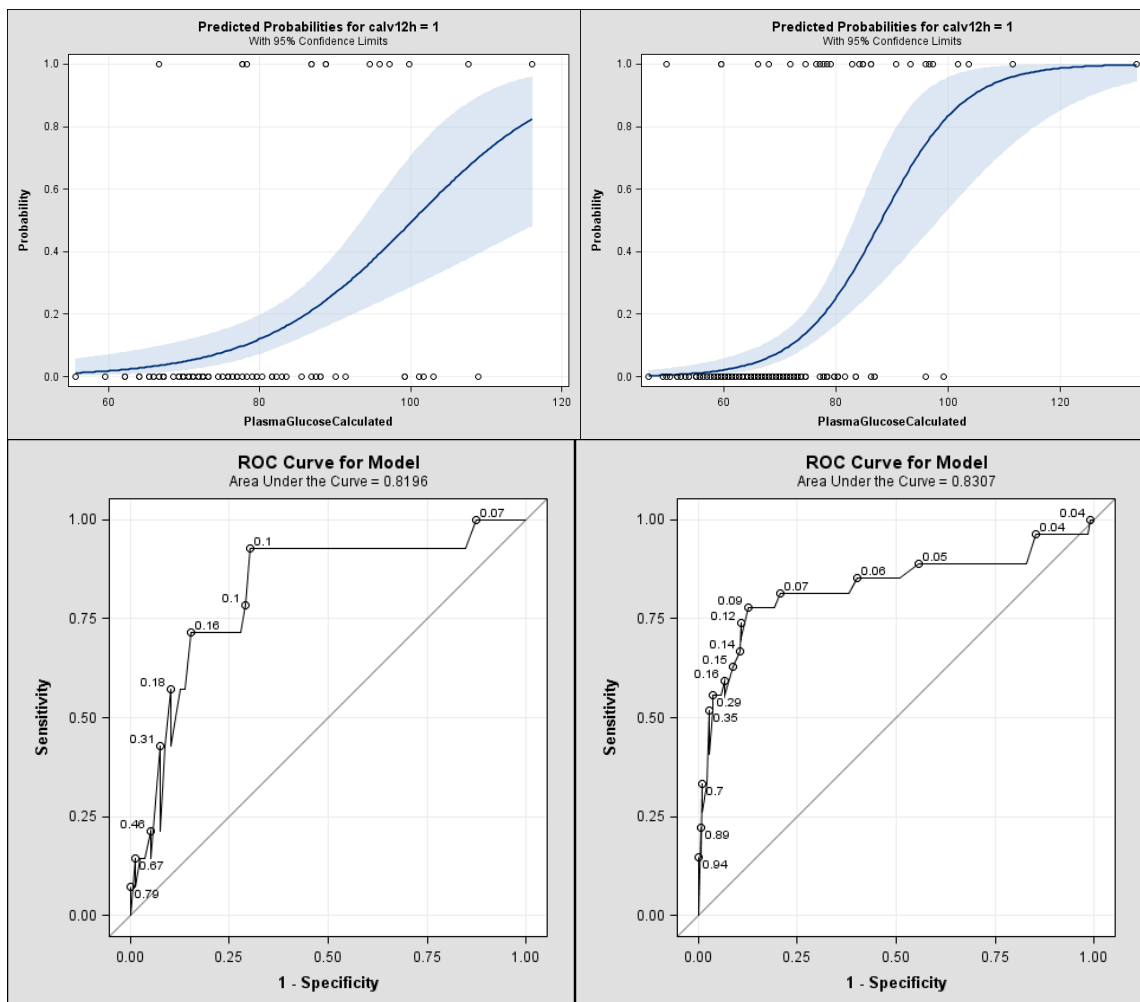


Figure 5.4 Binary logistic regression plot (top panels) of the relationship between the probability of parturition within 12 h and plasma glucose concentration (mg/dL) in 34 primiparous (left panel) and 72 multiparous (right panel) late gestation Holstein-Friesian cattle. The thick solid line is the logistic regression line and the shaded area represents the 95% confidence interval for the predicted probability. The open circles represent the plasma glucose concentration for cattle that calved ($P = 1.00$) or did not calve ($P = 0.00$) within 12 h. The bottom panels (left = primiparous, right = multiparous) represents the receiver-operating characteristic (ROC) curve for plasma glucose concentration as a predictor of parturition within 12 h. The diagonal thin line is the line of chance (no predictive ability). The optimal cutpoint for predicting parturition in primiparous cattle within 12 h was plasma glucose concentration > 82 mg/dL (area under the ROC curve = 0.82; Se = 0.71; Sp = 0.84), equivalent to $P = 0.14$ for the logistic regression equation. The optimal cutpoint for predicting parturition in multiparous cattle within 12 h was plasma glucose concentration > 72 mg/dL (area under the ROC curve = 0.83; Se = 0.74; Sp = 0.89), equivalent to $P = 0.10$ for the logistic regression equation.

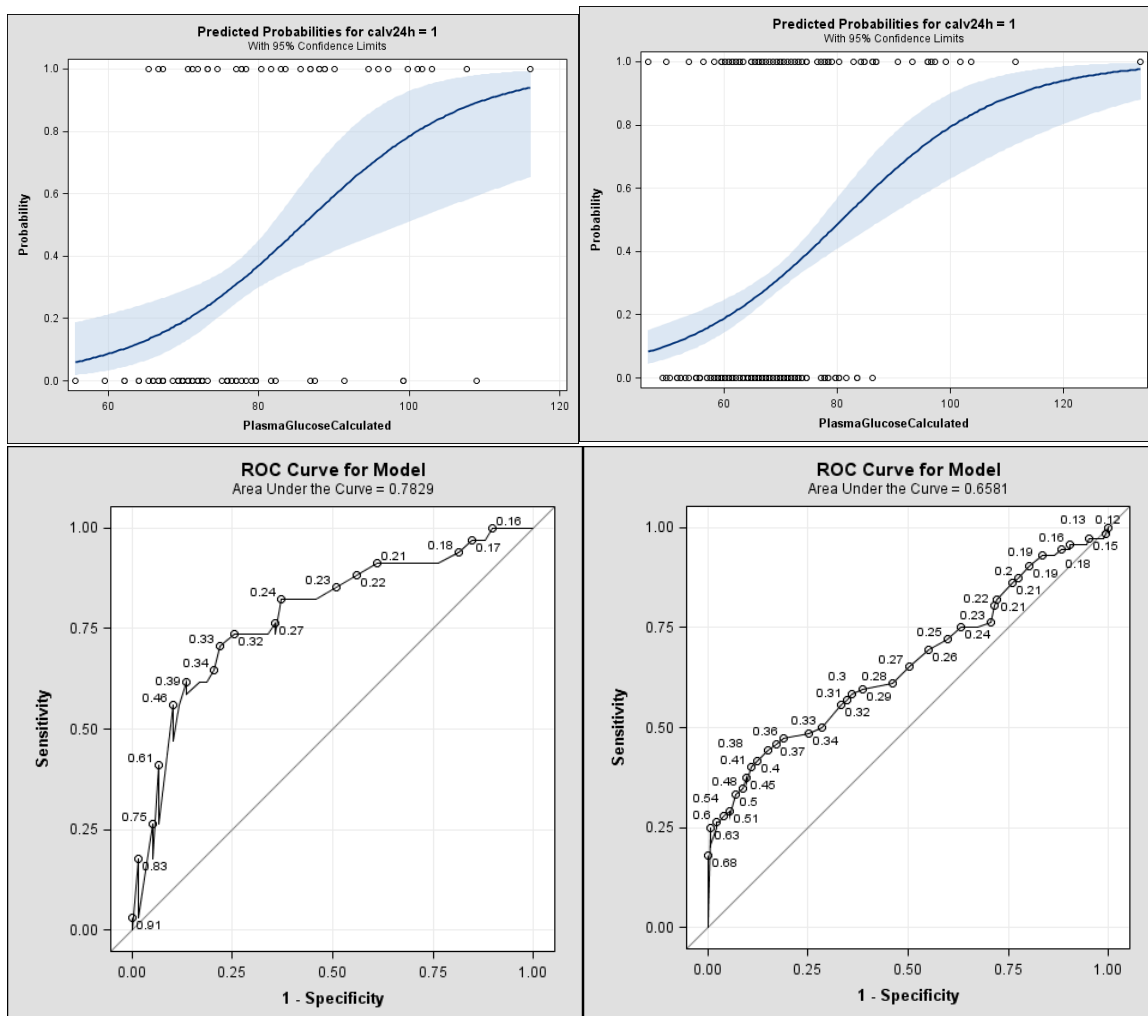


Figure 5.5 : Binary logistic regression plot (top panels) of the relationship between the probability of parturition within 24 h and plasma glucose concentration (mg/dL) in 34 primiparous (left panel) and 72 multiparous (right panel) late gestation Holstein-Friesian cattle. The thick solid line is the logistic regression line and the shaded area represents the 95% confidence interval for the predicted probability. The open circles represent the plasma glucose concentration for cattle that calved ($P = 1.00$) or did not calve ($P = 0.00$) within 24 h. The bottom panels (left = primiparous, right = multiparous) represents the receiver-operating characteristic (ROC) curve for plasma glucose concentration as a predictor of parturition within 24 h. The diagonal thin line is the line of chance (no predictive ability). The optimal cutpoint for predicting parturition in primiparous cattle within 24 h was plasma glucose concentration > 81 mg/dL (area under the ROC curve = 0.78; Se = 0.62; Sp = 0.86), equivalent to $P = 0.38$ for the logistic regression equation. The optimal cutpoint for predicting parturition in multiparous cattle within 24 h was plasma glucose concentration > 75 mg/dL (area under the ROC curve = 0.66; Se = 0.40; Sp = 0.89), equivalent to $P = 0.40$ for the logistic regression equation.

