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Impacts of calving management, calf risk factors, and difficult calvings on health and performance of beef calves

Pearson, Jennifer M.

UNIVERSITY OF CALGARY

Impacts of calving management, calf risk factors, and difficult calvings on health and performance of beef calves

by

Jennifer M. Pearson

A THESIS

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Abstract

Calf health and survival is crucial to successful cow-calf operations. Assisted calves are at a disadvantage compared to their herdmates because they may be injured, oxygen deprived, or less vigorous at birth. Determining evidence-based management practices to mitigate the effects of calving assistance on calf health and survival, as well as investigating risk factors associated with assisted calvings that affect transfer of passive immunity (TPI), morbidity, mortality, and growth, will help improve calf wellbeing. Therefore, the objectives of this thesis were to: benchmark the incidence of calving assistance and health outcomes, and describe current calving and colostrum management practices; to determine the impacts of subclinical trauma on calf vigour and TPI; and to investigate the impact of implementing pain mitigation at birth to assisted beef calves. Chapter 2 described current calving and colostrum management practices found on western Canadian cow-calf operations. Although the incidence of assisted calvings was low, the majority of producers assisted at least one calving, indicating the importance of understanding intervention and management strategies in compromised calves such as those assisted at birth. Chapter 3 quantified subclinical trauma associated with the degree of calving difficulty, and evaluated associations between subclinical trauma and calf vigour and TPI. Calves experiencing difficult births had elevated levels of subclinical trauma and decreased vigour. Subclinical trauma and reduced vigour were also associated with inadequate TPI. Chapters 4 and 5 investigated the clinical impacts of administering a non-steroidal anti-inflammatory drug to assisted beef calves at birth. In Chapter 4, calves administered meloxicam had greater average daily gain in the first week of life compared to placebo treated calves, but no effect was seen on pain and inflammatory mediators, vigour, TPI, health, or weaning growth. In Chapter 5, there was no effect of administering meloxicam to assisted calves on TPI, health, or growth, but vigour assessment and colostrum management were found to be important management tools associated with TPI, calf health, and growth. Therefore, calves assisted at birth experience subclinical trauma that affects their vigour and TPI. Pain mitigation strategies, vigour assessment, and colostrum management may be important tools to improve wellbeing in assisted beef calves.

Key words: beef calves, neonates, pain and inflammation, trauma, vigour, transfer of passive immunity, meloxicam, calf health

Preface

The following manuscripts have been published or submitted for publication. Jennifer M. Pearson was involved in the study design, data collection, analysis, result interpretation, and writing of the manuscripts with the guidance of the supervisors and co-authors. All authors contributed important intellectual content and provided critical review of the manuscripts. Written permission for reproduction of the articles in their entirety for this thesis has been obtained from the publishers and all co-authors.

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List of Symbols, Abbreviations and Nomenclature

Symbol	Definition
ºC	Degree Celsius
ADG	Average daily gain
AST	Aspartate aminotransferase
Bpm	Beats per minute (heart rate)
Bpm	Breaths per minute (respiratory rate)
BRD	Bovine respiratory disease
CI	Confidence interval
CK	Creatine kinase
Cox (1 or 2)	Cyclooxygenase enzyme
c-section	Caesarean section
DA	Difficult assist birth
EA	Easy assist birth
EDTA	Ethylenediamine tetra-acetic acid
EPD	Expected progeny difference
Eutocia	Normal calving
g	Gravitational force
G	Gravitational force
ID	Identification
IgG	Immunoglobulin G
IQR	Interquartile range
n	Sample size
NAHMS	National Animal Health Monitoring System
NCD	Neonatal calf diarrhea
NSAID	Non-steroidal anti-inflammatory drug
OR	Odds ratio
PCD	Preweaning calf diarrhea
PI	Passive immunity
RIA	Radioimmunoassay
RID	Radial immunodiffusion assay

SD	Standard deviation
SE	Standard error
TPI	Transfer of passive immunity
UA	Unassisted birth
US	United States
WCCCSN	Western Canadian Cow-Calf Surveillance Network

CHAPTER 1- INTRODUCTION

1.1 Canadian cow-calf industry

Canada is one of the top 11 countries for beef production in the world and is ranked 7th for beef exportation (Canfax Research Services, 2019). It is comprised of the cow-calf and feedlot sectors. Alberta is the major beef producing province, producing roughly 45% of the beef animals in Canada (Canfax Research Services, 2019). Amongst cow-calf producers, calf health and survival are predominant concerns (Murray et al., 2016a). One of the most important factors that impact calf health and survival is the amount of difficulty experienced during the birthing process (Sanderson and Dargatz, 2000; Mellor and Stafford, 2004). Specifically, dystocia is the predominant cause of preweaning mortality in western Canadian beef calves (BCRC, 2019).

1.1.1 Benchmarking cow-calf reproductive parameters

Calving management practices vary greatly depending on geographical region, size of the operation, and ranch facilities (NAHMS, 2009). Benchmarking herd parameters is commonly performed using herd records to monitor production outcomes, identify herd problems, and to establish goals for future production targets (Sanderson, 2005). General recommendations for calving production targets include: heifer pregnancy rate = 90%, cow pregnancy rate = 95%, calving interval = 365 days, calf crop = 90%, dystocia in cows <5%, dystocia in heifers <15%, and perinatal mortality <5% (Chenoweth, 2005). Although these parameters are not universal, they allow for baseline production monitoring and guide producers and veterinarians towards performance measurements and targets for each ranch individually.

1.1.2 Calving management practices

Forty percent of herds surveyed in the United States (US) maintained calving animals in specialized calving areas. A specialized calving area allows for more frequent observation intervals, timely calving or resuscitation intervention if needed and provides protection for dams and calves from the elements. The US producers surveyed observed heifers 3.6 times and cows 2.5 times in a 24-hour period for signs of calving difficulty and the majority of producers allowed heifers to labour for at least 3 hours prior to assistance (Dargatz et al., 2004). Although there is some understanding of the common management risk factors associated with assisted calving, such as a cow's body condition at calving and calving pen density (Grunert, 1979; Dufty, 1981), the frequency of these risk factors in western Canada is unknown.

Timely calving intervention is important for decreasing the risk of difficult calvings and stillbirths (Lombard et al., 2007; Villettaz Robichaud et al., 2017). Prolonged calving due to reduced uterine motility and cervical dilation associated with poor calving environments (e.g. human presence, confinement, etc.) can increase the risk of assisted calvings (Dufty, 1981). It has been reported that 50% of neonatal calving deaths could have been prevented if timely intervention had occurred (Dargatz et al., 2004). Assistance greater than one hour after the fetal hooves appear increased the severity of dystocia, duration of assistance, risk of downer cows from nerve damage, and reduced perinatal vigour in calves (Mee, 2004). Delaying assistance for greater than 2 hours increased calving duration and induced hyperlactatemia in the neonate (Egan et al., 2001; Mee, 2004). The recommendation that calving be assisted after about 60 minutes of labour to decrease the risk of calf stillbirth is based on normal calving times in Holstein cows (Schuenemann et al., 2011). Generally, it is common practice to allow dams to calve on their own unless they display signs of lack of progression or if malpresentation or malposture of the calf is visible. Recently, early intervention and assistance of calvings was investigated in relation to calf health and transfer of passive immunity (TPI) (Villettaz Robichaud et al., 2017). In that study, there was no negative effect of early assistance on stillbirth risk, vigour at birth, or TPI. Calves given late assistance at birth had higher risks of stillbirth and decreased vigour (Villettaz Robichaud et al., 2017).

1.2 Eutocia and dystocia

1.2.1 Normal calving physiology

To initiate parturition, the fetal adrenal glands release cortisol that increases 17 alpha hydroxylase in the placenta (Anderson et al., 1975). This decreases progesterone production by converting pregnenolone to estrogens, therefore increasing estradiols. Increasing concentrations of prostaglandin F2 alpha causes the myometrium to contract, creating pressure inside the uterus and rotating the fetus for delivery (Anderson et al., 1975). A normal calving (eutocia) can be defined by 3 stages of progress (Norman and Youngquist, 2007). Stage 1 is defined by relaxation and dilation of the cervix with rupture of the chorioallantois membrane (Jackson, 1995; Wehrend et al., 2006; Norman and Youngquist, 2007). This stage of parturition lasts 8 to 12 hours on average (Dufty, 1973; Miedema et al., 2011). Dilation of the cervix is achieved by decreasing cervical tone by the absence of progesterone and increasing mechanical pressure from the fetus (Taverne, 1992; Noakes et al., 2001). As the fetus engages the cervix, pressure receptors synapse in the spinal cord causing oxytocin release and increasing myometrial contractions to further dilate the cervix (Norman and Youngquist, 2007). Stage 2 of parturition is defined as the fetus passing through the birth canal and being delivered (Taverne, 1992; Norman and Youngquist, 2007; Mainau and Manteca, 2011). This stage of parturition lasts 1 to 4 hours on average and clinical signs are described as increasing myometrial contractions by the dam and visualisation of the fetal amniotic sac or fetal expulsion (Schuenemann et al., 2011). Stage 3 of parturition is defined as detachment of the placenta via vasoconstriction and myometrial contractions to dislodge the chorionic villi from the crypts (Noakes et al., 2001; Mainau and Manteca, 2011). This stage should not take longer than 12 hours and is considered pathologic by 24 hours after birth of the calf (Augustine, 2013).

1.2.2 Dystocia and calving assistance

There are several terms used to describe an abnormal birthing process in cattle. A dystocic birth is defined as a prolonged or difficult birth that may or may not require human assistance (Mee, 2004). An assisted birth may or may not have been a dystocic birth but the animal was assisted in delivery based on a person's decision to intervene (Mee, 2008). Calving ease is a subjective measure of the amount of effort required to deliver the calf (Mee, 2008). Due to the challenge of consistently and objectively describing dystocia or calving ease, whether the calving was assisted is considered the most accurate parameter by which to evaluate an abnormal birth in research studies.

The incidence of assisted births ranges depending on region and dam parity. In the US, the most recently published nationwide incidence of calving assistance in beef dams was 11.0% (NAHMS, 2009). Heifers had a 7.7% incidence of easy calving assistance and a 3.4% incidence of difficult calving assistance, while cows had a 3.2% incidence of easy calving assistance and 1.0% incidence of difficult calving assistance (NAHMS, 2009). In a previous study, Dargatz et al. (2004) found a 16.7% calving assistance risk in heifers and 2.3% calving assistance risk in mature cows in the US. In comparison to the US, Waldner (2014) found an incidence of any assistance during calving of 8.9% and severe dystocia incidence of 3.7% in western Canada. Heifers had an overall 22.1% incidence of assistance and cows had 5.8% incidence of assistance (Waldner, 2014). In Ontario, Canada, a survey reported an overall 5.8% incidence of calving assistance (McDermott et al., 1992). These surveys demonstrate regional and temporal differences in incidence of assistance at birth. Furthermore, the most recent benchmarking studies found that the majority of assisted births occur in heifers and were classified as easy assisted deliveries (McDermott et al., 1992; NAHMS, 2009; Waldner, 2014).

1.2.3 Causes of dystocia

The cause of dystocia can be categorised as either maternal or fetal in origin (Norman and Youngquist, 2007). Primary uterine inertia is a maternal origin of dystocia caused by failure of the myometrium to contract. This can be due to overstretching of the uterus by multiple fetuses, a defect in the myometrium, a deficit in parturient hormones, or muscular atony as it occurs with postparturient hypocalcemia (Norman and Youngquist, 2007). Secondary uterine inertia is caused by exhaustion of the myometrium after a prolonged parturition. Abnormalities of the birth canal such as a small maternal pelvis or pelvic deformities, incomplete dilation of the cervix, and remnants of the mullarian ducts cause obstructive dystocias (Norman and Youngquist, 2007). Although the cause is unknown, heifers have a higher risk of incomplete dilation of the cervix and vagina (Funnel and Hilton, 2016). Uterine torsions account for roughly 5-10% of all dystocias (Frazer et al., 1996; Laven and Howe, 2005). Fetal causes include abnormal presentation, position, or posture of the fetus, fetal deformities (e.g. schistosomus refleus, persomus elumbus), or fetal oversize such as fetal-maternal size mismatch, large offspring syndrome, or pituitary lesions causing excessive fetal growth (Norman and

Youngquist, 2007). Malpresentation (e.g. posterior presentation) of the fetus accounts for 13-22% of all dystocias (Funnel and Hilton, 2016) and is associated with a 5 times higher risk of stillbirth (Mee, 2008). Malposition (e.g. foreleg deviations, head deviations, etc.) accounts for 20-40% of calving assistance (Funnel and Hilton, 2016).

Greater than 50% of assisted calvings are caused by fetal-maternal size mismatch (Meijering, 1984; Berger et al., 1992), and the odds of an assisted calving increase greatly with every kilogram increase in birthweight (Johanson and Berger, 2003). Fetal-maternal size mismatch is the leading cause of assisted calvings in heifers and appears to be more prevalent in beef breeds rather than dairy breeds (Meijering, 1984). Decreasing the incidence of fetal-maternal size mismatch dystocias can be achieved through appropriate bull and heifer selection management practices as described later in this chapter.

Behavioral indicators associated with a dystocia include restless behavior, prolonged lying time, longer duration of tail elevation, and reduced abdominal contractions (Schuenemann, 2011; Barrier et al., 2012b). Dams with dystocic births also often have a prolonged time between visualization of the amniotic sac to birth of the calf (Schuenemann, 2011).

1.2.4 Negative effects of dystocia

1.2.4.1 Impacts on acidemia and hypoxemia

Newborn calves are born with a mixed metabolic and respiratory acidosis that normally resolves within the first 24 hours of life (Szenci, 1985; Homerosky et al., 2017a). In utero, oxygen and nutrient rich blood is delivered to the fetus via the umbilical vein. Waste products carried in the blood exits the fetus through the umbilical arteries and back to the placenta (Kasari, 1994). The fetus is under a high pressure, low flow, hypoxic environment until parturition and separation of the umbilicus (Kasari, 1994). During parturition, uterine contractions reduce uterine blood flow causing an increasingly hypoxic environment and separation of the umbilicus leads to acidemia and hypoxemia (Besser et al., 1990). Metabolic acidosis is caused by temporary anaerobic glycolysis from poorly perfused tissues, producing L-lactate, and respiratory acidosis is caused by a buildup of carbon dioxide from poor respiration (Bluel and Gotz, 2013). Hypoxemia stimulates a gasping reflex and modulates lung inflation to oxygenate the neonate's blood. Proper lung inflation leads to pressure changes that close shunts throughout the neonate's body and aid to expel normal fetal lung fluid (Kasari, 1994). Regular respiration will eliminate the carbon dioxide build-up and correct the respiratory acidosis, but metabolization and excretion of L-lactate must be done by the heart, kidney, and liver (Bellomo, 2002).

Calves experiencing a prolonged calving or increased force or duration of traction during calving assistance have a higher risk of acidemia and hypoxemia, which can lead to increased risk of stillbirth or decreased vigour in newborn calves (Meijering 1984; Breazile et al., 1988; Szenci et al., 1988; Vaala and House, 2002). Persistent acidemia can cause pulmonary arterioles to remain constricted and limit lung blood flow. Limited blood flow can lead to asphyxiation and death. Acidemia and hypoxemia can also lead to a depressed central nervous system and decreased muscle tonicity leading to decreased vigour (Dufty and Sloss, 1977). In a study investigating the effects of anoxia on calf vigour and mortality, calves experiencing anoxia for 6-8 minutes died, and those with severe acidemia and hypoxemia had delayed head righting, time to sternal recumbency, and increased time to stand and nurse (Dufty and Sloss, 1977). Hyperlactatemia has been strongly correlated with prolonged calvings and low blood pH in neonates (Bleul and Gotz, 2013; Homerosky, 2017a) and is associated with decreased vigour and increased mortality risk. (Homerosky et al., 2017a; Diesch et al., 2004).

Severely acidemic calves had decreased vigour, drank 50% less colostrum, and had 35% lower serum IgG concentration than those with normal pH levels (Boyd, 1989). Hypoxemia can prolong the period of IgG absorption, which may impact the health of compromised calves (Tyler and Ramsey, 1991). Calves with severe acidemia are at risk of failed TPI and preweaning morbidity and mortality (Szenci et al., 1988; Boyd, 1989; Besser et al., 1990; Schuijt and Taverne, 1994).

1.2.4.2 Impacts on calf vigour

Vigour assessment in newborns, such as the APGAR score, have been used in various neonatal species to classify their vitality at birth (Apgar, 1953; Randall, 1971; Veronesi et al., 2005, 2009). Assisted calves are often less vigorous and are described as taking longer to move into sternal recumbency, stand, walk, and nurse (Odde, 1988; Schuijt and Taverne, 1994; Barrier et al, 2012b).

Decreased vigour may be caused by trauma, prolonged calving assistance, or acidemia (Barrier et al., 2012b). Attempts have been made to identify acidemic and hypoxemic calves at birth based on APGAR or VIGOUR scores (Mulling, 1977; Zhang et al., 1999; Homerosky et al., 2017a). In a study by Homerosky et al. (2017a), specific physical exam parameters at birth were associated with blood gas disturbances and elevated blood L-lactate concentrations in neonatal beef calves. An incomplete tongue withdrawal and weak suckle response were associated with a decreased blood pH and elevated blood L-lactate concentration. An abnormal mucous membrane colour was also associated with elevated blood L-lactate concentrations. Other effects on calf health in assisted calves include taking significantly longer get into sternal recumbency and to stand, having lower packed cell volumes, and having higher plasma L-lactate concentrations (Diesch et al., 2004; Murray et al., 2015). Although not as thoroughly studied as acidemia and hypoxia, calves experiencing a traumatic birth may be less vigorous at birth as well as may have varying degrees of trauma, acidemia, and hypoxemia (Laven et al., 2012; Murray and Leslie, 2013). Currently, there is no literature describing the combination or varying degrees of these factors and the impacts they may have on calf vigour.

1.2.4.3 Impacts on transfer of passive immunity

Assisted calves are often born weak and less vigorous, which can interfere with normal neonatal behaviors such as ingesting colostrum in a timely fashion (Mellor and Stafford, 2004; Homerosky et al., 2017b). Due to the syndesmochorial structure of the bovine placenta, transfer of maternal antibodies across the placenta is not possible (Barrington and Parish, 2001). Therefore, calves are born agammaglobulinemic and depend on the consumption and absorption of colostral immunoglobulins for protective antibodies until their naive immune system has become more functional (Godden, 2008). Colostrum is also critical for the neonate because it provides nutrients, aids in thermoregulation, and assists with the maternal-neonatal bond (Godden, 2008; Cortese, 2009; Dwyer et al., 2016). Inadequate ingestion and absorption of colostrum leads to failed TPI (Weaver et al., 2000). Failed TPI is defined as calves with inadequate serum immunoglobulin (IgG) levels when measured between 1 and 7 days of age (Godden, 2008; McGee and Earley, 2019). The incidence of failed TPI varies by region and defined cut-off point of failed TPI. In a study of 932 western Canadian beef calves on 152 ranches, 6% of calves had inadequate levels of TPI (<8 g/L IgG concentration), 10% had marginal TPI (8-16 g/L), and 17% had sub-optimal TPI (16-24 g/L) (Waldner and Rosengren, 2009). Housing and management decisions may also impact TPI. In a Quebec study, 19% of beef calves had failed TPI (<10 g/L IgG concentration) and calving in a stanchion barn was a risk factor for failed TPI (Filteau et al., 2003).

Transfer of passive immunity is important because failed TPI is associated with increased preweaning morbidity, mortality, and decreased weight gain (Wittum and Perino, 1995; Dewell et al. 2006; Waldner and Rosengren, 2009). Specifically, Dewell et al. (2006) found calves with a serum IgG concentration less than 24 g/L were 1.6 times more likely to become ill and 2.7 times more likely to die in the preweaning period. Calves with higher serum IgG concentrations also weighed 3.35 kg more at 205 days of age than calves with lower serum IgG concentrations (Dewell et al., 2006).