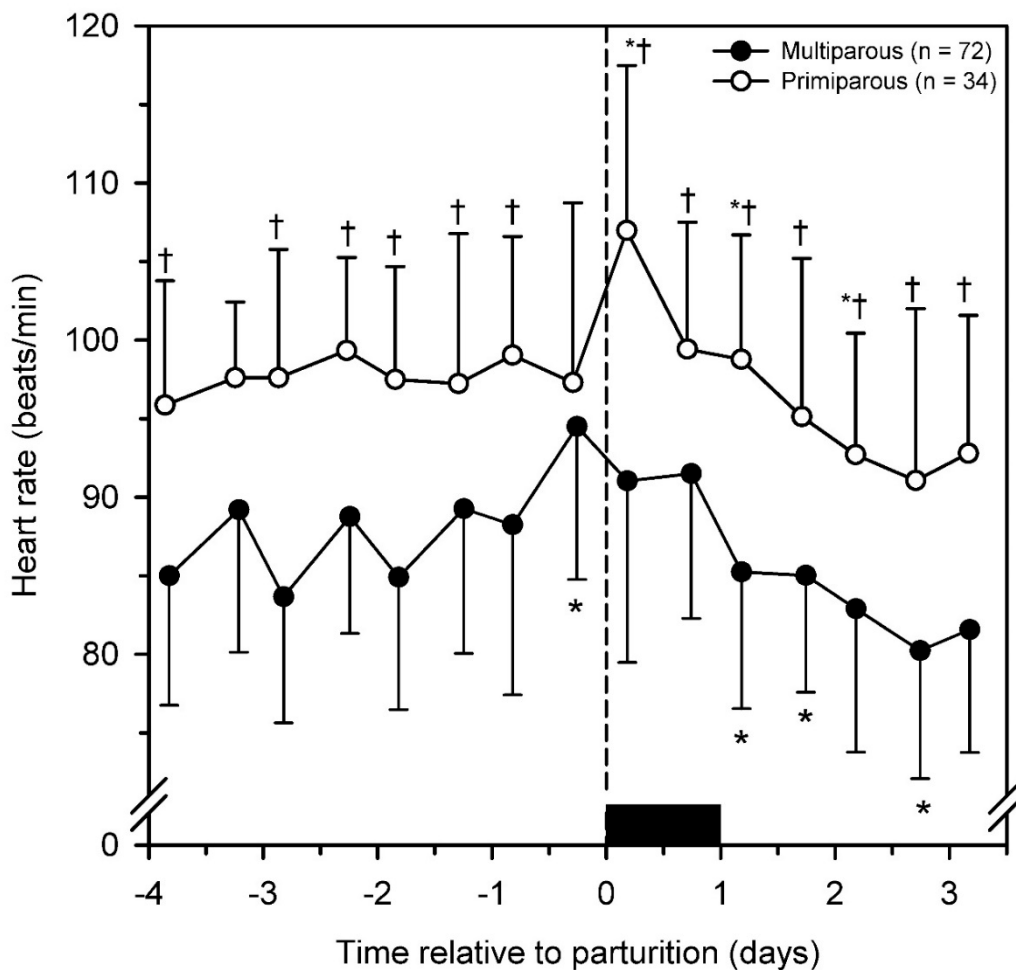


Figure 5.6 Mean heart rate (beats/min) for primiparous (open circles) and multiparous (filled circles) Holstein-Friesian cattle at 12 h intervals from 4 days prepartum to 3 days postpartum. Time is expressed as the geometric mean value which represents the time that data was recorded for each 12 h interval. The black rectangle is the 24 h period during which all cows calved. Data is presented as mean \pm SD. * $P < 0.0038$ (Bonferroni adjusted) compared to the value obtained 24 h previously. † $P < 0.0033$ (Bonferroni adjusted) compared to the value for multiparous cattle at the same time.

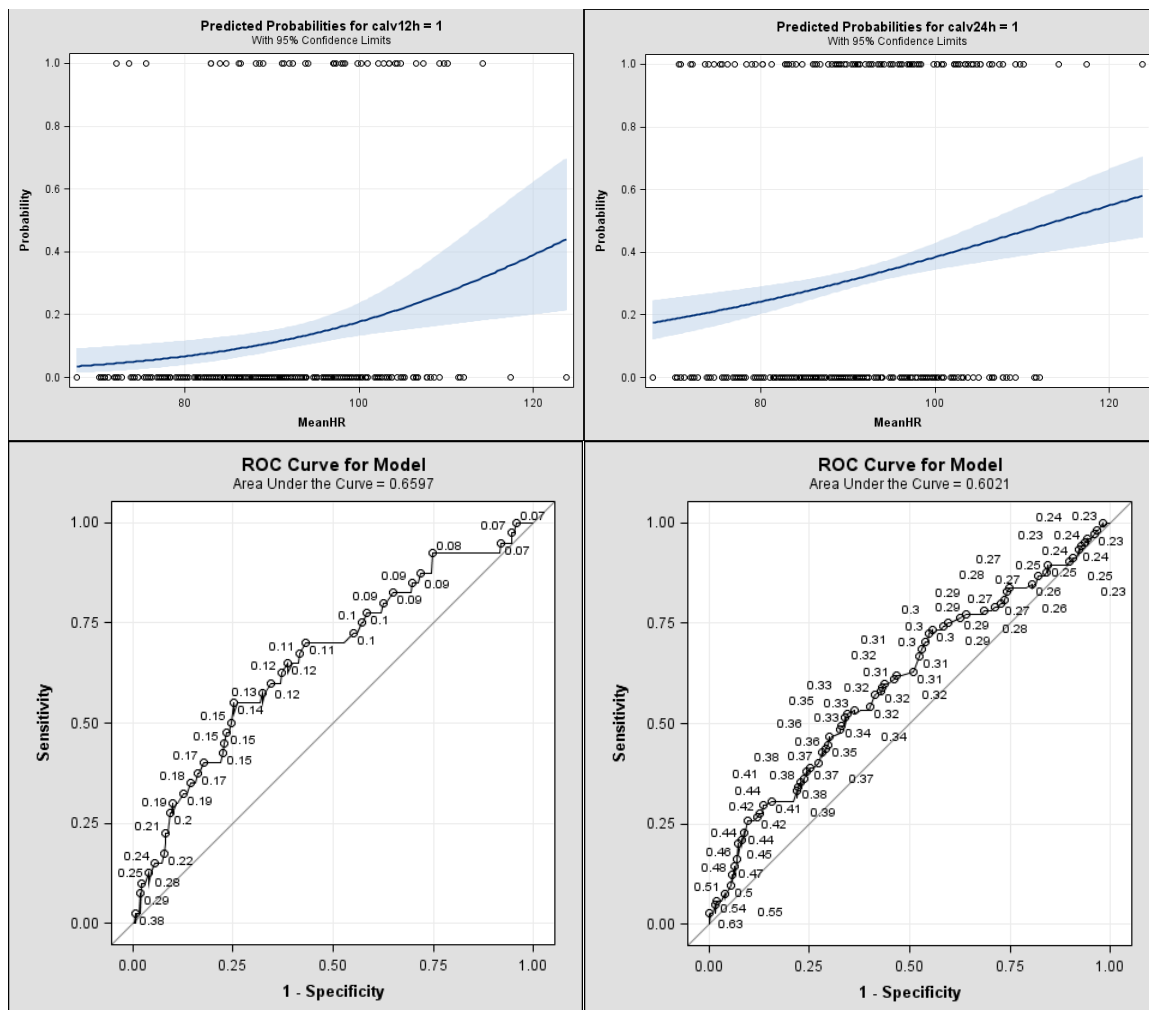


Figure 5.7 : Binary logistic regression plot (top panels) of the relationship between the probability of parturition within 12 h (left panel) and 24 h (right panel) and heart rate (beats/min) in 34 primiparous and 72 multiparous late gestation Holstein-Friesian cattle. The thick solid line is the logistic regression line and the shaded area represents the 95% confidence interval for the predicted probability. The open circles represent the heart rate for cattle that calved ($P = 1.00$) or did not calve ($P = 0.00$) within 12 h or 24 h. The bottom panels (left = 12 h, right = 24 h) represents the receiver-operating characteristic (ROC) curve for heart rate as a predictor of parturition. The diagonal thin line is the line of chance (no predictive ability). The optimal cutpoint for predicting parturition within 12 h was heart rate > 96 beats/min (area under the ROC curve = 0.66; Se = 0.55; Sp = 0.73), equivalent to $P = 0.14$ for the logistic regression equation. The optimal cutpoint for predicting parturition within 24 h was heart rate > 95 beats/min (area under the ROC curve = 0.60; Se = 0.48; Sp = 0.67), equivalent to $P = 0.34$ for the logistic regression equation.

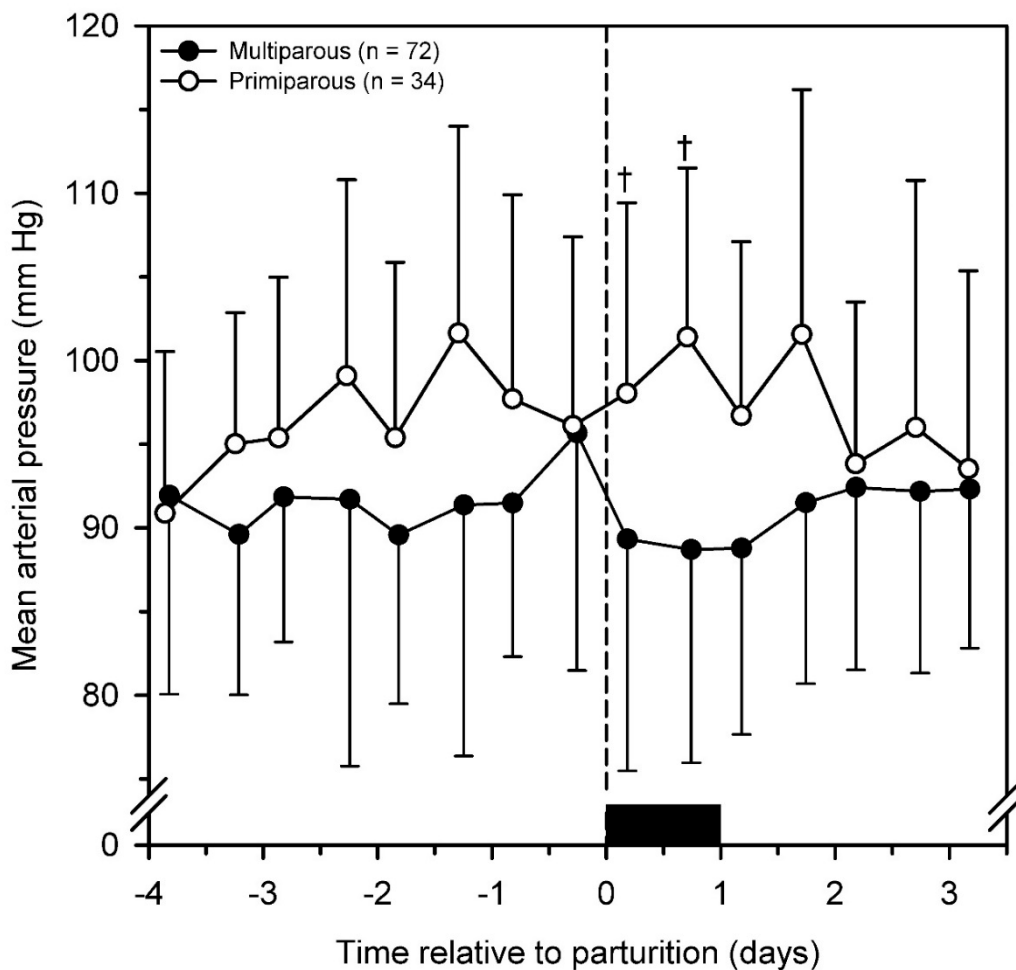


Figure 5.8 Mean arterial pressure (mmHg) for primiparous (open circles) and multiparous (filled circles) Holstein-Friesian cattle at 12 h intervals from 4 days prepartum to 3 days postpartum. Time is expressed as the geometric mean value which represents the time that data was recorded for each 12 h interval. The black rectangle is the 24 h period during which all cows calved. Data is presented as mean \pm SD. †P < 0.0033 (Bonferroni adjusted) compared to the value for multiparous cattle at the same time.

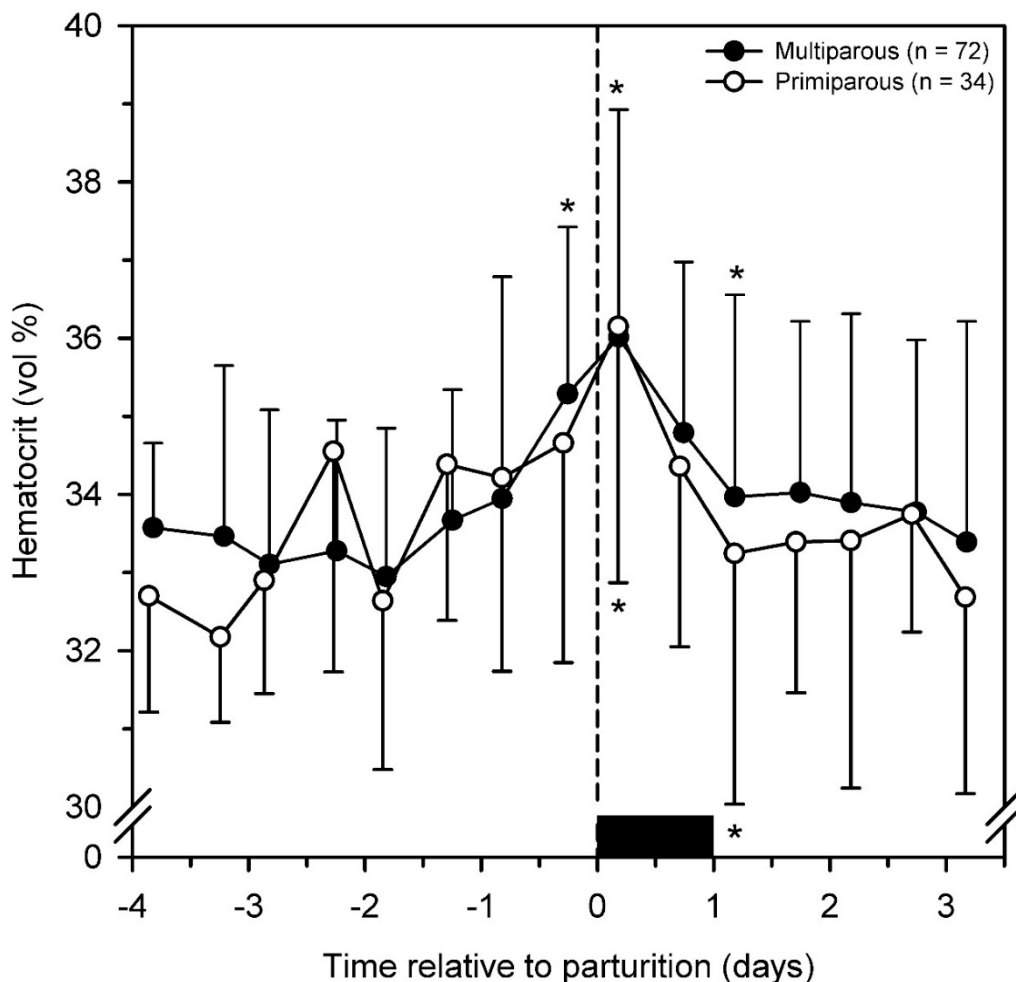


Figure 5.9 Hematocrit (vol %) for primiparous (open circles) and multiparous (filled circles) Holstein-Friesian cattle at 12 h intervals from 4 days prepartum to 3 days postpartum. Time is expressed as the geometric mean value which represents the time that data was recorded for each 12 h interval. The black rectangle is the 24 h period during which all cows calved. Data is presented as mean \pm SD. * $P < 0.0038$ (Bonferroni adjusted) compared to the value obtained 24 h previously.

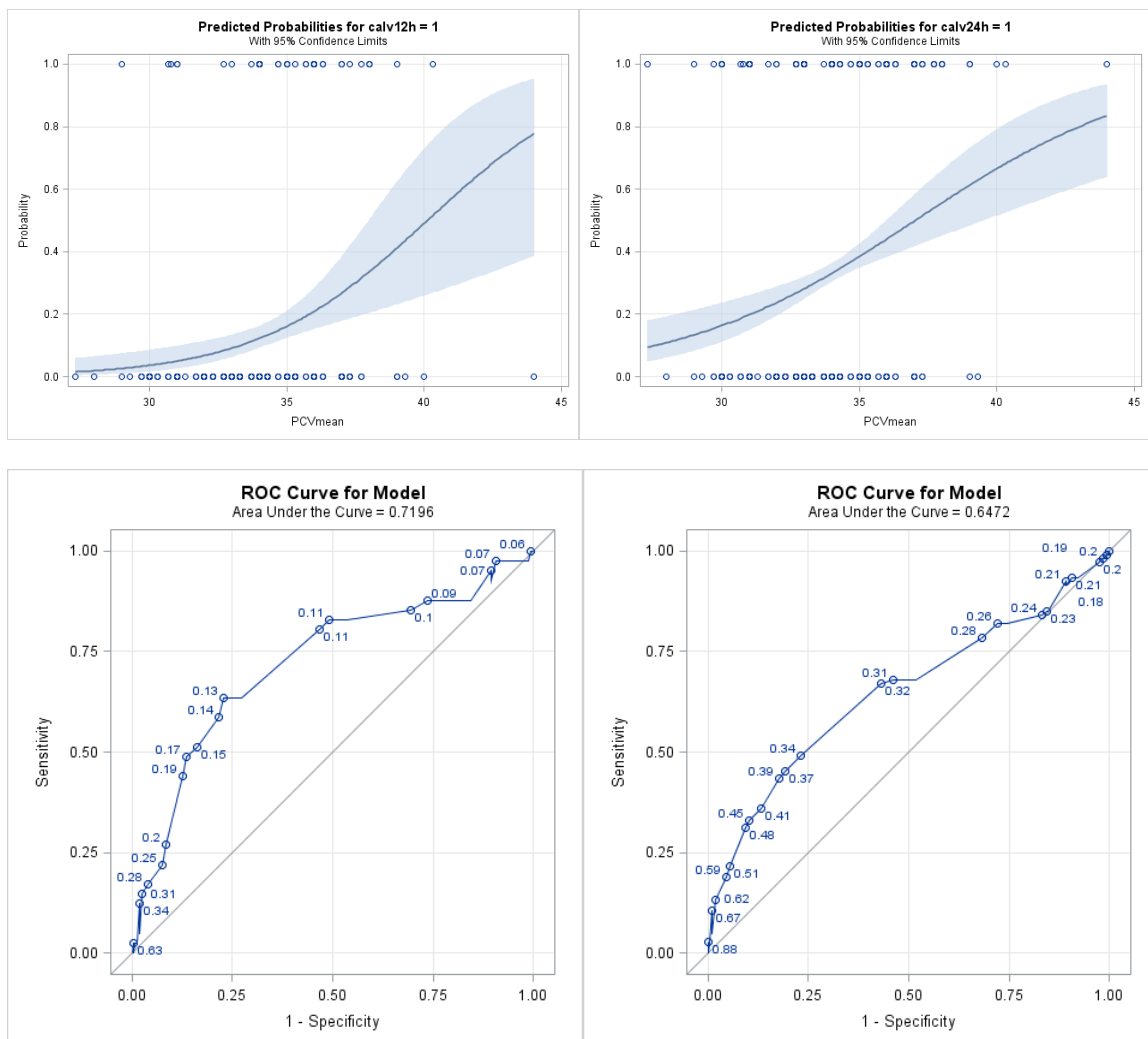


Figure 5.10 Binary logistic regression plot (top panels) of the relationship between the probability of parturition within 12 h (left panel) and 24 h (right panel) and hematocrit (vol %) in 34 primiparous and 72 multiparous late gestation Holstein-Friesian cattle. The thick solid line is the logistic regression line and the shaded area represents the 95% confidence interval for the predicted probability. The open circles represent the mean arterial pressure for cattle that calved ($P = 1.00$) or did not calve ($P = 0.00$) within 12 h or 24 h. The bottom panels (left = 12 h, right = 24 h) represents the receiver-operating characteristic (ROC) curve for hematocrit as a predictor of parturition. The diagonal thin line is the line of chance (no predictive ability). The optimal cutpoint for predicting parturition within 12 h was hematocrit > 34 vol % (area under the ROC curve = 0.72; Se = 0.63; Sp = 0.77), equivalent to $P = 0.13$ for the logistic regression equation. The optimal cutpoint for predicting parturition within 24 h was hematocrit > 35 vol % (area under the ROC curve = 0.65; Se = 0.45; Sp = 0.82), equivalent to $P = 0.36$ for the logistic regression equation.

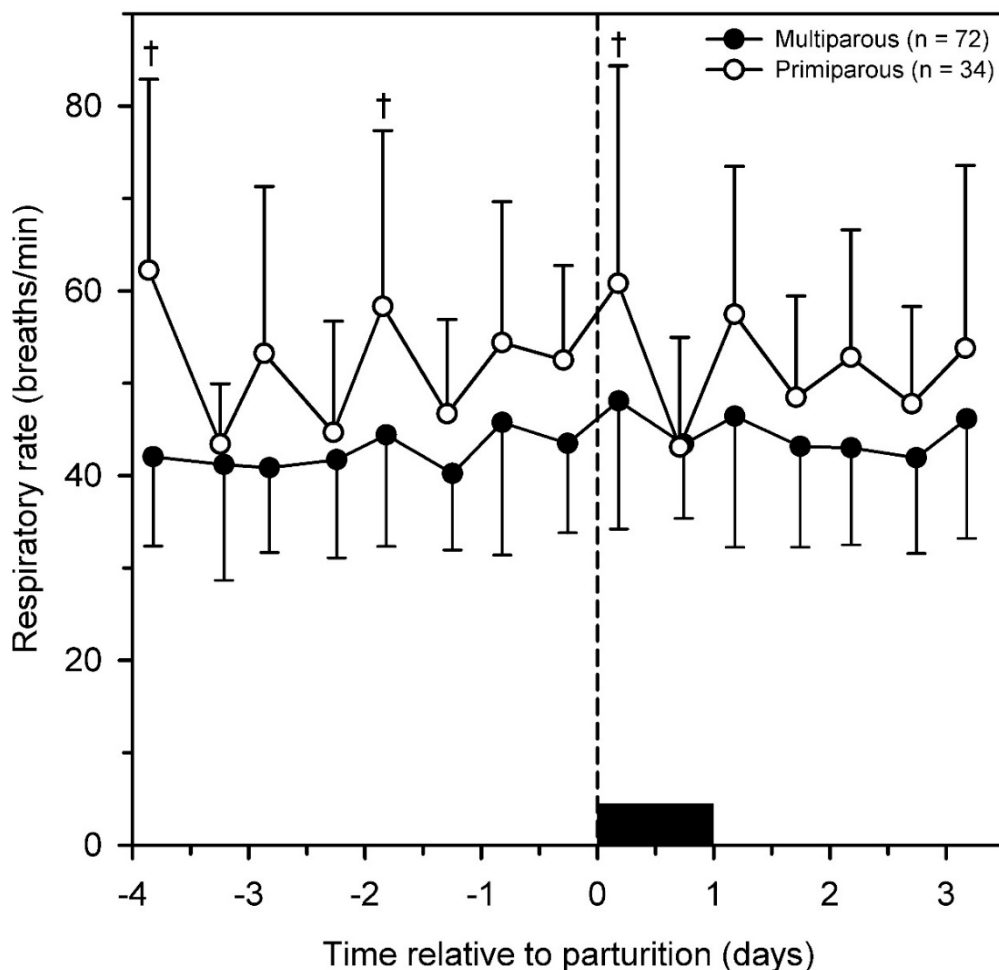


Figure 5.11 Respiratory rate (breaths/min) for primiparous (open circles) and multiparous (filled circles) Holstein-Friesian cattle at 12 h intervals from 4 days prepartum to 3 days postpartum. Time is expressed as the geometric mean value which represents the time that data was recorded for each 12 h interval. The black rectangle is the 24 h period during which all cows calved. Data is presented as mean \pm SD. $\dagger P < 0.0033$ (Bonferroni adjusted) compared to the value for multiparous cattle at the same time.