Risk factors for failed TPI include: being born to a heifer, being born as a twin, dystocia, severe acidemia at birth, and housing type (e.g. stanchion barns) (Odde, 1988; Besser et al., 1990; Weaver et al., 2000; Filteau et al., 2003; Waldner and Rosengren, 2009). Other factors influencing TPI include: the IgG concentration in the colostrum, the timing of consumption of colostrum, presence of the dam, season, and efficiency of absorption of IgG within the gut (Odde, 1988; Godden, 2008). Several studies have shown an association between assisted births and decreased serum immunoglobulins (Muggli et al., 1984; Odde, 1988; Gaspers, 2015). One study found no association between calving difficulty and serum IgG concentration but those calves were all fed 1 L of colostrum shortly after birth, similar to dairy calf management (Stott and Reinhard, 1978).

1.2.4.4 Impacts on calf health

Risk of mortality in the first day of life can range from 4 to 13% and half of all pre-weaning deaths occur within the first 24 hours of life (Berglund et al., 2003; Johanson and Berger, 2003). Calving assistance increases the risk of newborn calf mortality and this risk increases with increasing severity of calving difficulty (Bellows et al., 1987; Patterson, 1987; Wittum and Perino, 1995; Nix et al., 1998; Sanderson and Dargatz, 2000; Lombard, 2007). Specifically, mortality in assisted or caesarian-born calvings have been reported as high as 30 to 50% (Nix et al., 1998). Interestingly, it is estimated that 75% of neonatal mortality occurs in the first hour after birth and 90% of these calves that died were alive at the time of parturition (Mee, 2004).

The main causes of peripartum deaths are attributed to acidemia and trauma (Mee, 2004). In beef calves, dystocia is the most common cause of death resulting in over 50% of the preweaning incidence for mortality followed by disease (bovine respiratory disease (BRD) or preweaning calf diarrhea (PCD) accounting for 13% of deaths and weather exposure and hypothermia accounting for 6% of deaths (Bellows et al., 1987).

Risk factors for stillbirth include: low dam body condition score at parturition, being born to a heifer or cow older than 10 years old, being born as a twin, the body condition score of the dam (under or over conditioned), month of calving, low precipitation, and assistance at birth (Bellows et al., 1987; Waldner, 2014). Determining the presence of twins early on in the pregnancy may also help decrease calf losses caused by dystocia by appropriate observation and timely intervention at calving (Echternkamp et al., 2007).

Assisted calvings also have a risk of treatment for disease that is 2.4 times greater than that of unassisted calvings in the first 45 days of life (Toombs et al., 1994). Specifically, a difficult birth increases the odds of BRD or PCD in the preweaning period (Lombard et al., 2007). Management factors may play an important role in morbidity as well. Murray and colleagues (2016a) reported that herds that never intervened with calving assistance had 4.7% higher risk of PCD than those herds that did intervene with calving assistance.

1.2.5 Risk factors of dystocia

Dam risk factors for fetal-maternal size mismatch dystocias include: being a heifer, high birth weight, low body condition score as a yearling dam, low or high body condition score at calving, and small pelvic area (Dufty, 1981; Mee, 2008). Dam nutrition is important for ease of calving as well as for return to estrus (Mee, 2008). Underconditioned dams may not have the energy reserves to successfully deliver a calf leading to primary or secondary uterine inertia, while overconditioned dams have increased fat within the pelvic area, which increases their risk of an obstructive dystocia (Grunert, 1979; Quigley and Drewry, 1988; Mee, 2008; Funnel and Hilton, 2016). Mineral and hormone deficiencies in the dam such as calcium, phosphorous, copper, cobalt, selenium, iodine, sodium, and estradiol have also been associated with higher risk of dystocia caused by uterine inertia (O'Brien and Stott, 1977; Meijering, 1984; Corah and Ives, 1991; Graham, 1991). Dams confined around the time of calving can be at increased risk of dystocia due to stress and its negative effect on parturient hormones (Bontekoe et al., 1977; Dufty, 1981).

Calf risk factors for calving assistance include: being born male, being born to a twin, and a high birth weight (Meijering, 1984; Berger et al., 1992; Johanson and Berger, 2003; Lombard et al., 2007). Being born a male increases calving assistance risk as they often have larger body dimensions and higher birthweights than female calves (Meijering, 1984; Johanson and Berger, 2003; Lombard et al., 2007). Calves with higher birthweight are often larger, which contributes to fetal-maternal size mismatch dystocias (Johanson and Berger, 2003). Twins also have an increased calving assistance risk due to greater likelihood of malpresentation or malposition (Lombard et al., 2007).

1.2.6 Decreasing the risk of dystocia

Prevention of fetal-maternal size mismatch dystocias include sire and replacement heifer selection and appropriate dam nutrition (Funnel and Hilton, 2016). Sire selection for birthweight and calving ease through expected progeny differences (predicted genetic traits) can have a dramatic effect on the prevention of dystocias associated with large calf birth weights (Colburn et al., 1997). Replacement heifer selection and rearing is also an important management strategy to decrease the risk of dystocia. It is recommended that heifers be 65% of their mature body weight at the time of breeding and 85% of their mature body weight at the time of calving to decrease the risk of calving difficulty (Engelken, 2008). Although pelvic size measurements have been used in the past to predict mature pelvic size and risk of dystocia, selecting for larger pelvic size measurements has not decreased the risk of dystocia in heifers. It is currently recommended to cull replacement heifers below a minimum pelvic area measurement rather than selecting for larger pelvic size measurements (Larson et al., 2016).

1.3 Cattle welfare and pain management

Calf health and survival are major concerns of cow-calf producers (Murray et al., 2016a). Specifically, dystocia is considered painful for the calf and cow (Laven et al., 2012) and a welfare concern in the cattle industry (Moggy et al., 2017).

1.3.1 Cattle welfare

Animal welfare, as defined by the OIE, is “the physical and mental state of an animal in relation to the conditions in which it lives and dies” (OIE, 2019). The theory of animal welfare has evolved from one of the first documents known as the 5 Freedoms, proposed by the United Kingdom’s Farm Animal Welfare Council, to address public concern for the welfare of farm animals (Fraser, 2008). The Five Freedoms were defined to help monitor the husbandry practices of animals under human care. They summarise that farm animals should have freedom from hunger, malnutrition and thirst, freedom from fear and distress, freedom from heat stress or physical discomfort, freedom from pain, injury and disease, and freedom to express normal patterns of behaviour (Brambell Committee, 1965). Although they are commonly used to direct animal husbandry guidelines and animal welfare audits, they do not address today’s societal concerns of animal welfare such as pleasure or the complexities of fear and pain. It is not plausible to live in a world without fear or pain, but it is important to address fears and pain when considering animal welfare. Many animal welfare scientists consider the Five Freedoms to be too basic by not addressing the complexities of animal welfare such as the importance of positive welfare experiences (Mellor, 2016).

The Five Domains model was developed in response to the criticisms of the Five Freedoms. They consist of 4 physical or functional domains (nutrition, environment, health, and behaviour) and one affective experience domain (mental state) (Mellor and Reid, 1994). The Five Domains model addresses negative or positive experiences within the 4 physical domains and how they can effect the mental domain when describing the animal’s state of welfare (Mellor, 2016). This theory helps to describe a better understanding of animal husbandry and its effect on animal welfare, yet both the Five Freedoms model and Five Domains model fail to address the major ethical concerns of animal welfare researchers; understanding the welfare of animals through their function and through their feelings (Fraser, 2008).

A different theory to the Five Freedoms and Five Domains is a circle model outlined by Fraser et al. (1997). It describes the complex integration between animal welfare and ethical concerns by overlapping circles. Circle A represents the "adaptions possessed by the animal" and circle B represents the "challenges faced by the animal in its current circumstances" (Fraser et al., 1997). The areas of the circles that do not overlap represent the challenges animals may experience when they are unable to adapt to their environment. Area 1 represents "adaptations that no longer serve an important function" and area 2 represents "challenges for which the animal lacks corresponding adaptations" (Fraser et al., 1997). The middle overlap area represents "challenges for which the animal has corresponding adaptations" (Fraser et al., 1997). Overall, this animal welfare model takes into consideration the functionality and feelings of animals in response to their welfare as well as incorporates the major quality of life concerns animal welfare researchers attempt to address (Fraser et al., 1997).

Welfare can be negatively impacted by a multitude of issues surrounding calving such as stress, pain, injury, and disease. Specifically, the welfare of neonates can be impacted by injury, hypoxia, hypothermia, starvation, and mismothering (Mellor and Stafford, 2004). Pain experienced during calving is a fast growing topic in the beef industry (Laven et al., 2012, Murray et al., 2016a). World-wide, veterinary practitioners' and cattle producers' have ranked dystocia as one of the most painful conditions in cattle (Huxley and Whay, 2006; Moggy et al., 2017).

1.3.2 Pain

Pain, as defined by Molony and Kent (1997), is "an aversive feeling or sensation associated with actual or potential tissue damage resulting in physiological, neuroendocrine, and behavioral changes that indicate a stress response". It is a subjective experience impacting every individual differently (Millman, 2013). Therefore, measuring pain is performed indirectly and using multiple tools in combination, as no pain specific tests have been validated (Millman, 2013). Briefly, the physiologic pain response occurs through sensory pathways conducted through nociceptors located at the end of pain fibers. A noxious stimulus is recognised and transduced into an electrical impulse that transmits up the nerve fibers to the dorsal horn of the spinal cord. From there, a signal is modulated and transmitted to the brain for perception and interpretation and sympathetic neurons stimulate a nociceptive reflex response (Muir, 2009). Tissue damage and inflammation also elicit nociceptive responses through prostaglandin, histamine, bradykinin, cytokine, and chemokine release (Muir, 2009). These chemicals change the threshold of nociceptors and activate a hyperalgesic state (Anderson and Muir, 2005).

1.3.3 Measuring pain and inflammation in cattle

Cattle are prey animals and mask pain- and inflammation-related behaviours, making them challenging to study (Coetzee, 2013; Gleerup et al., 2015). Indirect measurements of pain include: behavioral, physiological, neuroendocrine, and production related changes (Millman, 2013; Coetzee, 2013). Behavioural signs of pain are often the most reliable indicators of pain due to the individual's experience, but they can be difficult to objectively measure (Mich and Hellyer, 2009; Millman, 2013). Examples of measurable behavioural signs of pain in cattle include: excessive vocalization, postural changes, limping, kicking, stamping of feet, grinding teeth, depression, reluctance to move, and inappetence (Millman, 2013). Recently, pain scales and cattle facial expressions have been investigated to combine multiple behaviours into an objective score (Gleerup et al., 2015). Behavioural indicators can also be objectively measured by observing the animal and counting the number of times they perform a behaviour (e.g. number of tail swishes) or the amount of time they perform a behaviour (e.g. lying time) (Coetzee, 2013). Other objective measurements of behavioural pain include using technology such as: accelerometers (to count the number of steps taken and lying position), electroencephalography (measuring brain activity), pressure algometers (amount of pressure applied to a painful site before animal moves away), infrared thermography (tissue temperature), pressure mats (lameness detection), and chute exit speeds (Coetzee, 2013; Johnson, 2016).

Non-invasive physiologic and autonomic measurements of pain include: changes in heart rate or respiratory rate, body temperature, and pupil size (Stewart et al., 2010). These assessments are measuring the activation of the autonomic nervous system and the hypothalamic-pituitary-adrenal axis through a stress response to a painful or stressful stimuli (Stewart et al., 2010).

Other commonly used methods to measure pain, stress, and inflammation include measuring physiological and neuroendocrine biomarkers in blood, saliva, or other bodily tissues. These include: cortisol and corticosterone, substance P, acute phase proteins (e.g. haptoglobin, fibrinogen, serum amyloid A), prostaglandins, cytokines, and adrenergic hormones. Cortisol is used as a measure of distress associated with stress or a painful stimuli (Mellor et al., 2000) and has been reported to be elevated in calves experiencing increased traction when being delivered by a difficult assist (Hoyer et al., 1990). Substance P is a neuropeptide that is released in response to stress, pain, and anxiety (Stewart et al., 2010; Coetzee, 2013). Acute phase proteins are released in response to infectious or inflammatory tissue injury and are routinely used to quantify the amount of tissue injury a painful procedure or condition exerts (Baunmann and Gauldie, 1994). Although less commonly measured, prostaglandins and cytokines are indicators of inflammation and tissue injury, and adrenergic hormones (e.g. adrenaline) are measurements of activation of the sympathetic pathway (Donalisio et al., 2012; Allen et al., 2013).

Production parameters are often measured when investigating pain mitigation strategies. These include: treatment for disease, mortality, feed intake, and weight gain (Stafford and Mellor, 2005; Coetzee, 2013).

Calves experiencing a difficult birth can experience trauma to their soft tissues and bones. Specifically, lesions identified from post-mortem examinations in association with a difficult or prolonged birth include: fractured or luxated vertebrae, ribs, and legs; crushing injuries; vascular compromise to soft tissues; and edema of the tongue or head due to prolonged periods in the dam's pelvic canal (Ferguson et al., 1990; Nagy, 2009). The degree of tissue damage, disease, or malfunction of organs are commonly determined in veterinary practice based on certain blood parameters. Muscle trauma can be measured by creatine kinase (CK) and aspartate aminotransferase (AST). Muscle and organ damage releases these enzymes into the blood. Creatine kinase is the most sensitive and specific indicator of muscle injury (Anderson et al., 1975) and its half-life is about 4 hours, so that CK decreases rapidly after muscle damage ceases (Cox and Onapitos, 1986; Lefebvre et al., 1994). While AST is not as specific for muscle damage as CK, a combined assessment of CK and AST are often used (Russell and Roussel, 2007). The half-life of AST is about 20 hours and changes more slowly than CK and a combination of CK and AST assessment can approximate the stage of muscle injury of the animal (Stockham and Scott, 2002; Russel and Roussel, 2007).

1.3.4 Pain mitigation in cattle

Commonly used analgesic therapies in cattle include: local anesthesia, sedative analgesics, and non-steroidal anti-inflammatory drugs (Anderson and Muir, 2005; Coetzee, 2011; Coetzee, 2013). Multimodal approaches are often used to improve pain mitigation for procedural or surgical pain in humans and animals to potentiate the efficacy and potency of analgesics (Anderson and Edmondson, 2013). Pre-emptive analgesic therapy is often considered more effective than post-procedural or analgesic therapy given after a painful experience. This is due to a decrease in length of efficacy and potency in humans and animals when administered after a painful stimulus has occurred (Anderson and Muir, 2005; Anderson and Edmondson, 2013; Coetzee, 2013).

Local or regional anesthesia acts by providing perineural anesthesia to a local or regional area, and at appropriate administration doses, has no systemic or behavioral effect (Garcia, 2015). They inhibit nerve polarization and prevent transduction and transmission of a painful stimuli to the dorsal horn (Coetzee, 2011). Examples of local or regional anesthesia include nerve blocks, regional limb blocks, and epidurals (Anderson and Muir, 2005). Although local or regional anesthesia offers sensory and motor nerve blockades to specific regions, they are not sufficient to address more generalised or systemic pain (Garcia, 2015).

Sedative analgesics are commonly used for their analgesic and sedative properties in cattle (Coetzee, 2011). Examples include alpha-2 adrenergic agonists (e.g. xylazine), N-methyl D-aspartate (NMDA) receptor antagonists (e.g. ketamine), and opioids (e.g. morphine) (Rankin, 2015). These analgesics act by different pathways and receptors but generally inhibit modulation, projection, and perception of pain to the brain (Coetzee, 2011). Specifically, alpha-2 adrenergic agonists act by inhibiting positive feedback mechanisms for norepinephrine release by activating alpha-2 adrenergic receptors (Rankin, 2015; Coetzee, 2011). N-methyl D-aspartate receptor antagonists cause a dissociative anesthetic effect in addition to analgesia (Berry, 2015). Opioids bind to spinal and supraspinal receptors preventing opioid nerve impulses (KuKanich and Wiese, 2015). In addition to sedation, other side effects of these analgesics include decreased cardiac output, respiratory depression, muscle relaxation, and depressed gastrointestinal motility, which may be counterproductive in neonates (Coetzee, 2011). Many of these sedative analgesics are regulated by drug enforcement agencies and require veterinary administration, therefore prescribing these drugs for use on cow-calf ranches is generally not feasible (Coetzee 2013).

The NSAID class of drugs provide a multimodal relief by analgesic, anti-inflammatory, and anti-endotoxic properties (Coetzee, 2013; Papich and Messenger, 2015). They are a favorable choice for analgesia because they are not a controlled or scheduled drug (drugs requiring documentation of use) and can be easily prescribed and dispensed (Papich and Messenger, 2015). The NSAIDs inhibit cyclooxygenase enzymes (COX). The COX enzymes are part of the arachidonic pathway producing prostaglandins and thromboxanes, which cause inflammation (Talcott, 2006; Papich and Messenger, 2015). The two most commonly referred to COX enzymes are COX-1 and COX-2. The COX-1 enzyme regulates physiological functions by synthesizing prostaglandins needed for cellular regulation. These functions include renal blood flow, gastric mucosal protection, and thromboxane production (platelet function) (Khan and McLean, 2012). The COX-2 enzyme regulates inflammatory mediators and are found in monocytes, fibroblasts, synoviocytes, and chondrocytes (Papich and Messenger, 2015). Potential adverse effects can occur with the use of NSAIDs. The most commonly reported adverse reaction is gastrointestinal toxicity, described as vomiting, diarrhea, anorexia, ulceration, and melena, and is well described in dogs and horses (Talcott, 2006). Renal injury causing clinical signs of polyuria and polydipsia has been described in humans and horses, but is not well documented in small animals (Papich and Messenger, 2015). Less common adverse effects include liver injury, platelet inhibition, depression, and ataxia (Talcott, 2006). These adverse effects have not been well documented in cattle.

In cattle, NSAIDs are one of the most commonly used form of pain control (Laven et al., 2012; Coetzee, 2013; Murray et al., 2016b). In a study of beef producers in Alberta in 2013, only 13% of surveyed beef producers reported using a pain medication in newborn calves after dystocia and 15% in the cows (Murray et al., 2016a). More recently, Moggy et al. (2017) stated that 33% and 28% of beef producers in western Canada reported giving an NSAID after dystocia to the cow and the calf, respectively.

Meloxicam is an NSAID with high bioavailability and prolonged half-life, making it a favorable choice for treating pain in cattle (Coetzee, 2013). A study evaluating the effects of meloxicam on vigour and subsequent health in dairy calves found those that received meloxicam at birth had significantly greater vigour and suckle responses as well as increased milk consumption compared to calves that received a placebo (Murray et al., 2016b).

Other NSAIDs have also been evaluated for their efficacy in improving calf health and welfare. Gladden et al. (2019) found that calves administered the NSAID ketoprofen within 3 hours of birth had improved behavioural indicators of welfare (increased play behaviour and decreased time spent in lateral recumbency) compared to calves that received a placebo. Although these findings are positive, when investigating physiological indicators of pain and inflammation, Gladden et al. (2018) found no effect of administering ketoprofen to calves shortly after birth on 24-hour cortisol, creatine kinase, plasma L-lactate, or total protein concentration.

Beef producers perceive that difficult births are painful and are administering NSAIDs to cows and calves after a difficult birth (Moggy et al., 2017), yet the efficacy of NSAIDs in neonatal beef calves experiencing an assisted calving has yet to be investigated. This suggests the need for more studies investigating the impacts of pain mitigation in assisted calves.

1.4 Conclusions

Calves that are assisted at birth have a higher risk of failed TPI, preweaning morbidity, mortality, decreased weight gain (Wittum and Perino, 1995; Sanderson and Dargatz, 2000; Dewell et al., 2006; Waldner and Rosengren, 2009). Pain mitigation strategies and risk factors associated with calf health should be investigated in these compromised, high-risk calves to improve calf welfare.