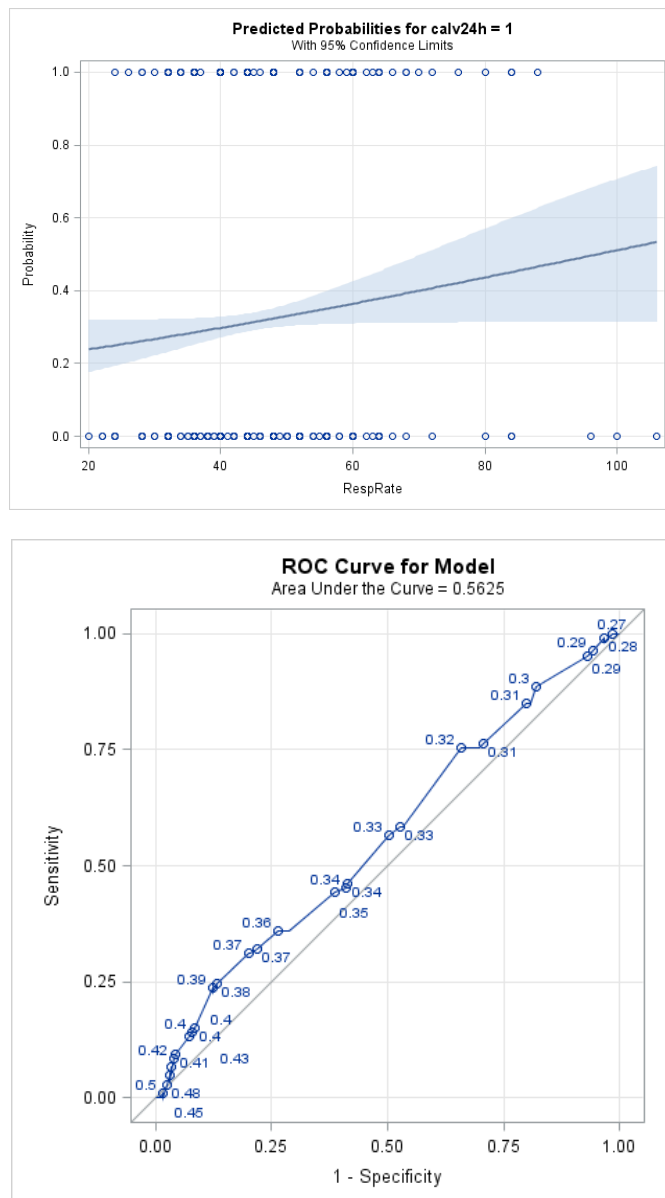


Figure 5.12 Binary logistic regression plot (top panel) of the relationship between the probability of parturition within 24 h and respiratory rate (breaths/min) in 34 primiparous and 72 multiparous late gestation Holstein-Friesian cattle. The thick solid line is the logistic regression line and the shaded area represents the 95% confidence interval for the predicted probability. The open circles represent the respiratory rate for cattle that calved ($P = 1.00$) or did not calve ($P = 0.00$) within 24 h. The bottom panel represents the receiver-operating characteristic (ROC) curve for respiratory rate as a predictor of parturition within 24 h. The diagonal thin line is the line of chance (no predictive ability). An optimal cutpoint for predicting parturition within 24 h could not be determined because the area under the ROC curve (0.56) was not significantly greater than 0.50

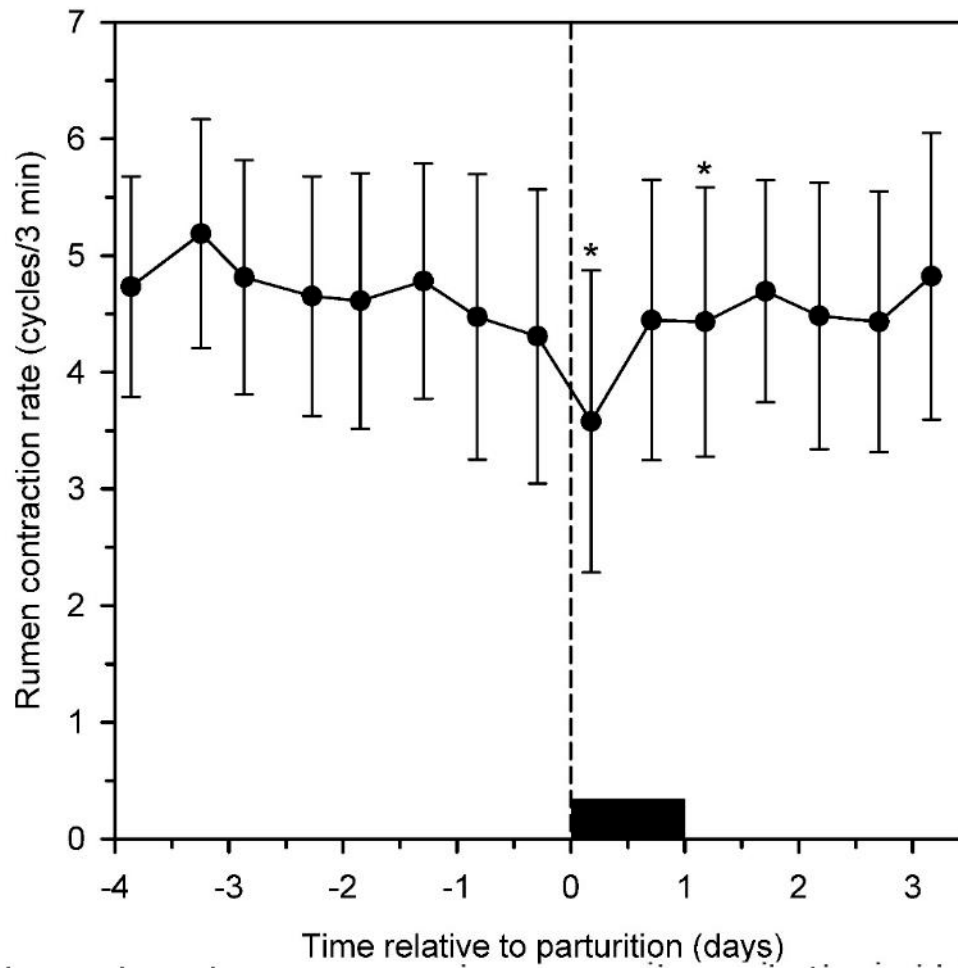


Figure 5.13 Rumen contraction rate (over 3 minutes) for 106 late gestation Holstein-Friesian cattle at 12 hour intervals from 4 days prepartum to 3 days postpartum. Data is presented as mean \pm SD. *P < 0.05 compared to values obtained 24 h previously.

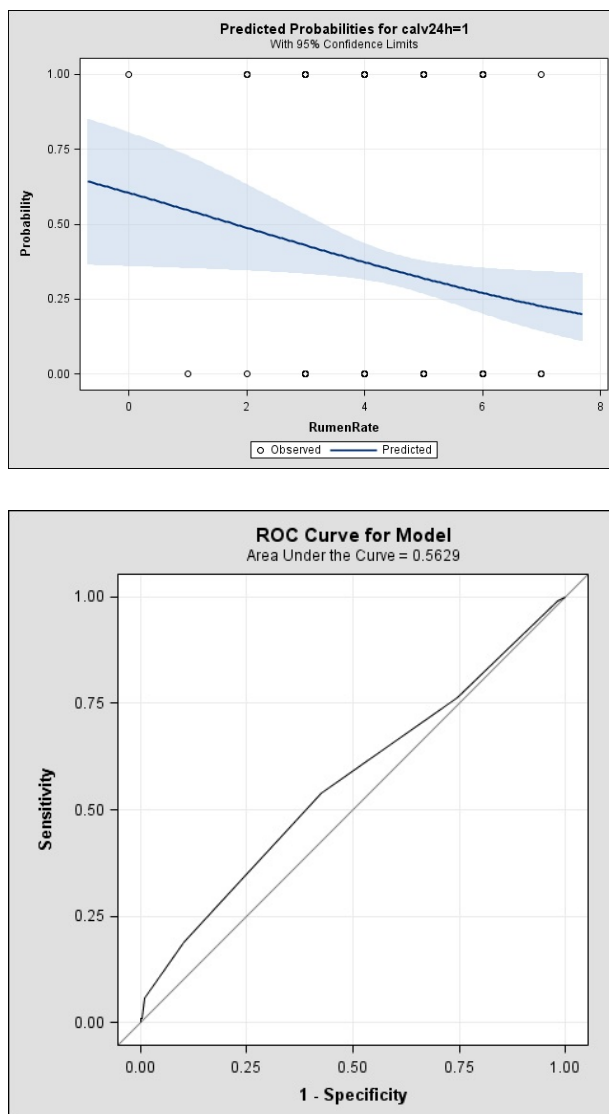


Figure 5.14 Binary logistic regression plot (top panel) of the relationship between probability of parturition within 24 hours and rumen contraction rate (over 3 minutes) in 106 late gestation Holstein-Friesian cattle. The thick solid line is the logistic regression line and the shaded area represents the 95% confidence interval for the predicted probability. The open circles represent the rumen contraction rate of cattle that calved ($P = 1.00$) or did not calve ($P = 0.00$) within 24 h (many data points are superimposed). The bottom panel represents the receiver-operating characteristic curve for rumen contraction rate used to predict parturition in Holstein-Friesian cattle. The diagonal thin line is the line of chance (no predictive ability). The optimal cutpoint for prediction of parturition occurred at < 4.2 rumen contractions (area under the ROC curve = 0.56; Se = 0.54; Sp = 0.58), equivalent to $P = 0.34$ for the logistic regression equation.

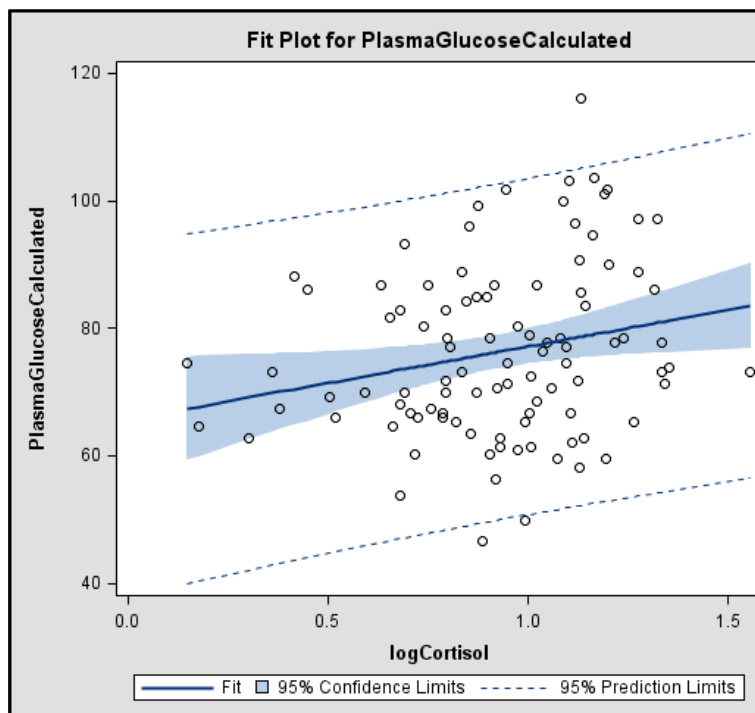


Figure 5.15 Scatterplot and linear regression analysis of the relationship between plasma glucose concentration (mg/dL) and \log_{10} (plasma cortisol concentration) in 32 primiparous and 67 multiparous late gestation Holstein-Friesian cattle. The thick solid line is the linear regression line and the shaded area represents the 95% confidence interval for the predicted line. Plasma glucose concentration was positively and linearly associated with \log_{10} (plasma cortisol concentration)

CHAPTER 6. CLINICAL PRESENTATION AND OUTCOME OF BEEF CATTLE UNDERGOING CESAREAN SECTION DUE TO DYSTOCIA: 173 CASES (2001-2010)

Abstract

Cesarean section is indicated for cattle with dystocia when assisted vaginal delivery and fetotomy are not viable options. This retrospective study aimed to characterize the signalment, history, fetal presentation, surgical management, and hospital discharge status of beef cattle undergoing cesarean section at a teaching hospital. Medical records of 173 beef cattle were reviewed and information on signalment, history, cause of dystocia, fetal presentation, anesthetic protocol, surgical management, number, sex, and weight of calves delivered (alive or dead), perioperative treatment, length of hospitalization, and discharge status were obtained. Male calves and calves that were born to dams with prolonged times between the first signs of labor and admittance into the teaching hospital had increased calf mortality. Numerically, calves with heavier birth weights and those born to primiparous cattle had increased mortality. Primiparous cattle bearing bull calves and bred to high birth weight EPD bulls should be observed closely at the time of parturition and early intervention should be done if dystocia is suspected. Cesarean section is a useful method to resolve dystocia as it has a high dam survivability.