Currently, there is no published research quantifying physiological biomarkers of trauma with degree of calving difficulty, nor have the effects of trauma after a difficult birth been investigated. Quantifying the amount of subclinical trauma experienced by a calf after a calving and understanding the relationship between that trauma and calf vigour and TPI may provide better understanding how an assisted calving impacts calves and potentially help develop pain mitigation strategies to decrease the side effects of experiencing a difficult birth.

There is no current research assessing the effects of an NSAID given at birth to newborn beef calves after an assisted calving. Treating newborn calves that have experienced a traumatic birth with an NSAID could potentially diminish the negative impacts by mitigating pain and inflammation. Treatment with an NSAID at birth could also potentially increase calf vigour, reduce the risk of failed TPI, and improve calf health and survival (Laven et al. 2012; Murray et al., 2016b).

In addition to the advantages pain mitigation strategies may provide for assisted calves, understanding current calving management practices will benefit producers and the beef industry in general. Specifically, identifying risk factors in the peri-partum period that are associated with calf morbidity and mortality could improve calf health and welfare. Although many herd-level risk factors and their impact on calf health have been studied (Ganaba et al., 1995; Sanderson and Dargatz, 2000; Woolums et al., 2013, Waldner, 2014; Murray et al., 2016a), current calving and colostrum management practices on western Canadian cow-calf operations have not been benchmarked recently.

1.5 Objectives

For the reasons outlined above, calves assisted at birth represent a vulnerable, at-risk group within the herd and are a population that should be investigated to improve overall herd health and productivity. Practical, evidence-based strategies that can mitigate the impacts of a difficult calving and improve transfer of passive immunity are important to ensure calf health and survival and optimize profits for cow-calf producers. Therefore, the aims of this thesis are to benchmark current calving and colostrum management practices, to determine the clinical impacts of calving assistance on pain and inflammatory mediators, transfer of passive immunity, health, and performance in beef calves, and to investigate the impact of implementing pain mitigation at birth to assisted beef calves.

The objectives of this thesis are to:

I. benchmark current calving and colostrum management practices on western Canadian cow-calf operations and investigate the relationship between herd demographics and herd-level incidence of calving assistance, treatment for disease, mortality, and frequency of calving and colostrum management practices,

II. quantify subclinical trauma and its association with calving difficulty, vigour assessment parameters, and serum IgG concentration,

III. investigate the impact of implementing an NSAID at birth to assisted beef calves on pain and inflammation, transfer of passive immunity, and calf health and growth, and

IV. determine calf-level risk factors associated with assisted calvings that impact transfer of passive immunity, health, and growth.

CHAPTER 2 – BENCHMARKING CALVING MANAGEMENT PRACTICES ON WESTERN CANADIAN COW-CALF OPERATIONS

2.1 Abstract

Benchmarking current calving management practices and herd demographics on western Canadian cow-calf production systems helps fill the gap in knowledge and understanding of how these production systems work. Further investigation into the relationships between management decisions and calf health may guide the development of management practices and protocols to improve calf health, especially in compromised calves after a difficult birth. Therefore, the objectives of this cross-sectional study were to describe current calving management practices on western Canadian cow-calf ranches and to investigate the association of herd demographics with average herd-level incidence of calving assistance, morbidity, mortality, and use of calving and colostrum management practices. Cow-calf producers were surveyed in January 2017 regarding herd inventory and management practices during the 2016 calving season. Ninety-seven of 110 producers enrolled in the Western Canadian Cow-Calf Surveillance Network responded. Average herd-level incidence of assisted calvings was 4.9% (13.5% heifers, 3.2% cows), stillbirths was 2.1% (3.3% heifers, 1.9% cows), preweaning mortality was 4.5%, and preweaning treatment for disease was 9.4% (3.0% neonatal calf diarrhea, 3.8% bovine respiratory disease, 2.6% other diseases). Greater than 90% of producers assisted calvings and would intervene with colostrum consumption if the calf did not appear to have nursed from its dam. Late calving herds (i.e. started calving in March or later) had significantly lower average herd-level incidence of assistance, treatment for disease, and mortality ($P < 0.05$). In earlier calving herds (i.e. started calving in January or February) producers had shorter intervals between checking on dams for signs of calving or intervening to assist with a calving ($P < 0.05$). In early calving herds

producers were more likely to perform hands-on colostrum management techniques such as placing the cow and calf together or feeding stored, frozen colostrum ($P < 0.05$). There were no associations between herd size and herd-level incidences or management techniques ($P > 0.05$). This study suggests that in western Canada earlier calving herds are more intensively managed whereas later calving herds are more extensively managed. Herd demographics may be important to consider when investigating factors associated with management strategies, health, and productivity in cow-calf herds.

2.2 Introduction

Alberta, Saskatchewan, and Manitoba, are the predominant beef producing provinces, producing roughly 77% of the beef animals in Canada (Canfax Research Services, 2019). Among the cow-calf sector, calf health and survival are critical (Murray et al., 2016a). Herd-level factors such as the month calving season began and herd size were associated with an increased risk of treatment for disease (Woolums et al., 2013; Murray et al., 2016a) and month calving season began and dam housing were associated with a higher risk of mortality (Ganaba et al., 1995; Sanderson and Dargatz, 2000; Waldner, 2014). At the individual-level, a difficult birth increases the risk of diseases and preweaning mortality (Sanderson and Dargatz, 2000; Mellor and Stafford, 2004). Difficult births have also been associated with decreased transfer of passive immunity (Waldner and Rosengren, 2009; Barrier et al., 2013). Calves with failure of transfer of passive immunity have a higher risk of preweaning morbidity, mortality, and decreased weight gain (Dewell et al., 2006, Waldner and Rosengren, 2009). Good quality and timely administration of colostrum are important to the health and productivity of compromised calves (Filteau et al., 2003; Homerosky et al., 2017). Despite these North American studies, calving management practices vary greatly depending on region, operation size, and available facilities (NAHMS, 2009). Calving and colostrum management practices and relationships between management practices and calf health on western Canadian cow-calf operations have not been sufficiently described nor explored. Filling this gap in knowledge has the opportunity to better understand how these production systems work and to potentially guide the development of future protocols. Therefore, the objectives of this study are to benchmark current calving and colostrum management practices on western Canadian cow-calf operations and to investigate the relationship between herd demographics and herd-level incidence of calving assistance, treatment for disease, mortality, and frequency of calving and colostrum management practices.

2.3 Materials and methods

The study was approved on January 9th, 2017 by the University of Calgary Research Ethics Board (REB16-1142). Producers enrolled in this study were participants in the Western Canadian Cow-Calf Surveillance Network (WCCCSN), which consisted of a convenience sample of approximately 110 herds from the provinces of Alberta, Saskatchewan, and Manitoba. Producers were contacted through veterinary practices. Herds were selected to reflect the 2011 Census of Agriculture (Statistics Canada, 2011) to represent the geographic distribution and herd size of herds with at least 100 breeding females. Additionally, producers were enrolled based on willingness to participate. In the WCCCSN, producers were asked to complete 3-4 surveys per year and to allow biological sampling of their herd every other year (Moggy et al., 2017; Waldner et al., 2017).

The survey for this study consisted of 51 questions. The first section included questions regarding number of workers, herd demographics (start and end of calving season, herd size), and cow and calf inventory. The second section of questions pertained to management factors such as: pregnant cow management, calving management, calving protocols, colostrum management, mismothering and crossfostering, and breeding management. The full survey can be found in Appendix A.

A pilot survey was circulated to a total of 5 cow-calf producers, veterinarians, and researchers. The survey was then revised for clarity prior to being distributed to the WCCCSN producers. Paper copies of the surveys were mailed to WCCCSN participants and an online version was also available. Data were recorded in commercially available spreadsheet software (Microsoft Excel, Microsoft Corporation, Redmond, Washington, USA) prior to analysis. Only winter/spring calving season inventory data and management practices were reported. Questions that were unanswered by respondents as well as questions where respondents marked more than one answer for a single-answer question were excluded from the descriptive analysis, so the number of herds reported for each question varied.

2.3.1 Herd demographics and animal inventory

The month of the start of calving season was determined by the date on which the second full term calf was born in the herd. April and May were combined due to the small number of herds (<5) that started calving in May. Total herd size was estimated by adding the number of heifers calved to the number of cows that calved. Animal inventory was calculated for calving assistance, stillborn calves, treatment for disease, and mortality. The frequency of assisted animals comprised of the number of calves assisted at birth for each herd divided by the total number of calves born (live or dead) on each herd for heifers or cows, respectively. The frequency of stillborn calves comprised of the number for the stillborn calves divided by the total number of born calves (live or dead) on each herd for heifers or cows, respectively. The frequency of treated calves in the preweaning period comprised of the number of calves treated for each category of disease (neonatal calf diarrhea [NCD], bovine respiratory disease [BRD], or other diseases) divided by the total number of liveborn calves in each herd. The frequency of dead calves in each age category comprised of the number of dead calves in the age category (i.e. 1-7 days of age, 7-30 days of age, 30 days to weaning) divided by the total number of eligible live calves in that category (i.e. total number of live calves minus the number of stillborn calves and of calves that died in previous mortality age category) in each herd.

2.3.2 Pregnant dam management

Respondents were asked to self-identify which type of housing for heifers and cows best fit their operation for the production periods: breeding to pregnancy diagnosis, overwintering period, and two months prior to the start of the calving season. Categories were: extensive grazing (cattle are housed on large land areas with a relatively large number of acres per animal and the main feed source being grazing or green feed), small pasture (cattle are housed on a small land area with a relatively low number of acres per animal with supplemental feed and/or grains provided as the main feed source either on the ground or in a feeder or feed bunk), or dry lot (cattle are housed in a cattle-dense dry lot [feedlot] with all feed and/or grains provided in a feeder or feed bunk).

2.3.3 Calving management

Calving management questions included: the timing when dams were moved to the calving area (i.e. >6 weeks, 3-6 weeks, 1-3 weeks, <1 week before calving), what reasons dams were moved into a calving barn either prior to or after calving (i.e. signs of impending calving, needing calving assistance, cold weather, mismothering, bad udder, crossfostering), the timing when dams were moved out of the calving area, the frequency that dams were checked for signs of calving (i.e. <30 minutes, 30-60 minutes, 60-90 minutes, 90-120 minutes, >120 minutes), which circumstances prompted a producer to intervene with calving assistance (i.e. feet or water bag [amniotic sac] showing, no progression by the dam, no assistance for heifers or cows), how soon intervention occurred, and under what circumstances the producer decided to call a veterinarian for assistance (i.e. when they discover something is abnormal, after they had attempted to deliver the calf but were unsuccessful, only if surgery was needed, or they do not call a veterinarian for calving assistance).

2.3.4 Calving protocols

The techniques producers used to resuscitate a calf were ranked and reported as a count for each category. These included whether the producer rubbed the calf vigorously, hung the calf over fence or gate, poured water in the calf's ear, or poked the nose of the calf with a finger or straw. Respondents indicated the information they recorded at calving (i.e. birthdate, identification number, calving ease, birthweight, other) and how they recorded that information (e.g. paper, computer, etc.). The drugs or other treatments that were administered to dams or calves after a difficult delivery (i.e. antibiotics, non-steroidal anti-inflammatory drugs, vitamins, etc.) were reported as well as the procedures performed (e.g. dehorning, castration, etc.) or products administered (e.g. vitamin and minerals, pain mitigation, etc.) to all calves within the first week of life.

2.3.5 Colostrum management

Producers were asked to respond to which criteria they used to verify if a calf had received colostrum and to rank techniques in the order they were most commonly used to ensure calves received colostrum (i.e. placed the cow and calf together, restrained the cow and allowed the calf to nurse, bottle-fed calves, or tube-fed calves). The source of colostrum used to assist calves with colostrum consumption (i.e. the dam's colostrum, a colostrum replacer product, frozen colostrum, or dairy colostrum) was also ranked in the order they were most commonly used.

2.3.6 Mismothering and crossfostering

Respondents reported dam's behaviour that commonly resulted in mismothering, the procedures performed to encourage bonding, and how dams that exhibited mismothering were managed. Techniques for fostering a calf onto a new dam were ranked by respondents and frequencies for each category and rank were calculated.

2.3.7 Breeding management

Breeding management questions included selection criteria and traits of bulls used to breed heifers. A Likert scale for reasons to cull a dam based on management issues such as aggressive behavior, lameness and bad foot conformation, bad udder conformation, mismothering, not pregnant, and poor body condition was reported and a frequency for each likelihood score was calculated.

2.3.8 Associations between herd demographics, herd-level incidence, and key management practices

Data were analysed using STATA® 14.1 software (StataCorp LP, College Station, TX). Descriptive statistics were calculated for all variables and tests for normality were performed on continuous variables. For normally distributed variables, means and standard deviations (SD) were calculated and for non-normally distributed variables, medians and interquartile ranges (IQR) were calculated. The range for variables were described and proportions of animals affected within a herd or by dam parity (i.e. heifer or cow) were calculated. The associations between herd demographics and herd-level incidences were investigated using Wilcoxon rank-sum tests. Herd demographics investigated as predictor variables included: herd size (small <300 dams; large ≥300 dams) and month calving started (early = January or February; late = March, April, or May) for heifers or cows, respectively. The correlation between herd size and month calving started was assessed using a Spearman rank correlation test. Continuous outcome variables for herd-level incidence included: percentage of heifers requiring calving assistance, percentage of cows requiring calving assistance, overall percentage of dams requiring calving assistance, percentage of stillborn calves born to heifers, percentage of stillborn calves born to cows, percentage of total stillborn calves, percentage of calves treated for disease, percentage of calves born to heifers that died preweaning, percentage of calves born to cows that died preweaning, and overall percentage of calves that died preweaning. The association between herd demographics and key management practices were assessed using Fisher Exact (if a group had a count less than 5) or Chi Square tests. Pairwise comparisons of significant associations were performed using a Bonferroni correction test. Key management practice outcomes included: colostrum management, resuscitation techniques, the frequency heifers or cows were checked during daylight or night-time hours, time to assist after an amniotic sac or feet have been visualized for heifers and cows, time to assist after no progression has been visualized for heifers and cows, and no calving assistance of cows. Multivariable linear and logistic regression models were attempted but are not reported because of issues with collinearity and frequent violation of model assumptions. The significance level was set at $\alpha = 0.05$.

2.4 Results

2.4.1 Herd demographics and animal inventory

Ninety-seven of 110 producers from Alberta (n = 49, 50.5%), Saskatchewan (n = 29, 30%), and Manitoba (n = 19, 19.5%) responded to the survey. The majority of producers defined their herds as commercial (n = 72, 74.2%), while the remainder defined their herds as either both commercial and purebred (n = 20, 20.6%), or just purebred (n = 5, 5.2%). Most producers did not have seasonal workers (Median = 0, IQR 0 - 1, range 0-3) and most had 2 full-time workers (IQR 1 - 2, range 0 - 10). The median herd size was 226 (IQR 158 - 337) and ranged from 37 - 2615 calving dams. Only 4 of the 97 herds (4.1%) calved in both the spring and fall. Eighteen of 92 (19.5%) herds started calving heifers in January, 18/92 (19.5%) herds started calving heifers in February, 34/92 (37%) herds started calving heifers in March, and 22/92 (24%) of herds started calving heifers in April or May. Two herds did not calve out heifers in 2016. Seventeen of 95 (17.9%) herds started calving cows in January, 19/95 (20.0%) herds started calving cows in February, 32/95 (33.7%) herds started calving cows in March, and 27/95 (28.4%) herds started calving cows in April or May. The mean calving season length was 58.9 days (SD 19.7) for heifers and 85.6 days (SD 26.2) for cows. Heifer calving season ranged from 10-129 days and cow calving season ranged from 37 - 189 days. Table 2.1 describes animal inventory during the 2015-2016 production cycle.

Overall, the average herd-level incidence of calving assistance was 4.9%. The incidence of calving assistance in heifers was 13.5% (median = 4.5 calves, IQR = 2.0-8.5 calves, range = 0-60 calves per herd) and in cows was 3.2% (median = 4 calves, IQR = 1-10 calves, range = 0-30 calves per herd). Very few dams (0.2% overall, 0.7% of heifers [range = 0-3 heifers per herd], and 0.15% of cows [range = 0-3 cows per herd]) required a Caesarian section to deliver their calves. The average herd-level incidence of twins born to heifers and cows was 1.4% (median = 0 sets of twins, IQR = 0-1 sets of twins, range = 0-6 sets of twins per herd) and 2.5% (median = 4.5 sets of twins, IQR = 2-7 sets of twins, range = 0-20 sets of twins per herd), respectively.

The average herd-level incidence of preweaning treatment for disease was 9.4%. Three percent of calves (median = 2 calves, IQR 0 – 6 calves, range 0 – 144 calves per herd) were treated for NCD, 3.8% (median = 4 calves, IQR 1 – 10 calves, range 0 – 249 calves per herd) were treated for BRD, and 2.6% (median = 2 calves, IQR 0 – 5 calves, range 0 – 70 calves per herd) were treated for other diseases. The average herd-level incidence of preweaning mortality was 4.5%. The percentage, median, IQR, and range of calves that died by age group is shown in Table 2.1.

2.4.2 Pregnant dam management

The majority of heifers and cows were housed in an extensive grazing management system from breeding to pregnancy confirmation and in small pastures during the overwintering period. The majority of heifers were managed in either small pastures or dry lots 2 months prior to calving, while cows typically continued to be managed on small pastures. Figure 2.1 describes the frequency of producers' responses for pregnant dam housing during these three pre-calving periods.

2.4.3 Calving management

The majority of respondents moved heifers (66.6%, 62/93) and cows (76%, 73/96) to designated calving areas <1-3 weeks prior to calving. Most of the time, heifers (56.5%, 52/92) and cows (55.8%, 53/95) were only moved into the barn if they needed assistance with parturition. Table 2.2 describes the management decisions prior to calving for heifers and cows. Most respondents assisted at least one of their heifers (95.7%; 89/93) or cows (89.6%; 86/96) with calving during the 2016 calving season. Very few respondents do not assist their heifers (2.1%; 2/95) or cows (6.3%; 6/95) with calving. Table 2.3 describes how frequently respondents would check heifers and cows for signs of calving and when they would intervene with calving assistance. Seventy-five percent (71/95) of producers would call a veterinarian for a difficult calving only after they had attempted to deliver the calf but were not successful. Only 3.2% (3/95) would not call a veterinarian for calvings.

2.4.4 Calving protocols

The majority of producers (58.3%, 56/96) record calving information in a calving notebook or by paper records only, 37% (36/96) of producers recorded calving information on paper and then transferred it to a computer, and 6.3% (6/96) entered calving information directly into a computer or hand-held electronic device. Date of birth (94.8%, 91/96), calf identification number (89.6%, 86/96), and calving ease score at calving (73.9%, 71/96) were the information most commonly recorded at calving. Less than half of producers surveyed recorded birthweight

(43.8%, 42/96) and other things (5.2%, 5/96) such as calf sex, coat colour, udder score, and dam temperament.

Various procedures were employed to resuscitate a calf and were ranked (Fig. 2.2). Other methods of resuscitation reported included blowing air into the calf's nose, chest compressions, using a calf resuscitating device, and epinephrine, and were used by 23.2% (23/96) producers. After a difficult calving, many producers administered an NSAID or antibiotics to dams (Table 2.4). The most commonly used NSAID reportedly used was meloxicam (53.5%, 23/43) and the most commonly reported antibiotic used was oxytetracycline (51.4%, 18/35) followed by penicillin (14.5%, 5/35). Forty-five percent of producers also administered an NSAID to calves after a difficult delivery (Table 2.4), the majority used meloxicam (46.5% 20/43). The majority of producers responded that all calves born received visual identification tags (92.7%, 89/96), were castrated (56.3%, 54/96), and received vitamin and mineral injections (44.8%, 43/96) within the first week of life. A small proportion of producers (8.3%, 8/96) disinfect the navels of calves within the first week of life.