Introduction

The incidence of dystocia in dairy cattle that requires mechanical extraction or surgical correction is 6.8% in heifers and 3.5% in cows (NAHMS 2009a). In comparison, fewer beef heifers and cows required assistance (3.9% and 1.1% respectively) via forced extraction or cesarean section (NAHMS 2009b). Cesarean section is indicated for dystocic cows when assisted vaginal delivery is ineffective and fetotomy is not an option. The incidence of cesarean section is associated with a number of risk factors including first parity, under 730 days of age at first calving, single male calf, long gestation period, long interval between first service and conception, long dry period, and having a previous cesarean section (Barkema, Schukken et al. 1992).

A variety of surgical techniques have been described to perform a cesarean section in cattle (Campbell and Fubini 1990, Parish, Tyler et al. 1995, Newman and Anderson 2005, Newman 2008, Vermunt 2008, Baird 2013). However, information relating to the outcomes of surgery in a teaching hospital setting has not been reported. The primary objective of this study was to characterize the signalment, history, presenting signs, fetal presentation, surgical management, and hospital discharge status of cattle undergoing cesarean section at a referral hospital. From this information we anticipated that factors associated with an unfavorable outcome to the fetus or dam would be identified.

Materials and methods

Criteria for inclusion of cases

The medical records of female cattle admitted to the Veterinary Teaching Hospital at Purdue University from January 2001 to December 2010 for treatment of dystocia were reviewed. Data was extracted from the medical records of beef cattle that underwent cesarean section for treatment of dystocia.

Medical record review

Information retrieved from the medical records from 2000 to 2010 included signalment, history, cause of dystocia, fetal presentation, anesthetic protocol, surgical management, number, sex, and weight of calves delivered (alive or dead), perioperative treatment, postoperative complications, and length of hospitalization. If the number of calves born was not recorded, it was assumed that a singleton was born. Information related to status at discharge from the hospital was also retrieved.

Reproductive examination

A standard method of examination was utilized for all cases. The dam was restrained in a chute and prepared for a vaginal examination in order to determine if vaginal delivery was possible. The perineal and vulval region was prepared with a surgical scrub using a warm povidone-iodine solution. A vaginal examination was then performed using a lubricated sterile obstetrical sleeve. A low epidural at the first intercoccygeal space was administered using 3 to 5 mL of 2% lidocaine in cattle that strained excessively. During the examination, the vaginal wall, cervical dilatation, size of the pelvis in relation to the fetus, presentation, position and posture of the fetus, and fetal viability (retraction of limb or suckle reflex) were evaluated. Palpation per rectum was not typically performed. Vaginal delivery was usually attempted unless an elective cesarean section was requested by the client or vaginal delivery had already been attempted by the referring veterinarian prior to presentation. When vaginal delivery was deemed not prudent, the dam was then prepared for a cesarean section.

Statistical Analyses

Data was expressed as median and range or mean \pm SD (standard deviation) and $P < 0.05$ was considered significant. The primary variables of interest were calf survival and dam survival. Continuous variables for the two survival categories were compared using the Mann-Whitney U test. Categorical variables for the two survival categories were

compared using Chi-square test; Fisher's exact test was used whenever the expected cell count was less than 5 in > 20% of the cells. A software program, SPSS version 22 (SPSS Inc., Chicago, IL), was used for statistical analysis.

Results

Animals

A total of 303 cattle were admitted over the 10 year study period for correction of dystocia. Of these 303 cattle, 173 (57.1%) beef cattle underwent cesarean section, comprising of 62 beef cross-breds (35.8%), 31 Aberdeen-Angus (17.9%), 29 Shorthorn (16.8%), 20 Hereford (11.5%), 13 Simmental (7.5%), 12 Maine-Anjou (6.9%), 3 Charolais (1.7%) as well as 1 each of Chianina (0.6%), Longhorn (0.6%), and Limousin (0.6%).

The median age of the cattle that underwent cesarean section was 29 months (2.4 years; range 13 to 148 months). Parity was recorded in 113 animals and consisted of 85 (75.2%) primiparous and 28 (24.8%) multiparous cattle. Of the multiparous cattle, 7 (6.2%) were 2nd parity, 7 (6.2%) were 3rd, 4 (3.5%) were 4th, 3 (2.7%) were 5th, and 5 (6.0%) were 6th or more. The median body condition score (on a scale of 1 to 9) for 100 animals was 5 (range 3 to 9). For 28 dams, 9 (34.6%) were pregnant to artificial insemination, 9 (34.6%) to embryo transfer, and 8 (30.8%) via natural service.

History

Information on the onset of dystocia to admission into the teaching hospital was available for 64 animals. Thirty-two (50.0%) had been in labor for < 3 h, 17 (26.6%) for > 3 to 6 h, 2 (3.1%) for > 6 to 9 h, 2 (3.1%) for >9 to 12 h, and 11 (17.2%) for more than 12 h.

Cesarean sections were mostly (53.2%) performed after normal hospital hours (between 17:00 and 08:00, and weekends). The indication for cesarean section was recorded for 155 cattle and included fetopelvic disproportion (n = 110, 71.0%),

malpresentation or malposition (n = 26, 16.8%), uterine torsion (n = 7, 4.5%), undilated cervix (n = 3, 1.9%), elective cesarean section (n = 3, 1.9%), schistosomus reflexus in the calf (n = 2, 1.3%), inadequate space due to twinning (n = 2, 1.3%), small vaginal tract (n = 1, 0.6%), and dead dam (n = 1, 0.6%) (Figure 6.1).

Peri-operative care of the dam

To reduce straining, 59 dams were administered a lidocaine epidural while 79 were not; the medical record did not comment on epidural administration in the remaining 35 animals. Antimicrobial administration was reported in 136 animals, which included ceftiofur sodium (n = 90 preoperative, n = 42 postoperative; 1.1 to 2.2 mg/kg [0.5 to 1.0 mg/lb], IM or SC q 24 h), ceftiofur crystalline free acid (n = 1 postoperative; 6.6 mg/kg [3.0 mg/lb], SC at base of ear), and procaine penicillin (n = 2 preoperative, n = 3 postoperative; 6000 i.u./kg [3000 i.u./lb], IM q24h). Flunixin meglumine (1.1 mg/kg [0.5 mg/lb], IV) was given to 113 dams either before or immediately after completion of the surgery.

Surgery

Regional anesthesia on the surgical site was reported in 137 cases and of these, 115 received one method of analgesia while 22 received a combination of two methods. Eighty-three (60.6%) animals received an inverted L block while 16 (11.7%) each received a paravertebral block, a line block, or a combination of a line block and a paravertebral block. Five (3.6%) cattle received a combination of an inverted L block and line block, while 1 animal (0.7%) received a combination of an inverted L block and a paravertebral block.

The left paralumbar fossa approach with the cow in a standing position was used in the majority of cases (n = 154, 89.0%). Other surgical methods used for cesarean section included ventral midline (n = 11, 6.4%), right paramedian (n = 3, 1.7%), and standing right paralumbar fossa (n = 3, 1.7%). Two (1.2%) dams had unrecorded surgical approaches.

Three major methods of uterine closure were employed depending on surgeon preference: a) single layer closure using a Utrecht pattern (n = 36, 22%) or a Lembert pattern (n = 1, 0.6%); b) two layer appositional and inverting pattern using a simple continuous then Cushing pattern (n = 5, 3.0%); simple interrupted sutures followed by a Cushing pattern (n = 1, 0.6%); and c) two layer inverting pattern such as a Lembert pattern then Cushing pattern (n = 98, 59.8%); Utrecht pattern then Cushing pattern (n = 9, 5.5%); a Lembert pattern followed by Utrecht pattern (n = 3, 1.8%); Cushing pattern then Lembert pattern (n = 2, 1.2%); Utrecht pattern then Lembert pattern (n = 1, 0.6%); two sequential Cushing patterns (n = 1, 0.6%]. The suture pattern used was not recorded in nine animals. From 161 reports that were recorded, the suture size and material used were 1 PDS® II (n = 155, 96.3%), 0 PDS®II (n = 2, 1.2%), 1 Vicryl® (n = 2, 1.2%), and 2 Vicryl®/Polysorb™ (n = 4, 2.4%) on swaged needles.

Fetal factors

Five pairs of twins were delivered (5.6%), producing a total of 178 calves from 173 cesarean sections. There were 49 (60.5%) right horn pregnancies and 32 (39.5%) left horn pregnancies from 81 recorded reports. There was a total of 113 records for calf sex and out of these, 88 (77.9%) were males (bull calves) and 25 (22.1%) were females (heifer calves).

The mean weight of 96 recorded calves was 106.4 ± 19.7 lb (range 57.0 – 170.0 lb). The mean weight of 64 recorded bull calves was 106.7 ± 19.0 lb (range 64.0 – 170.0 lb) and of 18 heifer calves was 104.4 ± 21.2 lb (range 57.0 – 137.0 lb). There was no significant difference ($P = 0.996$) between the birth weight of bull and heifer calves.

Post-operative management

One hundred animals were administered one or more doses of oxytocin (between 20 to 100 units, IM) post-operatively. Dams stayed for a median of 0 days (range 0 to 19) in the hospital before being discharged.

Calf and dam mortality

From the 168 available records of singleton births, 59.5% (n = 100) of the calves were alive when discharged from the hospital whereas 40.5% (n = 68) were born dead or died within 24 h of birth. When mortality within the sexes was observed from 113 records, a higher percentage (48.0%) of heifer calves were born dead or died within 24 h compared to 22.7% in bull calves. When compared between the sexes, there was significant difference between bull (n = 20) and heifer calf (n = 12) mortality (P = 0.013).

As for dams, 165 (95.4%) were alive while 8 (4.6%) were dead at the time of discharge. Post-operative complications were not documented because the majority of live dams were sent home immediately after surgery (n = 97, 58.8%).

From a total of 42 records, there were more dead calves born to primiparous cattle (n=32, 76.2%) than to multiparous cattle (n=10, 23.8%) but they did not show any significant difference (P = 0.96). There was a statistically significant association between the dystocia time and calf mortality (P < 0.001) when 62 records with both these parameters were analyzed. For dystocia times of < 3 h 24 calves were alive while 8 died, for > 3 to 6 h 6 were alive while 11 died, for 6 to 9 h 2 were alive while none died, and for > 12 h 8 died while 3 survived (Figure 6.2). There was no statistically significant association between dystocia times and dam mortality (P = 0.78).

No significant difference was observed in the survival of the calf (P = 0.75) or the dam (P = 0.36) between cesarean sections that were done during and those that were done after business hours. There was no significant difference (P = 0.73) in the weight of the calves that were alive (105.2 ± 16.0 lb) and dead (109.2 ± 26.3 lb) although they did differ numerically. Additionally, the horn of pregnancy also did not have a significant relationship (P = 0.263) with calf mortality.

Discussion

The major determinants of calf mortality in this study were the length of dystocia that was experienced by the dam and the gender of the calf. Numerically, calf mortality

increased when calves were born to primiparous cattle or had heavier birth weights. Overall calf survivability was low with 68 out of 168 (41%) calves born dead or died within 24 h of birth (one calf was euthanized due to multiple congenital defects).

In the present study, only 50% of animals were admitted into the hospital within 3 h of the onset of parturition. As the time of dystocia lengthened, the mortality of calves increased from the initial 25% (dystocia times of < 3 h) to 73% (dystocia times of > 12 h). The delay in admitting the dam to the hospital is highly influential on the outcome of surgery. It is essential for farm personnel to distinguish whether or when to intervene, how to intervene, and when to seek for veterinary assistance (Mee 2004). Timely intervention given to cattle in need can reduce the negative effects of dystocia on perinatal mortality (Johanson and Berger 2003, Schuenemann, Nieto et al. 2011). Regardless of the parity, it is suggested that personnel should assist cattle 70 minutes after the appearance of the amniotic sac or 65 minutes after feet appear outside the vulva. It is imperative that earlier obstetric intervention be given when an abnormal position or posture is seen immediately after the amniotic sac appears (Schuenemann, Nieto et al. 2011).

When analyzed within the gender, there was a higher death ratio in heifer calves than in their male counterparts and this finding is contrary to some studies (Chassagne, Barnouin et al. 1999, Mee, Berry et al. 2008). However, a study conducted in seven Midwestern states noted that large calves had greater mortality at first parity, and smaller calves at subsequent parities (Meyer, Berger et al. 2001). It was hypothesized that in later parities, the size of the birth canal is less limiting which gives preference to bigger and better developed calves. As most of the cattle presented were primiparous animals, this could be the reason as to why a higher death percentage was seen within the female calf group.

There were more dead calves delivered from primiparous compared to multiparous animals which was consistent with findings from other studies (Meyer, Berger et al. 2000, Mee, Berry et al. 2008) and this is once again related to the fetopelvic disproportion that is more common in primiparous animals (Nix, Spitzer et al. 1998,

Zhang, Nakao et al. 1999, NAHMS 2009a, NAHMS 2009b). Calves that were dead were found to weigh heavier than their live counterparts. Calf birth weight is one of the primary influencers of dystocia and the odds for dystocia increase by 13% per kg increase in birth weight (Johanson and Berger 2003). Heavier weights can also contribute to higher calving difficulties which may ultimately lead to higher perinatal mortality (Johanson and Berger 2003, Mee, Berry et al. 2008). It is also important that primiparous cattle be bred to bulls that have a low birth weight EPD (Expected Progeny Difference) to reduce the chances of the dam having large calves.

The incidence of cesarean section in beef cattle amongst all cattle admitted for dystocia at the teaching hospital was 57.1%. Dairy cattle were excluded in this study due to the small numbers that underwent surgery. More primiparous cattle (75.2%) underwent cesarean sections than their multiparous counterparts (25.8%) which showed that younger animals were more likely to need assistance at calving (Cattell and Dobson 1990, Meyer, Berger et al. 2001). Heifers have an odds ratio of 3.09 to undergo a cesarean section compared to older cows (Barkema, Schukken et al. 1992) and the former's smaller pelvic sizes increase their risk of dystocia at parturition (Bellows, Short et al. 1971, Price and Wiltbank 1978, Kolkman, Hoflack et al. 2009).

The main indication for cesarean section in beef cattle in this study was fetopelvic disproportion (Dawson and Murray 1992). The discrepancy between a large fetus and a small pelvic size leading to dystocia has been studied by various groups and inadequate pelvic area is correlated with dystocia in cattle (Mee 2008, Zaborski, Grzesiak et al. 2009).

Fetal malpresentation or malposition was the second highest cause of dystocia and this included fetuses that had a posterior or transverse presentation, dorsopubic position, malpositioned limbs, retroflexed head, or were breeched. Fetal malpresentation has been seen to have varying degrees of importance (from 0.9% to 20%) as a cause of dystocia (Philipsson 1976, Nix, Spitzer et al. 1998).

Uterine torsion was the third highest indication for cesarean sections (3.9%) in this study although it has been seen to occur in 5 to 10% of animals in a given study

population (Frazer, Perkins et al. 1996, Laven and Howe 2005). Underdiagnosis of this condition could be due to the infrequent rectal examinations performed when an animal is presented for dystocia as some cases of vaginal involvement are not evident even on speculum examination (Frazer, Perkins et al. 1996). Clinicians in our hospital routinely perform a vaginal examination in cattle with dystocia and rarely perform palpation per rectum. Of the uterine torsion cases, 62% needed a cesarean section (Frazer, Perkins et al. 1996) which indicates that surgery has a moderate likelihood to occur when one is presented with a torsed uterus. In a study done on 55 field cases in dairy cattle, multiparous cattle were at greater risk of uterine torsion (Aubry, Warnick et al. 2008) which may explain the reason for the low incidence in the present study due to more primiparous cattle being presented for dystocia.

Ceftiofur and procaine penicillin G were the antimicrobials of choice administered peri-operatively to the dams, with the overwhelming majority of animals receiving ceftiofur sodium (NAXCEL[®], Zoetis). Ceftiofur was selected based on clinician preference and its relatively short pre-slaughter withdrawal period (4 days for NAXCEL[®]) and zero milk withdrawal period (NAXCEL(R) 2006, EXCEDE(R) 2011); although the milk withdrawal time is not a relevant parameter for beef cattle. Procaine penicillin G has a pre-slaughter withdrawal period of 4 days and milk withdrawal period of 48 h. Antimicrobials are routinely recommended when cesarean sections are performed as peritonitis, incisional infection, and endometritis in association with retained placenta were regularly seen in animals that did not receive them (Brounts, Hawkins et al. 2004). Oxytetracycline is another antimicrobial that has been administered perioperatively in abdominal surgeries (Chicoine, Dowling et al. 2008). However, this drug has a pre-slaughter withdrawal period of 28 days and a milk withdrawal period of 96 h which does not make it a drug of choice in the teaching hospital.

Most practitioners prefer administering antimicrobials postoperatively although there is limited proof of its efficacy compared to a preoperative administration (Haven, Wichtel et al. 1992, Chicoine, Dowling et al. 2008) but protection against infection is deemed best when antimicrobials are present in tissues before microbial inoculation

happens (Gyssens 1999). There is no justification for antimicrobial use when clean operations are done under optimal aseptic conditions (Klein and Firth 1988) and antimicrobials should not be a crutch for poor aseptic technique.

Oxytocin was given postoperatively to aid uterine involution and placental passage (Beagley, Whitman et al. 2010). A dose as low as 30 IU of oxytocin, given immediately after calving and again 2 to 4 h later, has been observed to reduce the occurrence of retained placentas in cattle (Mollo, Veronesi et al. 1997) which negates the necessity for high doses. Not all dams were given oxytocin as they had live calves that suckled from them and this stimulated endogenous oxytocin release. The majority of dams (57.8%) were immediately discharged from the hospital after undergoing surgery as the clinician determined that there was no need for further post-operative monitoring.

The most common regional anesthesia technique administered was the inverted L block. It is a relatively simple technique that uses a local anesthetic agent (typically lidocaine) administered non-specifically in the form of an inverted L (caudal to the last rib and ventral to the transverse processes of the lumbar vertebrae) to block nerves that enter the surgical field (Mama 2013). Compared to other methods like the paravertebral block, the inverted L block is more technically straightforward, quicker, and involves less skill while still able to provide sufficient anesthesia and analgesia. This is especially important in emergency situations when surgical preparation time is kept to a minimum. This method however requires the use of larger amounts of anesthetic drugs and there is a tendency to infiltrate more local anesthetic than is needed in heavy muscled or fat beef cattle. Although to our knowledge there is no data on systemic lidocaine toxicity (Meyer, Kästner et al. 2010), an estimated maximal dose of 10 mg/kg (4.5 mg/lb) body weight has been proposed (Anderson and Edmondson 2013) and this should always be considered. With this threshold, the maximum safe dosage of 2% (20 mg/ml) lidocaine HCl for a 700 kg cow would be 350 ml (Anderson and Edmondson 2013). The paravertebral and line block were the second most used regional blocks. Paravertebral blocks were not as popular as inverted L blocks due to the requirement of

greater skill and the difficulty in locating anatomic structures (Skarda 1996) especially in fat or well-muscled beef cattle. The line block involves infusing local anesthetic into the incision site (Edmondson 2008) and in the teaching hospital some technicians and clinicians place this block behind the last rib to supplement the paravertebral block especially when left paralumbar flank approaches were incised more ventrally. A major disadvantage of the line block is that the anesthetic agent may delay incisional site healing due to myotoxicity (Hogan, Dotson et al. 1994) and inhibition of the first two stages of healing which are inflammatory and granulation/proliferation (Brower and Johnson 2003) as well as cause incisional edema and hematoma (Skarda 1996). However, in the teaching hospital line blocks were generally performed cranial to the incision site in order to block nerves proximal to the incision and wound healing was deemed to not be compromised in this case.

A caudal epidural block was given to 43% of cattle that had reports of being given local anesthesia. This block is recommended for cesarean sections as it eliminates straining (Frazer and Perkins 1995) and tenesmus (Mama 2013). This study saw the usage of 3 to 5 mL of local anesthetic for the epidural block which is a safe amount as only doses greater than 10 mL (in 450 kg cattle) can cause hindlimb incoordination and recumbency (Skarda 1996). However, 6 to 7 mL of lidocaine should be considered the maximal amount administered due to a high percentage of animals being recumbent when this dosage was exceeded (Horstman, personal communication).

The most common surgical approach in this study was via the left paralumbar fossa with the dam standing. This method requires minimal restraint and assistance because a chute with a head catch was all that was required. With this approach, the rumen prevents evisceration of the intestines during surgery (Noorsdy 1979) and the mammary veins are avoided. In cases where the fetus is of reasonable size, is alive or just died recently, this is a good method to employ (Noorsdy 1979). Most animals that are admitted with dystocia are generally in good condition and have the demeanor to go through a standing surgery. In the present study, the recumbent approach (ventral midline and right paramedian) was not commonly used and only considered when the

dam was recumbent, the fetus was dead, or the uterus was contaminated. One recumbent midline cesarean section was elected upon the request of the owner who had a bad experience with a flank incision that was performed at another practice. This ventral approach makes it easier for fetal and uterine debris to be evacuated, and minimizes spillage into the peritoneal cavity (Noorsdy 1979). Before the uterine incision is closed the entire uterus should be thoroughly examined to ensure that a twin fetus is not overlooked (Frazer and Perkins 1995).

The most common uterine closure method used was a Lembert pattern oversewn with a Cushing pattern which ensured an adequate inverting closure (Frazer and Perkins 1995). Two layer closures such as these are indicated whenever there is a risk of leakage or excessively contaminated uterine fluid (Kolkman, De Vlieghe et al. 2007). The Utrecht pattern was the second most common method of suturing used and was usually done when uterine tissue did not appear compromised and a one layer pattern was deemed sufficient. This technique was developed due to findings that adhesions frequently develop between the uterus and visceral organs and they start at the ends of the incision where knots were tied as well as wherever suture patterns were exposed. The usage of this pattern to close the uterus has been associated with improved fertility of the dam (Lyons, Karvountzis et al. 2013). Therefore, it is imperative to bury all knots (Kolkman, De Vlieghe et al. 2007, Baird 2013) within the suture line.