2.4.5 Colostrum management

The majority of respondents verified if a calf had received colostrum by visualizing the calf nursing (93.7%, 89/95), determining if the cow's udder did not look full (83.2%, 79/95), or assessing if the calf appeared full (44.2%, 42/95). Only 3.2% (3/95) of respondents did not check to see if the calf received colostrum. The most common techniques ranked first to ensure a calf received colostrum included: restraining the cow and helping the calf nurse (43.2%, 41/95), placing the cow and calf together in a pen (41.1%, 39/95), and tube feeding (24.2%, 23/95) or bottle feeding the calf (18.9%, 18/95). Only 1.1% (1/95) of respondents reported not intervening with colostrum consumption in their calves. The majority of respondents ranked the number one source of colostrum for the calf as being from the calf's dam (68.7%, 66/96) followed by a colostrum replacement product (38.5%, 37/96). Nine percent (9/96) of producers indicated that they sometimes used dairy colostrum as a source of colostrum for calves.

2.4.6 Mismothering and crossfostering

Overall, very few dams were managed for mismothering (1.2%). Heifers had a higher frequency of being managed for mismothering at 3.6% (median=1 heifer, IQR 0 – 2 heifers, range 0-12 heifers per herd) than cows at 0.8% (median=1 cow, IQR 0 – 2 cows, range 0-20 cows per herd). The most common behaviors ranked highest for mismothering included cow not allowing calf to nurse (39.4%, 37/94) followed by the cow abandoning the calf (28.7%, 27/94), having twins and rejecting one or both calves (26.6%, 25/94), and the cow showing aggressive behavior towards her calf (18.1%, 17/94). The majority of producers would either give a heifer one more chance (37.6%, 35/93) or closely monitor her at the next calving season (34.4%, 32/93) if she had mismothered her calf, while the majority of producers would remove cows from the herd (53.8%, 50/93) if she was managed for mismothering or closely monitor her at the next calving season (25.8%, 24/93). The most common procedures ranked first to be used to manage mismothering included housing the cow and calf together (56.4%, 53/94) followed by restraining the cow in a chute and assisting the calf to nurse (50.0%, 47/94). Few producers ranked keeping calves separate but close and confined (9.6%, 9/94), sedating the cow with a drug (2.1%, 2/94), or crossfostering the calf onto another cow (2.1%, 2/94) as common methods to manage mismothering.

During the 2016 calving season, few calves (0.3%) were fostered onto new dams due to mismothering (median=0 calves, IQR 0 – 1 calves, range 0-12 calves per herd). The proportion of calves fostered onto a new dam due to twinning was 1.1% (median 2 calves, IQR 1 – 4 calves, range 0 – 40 calves per herd) and the proportion of calves fostered due to death of the dam was 0.2% (median=0 calves, IQR 0 – 1 calves, range 0 – 3 calves per herd). The most common highest ranked procedures used to manage crossfostering included placing the dead calf's hide onto the foster calf (56.3%, 54/96) followed by placing the cow and calf together (36.6%, 34/95) and placing the placenta from the foster cow onto the new calf (20%, 19/95). Few producers ranked scent masking powder (6.3%, 6/96), putting grain on the foster calf (6.3%, 6/95), or sedating the foster dam (5.2%, 5/96) as methods to manage crossfostering.

2.4.7 Breeding management

When selecting a bull to breed replacement heifers, the majority of producers reported the bull's birthweight (33.7%, 32/95) or expected progeny difference (EPD) for calving ease (24.2%, 23/95) as the most important traits. Less frequently reported answers included: physical appearance (13.7%, 13/95), other traits not listed (10.5%, 10/95), breed reputation for calving ease (9.5%, 9/95), and pedigree (8.4%, 8/95). The more frequently selected answers for cows to be culled from the herd include aggressive behavior towards people, bad foot conformation, bad udder conformation, mismothering behaviors, and a nonpregnant diagnosis at fall pregnancy confirmation (Table 2.5).

2.4.8 Associations between herd demographics, herd-level incidence, and key management practices

Herd size, categorised as small or large, was not correlated with the month calving started for heifers (rho = 0.029, P = 0.8) and cows (rho = 0.11, P = 0.3). The month calving started for heifers was highly correlated with the start of calving month for cows (rho = 0.88, P< 0.0005). Herds that started calving heifers in later months had lower average herd-level incidence of calving assistance and preweaning treatment for disease than those herds calving heifers in earlier months (Table 2.6). Herds that started calving cows in later months had lower herd-level incidence of calving assistance, stillbirths, preweaning treatment for disease, and total preweaning mortality compared to those herds that started calving in earlier months (Table 2.6). Producers that had later calving heifer and cow herds were less likely to place a cow and calf together to encourage colostrum consumption (heifer and cow: OR = 0.16, P = 0.001) or to feed frozen colostrum (heifer: OR = 0.41, P = 0.04; cow: OR = 0.3, P = 0.01). There was no difference between early and late calving herds and resuscitation techniques (P > 0.05). Producers with earlier calving heifer herds were more likely to check on heifers and cows more frequently during daylight and night-time hours than those with later calving herds (Table 2.7). The odds that producers would intervene with a heifer calving after observing the amniotic sac for 60 to 90 minutes instead of < 60 minutes was 4.3 times higher in early calving herds compared to late calving herds (P = 0.002; Table 2.8). There were no other differences in how long producers waiting to intervene with calving based on when their herd calved (Table 2.8). There was no association between early and late calving herds and whether or not producers assisted cows with calving (P = 0.25).

There was no association between herd size and average herd-level incidence of calving assistance, disease, mortality, or management techniques ($P > 0.05$).

2.5 Discussion

This survey describes calving and colostrum management practices on western Canadian cow-calf ranches. In general, this survey indicates that the majority of respondents followed many recommended calving and colostrum management practices, but that record-keeping and herd-level incidences of morbidity and mortality could be improved. Producers with earlier calving herds have higher incidence of calving assistance, stillbirth, treatment for disease, and morbidity but there was no association with herd size. Producers with earlier calving herds use more intensive calving and colostrum management techniques than producers with later calving herds as well.

In this study, over 90% of producers moved their heifers and cows to a designated calving area, in contrast to 40% of U.S. herds surveyed (Dargatz et al., 2004). A specialized calving area to maintain calving dams is important to increase observation intervals, allow timely intervention, and provide protection from the elements (Dargatz et al., 2004). Although a specialized calving area may allow for increased observation intervals and timely intervention if needed, decreased uterine motility and incomplete cervical dilation have been associated with environmental stressors such as frequent presence of an observer and confined calving spaces in heifers and ewes (Bontekoe, et al., 1977; Dufty, 1981). The majority of producers of herds surveyed checked their heifers and cows multiple times a day, which was similar to a U.S. survey where producers would observe heifers 3.6 times and cows 2.5 times in a 24-hour period (Dargatz et al., 2004).

Timely intervention is important to decrease the severity of dystocia, risk of nerve damage and recumbency of the dam, and negative consequences of a prolonged delivery for the calf (Nix et al., 1998; Mee, 2004; Lombard et al., 2007). The recommendation that a calving be assisted after 70 minutes after the amniotic sac was visualized or 65 minutes after feet were visualized to decrease the risk of calf stillbirth was based on normal calving times in Holstein cows (Schuenemann et al., 2011). The majority of western Canadian cow-calf producers in this survey would assist a heifer or cow in less than 90 minutes if they appeared to have a prolonged or difficult calving while in comparison, the majority of U.S. producers allowed heifers to labor 2.8 hours or 3.5 hours for cows prior to assistance (Dargatz et al., 2004). Producers of earlier calving herds had greater odds of intervening with a heifer calving after observing the amniotic sac for 60 to 90 minutes instead of < 60 minutes compared to late calving herds. This may be due to the fact that producers of earlier calving herds are more likely to be observing dams for signs of calving more frequently and so may wait slightly longer before assisting with a calving in comparison to producers of later calving herds that may not have seen that dam as recently and may intervene slightly sooner. Although in this study the frequency of observations and interventions for calving assistance was not investigated as a risk factor for the average herd-level incidence of calving assistance and stillbirths, it may be an important factor affecting stillbirth rates in beef calves and should be investigated in future studies.

The average herd-level incidence of calving assistance in this survey was 4.9%, with 13.5% assistance of heifers and 3.2% assistance of cows. A previous Canadian study demonstrated an overall herd-level assistance risk of 8.8% in western Canadian cow-calf herds surveyed in 2001 (Waldner, 2014). Our survey findings were similar to reports from U.S. cow-calf herds that reported a 4.8% overall assistance risk, with 11.6% assistance of heifers and 4.3%

assistance of cows (NAHMS, 2009). The majority of difficult calvings are influenced by maternal body size, calf size, and by sire qualities (e.g. confirmation, birthweight, etc.) (Meijering, 1984). In the current study, the majority of producers selected bulls to breed to their heifers based on the bull's birthweight and calving ease EPD. Management decisions such as bull selection may influence the incidence of calving difficulties on cow-calf operations (Meijering, 1984; Larson et al., 2004; Funnel and Hilton, 2016). Although the incidence of calving assistance was low (4.9%) in this population, over 90% of producers assisted at least one heifer or cow, indicating that calving assistance and the associated management are widespread issues faced by producers on cow-calf operations.

Individual risk factors associated with calving assistance have been well studied (Meijering, 1984; Mee, 2004) but herd-level management and demographics have not. In this study, later calving herds had lower herd-level calving assistance risk for both heifers and cows. The findings of the present study are similar to a previous study that found that individual calves born in January or February had a higher calving assistance risk than those born in March and April (Waldner, 2014). This association may be due to more extensive calving management practices used by producers with spring calving operations in Alberta (Pang et al., 1998). Alternatively, it may be related to a lack of record-keeping, as 26% of herds surveyed in this study did not record calving ease score, a subjective score of the degree of calving difficulty and required level of assistance. Proportions of calving assistance in early versus late calving herds did not differ in a previous study conducted in Alberta, Canada (Pang et al., 1998); however, there were few assisted calvings reported in that study population. That study also differed from the present one in the definition of "early calving season". Pang et al. (1998) defined early calving season as starting in April and a late calving season as starting in May and June, whereas in the current study, early calving started in January and February and late calving started in March, April, or May.

Having an assisted calving, being born to a heifer or cow older than 10 years old, and being born of a twin are risk factors associated with stillbirth in beef calves (Waldner, 2014). In previous Canadian studies, the stillbirth risk ranged from 2.7 to 4.4% (Ganaba et al., 1995; Waldner, 2014), which was greater than the overall herd-level stillbirth risk of 2.1% (heifers = 3.3% and cows = 1.9%) in our study. Risk of mortality in the first day of life has been reported to range from 4 to 13% and half of all pre-weaning deaths occur within the first 24 hours of life (Berglund et al., 2003; Johanson and Berger, 2003). Mortality associated with an assisted or caesarian-born calf has been reported as high as 30 to 50% (Nix et al., 1998). Later calving herds had lower herd-level stillbirth and mortality risks in this survey. Decreased stillbirth risks are reported in herds with frequent calving supervision (Hodge et al., 1982); however, later calving herds in this survey supervised calvings less frequently than early calving herds. We hypothesize that stillbirth risks may have been lower in late calving herds due to an underreporting of stillbirths by extensively managed herds who monitor dams for signs of calving less frequently. Increased stillbirth risk is also seen in herds with higher incidence of dystocia and those that calve in small pens (Dufty, 1981; McDermott et al., 1992), as described in early calving herds in this study.

In this study, the herd-level treatment for disease was 9.4%, with 3.0% of calves being treated for NCD, 3.8% for BRD, and 2.6% for other diseases. This is similar to a previous study reporting 4.9% calves were treated for NCD and 3.0% for BRD (Murray et al., 2016a). Risk factors for increase in herd-level incidence of calfhood disease in that study were: not intervening at parturition, castration using small elastrator bands, and larger herd size. Similarly, in the current survey, a lower incidence of calves being treated for disease was observed in later calving herds, which also had a lower herd-level calving assistance risk. This may be due to more extensive management techniques such as less confinement, which is associated with lower morbidity (Sanderson and Dargatz, 2000) and less frequent management interventions for treating disease.

Calves experiencing a difficult birth have a higher risk of morbidity and mortality in the preweaning period (Lombard et al., 2007). Inadequate transfer of passive immunity through colostrum consumption contributes to an increased risk of preweaning morbidity (Larson et al., 2004; Waldner and Rosengren, 2009). This may be due to increased time to stand and nurse or decreased absorption of colostral immunoglobulins (Vasseur et al., 2009; Barrier et al., 2012b). Therefore, management techniques to decrease the risk of inadequate transfer of passive immunity and subsequent morbidity and mortality are important (Filteau et al., 2003; Murray et al., 2016a). Murray et al. (2016a) found that in herds where producers verified that the calf nursed and who intervened with colostrum administration had lower mortality in calves in the first week of life. Although the majority of beef producers in this survey do confirm colostrum ingestion and intervene with various methods of colostrum consumption, in later calving herds, producers were less likely to perform laborious colostrum intervention strategies such as placing the cow and calf together or feeding stored, frozen colostrum. This suggests that producers who have earlier calving herds may practice more intensive colostrum management techniques than those who have later calving herds.

Although this study reports current calving and colostrum management techniques, it was not possible to perform multivariable regression modeling to investigate more fully the risk factors for herd-level incidence of morbidity and mortality due to issues of collinearity, a lack of variability within the data, and frequent violations of model assumptions. Future studies looking at the associations between management factors could help fill in the gap in knowledge of herd-level risk factors for calf health. Also, the results of this study should be interpreted with caution as unmeasured herd characteristics and management factors not investigated may influence the relationships found. It is important to note that the majority of producers keep paper records and only recorded calving date and calf ID, clearly indicating that data collection by cow-calf producers could be improved and be used to benefit their decision making process. As such, estimating herd-level incidence of calving assistance, morbidity, and mortality may be underestimated.

2.6 Conclusions

Overall, this survey described current calving and colostrum management practices and found that although the incidence of calving assistance is low, the majority of producers do assist at least one calving and check to make sure calves consume colostrum. It also demonstrates how intervention strategies may differ between producers who have early and late calving herds and suggests that those who calve earlier have more intensively managed herds. Herd demographics may be important to consider when investigating risk factors associated with management strategies in cow-calf herds.

Table 2.1. Demographics of heifer, cow, and calf inventory during the 2015-2016 production cycle[1].

Inventory Category		Median	Interquartile range	Range	Average herd-level incidence
Dams that calved					
	Heifers	35	26-62	7-400	-
	Cows	192	133-291	24-2325	-
Dams that died during calving season					
	Heifers	0	0-0	0-3	0.4%
	Cows	0	0-1	0-5	0.4%
Dams that died from the end of calving season to the fall					
	Heifers	0	0-0	0-4	-
	Cows	0	0-1	0-20	-
Dams that aborted[2]					
	Heifers	0	0-1	0-10	1.7%
	Cows	1	0-4	0-50	1.4%
Total calves born[3]					
	Heifers	35.5	27.5-68	7-400	-
	Cows	200	135-301	24-2325	-
Live calves born					
	Heifers	34	25-62	6-287	-
	Cows	190.5	133-292	23-2305	-
Stillborn calves[4]					
	Heifers	1	0-2	0-18	3.3%
	Cows	3	2-6	0-26	1.9%
Calves that died 1-7 days of age					
	Heifers	0	0-1	0-5	0.7%
	Cows	1	0-2	0-10	0.7%
Calves that died from 7-30 days of age					
	Heifers	0	0-1	0-8	1.1%
	Cows	1	0-2	0-11	0.6%
Calves that died from 30 days to weaning					
	Heifers	0	0-1	0-38	1.3%
	Cows	1	0-3	0-30	0.9%

[1]Data collected from 97 cow-calf ranches surveyed through the Western Canadian Cow-Calf Surveillance Network

[2]Dams that gave birth to a calf that was not full term
[3]Calves born alive and dead
[4]Calve that were born dead but full term, or alive but died by 24 hours of age

Table 2.2. Respondents report of management practices pertaining to dam movement to and from the calving area and calving barn usage for heifers and cows[1].

Dam Management in the Calving Area	Heifers		Cows	
	Percent	Count	Percent	Count
When are dams moved to the calving area prior to calving?				
Calving occurs where overwintered	10.8%	10/93	10.4%	10/96
>6 weeks	5.4%	5/93	4.2%	4/96
3-6 weeks	17.2%	16/93	9.4%	9/96
1-3 weeks	38.7%	36/93	41.7%	40/96
<1 week	27.9%	26/93	34.3%	33/96
When are dams moved into the barn during calving?				
Signs suggest calving within 24 hours	10.9%	10/92	7.4%	7/95
Active calving	16.3%	15/92	13.7%	13/95
Only if dam needs assistance	56.5%	52/92	55.8%	53/95
I do not bring dams into the barn	16.3%	15/92	23.1%	22/95
When are cow-calf pairs moved into the barn after calving?[2]				
Cold weather	59.5%	53/89	54.4%	49/90
Mismothering	61.8%	55/89	65.6%	59/90
Bad udder	29.2%	26/89	52.2%	47/90
Crossfostering	58.4%	52/89	65.6%	59/90
Other	19.1%	17/89	20.0%	18/90
When are cow-calf pairs moved out of the calving area?				
Moved as soon as possible	21.1%	19/90	17.0%	16/94
Moved in batches every 24 hours	15.6%	14/90	18.1%	17/94
Moved at >24 hours but less than 1 week after birth	22.2%	20/90	19.2%	18/94
Moved in groups every 1-2 weeks	18.9%	17/90	12.8%	12/94
Remain in calving area until the end of the calving season	13.3%	12/90	15.9%	15/94
Pairs stay in calving area, un-calved dams are moved to a fresh pasture	1.1%	1/90	5.3%	5/94
Other	7.8%	7/90	11.7%	11/94

[1]Data from 97 cow-calf ranches surveyed through the Western Canadian Cow-Calf Surveillance Network
[2]Question was formatted as check all that apply

Table 2.3. Respondents report of management decisions pertaining to the frequency producers check dams for signs of calving and how long they waited before intervention with calving assistance for heifers and cows[1].

Management Decisions for Calving and Intervention	Heifers		Cows	
	Percent	Count	Percent	Count
How often are dams checked during daylight hours?				
At least hourly or every 1-2 hours	25.3%	24/95	21.2%	20/94
3-6 times a day	56.8%	54/95	50.0%	47/94
Twice daily	11.6%	11/95	24.5%	23/94
Once daily or other	6.3%	6/95	4.3%	4/94
How often are dams checked during night-time hours?				
At least hourly or every 1-2 hours	18.5%	17/92	19.3%	18/93
3-6 times a day	32.6%	30/92	28.0%	26/93
Twice daily	16.3%	15/92	14.0%	13/93
Once daily or other	32.6%	30/92	38.7%	36/93
How long do you wait to assist when water bag (amniotic sac) or feet are showing?				
< 60 minutes	34.5%	29/84	29.6%	24/81
60 minutes to 90 minutes	39.3%	33/84	34.6%	28/81
90 minutes to 120 minutes	17.9%	15/84	18.5%	15/81
> 120 minutes	8.3%	7/84	17.3%	14/81
How long do you wait to assist when no progression is seen?				
< 60 minutes	34.5%	29/84	29.6%	24/81
60 minutes to 90 minutes	39.3%	33/84	34.6%	28/81
90 minutes to 120 minutes	17.9%	15/84	18.5%	15/81
> 120 minutes	8.3%	7/84	17.3%	14/81

[1]Data collected from 97 cow-calf ranches surveyed through the Western Canadian Cow-Calf Surveillance Network

Table 2.4. Respondents report of treatments administered to the cow or calf after a difficult delivery[1].