The most used suture type, was the 1 PDS®II (polydioxanone) suture (Ethicon®, Somerville, NJ, USA), while the others were 0 PDS®II, 1 Vicryl® (polyglactin 910; Ethicon®, Somerville, NJ, USA), and 2 Vicryl®/Polysorb™ (Covidien, New Haven, CT, USA). Both Vicryl® and Polysorb™ are made of polyglycolic acid and were analyzed under the same category. Catgut has been used frequently for uterine closure (Dawson and Murray 1992, Frazer and Perkins 1995, Baird 2013) but in the present study, synthetic suture material was preferred due to availability and surgeon preference. Synthetic absorbable monofilament sutures have been recommended to optimally avoid periuterine adhesions and reduce the potential risk concerned with transmissible spongiform encephalopathy when chromic catgut is used (Kolkman, De Vlieghe et al.

2007). Compared to catgut, polyglycolic acid sutures produce a milder inflammatory reaction but is more expensive and causes more drag due to its braided structure. However, there was no correlation between the presence of adhesions with the use of either polyglycolic acid or catgut (Mijten, de Kruif et al. 1997). Also, surgical skills and technique are important in cesarean sections as calf mortality has been seen to increase with longer surgery durations (Lyons, Karvountzis et al. 2013).

Generally beef herds have a lower twinning rate compared to dairy herds (Komisarek and Dorynek 2002). The twinning rate seen in this study (5.6%) was higher than the rate typically reported for beef cattle (0.4 to 4.6%) (Erdheim 1942, Rutledge 1975). The possible increased incidence of twinning observed in this study could be due to the fact that we did not observe whole herds but rather a selected group of cattle that were brought in with dystocia and this skewed the data towards a higher twinning rate. A higher percentage of bull calves, considered a risk factor for cesarean section compared to heifer calves (Barkema, Schukken et al. 1992), were delivered and their average weight was heavier than heifer calves. As calf sex and weight are related, both these factors influence dystocia (Laster, Glimp et al. 1973) and subsequently increase the number of cesarean sections performed. A much higher percent of right uterine horn pregnancies were observed in this study compared to the left horn and this is consistent with observations that the right ovary of cattle is functionally more active than the left (Reece and Turner 1938). On the other hand, another study (Giraldo, Hylan et al. 2010) noted that pregnancy rates were similar for left and right uterine horns.

A high percentage of dams that underwent cesarean section in the present study were alive at the time of discharge from the hospital (95%) which shows that this is an effective method of dealing with dystocia. This survival rate was higher when compared to previous findings of 86% for a live calf, 79% when the calf was dead, and 33% with an emphysematous fetus (Bouchard, Daignault et al. 1994). The relative high survivability may have been influenced by the surgeries being done in a teaching hospital setting due to there being more technically skilled staff is available and the relatively easier adherence to aseptic principles compared to field surgeries. Some key aspects that have

been seen to increase the 14 day survival rate of dams were the exteriorization of the uterus and removal of abdominal blood clots, the calf being female, the presence of fetopelvic disproportion, and the absence of retained placenta at 24 to 48 h post cesarean section (Lyons, Karvountzis et al. 2013).

A major limitation of this study was that only the status of the animal at discharge was evaluated and no follow up on the survivability, postoperative complications, and subsequent fertility of the dams was done. Additionally, a hospital based study is not representative of operations done in the field and the factor that different veterinary surgeons were involved in the cesarean sections was not taken into consideration. Finally, as can be seen in retrospective studies, loss of information due to inconsistent record keeping prevented this study from investigating all parameters for each patient.

Conclusion

Early intervention in dystocic cattle is recommended to decrease the incidence of perinatal mortality and reduce injury to the dam (Schuenemann, Nieto et al. 2011). Primiparous cattle bearing bull calves and bred to high birth weight EPD bulls should be observed closely at the time of parturition as they have higher chances of experiencing dystocia. Lastly, cesarean section is a useful method to resolve dystocia as could be observed from the high dam survivability.

References

- Anderson, D. E. and M. A. Edmondson (2013). "Prevention and Management of Surgical Pain in Cattle." Veterinary Clinics of North America: Food Animal Practice **29**(1): 157-184.
- Aubry, P., et al. (2008). "A study of 55 field cases of uterine torsion in dairy cattle." The Canadian Veterinary Journal **49**(4): 366-372.
- Baird, A. (2013). Bovine Urogenital Surgery. Turner and McIlwraith's Techniques in Large Animal Surgery, John Wiley & Sons, Inc.: 235-271.
- Barkema, H., et al. (1992). "Caesarean section in dairy cattle: A study of risk factors." Theriogenology **37**(2): 489-506.
- Beagley, J., et al. (2010). "Physiology and treatment of retained fetal membranes in cattle." Journal of Veterinary Internal Medicine **24**(2): 261-268.
- Bellows, R., et al. (1971). "Cause and effect relationships associated with calving difficulty and calf birth weight." Journal of Animal Science **33**(2): 407-415.
- Brounts, S. H., et al. (2004). "Outcome and subsequent fertility of sheep and goats undergoing cesarean section because of dystocia: 110 cases (1981-2001)." Journal of the American Veterinary Medical Association **224**(2): 275-281.
- Brower, M. C. and M. E. Johnson (2003). "Adverse effects of local anesthetic infiltration on wound healing." Regional Anesthesia and Pain Medicine **28**(3): 233-240.
- Campbell, M. and S. Fubini (1990). "Indications and surgical approaches for cesarean section in cattle." The Compendium on continuing education for the practicing veterinarian (USA) **12**(2): 285-291.
- Cattell, J. and H. Dobson (1990). "A survey of caesarean operations on cattle in general veterinary practice." The Veterinary Record **127**(16): 395-399.
- Chassagne, M., et al. (1999). "Risk factors for stillbirth in Holstein heifers under field conditions in France: a prospective survey." Theriogenology **51**(8): 1477-1488.
- Chicoine, A. L., et al. (2008). "A survey of antimicrobial use during bovine abdominal surgery by western Canadian veterinarians." The Canadian Veterinary Journal **49**(11): 1105-1109.
- Dawson, J. and R. Murray (1992). "Caesarean sections in cattle attended by a practice in Cheshire." The Veterinary Record **131**(23): 525-527.

Edmondson, M. A. (2008). "Local and regional anesthesia in cattle." Veterinary Clinics of North America: Food Animal Practice **24**(2): 211-226.

Erdheim, M. (1942). "The incidence of right and left horn pregnancies in dairy and beef cattle." Journal of the American Veterinary Medical Association **100**: 343-344.

EXCEDE(R) (2011). [package insert] Division of Pfizer Inc, New York, New York, Pharmacia & Upjohn Company.

Frazer, G., et al. (1996). "Bovine uterine torsion: 164 hospital referral cases." Theriogenology **46**(5): 739-758.

Frazer, G. S. and N. R. Perkins (1995). "Cesarean section." Veterinary Clinics of North America: Food Animal Practice **11**(1): 19-35.

Giraldo, A., et al. (2010). "Distribution of sexes within the left and right uterine horns of cattle." Theriogenology **73**(4): 496-500.

Gyssens, I. C. (1999). "Preventing postoperative infections." Drugs **57**(2): 175-185.

Haven, M., et al. (1992). "Effects of antibiotic prophylaxis on postoperative complications after rumenotomy in cattle." Journal of the American Veterinary Medical Association **200**(9): 1332-1335.

Hogan, Q., et al. (1994). "Local anesthetic myotoxicity: a case and review." Anesthesiology **80**(4): 942-947.

Johanson, J. and P. Berger (2003). "Birth weight as a predictor of calving ease and perinatal mortality in Holstein cattle." Journal of Dairy Science **86**(11): 3745-3755.

Klein, W. and E. Firth (1988). "Infection rates in clean surgical procedures with and without prophylactic antibiotics." The Veterinary Record **123**: 542-543.

Kolkman, I., et al. (2007). "Protocol of the caesarean section as performed in daily bovine practice in Belgium." Reproduction in Domestic Animals **42**(6): 583-589.

Kolkman, I., et al. (2009). "Evaluation of the Rice pelvimeter for measuring pelvic area in double muscled Belgian Blue cows." Livestock Science **121**(2): 259-266.

Komisarek, J. and Z. Dorynek (2002). "Genetic aspects of twinning in cattle." Journal of Applied Genetics **43**(1): 55-68.

Laster, D. B., et al. (1973). "Factors affecting dystocia and the effects of dystocia on subsequent reproduction in beef cattle." Journal of Animal Science **36**(4): 695-705.

Laven, R. and M. Howe (2005). "Uterine torsion in cattle in the UK." Veterinary Record **157**(3): 96.

Lyons, N. A., et al. (2013). "Aspects of bovine caesarean section associated with calf mortality, dam survival and subsequent fertility." The Veterinary Journal **197**(2): 342-350.

Mama, K. (2013). Anesthesia and fluid therapy. Turner and Mcllwraith's Techniques in Large Animal Surgery, John Wiley & Sons, Inc.: 7-31.

Mee, J. (2008). "Prevalence and risk factors for dystocia in dairy cattle: A review." The Veterinary Journal **176**(1): 93-101.

Mee, J. F. (2004). "Managing the dairy cow at calving time." Veterinary Clinics of North America: Food Animal Practice **20**(3): 521-546.

Mee, J. F., et al. (2008). "Prevalence of, and risk factors associated with, perinatal calf mortality in pasture-based Holstein-Friesian cows." Animal **2**(4): 613-620.

Meyer, C., et al. (2000). "Interactions among factors affecting stillbirths in Holstein cattle in the United States." Journal of Dairy Science **83**(11): 2657-2663.

Meyer, C. L., et al. (2001). "Phenotypic trends in incidence of stillbirth for Holsteins in the United States." Journal of Dairy Science **84**(2): 515-523.

Meyer, H., et al. (2010). "Cardiopulmonary effects of dorsal recumbency and high-volume caudal epidural anaesthesia with lidocaine or xylazine in calves." The Veterinary Journal **186**(3): 316-322.

Mijten, P., et al. (1997). "Comparison of catgut and polyglactin 910 for uterine sutures during bovine caesarean sections." The Veterinary Record **140**(17): 458-459.

Mollo, A., et al. (1997). "The use of oxytocin for the reduction of cow placental retention, and subsequent endometritis." Animal Reproduction Science **48**(1): 47-51.

NAHMS (2009a). Dairy 2007: Part IV Reference of dairy cattle health and management practices in the United States, 2007, US Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services, National Animal Health Monitoring System.

NAHMS (2009b). Beef 2007-08 Part III: Changes in the U.S. Beef Cow-calf Industry, 1993-2008, US Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services, National Animal Health Monitoring System. **3**.

- NAXCEL(R) (2006). [package insert] Division of Pfizer Inc, New York, New York, Pharmacia & Upjohn Company.
- Newman, K. D. (2008). "Bovine cesarean section in the field." Veterinary Clinics of North America: Food Animal Practice **24**(2): 273-293.
- Newman, K. D. and D. E. Anderson (2005). "Cesarean section in cows." Veterinary Clinics of North America: Food Animal Practice **21**(1): 73-100.
- Nix, J., et al. (1998). "A retrospective analysis of factors contributing to calf mortality and dystocia in beef cattle." Theriogenology **49**(8): 1515-1523.
- Noorsdy, J. (1979). "Selection of an incision site for cesarean section in the cow." Veterinary Medicine Small Animal Clinician **74**(4): 530-537.
- Parish, S., et al. (1995). "Left oblique celiotomy approach for cesarean section in standing cows." Journal of the American Veterinary Medical Association **207**(6): 751-752.
- Philipsson, J. (1976). "Studies on calving difficulty, stillbirth and associated factors in Swedish cattle breeds: I. General introduction and breed averages." Acta Agriculturae Scandinavica **26**(2): 151-164.
- Price, T. and J. Wiltbank (1978). "Dystocia in cattle a review and implications." Theriogenology **9**(3): 195-219.
- Reece, R. and C. Turner (1938). "The functional activity of the right and left bovine ovary." Journal of Dairy Science **21**(1): 37-39.
- Rutledge, J. (1975). "Twinning in cattle." Journal of Animal Science **40**(5): 803-815.
- Schuenemann, G., et al. (2011). "Assessment of calving progress and reference times for obstetric intervention during dystocia in Holstein dairy cows." Journal of Dairy Science **94**(11): 5494-5501.
- Skarda, R. T. (1996). "Local and regional anesthesia in ruminants and swine." The Veterinary Clinics of North America: Food Animal Practice **12**(3): 579-626.
- Vermunt, J. J. (2008). "The caesarean operation in cattle: A review." Iranian Journal of Veterinary Surgery Suppl: 82-100.
- Zaborski, D., et al. (2009). "Factors affecting dystocia in cattle." Reproduction in Domestic Animals **44**(3): 540-551.