Treatments Administered for a Difficult Delivery[2]	Calf		Cow	
	Percent	Count	Percent	Count
Nonsteroidal anti-inflammatory drug	44.7%	43/96	44.8%	43/96
Antibiotics	10.5%	10/95	36.5%	35/96
Vitamins or minerals	-	-	2.1%	2/96
Vitamins ADE injection	31.3%	30/96	-	-
Selenium/Vitamin E injection	35.4%	34/96	-	-
Lidocaine epidural	-	-	2.1%	2/96
Oxytocin	-	-	28.1%	27/96
Dip navel	8.3%	8/96	-	-
Other	4.2%	4/96	6.3%	6/96
Do not administer anything	34.4%	33/96	33.3%	32/96

[1]Data collected from 97 cow-calf ranches surveyed through the Western Canadian Cow-Calf Surveillance Network
[2]Questions were formatted as check all that apply

Table 2.5. Frequency of respondents reporting the likelihood they will cull cows for various behaviors or conditions[1].

Behavior or Condition	Very Unlikely		Unlikely		Possible		Likely		Very Likely	
	Percent	Count	Percent	Count	Percent	Count	Percent	Count	Percent	Count
Aggressive behavior	4.2%	4/95	3.2%	3/95	12.6%	12/95	15.8%	15/95	64.2%	61/95
Bad foot conformation	2.1%	2/95	1.1%	1/95	14.7%	14/95	43.2%	41/95	38.9%	37/95
Bad udder conformation	2.1%	2/96	0%	0/96	8.3%	8/96	38.5%	37/96	51.1%	49/96
Calf dead at birth	5.5%	5/91	10.9%	10/91	45.1%	41/91	13.2%	12/91	25.3%	23/91
Lameness	1.1%	1/94	10.6%	10/94	30.9%	29/94	37.2%	35/94	20.2%	19/94
Mismothering behaviours	2.1%	2/96	1.0%	1/96	32.3%	31/96	36.5%	35/96	28.1%	27/96
Not pregnant in the fall	3.2%	3/95	1.0%	1/95	2.1%	2/95	7.4%	7/95	86.3%	82/95
Poor body condition	2.1%	2/95	10.5%	10/95	43.2%	41/95	18.9%	18/95	25.3%	24/95

[1]Data from 97 cow-calf ranches surveyed through the Western Canadian Cow-Calf Surveillance Network

Table 2.6. Comparison of early (January or February) and late (March, April, or May) start of calving and herd-level incidence of calving assistance, stillbirths, and preweaning treatment for disease and mortality by dam parity (heifer or cow)[1].

[1]Data from 97 cow-calf ranches surveyed through the Western Canadian Cow-Calf Surveillance Network.

Herd-level Incidence	Early		Late		P Value
	Median	Interquartile Range	Median	Interquartile Range	
Calving assistance					
Heifer	18.2%	10 – 28.6	7.9%	3.6 – 13.3	<0.0005
Cow	5.3%	2.2 – 8.4	1.3%	0.6 – 2.2	<0.0005
Stillbirth					
Heifer	3.1%	0 – 5.9	1.5%	0 – 3.5	0.08
Cow	2.1%	0.9 – 3.5	1.3%	0.7 – 2.1	0.01
Preweaning treatment for disease					
Heifer’s calves	8.3%	3.3 – 20.6	3.4%	0.8 – 6.9	0.0008
Cow’s calves	5.9%	3.3 – 20.6	3.2%	0.8 – 8.2	0.001
Preweaning mortality					
Heifer’s calves	2.4%	0 – 6.0	0.6%	0 – 3.6	0.1
Cow’s calves	1.9%	1.3 – 3.5	1.8%	1.1 – 3.0	0.02

Table 2.7. Comparison of early (January or February) and late (March, April, or May) start of calving and frequency of respondents reporting key management practices such as frequency of checking dams for signs of calving for heifers and cows[1].

Management decisions for frequency of checking dams for signs of calving	Early	Late	P Value	Pairwise Comparisons: Odds Ratio[2] (P Value)		
	Count (%)	Count (%)		1-2 hrs. vs 3-6x/day	1-2 hrs. vs 1-2x/day	3-6x/day vs 1-2x/day
Frequency of checking heifers during daylight hours			0.003			
At least hourly or every 1-2 hours	17	7		6.6 (0.001)	-	-
3-6 times a day	14	38		-	19.4 (0.001)	-
Once to twice a day	1	8		-	-	2.9 (0.1)
Frequency of checking cows during daylight hours			0.0001			
At least hourly or every 1-2 hours	16	4		9.1 (0.001)	-	-
3-6 times a day	14	32		-	84.0 (<0.0005)	-
Once to twice a day	1	21		-	-	9.2 (0.002)
Frequency of checking heifers during night-time hours			0.0005			
At least hourly or every 1-2 hours	12	5		2.9 (0.004)	-	-
3-6 times a night	13	16		-	32.5 (<0.0005)	-
Once to twice a night	0	14		-	-	12.4 (0.004)
Frequency of checking cows during night-time hours			0.0001			
At least hourly or every 1-2 hours	14	4		4.1 (0.02)	-	-
3-6 times a night	12	14		-	42.0 (<0.0005)	-
Once to twice a night	0	13		-	-	12.1 (0.004)

[1]Data from 97 cow-calf ranches surveyed through the Western Canadian Cow-Calf Surveillance Network
[2]Odds ratios are interpreted as the odds of checking at the less frequent interval rather than the more frequent interval was this many times higher in late calving herds compared to early calving herds.

Table 2.8. Comparison of early (January or February) and late (March, April, or May) start of calving and frequency of respondents reporting key management practices such as frequency of calving intervention for heifers and cows[1].

	Early	Late	
Management decisions for calving intervention	**Count (%)**	**Count (%)**	**P Value**
Time to assist heifer when water bag (amniotic sac) or feet are showing			0.011[2]
< 60 minutes	8	19	
60-90 minutes	21	11	
90-120 minutes	3	11	
>120 minutes	3	4	
Time to assist cow when water bag (amniotic sac) or feet are showing			0.43
< 60 minutes	11	13	
60-90 minutes	13	15	
90-120 minutes	6	8	
>120 minutes	3	11	
Time to assist heifers when no progression is seen			0.48
<60 minutes	19	31	
60-90 minutes	6	13	
90-120 minutes	8	6	
>120 minutes	2	4	
Time to assist cows when no progression is seen			0.58
<60 minutes	18	22	
60-90 minutes	8	20	
90-120 minutes	3	4	
>120 minutes	5	7	

[1] Data from 97 cow-calf ranches surveyed through the Western Canadian Cow-Calf Surveillance Network
[2]Pairwise comparison reported in text

Figure 2.1. Frequency of respondents self-identifying the type of housing of heifers and cows at different management periods from breeding to prior to calving on 97 cow-calf ranches surveyed through the Western Canadian Cow-Calf Surveillance Network. Extensive grazing was defined as cattle housed on large land areas with a relatively large number of acres per animal and the main feed source being grazing or green feed. Small pasture was defined as cattle housed on a small land area with a relatively low number of acres per animal with supplemental feed and/or grains provided as the main feed source either on the ground or in a feeder or feed bunk. Dry lot was defined as cattle housed in a cattle-dense dry lot (feedlot) with all feed and/or grains provided in a feeder or feed bunk.

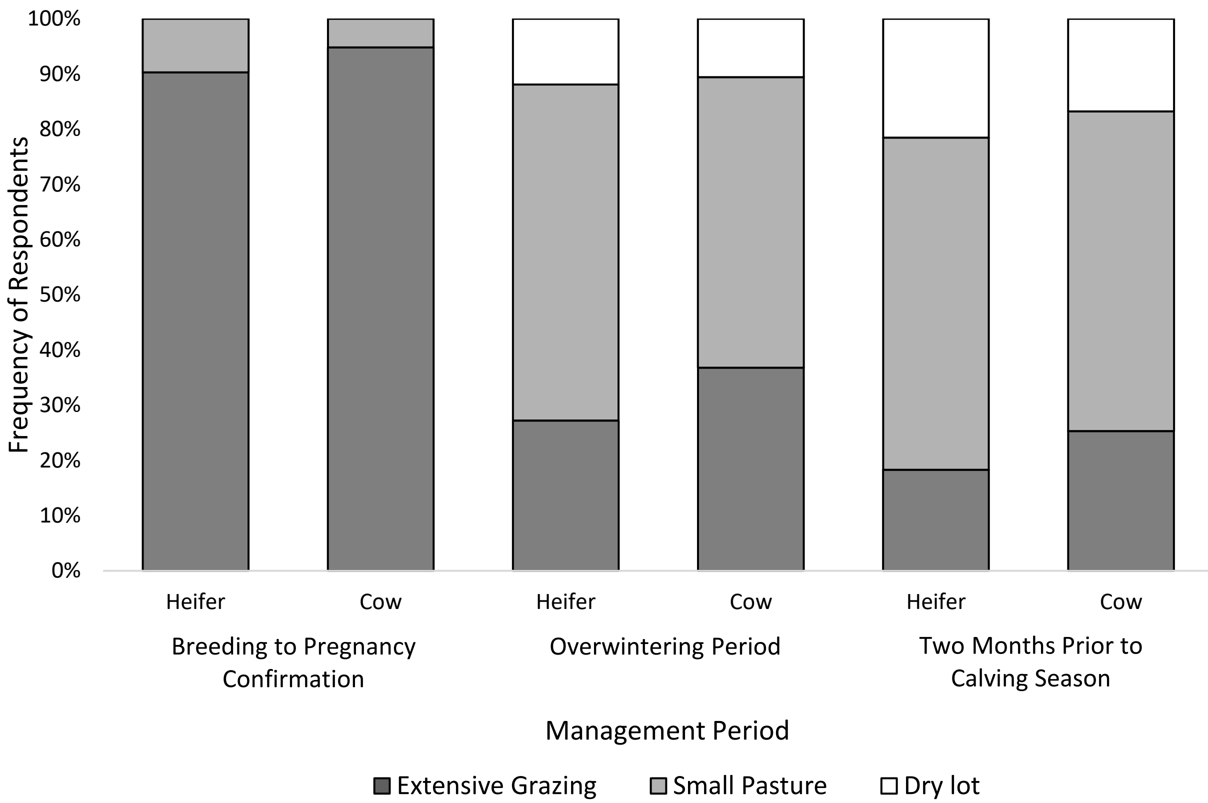
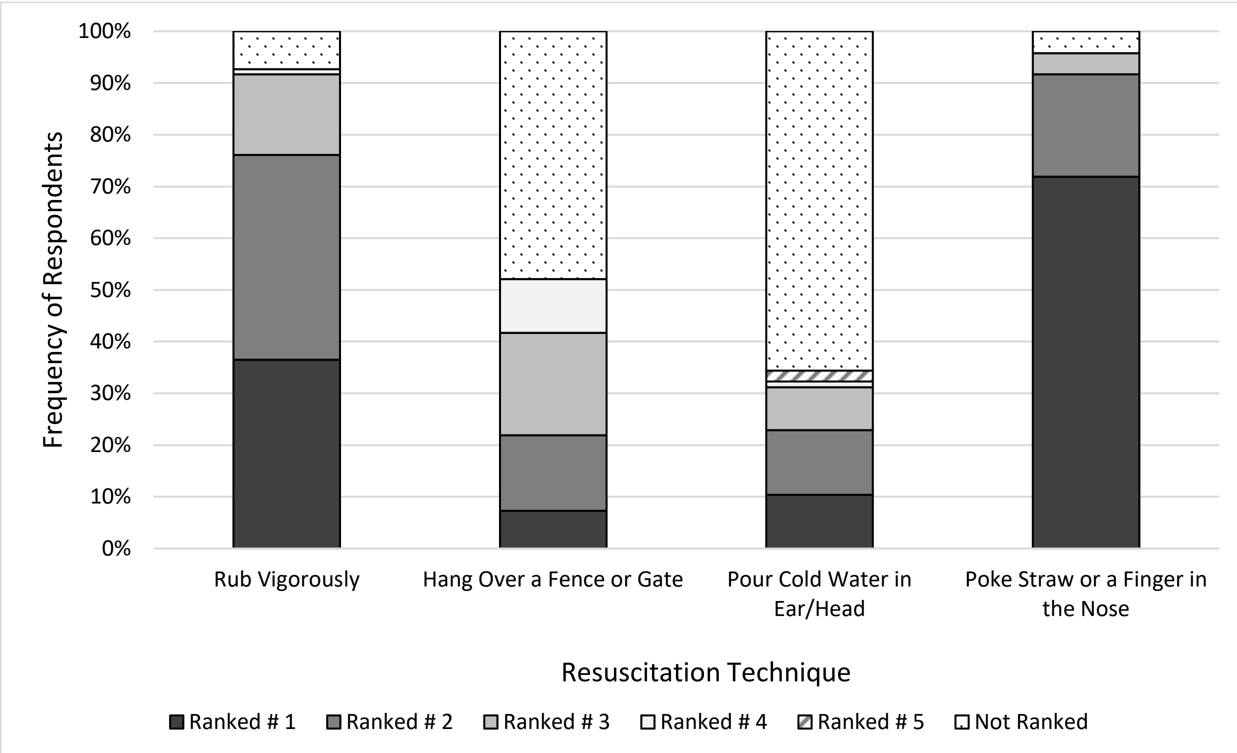


Figure 2.2. Frequency of respondents ranking resuscitation techniques from most to least commonly used on 97 cow-calf ranches surveyed through the Western Canadian Cow-Calf Surveillance Network.



CHAPTER 3 – QUANTIFYING SUBCLINICAL TRAUMA ASSOCIATED WITH CALVING DIFFICULTY, VIGOUR, AND PASSIVE IMMUNITY IN NEWBORN BEEF CALVES

3.1 Abstract

This cross-sectional study quantifies subclinical trauma associated with calving difficulty, calf vigour, and passive immunity (PI) in newborn beef calves. The degree of calving difficulty was categorised into: unassisted, easy assist (1 or 2 people manually pulling to deliver the calf), and difficult assist (more than 2 people pulling, a fetal extractor (i.e. calf jack), or caesarian section). Vigour assessment occurred at 10 minutes and blood sampling at 24-hours after birth in 77 beef calves. The measured blood parameters associated with trauma were creatine kinase (CK), aspartate aminotransferase (AST), and haptoglobin. Serum immunoglobulin (IgG) concentration was measured, and an IgG concentration ≥24g/L was considered as adequate PI. Calving difficulty was associated with elevated levels of CK (P=0.002) and AST (P=0.01), weak suckle reflex (P=0.001), abnormal mucous membrane colour (P<0.0001), and decreased odds of adequate PI (P=0.004). Elevated levels of CK and AST were associated with abnormal mucous membrane colour, incomplete tongue withdrawal, and weak suckle reflex at birth (P<0.001). An incomplete tongue withdrawal (P=0.005) and weak suckle reflex (P=0.02) were associated with decreased IgG concentrations. Abnormal mucous membrane colour, incomplete tongue withdrawal, and a weak suckle reflex were associated with decreased odds of having adequate PI (P<0.05). Haptoglobin was not associated with any of the parameters measured. Subclinical trauma was associated with calving difficulty, decreased vigour, and decreased odds of having adequate PI. Understanding the impacts of a traumatic birth may aid the development of management strategies for compromised newborn beef calves.

3.2 Introduction

Calf health and survival is crucial to successful cow-calf operations. Although the majority of producers rank calving ease and birth weight as their most important selection criteria when purchasing replacement bulls (NAHMS, 2009), approximately 9% of calvings are assisted in western Canada (Waldner, 2014). This proportion fluctuates between herds and between different years, but almost all cow-calf operations have some calvings that require assistance each season.

Calves that are assisted at birth are more likely to experience trauma or oxygen deprivation during the birthing process, which may negatively influence their vigour (Bellows et al., 1987; Vaala and House, 2002; Bleul and Gotz, 2013). Trauma caused by an assisted calving includes: fractured or luxated vertebrae, ribs, and legs; crushing injuries; vascular compromise to soft tissues; and edema of the tongue or head due to prolonged periods in the dam's pelvic canal (Ferguson et al., 1990; Nagy, 2009). Assisted calves also have a higher risk of acidemia and hypoxia, which can lead to decreased vigour, and decreased transfer of colostral immunoglobulins (Szenci et al., 1988; Besser et al., 1990; Schuijt and Taverne, 1994). Failed transfer of passive immunity (PI) is caused by the inadequate ingestion or absorption of enough good quality colostrum (Weaver et al., 2000) and is associated with increased pre-weaning morbidity and mortality (Wittum and Perino, 1995; Dewell et al., 2006.

Higher risk of stillbirth and preweaning morbidity and mortality are consequences of difficult calvings (Patterson et al., 1987; Sanderson and Dargatz, 2000; Waldner, 2014). However, the extent or severity of trauma, and the impacts of that trauma on calf well-being have not been well described. Unless the trauma is obvious (e.g. fractures), on farm this trauma often goes undiagnosed and therefore, untreated (Ollivett et al., 2018). The degree of tissue damage, disease, or organ malfunction are commonly assessed in veterinary practice based on certain biochemical parameters measured in blood or other tissues. Muscle trauma, inflammation, or other muscular pathological processes can be measured by serum creatine kinase (CK) and aspartate aminotransferase (AST). These enzymes are released into the plasma after muscle or other organ damage have occurred (Russell and Roussel, 2007). Currently, there is no published research quantifying the relationship of these blood parameters with the trauma of calving difficulty.

Therefore, the objective of this study was to quantify subclinical trauma, as measured by elevated muscle enzymes and haptoglobin, a marker for inflammation, and its association with calving difficulty, vigour assessment parameters, and serum IgG concentration. It is hypothesized that elevated levels of CK, AST, and haptoglobin will be associated with greater calving difficulty, reduced vigour, and failed transfer of passive immunity, and calves with reduced vigour are suspected to have increased odds of failed transfer of passive immunity.

3.3 Materials and methods

The study was approved February 3rd, 2014 by the University of Calgary Veterinary Sciences Animal Care Committee (AC13-0324) and was conducted in accordance with guidelines established by the Canadian Council on Animal Care. The data were collected in March 2014 in Alberta, Canada from 77 calves that were enrolled as described previously (Homerosky et al., 2017a,b). A privately-owned cow-calf operation located in southern Alberta was enrolled as the study herd. It consisted of approximately 800 Hereford and Hereford x Red Angus cows and heifers. Animals were enrolled using a purposive sampling regime to represent both mature cows and heifers and include unassisted and assisted calvings. Pregnant dams were monitored in small pastures close to the calving barn and checked hourly for signs of calving. Unassisted dams were allowed to calve without assistance in the pasture, and the calves were brought into the barn within 10 minutes of birth. Failure to calve or make progression within one hour of estimated onset of stage two labour (e.g. amniotic sac visible, feet present, strong abdominal contractions, etc.) resulted in the dam being walked to the nearby calving barn for vaginal examination and assisted delivery of the calf. If the calf was unable to be delivered vaginally, a veterinarian examined the dam, and if necessary, a caesarean section (C-section) was performed.

At-birth data that was collected included: date and time of calving, calving ease score, presentation and posture of the calf, dam parity, calf sex, and calf birth weight. The subjective measure of calving ease score was categorised as unassisted (UA), easy assist (EA), or difficult assist (DA). Easy assists were defined as one or two people manually pulling to extract a calf. Difficult assists were those that required more than two people, a fetal extractor (i.e. calving jack; Dr. Franks Calf Puller, Neogen), or C-section. The presentation of the calf was defined as anterior versus posterior, and any abnormal posture (e.g. head ventroflexed, leg malpositioned, etc.) was also recorded for assisted calvings.

Within 10 minutes of birth, all calves were placed in sternal recumbency and evaluated for vigour parameters. The vigour parameters used in this study were examined in Homerosky and colleagues (2017a,b) and were associated with acidemia (mucous membrane colour and tongue withdrawal) and likelihood of standing to nurse without human assistance within 4 hours of birth (suckle reflex). Mucous membrane colour was categorised into pink (light pink or dark pink) or abnormal (blue-purple, white, dark red) by visual examination of the oral mucous membranes. Tongue withdrawal was categorised as complete or incomplete depending on whether the calf withdrew the tongue back into its mouth fully or not when the tongue was pulled from the its mouth. Suckle reflex was categorised as strong or weak by placing a finger in the calf's mouth and feeling if it suckled the finger. Calves born dead or that did not survive to 10 minutes were not enrolled.

After vigour assessments were performed, cow-calf pairs were placed in individual box stalls and monitored for colostrum consumption. If calves were not observed nursing from the dam by 4 hours after birth, research personnel intervened with colostrum consumption first by assisting the calf to nurse from the cow in a chute. If the calf did not nurse from the dam, the dam was hand-milked, and the calf bottle or tube fed 0.5-1.25 L of colostrum by 6 hours, as per on-farm protocols.

A blood sample was collected from each calf by jugular venipuncture at approximately 24 h after birth (Homerosky et al., 2017a) using a 10 mL silicon-coated serum separator vacutainer tube and 20 G x 2.54 cm needle (BD Vacutainer). Whole blood samples were stored at 4 ºC until processed. Within 12 hours of collection, samples were centrifuged at 1400 G for 20 min. Serum was extracted and frozen at -80 ºC until further analysis.

Biochemistry profile analysis was performed on 24-hour post-birth serum samples using a Beckman AU680 chemistry panel machine (Beckman/Coulter) at the IDEXX Reference Laboratories (Calgary, AB). Haptoglobin analysis was performed by photometric analysis using the 6000 c501 biochemistry analyser (Roche Cobas) at the Animal Health Laboratory, University of Guelph (Guelph, ON). Serum IgG concentrations were also measured in the 24-hour serum samples using an in-house radial immunodiffusion assay (RID) at the Saskatoon Colostrum Company Ltd. Quality Assurance Laboratory (Saskatoon, SK), as described by Chelack et al. (1993).

Data were analysed using STATA® 14.1 software (StataCorp LP). Descriptive statistics and tests for normality were performed on all continuous variables. Adequate PI was categorised as serum IgG concentration above a cut-point of 24 g/L (Waldner and Rosengren, 2009). To assess differences between proportions of assisted heifers and cows, a Fisher's Exact test and pairwise comparisons were performed. To evaluate the association of calving ease score with the continuous blood parameters indicative of trauma and serum IgG concentration, Kruskal Wallis tests were performed on the non-parametric outcomes (CK, AST, and haptoglobin) and one-way ANOVA was performed on the parametric outcome (serum IgG concentration). To determine the association of calving ease score on the categorical outcomes of vigour and adequate PI, a Fisher's Exact test was used. To assess the association of blood parameters indicative of trauma on the categorical outcomes of vigour, Wilcoxon Rank Sum tests were performed. To evaluate the association of vigour on serum IgG concentration, a Student's T test was performed, and a Fisher's Exact test was performed to evaluate the association of vigour with adequate PI. Pairwise comparisons between calving ease score, vigour parameters, and adequate PI were done using a Bonferroni correction test. Odds ratios (OR) were calculated; however, when a cell had a zero for its count, 0.5 was added to all cells for the calculation (Pagano and Gauvreau, 2000).

3.4 Results

Data were collected from calves born to 50 mature cows (65%) and 27 heifers (35%). Forty-one heifer calves (53%) were enrolled and 36 bull calves (47%). As reported previously, there was no difference between the proportion of total assisted births between heifers and cows, nor in the average birth weight between bull and heifer calves (Homerosky et al., 2017a). A heifer was more likely to be a DA than an EA compared to cows (P = 0.0008), but the proportions did not differ between the other groups (*P* > 0.06). The majority of calves were born in anterior presentation (91%) and normal posture (84%). The population sampled categorised by calving ease score is reported (Table 3.1). Median birth weight and interquartile range by calving ease score was 38.4 kg (37.5-41.0) for UA, 40.7 kg (36.4-45.7) for EA, and 39.7 kg (36.1-43.3) for DA.

Twenty-two calves were categorised as UA (28.6%), 41 as EA (53.2%), and 14 as DA (18.2%), as previously reported (Homerosky et al., 2017a). Two of the 14 DA calves categorised as DA were born via C-section. They were categorised as a DA because there were extensive efforts made by the farm personnel to deliver the calves vaginally prior to surgical intervention by a veterinarian. Difficult assists were associated with elevated CK and AST levels as compared to EA and UA (Table 3.2). There was no association between calving ease score and haptoglobin levels or serum IgG concentrations (Table 3.2). Calving ease score had an effect on suckle reflex and mucous membrane colour. Difficult assists were associated with a higher proportion of calves with weak suckle reflexes when compared to UA (OR = 45.0, *P* = 0.0004) and EA (OR = 4.9, *P* = 0.02). Difficult assists were associated with a higher proportion of calves with abnormal mucous membrane colour when compared to UA (OR = 45.0, *P* = 0.0004) and EA (OR = 9.3, *P* = 0.02). Twenty-two (100%) UA calves, 38 (92.7%) EA calves, and 9 (62.3%) DA calves had adequate PI. Difficult assists were associated with a higher proportion of calves with inadequate PI when compared to UA (OR = 26.1, *P* = 0.005) and EA (OR = 7.04, *P* = 0.019).

An abnormal mucous membrane colour at birth was associated with significantly elevated CK and AST levels (Table 3.3). An incomplete tongue withdrawal and weak suckle reflex were associated with elevated CK, AST, and decreased serum IgG concentrations (Table 3.3). Haptoglobin was not associated with any vigour parameters (Table 3.3). Abnormal vigour parameters (abnormal mucous membrane colour, incomplete tongue withdrawal, and weak suckle reflex) were associated with higher odds of inadequate PI ($P<0.05$) (Table 3.4).

3.5 Discussion

In the present study, DA calvings were associated with increased tissue trauma, as evidenced by elevated CK and AST levels, higher odds of reduced vigour, and higher odds of inadequate PI, indicating that a more difficult birth causes more tissue trauma and impacts calf vigour and PI. Although many textbooks may report that difficult calvings cause trauma, it has not been fully investigated nor quantified. Undiagnosed trauma is often observed at necropsy in the form of subcutaneous bruising (Bellows et al., 1987; Waldner et al., 2010). In the present study, no fractures or obvious signs of trauma were diagnosed at birth, but the calves experiencing a DA had elevated levels of blood parameters associated subclinical trauma. Subclinical trauma caused by a difficult birth may be more prevalent than previously recognised. A randomised clinical trial for a viral respiratory vaccine unexpectantly found a prevalence of 6% rib fractures in dairy calves during thoracic ultrasonography (Ollivett et al., 2018). Those authors found that these undiagnosed rib fractures were associated with assisted calving and with decreased average daily gain (Ollivett et al., 2018). Therefore, subclinical trauma may have long-term affects on calf health and production.

Calves that experienced a DA in this study had significantly elevated CK and AST values compared to UA and EA calves. Serum CK is a sensitive and specific biochemical indicator that can detect subclinical muscle injury and trauma (Anderson et al., 1976). The half-life of serum CK is approximately 4 hours and values decrease rapidly if the cause of muscle damage ceases (Cox and Onapitos, 1986; Lefebvre et al., 1994). Aspartate aminotransferase has a half-life of about 20 hours and changes more slowly than CK (Stockham and Scott, 2002). Therefore, subclinical trauma experienced at birth can be detected at 24 hours of age using a combined assessment of CK and AST (Russell and Roussel, 2007). Few studies have quantified serum biochemical results in newborn calves and those authors found elevated CK levels at birth that declined over time (Egli and Blum, 1998; Knowles et al., 2000). They hypothesized these findings were due to trauma associated with birth, but they did not specifically investigate the association with varying degrees of calving difficulty. The present study demonstrated subclinical trauma was associated with difficult births as measured by elevated levels of CK and AST, and this differed from easy assisted and unassisted births.

Subclinical trauma was associated with reduced vigour, and serum IgG concentrations were significantly lower in calves with weak suckle reflexes and an incomplete tongue withdrawal. Various assessment of newborns, such as the APGAR score, have been used in various neonatal species to classify their vigour at birth (Apgar, 1953; Randall, 1971; Veronesi et al., 2005). A difficult birth can result in a less vigorous neonate, which subsequently leads to a prolonged time to stand and time to suckle from the dam (Poppe et al., 2006; Barrier et al., 2012b; Murray, 2013). The present study is consistent with other studies demonstrating that calves with prolonged or difficult calvings had reduced vigour compared to calves assisted earlier during the parturition process (Vilettaz Robichaud et al., 2016) or unassisted calvings (Riley et al., 2004). Reduced vigour and vitality have been shown to be associated with acidemia, hypoxia, and elevated L-lactate (Bleul and Gotz, 2013; Homerosky et al., 2017a). Acidemia or hypoxemia could be another physiological explanation for reduced vigour in assisted calves. The relationship between subclinical trauma and hypoxia as a result of a difficult calving was not investigated but should be investigated in future studies.

Reduced vigour has also been associated with inadequate PI in beef and dairy calves (Homerosky et al., 2017b; Barrier et al., 2013). A previous analysis performed on this sampled population showed that calves with a weak suckle reflex had higher odds of failing to consume colostrum on their own by 4 hours, and that there was an association between those that failed to consume colostrum by 4 hours and inadequate transfer of passive immunity (Homerosky et al., 2017b). Vasseur et al. (2009) found that a dairy calf's overall vigour (defined as attempting to stand within 1 hr of birth) was associated with colostrum intake. They also found birthweight, vigour during feeding, and vigour during the first hour of life were associated with the quantity of colostrum ingested. Although the outdoor birthing environment for UA calves was different than the indoor birthing environment of EA and DA calves, there was no difference in vigour parameters between UA and EA calves. This suggests environmental factors had negligible effect on calf vigour in this study.

In this study, calving ease score was not associated with the continuous outcome of serum IgG concentration, but it was significantly associated with the dichotomised outcome of adequate PI. This may indicate that even if the mean concentration of immunoglobulin is not significantly different by calving ease score, a difficult calving still influences the likelihood of a calf reaching a threshold of adequate PI. The purpose of using a standard cut-off for serum IgG concentration is to determine which calves are at an increased risk for morbidity and mortality (Waldner and Rosengren, 2009). Although no association between calving ease score and serum IgG concentration was reported in this study, others have reported a decrease in serum IgG concentration with increasing calving difficulty (Muggli et al., 1984; Barrier et al., 2013; Gaspers, 2015). Our lack of significant differences may be due to a small proportion of calves having low concentrations of IgG, as all calves received colostrum by 6 hours after birth. One similar study found no association between calving difficulty and serum IgG concentrations when those calves were all fed 1 L of colostrum shortly after birth (Stott and Reinhard, 1978). A limitation to this study was the variation in the quality, volume, and method of colostrum consumption. It is well documented that high quality colostrum and larger concentrations of colostral IgG fed to dairy calves improves passive immunity (Godden, 2008), but that was not standardized in this study due to on-farm protocols.

Haptoglobin did not differ significantly among calving ease scores, nor was it associated with reduced vigour. Haptoglobin is one of the major acute phase proteins in cattle (Eckersall and Bell, 2010) and is released in the early stages of inflammation and infection or after tissue damage (Koj, 1985; Murata et al., 2004). Although acute phase proteins are not specific to a certain disease, they are quite sensitive to inflammation and can detect subclinical disease in some species (Cerón et al., 2005). Similar to the results of the present study, Alsemgeest et al. (1995) reported that haptoglobin was undetectable or in low concentrations in newborn calves after different types of obstetrical help. They suggested that the trauma of parturition did not increase acute phase proteins in neonates due to the inability of the immature liver to produce the protein (Alsemgeest et al., 1995).

Although the primary objective of this study was achieved, there were limitations. One is the lack of control over variables in the environment and potential confounders that exist on a commercial ranch. However, this is balanced with the increased external validity of using such a ranch compared to a research facility. It was not feasible to select at random the animals in this study. They were enrolled based on a purposive sampling of cattle calving within a 24-day period and that could be handled without injury to the animal handlers or excessive stress to the periparturient dam. On this ranch, the animals were intensely managed. Early intervention to increase the proportion of live-born calves may have inflated the number of calves in the easy assisted group and underestimated the unassisted group, if those animals had been given more time to calve. Interestingly, only difficult assists, which likely represent "true dystocias", had significantly elevated blood parameters associated with trauma, reduced vigour, and increased odds of inadequate PI. In situations where the dam's birth canal is fully dilated, early intervention may indicate a positive management decision to aid in the prevention of calves becoming compromised due to a prolonged calving (Villettaz Robichaud et al., 2016). Although not assessed in this study, it is important to note that the degree of interaction between the dam and calf may influence the vigour, time to stand, and time to nurse in neonatal calves (Lidfors, 1996; Ribeiro et al., 2007). Also, further studies to investigate pain and inflammation associated with difficult calvings is warranted as this may impact calf vigour and health.

3.6 Conclusions

Difficult births lead to elevated indicators of subclinical trauma and decreased vigour in the neonate, which can be quantified by measuring serum CK, AST, and vigour parameters, respectively. Trauma and reduced vigour can lead to inadequate transfer of PI. These findings suggest further studies are needed to investigate appropriate management practices to decrease the impacts of a difficult calving on calf health.

Table 3.1. Descriptive statistics of 77 cow-calf pairs by calving ease score.

Variable	**Unassisted**[1]	**Easy Assist**[2]	**Difficult Assist**[3]
Dam			
Heifers	8 (29.6%)	9 (33.3%)	10 (37.0%)
Cows	14 (28.0%)	32 (64.0%)	4 (8.0%)
Calf sex			
Bull	5 (13.9%)	24 (66.7%)	7 (19.4%)
Heifer	17 (41.5%)	17 (41.5%)	7 (17.0%)

[1]Calf delivered without assistance at birth

[2]One or two people pulling to extract a calf

[3]More than two people pulling, a fetal extractor, or Caesarian section used to extract a calf

Table 3.2. Descriptive statistics for blood parameters indicative of trauma and serum immunoglobulin G (IgG) concentrations measured at 24 hours by calving difficulty in 77 cow-calf pairs*.

Blood Parameter	**Unassisted**[3]	**Easy Assist**[4]	**Difficult Assist**[5]	**P-value**
CK (IU/L)[1,6]	233.5 (192 - 343)	310 (228 - 458)	696 (268 - 1441)	0.002
AST (IU/L)[1,7]	61.5 (55 - 73)	71 (59 - 82)	78 (63 - 119)	0.01
Haptoglobin (g/L)[1]	0.15 (0.13 - 0.16)	0.14 (0.13 - 0.16)	0.14 (0.13 - 0.15)	0.9
Serum IgG (g/L)[2]	47.4 (42.2 - 52.6)	43.3 (39.3 - 47.4)	36.6 (24.6 - 48.7)	0.1

[1]Median (1st interquartile to 3rd interquartile) reported for non-normally distributed variables
[2]Mean (95% CI) reported for normally distributed variables
[3] Calf delivered without assistance at birth
[4]One or two people pulling to extract a calf
[5]More than two people pulling, a fetal extractor, or Caesarian section used to extract a calf
[6]Creatine kinase
[7]Aspartate aminotransferase
*Pairwise comparisons reported in text

Table 3.3. Descriptive results for blood parameters indicative of trauma and serum immunoglobulin G (IgG) concentration by vigour parameters in 77 cow-calf pairs.

Variable	**Categories**		**P-value**
Mucous Membrane Colour	**Pink (n = 66)**	**Abnormal (n = 11)**	
CK (IU/L)[1,3]	270 (218 - 401)	878 (514 - 4178)	<0.0001
AST (IU/L)[1,4]	67 (57 - 78)	94 (71 - 130)	0.002
Haptoglobin (g/L)[1]	0.14 (0.13 - 0.15)	0.14 (0.13 - 0.19)	0.3
Serum IgG (g/L)[2]	44.4 (41.5 - 47.5)	36.0 (20.0 - 51.9)	0.07
Tongue Withdrawal	**Complete (n = 60)**	**Incomplete (n = 15)**	
CK (IU/L)[1,3]	270 (212.5 - 411.5)	584 (309 - 1441)	0.0004
AST (IU/L)[1,4]	67 (55.5 - 77.5)	82 (76 - 119)	0.0009
Haptoglobin (g/L)[1]	0.14 (0.13 - 0.16)	0.15 (0.13 - 0.16)	0.4
Serum IgG (g/L)[2]	45.5 (42.0 - 49.0)	33.8 (25.2 - 42.4)	0.005
Suckle Reflex	**Strong (n = 63)**	**Weak (n = 14)**	
CK (IU/L)[1,3]	269 (206 - 420)	544 (309 - 1441)	0.0005
AST (IU/L)[1,4]	67 (55 - 77)	88.5 (76 - 130)	0.0002
Haptoglobin (g/L)[1]	0.14 (0.13 - 0.16)	0.135 (0.13 - 0.16)	0.9
Serum IgG (g/L)[2]	45.0 (41.7 - 48.3)	35.3 (24.7 - 45.9)	0.02

[1]Median (1st interquartile to 3rd interquartile) reported for non-normally distributed variables
[2]Mean (95% CI) reported for normally distributed variables
[3]Creatine kinase
[4]Aspartate aminotransferase

Table 3.4. Descriptive results for vigour parameters by passive immunity in 77 cow-calf pairs.

Variable	Passive Immunity		OR	P-value
Mucous Membrane Colour	**Inadequate[1] (n = 8)**	**Adequate[2] (n = 69)**		
Abnormal (n = 11)	5	6	17.5	0.001
Pink (n = 66)	3	63		
Tongue Withdrawal	**Inadequate[1] (n = 8)**	**Adequate[2] (n = 67)**		
Incomplete (n = 15)	4	11	5.09	0.046
Complete (n = 60)	4	56		
Suckle Reflex	**Inadequate[1] (n = 8)**	**Adequate[2] (n = 69)**		
Weak (n = 14)	4	10	5.9	0.03
Strong (n = 63)	4	59		

[1]Inadequate passive immunity (serum immunoglobulin concentration < 24 g/L)
[2]Adequate passive immunity (serum immunoglobulin concentration ≥ 24 g/L)

CHAPTER 4 – CLINICAL IMPACTS OF ADMINISTERING A NON-STEROIDAL ANTI-INFLAMMATORY DRUG TO BEEF CALVES AFTER ASSISTED CALVING ON PAIN AND INFLAMMATION, PASSIVE IMMUNITY, HEALTH, AND GROWTH

4.1 Abstract

Assisted calves are often born weak, injured, or oxygen deprived, and have a higher risk of morbidity and mortality. The objective was to investigate the impact of using pain mitigation at birth in assisted beef calves on physiological indicators of pain and inflammation, passive immunity, health, and growth. Thirty-three primiparous cow and their calves requiring assistance at birth on 2 ranches located in southern Alberta were enrolled. Data collected at birth included: date and time of calving, calf sex, meconium staining, presentation of calf, and calving difficulty (easy assist: 1 person manually delivered the calf; difficult assist: delivery by 2 or more people, or mechanical assistance). Within 10 minutes of birth, calves were stratified by calving difficulty, randomized to a medication group, and received a subcutaneous dose of meloxicam (0.5 mg/kg body weight) or an equivalent volume of placebo. Cow-calf pairs were then placed in individual box stalls for observation and sampling. At birth, 1 hour, 4 hours, and 24 hours after birth, heart rate, respiratory rate, and rectal temperature were assessed, and blood samples collected to measure indicators of pain and inflammation (cortisol, corticosterone, substance P, and haptoglobin). Serum immunoglobulin (IgG) concentration and failed transfer of passive immunity (serum IgG concentration less than 24 g/L) were assessed in the 24 hours blood samples. Preweaning treatment for disease and mortality information was collected, and calves were weighed at 7-10 days of age and at weaning. Of the 33 calves enrolled, 17 calves received meloxicam and 16 calves received a placebo. Meloxicam-medicated calves had significantly greater average daily gain to 7-10 days of age ($P = 0.05$) (mean = 0.9 kg/d; SE= 0.10), compared to placebo-medicated calves (mean = 0.6 kg/d; SE = 0.12). There was no significant effect of

meloxicam on physiological indicators of pain and inflammation, time to stand, time to nurse, passive immunity, health outcomes, or ADG to weaning ($P > 0.1$). Although this was a small sample population, meloxicam given to assisted calves at birth improved ADG in the first week of life, which may indicate an important production management tool for improving well-being in assisted calves.