Zhang, W., et al. (1999). "Relationship of maternal plasma progesterone and estrone sulfate to dystocia in Holstein-Friesian heifers and cows." The Journal of Veterinary Medical Science **61**(8): 909-913.

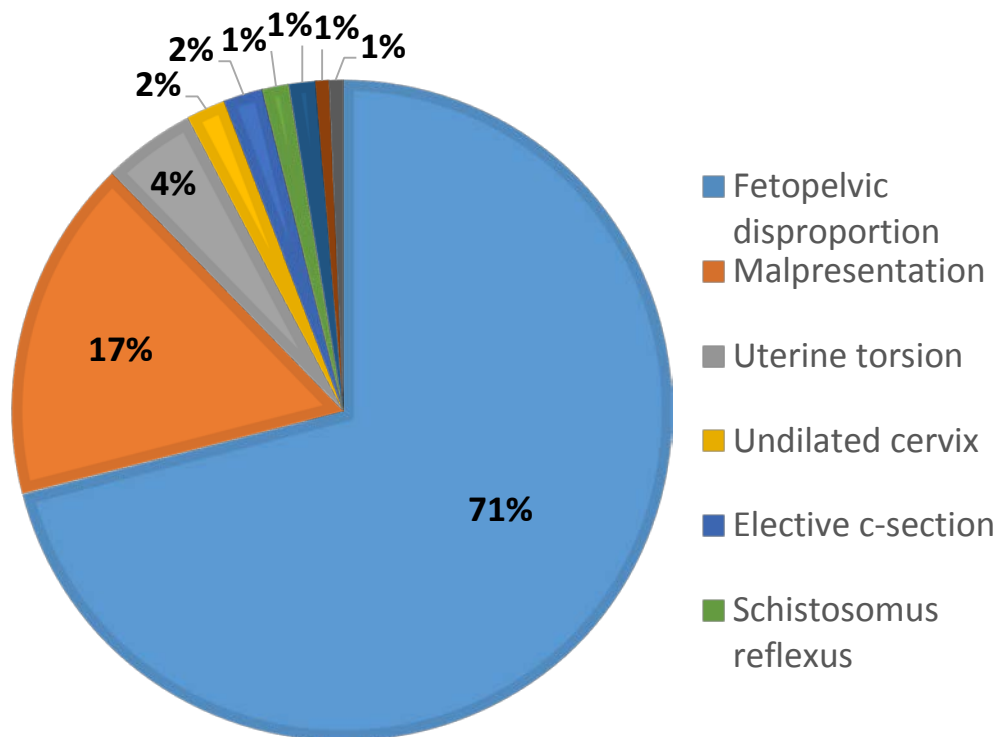


Figure 6.1 Pie chart of the indications for cesarean section in 155 beef cattle admitted to the Purdue University Veterinary Teaching Hospital between 2001 and 2010.

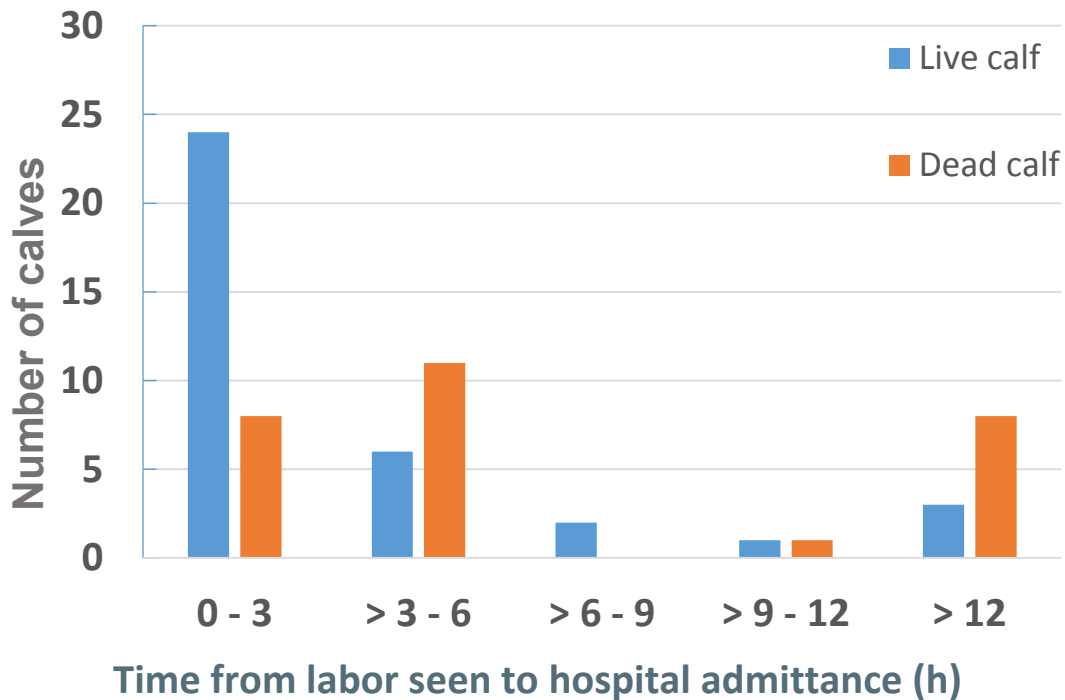


Figure 6.2 Bar graph of the number of calves that were alive at discharge or dead at or within 24 h of birth in relation to the time from labor was first seen to hospital admittance from cattle that underwent cesarean section at the Purdue University Veterinary Teaching Hospital between 2001 and 2010.

CHAPTER 7. SUMMARY AND CONCLUSIONS

The process of parturition is initiated by the fetus following activation of the fetal hypothalamus-pituitary-adrenal axis that stimulates the release of cortisol. Fetal hypercortisolemia decreases the placental production of progesterone and increases the placental production of estrogen as progesterone is aromatized and converted to estrogen. The consequent increase in the maternal plasma estrogen concentration has been related to the degree of sacrosciatic ligament relaxation, while the decrease in maternal plasma progesterone concentration removes its ability to maintain uterine quiescence and decreases body temperature due to the loss of progesterone's thermogenic effect. Increased uterine motility is associated with the pain and stress of labor which leads to the increase in plasma cortisol and glucose concentrations in the dam. Pain also activates the sympathetic nervous system and causes an increase in heart rate and hematocrit; the rumen contraction rate is decreased, in part, due to a decrease in feed intake.

In order to predict the time of parturition, it is helpful to use an upstream parameter to provide a sensitive and specific test and provide ample time for assistance in case of dystocia. Our current understanding indicates that the most upstream parameter is fetal plasma cortisol concentration but it is not practical to measure this parameter. Therefore, the decrease in plasma progesterone concentration in the dam appears to provide the best prediction of parturition in cattle. However, the need to perform repeated blood draws and submit the sample for laboratory analysis is not practical. Future studies that utilize rapid and portable test kits to measure urinary or salivary progesterone concentration or their metabolites such as pregnanediol-3-glucuronide would be helpful as these samples are easier to obtain than blood samples.

At the present time, the most practical, low cost, and reasonably accurate point of care test to predict the time of parturition in cattle is the glucometer to evaluate blood glucose concentration.

Chapter three revealed that the best predictor for calving difficulty score is the ratio of the calf front hoof circumference with the maternal intrapelvic area while chapter six conveyed the importance of timely intervention in dystocic animals to ensure survivability of the calf.

A limitation of the studies presented in chapters three to five is the usage of only one breed of cattle that was housed on one farm. Although the results have a good chance of being extrapolated to other dairy herds with similar breeds, it would be useful to conduct the same study on different farms using a variety of breeds to observe repeatability and if results differ amongst breeds. The retrospective cesarean study on the other hand had no follow up on postoperative complications, subsequent fertility, and lifespan of the animal. The study also evaluated animals in a hospital environment and results cannot be easily extrapolated to field surgeries where most cesarean sections in beef cattle occur.

Collectively, the results presented in this thesis provide methods to predict dystocia and parturition in late gestating cattle as well as highlight factors that help ensure favorable outcomes from cesarean sections.

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Changes in Rectal Temperature, Sacrosciatic Ligament Relaxation, and Plasma Progesterone Concentration at 24 hours Before Parturition in Holstein-Friesian Cattle. American Association of Bovine Practitioners 46th Annual Conference Milwaukee, WI, September 2013.

Associations between Calving Difficulty Score and Intrapelvic Dimension, Calf Hoof Circumference, and Calf Birth Weight in Holstein-Friesian Cattle. American Association of Bovine Practitioners 46th Annual Conference Milwaukee, WI, September 2013.

Evaluation of 2 Chute-Side Tests for the Detection of Leukocytes and Bacteria in Semen from Yearling Bulls. American Association of Bovine Practitioners 44th Annual Conference St Louis, MO, September 2011.

Regional and State

Changes in plasma progesterone concentration, rectal temperature, and sacrosciatic ligament relaxation at 24 hours before parturition in Holstein-Friesian cattle. *Indiana Bovine Interest Group Meeting*, Indianapolis, IN, 2013.

Local

Ability of pelvimetry and calf front hoof circumference to predict dystocia and calving difficulty score in Holstein-Friesian cattle. Veterinary Clinical Sciences Resident and Intern Seminar. West Lafayette, IN, February 2014

Changes in rectal temperature, sacrosciatic ligament relaxation, plasma progesterone concentration, and plasma glucose concentration in periparturient dairy cattle. 26th Annual Phi Zeta Abstract and Poster Competition. West Lafayette, IN, April 2013.

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					A&I	
Professional Courses						
Applications and Integrations I	VM82000	3	Tutor	8	5	2014
Applications and Integrations I	VM82000	3	Tutor	8	6	2013

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American Association of Bovine Practitioners 46th Annual Conference
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Annual Purdue Veterinary Medicine Fall Conference 2012 – 2014
West Lafayette, IN

Student American Veterinary Medical Association Symposium 2012
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Indiana Veterinary Medical Association Annual Meeting 2012
February 9 – 12, Indianapolis, IN

Scientific Writing Workshop 2012
February 11, West Lafayette, IN

American Association of Bovine Practitioners 44th Annual Conference
September 22 – 24 2011, St Louis, MO

21st ADSA Discover Conference: Improving Reproductive Efficiency of Lactating Dairy
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VCS Graduate Student Competitive Research Funds (2012-2013)
Determination of the ability of urine and plasma progesterone concentrations, and
blood and plasma glucose concentrations to predict the time of parturition in dairy
cattle
Co-PI: Mark Wen Han Hiew; PI: Dr Peter Constable; Co-I: Dr Larry Horstman, Dr Jon
Townsend

Ph.D. Thesis Title

Prediction of parturition and dystocia in Holstein-Friesian cattle, and cesarean
section in dystocic beef cattle. Purdue University, 2014.

D.V.M. Thesis Title

Evaluation of different extenders on the viability and abnormality of goat spermatozoa. Universiti Putra Malaysia, 2008.

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