4.2 Introduction

Calf health and survival are predominant concerns of cow-calf producers (Murray et al., 2016a). An important factor that affects calf health and survival is the difficulty experienced during the birthing process (Sanderson and Dargatz, 2000; Mellor and Stafford, 2004). Assisted calving is when a decision is made to intervene and deliver a calf and a degree of difficulty may be assigned to that calving (Mee, 2008). Incidence of assisted births in beef cows ranges from 5 to 20% in heifers and 1 to 4% in mature cows in North America (Dargatz et al., 2004; NAHMS, 2009; Waldner, 2014). Assisted calves have a higher risk of trauma and oxygen deprivation, and are less vigorous (Ferguson et al., 1990; Bleul and Gotz, 2013; Homerosky et al., 2017a). This can lead to delayed colostrum consumption (Mellor and Stafford, 2004; Homerosky et al., 2017b). Inadequate ingestion of good quality colostrum leads to failed transfer of passive immunity, which is associated with preweaning morbidity, mortality, and lower ADG (Wittum and Perino, 1995; Dewell et al., 2006). Further, dystocias are considered extremely painful for the cow and calf (Huxley and Whay, 2006; Mainau and Manteca, 2011; Barrier et al., 2012a). Non-steroidal anti-inflammatory drugs (NSAIDs) are increasingly being used for cattle pain management (Murray et al., 2016a; Moggy et al., 2017). Practical strategies that can mitigate effects of a difficult calving and improve acquired passive immunity are important to ensure calf health and survival and optimize profit for cow-calf producers. Therefore, the objective was to investigate the impact of implementing pain mitigation at birth to assisted beef calves. The hypothesis was that administering meloxicam at birth to assisted calves would decrease pain and inflammation, improve acquisition of passive immunity, decrease the risk for morbidity and mortality, and increase growth.

4.3 Materials and methods

The study was approved by the University of Calgary Veterinary Sciences Animal Care Committee (AC15-0150) and was conducted in accordance with guidelines established by the Canadian Council on Animal Care. Sample size calculations were based on previous work by this group looking at physiological indicators of trauma in calves at 24 hours of age in relation to calving score (Pearson et al., 2019a). A sample size of 16 calves per medication group was deemed necessary to detect a significant difference between the mean values of aspartate aminotransferase, an indicator of muscle trauma, in unassisted (mean = 61.9 IU/L; SD = 14.4) and difficult assisted calvings (mean = 92.3 IU/L; SD = 37.1) based on a significance level of 0.05 and 80% power. The data were collected from January to May of 2016 on two cow-calf operations located in southern Alberta, Canada. The operations were selected based on relationships with local cow-calf veterinary consultants, number of heifers to calve, and proximity to the University of Calgary. Thirty-three primiparous dams (Ranch A = 20; Ranch B = 13) were enrolled in the study. Ranch A consisted of 185 primiparous dams (either purebred registered Angus or crossbred commercial cattle), and Ranch B consisted of 150 crossbred primiparous dams. On both ranches, pregnant dams were monitored in outdoor pre-calving pens close to the calving barn and checked hourly for signs of calving. On Ranch A, during cold weather the majority of dams were brought into a heated barn with individual, 12 ft. by 12 ft. stalls bedded with straw. One dam on Ranch A was recumbent and unable to walk to the barn during calving so was assisted outside in the pre-calving pen. Dams were observed either by camera surveillance (GoPro Hero3+, GoPro Inc., San Mateo, CA) or by visual surveillance from a distance for signs of impending parturition. On Ranch B, dams were allowed to calve outside unless they required assistance. Failure to calve or make progression within 1 to 2 hours of estimated onset of stage 2 labor (e.g. amniotic sac visible, feet present, strong abdominal contractions, etc.) resulted in the dam being moved into a chute for vaginal examination and delivery of the calf. Twins and deliveries by Caesarian-section were excluded from this study.

Data collected at the time of birth included: date and time of calving, ambient temperature, calf sex, meconium staining, presentation of the calf (anterior versus posterior), and calving difficulty. Calving difficulty was classified as either an easy assist (1 person pulling to deliver the calf), or difficult assist (2 or more people pulling to deliver the calf or mechanical assistance). Within 10 minutes of birth, a physical examination and evaluation of calf vigor were performed as described by Homerosky and colleagues (2017a,b). Mucous membrane colour was categorised into pink (light pink or dark pink) or abnormal (blue-purple, white, dark red) by visual examination of the oral mucous membranes. Tongue withdrawal was categorised as complete or incomplete when the tongue was pulled from the calf's mouth and the extent to which it withdrew the tongue back into its mouth determined. Suckle reflex was categorised as strong or weak by placing a finger in the calf's mouth and feeling if it suckled the finger. These vigour parameters are associated with acidemia (Homerosky et al., 2017a) and likelihood of a calf standing to nurse on its own within 4 hours after birth (Homerosky et al., 2017b). Presence of meconium staining (yes or no), heart rate, respiratory rate, and rectal temperature were also recorded at birth. Calves were transported in a calf sled to a digital scale to measure the birth weight of the calf.

Assisted calves were randomized to a medication group using a computer-assisted randomization chart (Microsoft Excel, Microsoft Corporation, Redmond, Washington) stratified by calving difficulty (easy assist or difficult assist). Calves received a subcutaneous dose of meloxicam (Metacam®, 20 mg/ml, 0.5 mg/kg body weight, Boehringer Ingelheim, Ingelheim, Germany) or an equivalent volume of placebo (sterile saline with 2% oxytetracycline [Oxymycine LP®, 100mg/ml, Zoetis Canada Inc., Kirkland, QC] to match the colour of meloxicam). The amount of oxytetracycline that would be injected was 4.4×10^{-6} mg/kg body weight, which is a fraction of the concentration of therapeutic oxytetracycline (6.6 mg/kg body weight) and likely would not impact the results of this study. Ranch and research personnel were blinded to the treatment group. On-farm protocol dictated that all dams assisted at calving receive meloxicam (Meloxicam Oral Suspension, 15 mg/ml, 1.0 mg/kg body weight, Bow Valley Research, Calgary, AB at Ranch A; Metacam® injectable solution, 20mg/ml, 0.5 mg/kg body weight at Ranch B).

Sampling time points for all calvings enrolled included: birth (within 10 minutes of delivery), 1 hour, 4 hours, 24 hours, and 7 to 10 days post-delivery. All calves had blood drawn from the jugular vein by vacutainer needle (20-gauge x 1 inch; Airtite Product Co. Inc., Virginia Beach, VA). At each time point, blood was collected into a vacutainer (BD Vaccutainer®, BD, Franklin Lakes, NJ) coagulation tube (10 ml), EDTA tube (6 ml), and heparinized tube (10 ml). After blood collection, a drop of heparinized whole blood was placed on a lactate strip and analysed immediately for L-lactate concentrations (Lactate Pro, Arksay, Japan; or Lactate Plus Meter, Nova Biomedical, Watham, MA). Each EDTA tube had 300 uL of benzamidine hydrochloride (Sigma-Aldrich, St. Louis, MO) solution (a protease inhibitor) added and was inverted 10 times to mix. Heparinized and EDTA tubes were then centrifuged at 3000 x g for 10 minutes (LW Scientific E8, Lawrenceville, GA). Coagulating tubes were allowed to clot first and then centrifuged for 20 minutes at 3000 x g. Serum or plasma were removed from blood collection tubes, placed in 2 ml cryotubes, and immediately frozen at -18°C. Once a week, samples were transported to the University of Calgary Faculty of Veterinary Medicine and placed in a -80°C freezer until further analysis.

After the at-birth examination and sampling, cow-calf pairs were placed in individual box stalls for observation and sampling until after the 24-hour sample collection. Latency to stand and nurse were recorded and if the calf had not sucked within 1 to 4 hours, the on-farm protocol recommended calves be bottle- or tube-fed 1 L of maternal colostrum or colostrum replacer (Calf Choice Total, Saskatoon Colostrum Co. LTD, Saskatoon, SK at Ranch A; ImmuStart 50, Imu-Tek, Fort Collins, CO at Ranch B). The cow-calf pairs were then moved to an outside pen measuring approximately 30 x 30 meters to be observed by the ranch personnel.

At 7 to 10 days of age, calves were restrained in a calf chute with a built-in scale (7L Livestock Equipment Ltd., Brandon, MB) for body weight measurement and blood collection.

Table 4.1 summarizes the parameters evaluated at the different sampling times. Serum cortisol and corticosterone concentrations were measured by an Agilent 1200 binary liquid chromatography system connected with an AB SCIEX QTRAP® 5500 tandem mass spectrometer equipped with electrospray ionization source in the Wynne-Edwards Research Lab at the University of Calgary (Calgary, AB). Haptoglobin concentrations were measured by photometric analysis using the Roche Cobas 6000 c501 biochemistry analyzer (Laval, Quebec) in the Animal Health Laboratory at the University of Guelph (Guelph, ON). Substance P concentrations were measured by radioimmunoassay (RIA) in the Pharmacology Analytical Support Team Laboratory at the Iowa State University, Veterinary Diagnostic Laboratory (Ames, IA) as described by Van Engen et al. (2014). Serum IgG concentrations were measured using an in-house RIA in the Quality Assurance Laboratory of the Saskatoon Colostrum Company Ltd. (Saskatoon, SK) as described by Chelack et al. (1993). Serum biochemistry profile analysis was performed on a Beckman AU680 chemistry panel machine (Beckman/Coulter, Mississauga, ON) at the IDEXX Reference Laboratories (Calgary, AB). The concentration of plasma meloxicam was measured in heparinized blood samples using high performance liquid chromatography (Shimadzo LC-10A, Shimadzu Scientific Instruments, Columbia, MD) and was performed as described by Vivancos et al. (2015). Meloxicam concentrations were assessed in samples from meloxicam-treated calves on both ranches to ensure therapeutic levels were reached when it was administered to neonatal calves at birth. It was also measured in the samples from placebo-treated calves on both ranches to determine if they had absorbed any meloxicam through the milk because all dams were treated with meloxicam after calving.

Treatment and mortality data of all calves enrolled was recorded by ranch personnel. Date, suspected disease, and drugs used were recorded for treatment of disease in the preweaning period. Calves that died during the preweaning period were submitted to the University of Calgary Faculty of Veterinary Medicine Diagnostic Services Unit for gross and histological examination. Individual weaning weights were collected on calves at weaning.

Data were analysed using STATA® 14.1 software (StataCorp LP, College Station, TX) to investigate the relationships of medication group (placebo versus meloxicam) with physiological indicators of pain and inflammation, passive immunity, and calf health and growth.

Descriptive statistics and tests for normality were performed on all continuous variables. Multicollinearity was assessed using Spearman's rank correlation. Exact logistic regression was used to evaluate: failed transfer of passive immunity (determined using less than 24 g/L of serum IgG as a cut-point), standing by 1 hour, nursing by 1 hour, treatment, and mortality in the preweaning period. Multivariable linear regression modeling was performed for the following outcome variables: serum IgG concentration, 24-hour L-lactate, 24-hour haptoglobin, 7- to 10-day haptoglobin, 7- to 10-day ADG, and weaning ADG. Average daily gain was calculated by subtracting the birthweight of the calf from the measured weight and dividing by the age (in days) of the calf at the time of the measured body weight. Mixed multivariable linear regression modeling for repeated measures were performed for the following outcome variables: cortisol, corticosterone, substance P, heart rate, respiratory rate, and rectal temperature. Ranch, calving difficulty, and at-birth parameters of the corresponding outcome variable were offered as fixed effects to the models. Calf enrollment was offered as a random effect in the repeated measures models. Passive immunity models (i.e. serum IgG concentration and failed transfer of passive immunity) also had method of colostrum administration (nursed from dam or assisted by bottle or esophageal tube) and type of colostrum (dam colostrum or colostrum replacement product) offered as covariates. Birthweight, serum IgG concentration, and failed transfer of passive immunity were offered as potential covariates to the treatment for disease and mortality models. In addition, treatment for disease was offered to the ADG models. All models were analysed using forward selection model building strategies. Non-significant terms were removed, except for medication group, which was forced into the model because it was the variable of interest. Additionally, partial F-tests were used when categorical variables were removed from the models. The significance level to be retained in the model was set at $\alpha = 0.05$. Models were checked for assumptions by Cook-Weisberg test for heteroscedasticity and Shapiro-Wilk W test for normality. Residuals were assessed visually by residual-versus-fitted plots. Outliers and leverage were assessed using Cook's Distance, Studentized DFIT, and DFBETAs. Individuals that were outliers or leveraged the model were removed and the data re-analysed to determine if the resulting model was different. If the models were the same, the individual remained in the model. Models that did not fit the assumptions had variables transformed for normal distribution, using a transformation selected by visual assessment of several transformations determined by using the "gladder" command. All significant covariates were checked for interactions within each model. Two-sample T tests were performed to compare 24-hour hepatic enzymes (alkaline phosphatase, aspartate aminotransferase, and alanine aminotransferase) and renal biochemical parameters (urea and creatinine) between meloxicam and placebo groups to assess impacts of the medication on hepatic and renal function.

4.4 Results

Eleven of the enrolled births were easy assists and 22 were difficult assists. Only 1 difficult assisted calf presented posteriorly. One of the 22 difficult assist calves was delivered manually by 2 or more people. The others were all delivered by mechanical traction. Six of the 22 difficult assisted calves had meconium staining at birth. None of the easy assist calves had meconium staining. Seventeen calves received meloxicam and 16 calves received placebo. Table 4.2 describes the demographics of calves enrolled in the study by medication group. The average meloxicam concentration in meloxicam-treated calves at birth, 1 hour, 4 hours, and 24 hours were no detectable levels of meloxicam, 2957.8 ng/ml (SD = 3080.2), 2429.3 ng/ml (SD = 485.6), and 1696.0 ng/ml (SD = 488.9), respectively. Placebo-treated calves did not have detectable levels of meloxicam at birth, 1 hour, and 4 hours of age. At 24 hours, 7 of the 16 placebo treated calves (5/10 from Ranch A and 2/6 from Ranch B) had low levels of detectable meloxicam in the serum (mean = 15.4 ng/ml; SD = 17.9), which could only have been absorbed from the dam's milk.

The majority of vigour parameters were normal by 1 hour, so this precluded further analysis aside from describing the at-birth vigour parameters prior to product administration. Twenty-one of 33 calves had weak suckle reflexes at birth, 8 of 33 had incomplete tongue withdrawal reflexes, and 7 of 33 had abnormal mucous membrane colours. Five of the 33 (15%) calves were treated for disease in this study (meloxicam group: n = 1; placebo group: n = 4). Six of the 33 (18%) calves died prior to weaning (meloxicam group: n = 3; placebo group: n = 3).

There were no significant differences ($P \geq 0.17$) between meloxicam-treated and placebo-treated calves for 24-hour L-lactate, 24-hour haptoglobin, and 7- to 10-day haptoglobin. Table 4.3 reports these models, including the significant covariates. Similarly, there were no significant differences between medication groups ($P \geq 0.12$) when comparing repeated measures of cortisol, corticosterone, substance P, heart rate, and rectal temperature over the 24-hour period. Table 4.4 reports the mixed multivariable linear regression repeated measure models for cortisol, corticosterone, substance P, heart rate, respiratory rate, and rectal temperature and significant covariates included. Respiratory rate was significantly associated with medication given (P = 0.025) when taking into account an interaction between medication group and calving difficulty. The only significant pairwise comparison was between placebo-treated easy and difficult assisted calves (P = 0.02): easy assists receiving a placebo had a mean respiratory rate of 46.0 bpm (SE = 3.49) while difficult assists receiving a placebo had a mean respiratory rate of 55.0 bpm (SE = 1.83). Overall, the means for placebo and meloxicam treated calves' respiratory rates were 52.2

bpm (SE = 1.75) and 51.1 bpm (SE = 1.59), respectively, which was not significantly different ($P = 0.6$). The raw means (SD) for each pain or inflammatory mediator by medication group can be found in the supporting document (Appendix B).

The odds of standing by 1 hour, nursing by 1 hour, and having failed transfer of passive immunity, and serum IgG concentrations were not significantly different between placebo and meloxicam medicated groups ($P \geq 0.18$), as reported in Table 4.5. Preweaning treatment and mortality risk were not significantly different between calves medicated with a placebo or meloxicam ($P \geq 0.31$). Meloxicam-treated calves had significantly higher ADG to 7-10 days of age ($P = 0.05$; mean = 0.9 kg; SE = 0.10), compared to placebo-treated calves (mean = 0.6 kg; SE = 0.12). Serum IgG concentration and ranch were also important factors associated with ADG to 7-10 days (Table 4.5). Average daily gain to weaning was not statistically different in meloxicam-treated calves compared to placebo-treated calves when taking into account an interaction between ranch and treatment for disease (Table 4.5).

There was no significant difference between meloxicam and placebo treated calves on hepatic enzymes and renal biochemical parameters (alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, urea, and creatinine) ($P \geq 0.22$).

4.5 Discussion

The pain calves experience during calving is a topic of increasing interest in the beef industry (Laven et al., 2012). In a study of beef producers in Alberta in 2013, only 13% of surveyed beef producers reported using a pain medication in newborn calves after dystocia and 15% in the cows (Murray et al., 2016a). More recently, Moggy and colleagues (2017) stated that 28% and 33% of beef producers in western Canada reported giving an NSAID after dystocia to the calf and cow, respectively. Non-steroidal anti-inflammatory drugs provide a multimodal relief by analgesic, anti-inflammatory, and anti-endotoxic effects (Coetzee, 2013). Meloxicam is an NSAID with high bioavailability and a prolonged half-life, making it a favorable choice for treating pain in cattle (Coetzee, 2013). Therefore, the hypothesis for this study was that administering meloxicam at birth to assisted calves would decrease pain and inflammation, improve acquisition of passive immunity, decrease the risk for morbidity and mortality, and increase growth. Although NSAIDs are designed to decrease pain and inflammation (Coetzee, 2011), no association was found in the measured physiological indicators of pain and inflammation between meloxicam and placebo medicated calves in the present study and did not support our hypothesis. This is in agreement with recent work investigating the effects of another NSAID, ketoprofen, on stress biomarkers in calves (Gladden et al., 2018). In that study, the authors found no effect of administering an NSAID within 3 hours of birth, on cortisol, creatine kinase, plasma L-lactate, or total protein concentration at 24 hours of age.

Other studies investigating painful management interventions such as castration and dehorning have found a decrease in pain and stress indicators after administering an NSAID (Coetzee, 2011; Stock and Coetzee, 2015). In a study investigating various analgesics, including meloxicam, given at the time of dehorning, had lower substance P than control calves, but no difference in haptoglobin or mean serum cortisol levels (Glynn et al., 2013). They also found increased ADG to 7 days after dehorning in medicated calves versus unmedicated calves. In other meloxicam specific studies, calves receiving meloxicam in association with dehorning, had decreased cortisol, substance P, and prostaglandin $E_{2,}$ levels, decreased heart rate, and increased ADG to 10 days after dehorning compared to placebo (Coetzee et al., 2012; Allen et al., 2013). In a castration study, substance P levels decreased, but not serum cortisol in calves medicated with meloxicam compared to controls (Coetzee et al., 2008). Contrary to the above studies, Melendez et al. (2017) did not find an association between the use of meloxicam before or at the time of castration on substance P or salivary cortisol levels up to 240 minutes after castration. Together, the results of these studies indicate the complexity of pain physiology, and detecting and treating pain in calves.

Serum cortisol and substance P are commonly used biomarkers for the evaluation of analgesic treatments (Coetzee, 2013). Cortisol, as measured by peak concentration or duration, is used as a measure of distress associated with painful stimuli (Mellor et al., 2000). An increase in tractive forces on a calf has been shown to lead to increased levels of cortisol in neonatal calves (Hoyer et al., 1990). Although cortisol is commonly evaluated in pain mitigation studies, it was not significantly different by medication groups in this study. This may be because cortisol is already elevated due to stimulation of the fetal adrenal-pituitary axis to initiate parturition (Breazile et al., 1988). Substance P is a neuropeptide released in response to pain, stress, and anxiety (Coetzee, 2013). Although it has gained popularity in pain mitigation studies, results have not been consistent (Coetzee et al., 2008; Melendez et al., 2017).

Haptoglobin at 24 hours and 7 to 10 days of age was not significantly different by medication group. Murray and coworkers (2014) found no association between calving difficulty and haptoglobin levels but did find higher concentrations of haptoglobin in calves with higher rectal temperatures and depressed attitudes in the first few days after birth. Haptoglobin is an acute phase protein released by the liver after infectious or inflammatory tissue injury (Baumann and Gauldie, 1994). Acute phase proteins are commonly used in veterinary medicine to quantify tissue damage but a lack of significant differences at birth may be due to the immature inflammatory response in the neonate (Alsemgeest et al., 1995; Schroedl et al., 2003)

Other indirect, physiological indicators of pain and inflammation such as heart rate, respiratory rate, and body temperature have been investigated in painful procedures in cattle (Stewart et al., 2010; Coetzee, 2011). Respiratory rate was significantly different by medication group in this study. The effect was influenced by an interaction between medication and calving difficulty and driven by a significant difference between easy and difficult assists among placebo-treated calves. Although there was a significant difference, the differences were small and deemed not clinically relevant. The normal respiratory rate of the bovine neonate ranges from 36 to 60 bpm (Dufty and Sloss, 1977), and the mean respiratory rate amongst calves medicated with meloxicam or a placebo were within the normal range. Although respiratory rate may be associated with pain, it is also associated with hypoxia, hypercapnia, and acidemia in neonates, which may confound its relevance in neonatal pain studies (Breazile et al., 1988; Bleul and Gotz, 2013). Heart rate, respiratory rate, and temperature are regulated by the sympathetic nervous system in reaction to pain, and therefore a difference might be expected between calves medicated with analgesics versus controls, as reported in other studies (Mohankumar et al., 2012; Kovacs et al., 2014). Previous work investigating analgesic and anti-inflammatory mitigation with meloxicam given to calves at the time of a painful procedure has found decreased respiratory rates compared to control calves (Heinrich et al., 2009; Cagnardi et al., 2017).

The effect of an NSAID on appetite and growth has been evaluated in several studies (Todd et al., 2010; Glynn et al., 2013; Murray et al., 2016b). Our hypothesis was that treated calves would be less painful, get up and nurse more frequently, and therefore gain more weight. Another hypothesis for increased appetite and growth may be due to the decreasing pro-inflammatory cytokine pathways that may affect metabolism and nutrient intake (Johnson, 1998). The only notable impacts of administering meloxicam at birth in this study were an increase in ADG to 7 to 10 days. Ranch and serum IgG concentration were significant covariates for ADG to 7 to 10 days of age, indicating that the ranch management and colostrum consumption are also important factors for weight gain in the first week of life. These findings were expected because management practices differed on the two ranches. In addition to immunoglobulin absorption, colostrum contains other important factors that impact calf health such as nutrients, immune cells, growth factors, and antimicrobial properties, which may explain why IgG concentrations (an indicator of colostrum absorption) were associated with weight gain (Godden, 2008).

A difference in ADG between medication groups was not found at weaning. Whether the calves were treated for disease in the preweaning period did affect their ADG to weaning, although this was influenced by which ranch they lived on. In other pain studies, calves that were medicated with meloxicam had greater ADG to 7-10 days after dehorning compared to unmedicated calves (Coetzee et al., 2012; Glynn et al., 2013). Murray and colleagues (2016b) investigated the use of meloxicam given to dairy calves at birth, and found greater milk intake, better health in the first 8 weeks, and greater vigour, but no significant effect on ADG. A similar study (Todd et al., 2010) investigated the impacts of an NSAID given to calves with diarrhea. They found that calves treated with meloxicam consumed starter ration sooner, had higher odds of finishing daily allotted milk, gained weight at a faster rate, and weaned earlier.

Serum IgG concentrations have been reported to be lower in calves born to a heifer, via dystocia, or as a twin, and the odds of treatment or death increased when serum IgG concentrations were below 24g/L (Waldner and Rosengren, 2009). Although in the present study serum IgG concentrations and failed transfer of passive immunity were not significantly different by medication group, serum IgG concentration was an important factor that influenced ADG to 7 to 10 days of age. Other studies have shown that lower IgG concentrations were associated with higher morbidity, mortality, and lower ADG in beef calves (Dewell et al., 2006). Our lack of significant difference between medication groups on passive immunity may have been due to on-farm protocols to intervene with colostrum consumption by 1 to 4 hours after birth, as is currently recommended to decrease the risk of failed transfer of passive immunity and associated health issues (Godden, 2008).

The risk of acidemia and hypoxemia is higher in assisted calves, which can lead to increased risk of stillbirth or decreased vigour in newborn calves (Breazile et al., 1988; Vaala and House, 2002). Blood gas disturbances, lower packed cell volumes, and elevated blood L-lactate concentrations are associated with severe acidemia and hypoxemia at birth (Homerosky et al., 2017a). Other outcomes associated with acidemia and hypoxia at birth include taking longer to stand, increased risk of failed transfer of passive immunity, and preweaning morbidity and mortality (Szenci et al., 1988; Boyd, 1989; Besser et al., 1990; Schuijt and Taverne, 1994). Vigour assessments can include reflexes such as tongue withdrawal and suckle reflex, as well as time to stand and nurse (Barrier et al., 2012b; Murray et al., 2016b; Homerosky et al., 2017a,b). In this study, the vigour assessments indicated that some calves were less vigorous at birth than other calves. Although it was not possible to investigate the impact of meloxicam on the clinical assessment of vigour in the present study, there was no significant difference between calves that received meloxicam versus a placebo in their time to stand or nurse within one hour. Behaviors such as time to stand and nurse were expected to be impacted by treatment of meloxicam medicated calves because changes in behaviors associated with pain and distress are decreased in calves treated with meloxicam after painful stimuli such as dehorning, castration, or a difficult birth (Heinrich et al, 2010; Murray et al., 2016b; Olson et al., 2016). However, it was not the case in this study.

Factors such as weakness, trauma, and subsequently failed transfer of passive immunity, can lead to increased risk of morbidity and mortality in the preweaning period (Bellows et al., 1987; Wittum and Perino, 1995; Vaala and House, 2002). Specifically, a difficult birth increases the risk of mortality in the first 24 hours of life (stillbirth), the first 30 days of life, and increases the odds of bovine respiratory disease and preweaning calf diarrhea (Nix et al., 1998; Lombard et al., 2007). In the current study, there was no association between calves medicated with meloxicam or a placebo at birth on treatment and mortality outcomes. This could be because the sample size was not sufficient to measure this difference with so few calves that were treated for disease (n = 5) or that died (n = 6), despite this being a large proportion of calves that were enrolled in the study. There were differences in treatment and mortality risks between the two farms, which had different periparturient management procedures. This could be explained by the findings in other studies that associated high difficult calving rates and calving management practices with high herd-level calf morbidity (Sanderson and Dargatz, 2000). Cow-calf preweaning mortality is about 7%, and most preweaning mortality occurs in first 3 days of life, usually due to dystocia (Patterson et al., 1987). Half of the calf deaths in this study were within the first 4 days of life and were associated with complications of a difficult birth. The much higher mortality risk (18%) in the present study population is attributable to the fact that only assisted calvings were enrolled.

Potential weaknesses of this trial include the selection of sample size and complexities with using reference values that are not based on neonatal animals. Post hoc sample size calculations for this study indicated a higher number of animals than the *a priori* sample size calculations, and post hoc power calculations suggested the sample size was too small to detect a significant difference. Predicting when a heifer or cow will need assistance at birth is difficult and dependant on multiple management variables. This criteria limited the number of assisted calves available to be enrolled in this study. Due to the challenge of consistently and objectively describing dystocia, assistance at birth stratified by calving difficulty was considered the most accurate way of categorizing calvings for this study. This may lead to some misclassification due to subjectivity of the measure and the influence of on-farm protocols to decide when to intervene.

Neonatal physiology is quite complex and variable in dystocic calves. Determining when stage 1 or stage 2 labor actually begins is difficult to measure, which may affect the duration of calving prior to the decision to intervene with delivery, and can increase the variability in physiological parameters. Other effects of neonatal physiology that impact calf vigour and viability include hypoxemia and acidemia. It is difficult to determine at birth, without further blood analysis, if a calf is less vigorous because of trauma due to a difficult calving, or because of hypoxia and acidosis caused by a prolonged calving, or both. It is not expected that an NSAID would improve vigour if the calf was hypoxic or acidemic, which may have impacted the findings of this study.

Although few positive effects of meloxicam were found in this study, no negative effects were detected either. There were no pathological findings consistent with NSAID toxicity upon gross necropsy and histological examination of calves that died. There was no difference between meloxicam and placebo treated calves on hepatic and renal biochemical enzymes to indicate a negative effect of meloxicam on neonatal calves. Although there was no difference between medication groups, calving in either group demonstrated biochemical parameters outside the reference range for adult cattle used by the laboratory. There are few references indicating normal biochemical parameters for neonatal calves in the first 24 hours of life or any age-related changes (Knowles et al., 2000; Mohri et al., 2006), which indicates a need for further investigation in the physiology of organ function in newborn calves.

Methods described to assess pain in cattle include physiologic changes (serum cortisol, heart rate, feed intake, ADG), neuroendocrine changes (substance P, infrared thermography, heart rate variability, skin electrical impedance, and electroencephalography), and behavioral changes (visual scoring systems, videography, vocalization, chute behavior, pedometers and accelerometers) (Coetzee, 2013). Although physiologic and neuroendocrine changes were measured in this study, behavioral pain assessment was not. This was due to on-farm protocols that intervened frequently with the cow-calf pairs throughout the 24-hour period. Future studies investigating pain associated with assisted calvings might evaluate behavioral effects as well as other physiologic and neuroendocrine changes to better understand pain associated with assistance at birth.

4.6 Conclusions

This study demonstrated a potential growth benefit to meloxicam medicated calves assisted at birth by an increased ADG of 0.3 kg/d in the first 7 to 10 days of life. It did not find an effect of administering meloxicam at birth to assisted calves and there was no decrease in physiological indicators of pain and inflammation, or improvements in passive immunity or health. Future studies are warranted to further investigate how meloxicam affects neonatal pain and inflammation as well as how it is associated with calf health and productivity. Although this was a small study, improvements in early growth suggest meloxicam given to assisted calves at birth may indicate an important production management tool for improving production and wellbeing in assisted calves.

Table 4.1. Age of the calf when parameters were evaluated in 33 beef calves assisted at delivery and randomly assigned to a subcutaneous meloxicam (Metacam®, 20 mg/ml, 0.5 mg/kg body weight, Boehringer Ingelheim, Ingelheim, Germany) or placebo (0.025 ml/kg) medication group at birth.

At-Birth	1 hour	4 hours	24 hours	7 to 10 days	Weaning
Body weight				Body weight	Body weight
Cortisol	Cortisol	Cortisol	Cortisol		
Corticosterone	Corticosterone	Corticosterone	Corticosterone		
Substance P	Substance P	Substance P	Substance P		
Heart Rate	Heart Rate	Heart Rate	Heart Rate		
Respiratory Rate	Respiratory Rate	Respiratory Rate	Respiratory Rate		
Rectal Temperature	Rectal Temperature	Rectal Temperature	Rectal Temperature		
L-lactate			L-Lactate		
Haptoglobin			Haptoglobin	Haptoglobin	
			Serum IgG		
			Serum Chemistry		
					Treatment
					Mortality

Table 4.2. Demographics of 33 beef calves by medication group. Calves were administered a dose of either subcutaneous meloxicam (Metacam®, 20 mg/ml, 0.5 mg/kg body weight, Boehringer Ingelheim, Ingelheim, Germany) or placebo (0.025 ml/kg) at birth. All parameters are presented as counts unless otherwise stated.

		Placebo	Meloxicam	Overall
Ranch				
	Ranch A	10	10	20
	Ranch B	6	7	13
Breed				
	Angus	5	7	12
	Crossbred	11	10	21
Calf Sex				
	Bull	12	13	25
	Heifer	4	4	8
Meconium staining				
	No	11	16	27
	Yes	5	1	6
Ambient Temperature, ºC (median, IQR)		10.0 (6.9 - 11.1)	11.7 (10 - 12.2)	10.9 (9.4-11.7)
Birthweight, kg (mean, SD)		39.9 (5.4)	39.6 (8.1)	39.8 (6.8)

Table 4.3. Multivariable linear regression models of blood physiological parameters of acidemia or inflammation in 33 beef calves assisted at birth and medicated with subcutaneous meloxicam (Metacam®, 20 mg/ml, 0.5 mg/kg body weight, Boehringer Ingelheim, Ingelheim, Germany) or placebo (0.025 ml/kg).

	Coefficient	**Standard Error**	**P Value**
24-h L-Lactate, mmol/L			
Medication Group			
Placebo	Referent	-	-
Meloxicam	-0.4	0.4	0.41
Birth L-Lactate, mmol/L	0.2	0.07	0.02
24-h Haptoglobin, g/L[1]			
Medication Group			
Placebo	Referent	-	-
Meloxicam	0.06	0.04	0.17
Birth Haptoglobin, g/L	4.4	0.7	<0.0001
7- to 10-day Haptoglobin, g/L[2]			
Medication Group			
Placebo	Referent	-	-
Meloxicam	3.6	8.0	0.66
Ranch			
Ranch A	Referent	-	-
Ranch B*	-22.2	8.5	0.01

[1] Log transformation
[2] $1/x^2$ transformation
*Due to the transformation, the sign is reversed (Ranch A had lower 7 to 10 day Haptoglobin than Ranch B).

Table 4.4. Mixed linear regression repeated measures models of blood parameters and physical examination findings associated with pain or inflammation in 33 beef calves assisted at birth and medicated with subcutaneous meloxicam (Metacam®, 20 mg/ml, 0.5 mg/kg body weight, Boehringer Ingelheim, Ingelheim, Germany) or placebo (0.025 ml/kg).

	Coefficient	Standard Error	P Value
Cortisol, ng/ml			
Medication Group			
Placebo	Referent	-	-
Meloxicam	-1.7	3.6	0.62
Ranch			
Ranch A	Referent	-	-
Ranch B	-22.8	14.5	0.11
Calving Difficulty			
Easy	Referent	-	-
Difficult	7.6	3.9	0.05
At-birth[1] Cortisol	-0.7	0.4	0.08
Time Sampled			
1 hour	Referent	-	-
4 hours	-20.9	3.5	<0.0001
24 hours	-48.4	3.5	<0.0001
Farm by At-birth Cortisol Interaction	0.4	0.2	0.009
Corticosterone,[2] ng/ml			
Medication Group			
Placebo	Referent	-	-
Meloxicam	0.2	0.1	0.122
Ranch			
Ranch A	Referent	-	-
Ranch B	0.3	0.1	0.021
At-birth[1] Corticosterone	0.4	0.06	<0.0001
Time Sampled			
1 hour	Referent	-	-
4 hours	-1.1	0.2	<0.0001
24 hours	-1.8	0.1	<0.0001
Substance P,[3] pg/ml			
Medication Group			
Placebo	Referent	-	-
Meloxicam	-0.002	0.0001	0.20
At-birth[1] Substance P	-0.0001	0.00002	<0.0001
Time Sampled			
1 hour	Referent	-	-
4 hours	-0.02	0.004	<0.0001
24 hours	-0.03	0.003	<0.0001
Heart Rate,[4] bpm			
Medication Group			

Placebo	Referent	-	-
Meloxicam	-0.3	0.2	0.23
Time Sampled			
1 hour	Referent	-	-
4 hours	-0.5	0.2	0.02
24 hours	-0.8	0.2	<0.0001
Respiratory Rate, bpm			
Medication Group			
Placebo	Referent	-	-
Meloxicam	17.9	8.0	0.02
Calving Difficulty			
Easy	Referent	-	-
Difficult	12.5	3.4	<0.0001
Time Sampled			
1 hour	Referent	-	-
4 hours	-0.6	2.1	0.77
24 hours	3.0	3.1	0.32
Calving Difficulty by Medication Interaction	-10.5	4.6	0.02
Rectal Temperature, C°			
Medication Group			
Placebo	Referent	-	-
Meloxicam	0.05	0.1	0.74
Time Sampled			
1 hour	Referent	-	-
4 hours	-0.2	0.1	0.16
24 hours	-0.2	0.1	0.10

[1]"At-birth" refers to baseline measurements of that outcome variable taken within 10 minutes of birth

[2]Log transformation

[3]1/(square root) transformation

[4]Square root transformation

Table 4.5. Logistic and linear regression models for outcomes associated with passive immunity and average daily gain in 33 beef calves assisted at birth and medicated with subcutaneous meloxicam (Metacam®, 20 mg/ml, 0.5 mg/kg body weight, Boehringer Ingelheim, Ingelheim, Germany) or placebo (0.025 ml/kg).

	Odds Ratio	P Value
Failure to Stand by 1 hour		
Medication Group		
Placebo	Referent	-
Meloxicam	1	1.0
Ranch		
Ranch A	Referent	-
Ranch B	13.2	0.003
Nursing by 1 hour		
Medication Group		
Placebo	Referent	-
Meloxicam	0.7	1.0
Failed Transfer of Passive Immunity		
Medication Group		
Placebo	Referent	-
Meloxicam	0.2	0.36
Method Colostrum Consumed		
Nursed from Cow	Referent	-
Tubed or Esophageal Fed	13.6	0.01
	Coefficient (SE)	**P Value**
Serum IgG, g/L		
Medication Group		
Placebo	Referent	-
Meloxicam	6.1 (4.4)	0.176
Calving Difficulty		
Easy	Referent	-
Difficult	-14.4 (4.6)	0.004
Average Daily Gain to 7 to 10 days, kg		
Medication Group		
Placebo	Referent	-
Meloxicam	0.29 (0.1)	0.05
Ranch		
Ranch A	Referent	-
Ranch B	0.4 (0.2)	0.01
Serum IgG Concentration (g/L)	0.01 (0.005)	0.03
Average Daily Gain to Weaning, kg		
Medication Group		
Placebo	Referent	-
Meloxicam	0.05 (0.05)	0.3
Ranch		

Ranch A	Referent	-
Ranch B	-0.2 (0.06)	0.003
Treatment for Disease		
No	Referent	-
Yes	0.5 (0.3)	0.1
Treatment for Disease by Ranch Interaction	-0.3 (0.1)	0.04

CHAPTER 5 – A RANDOMISED CONTROL TRIAL INVESTIGATING THE EFFECTS OF ADMINISTERING A NON-STEROIDAL ANTI-INFLAMMATORY DRUG TO BEEF CALVES ASSISTED AT BIRTH AND RISK FACTORS ASSOCIATED WITH PASSIVE IMMUNITY, HEALTH AND GROWTH

5.1 Abstract

Objectives were to investigate impacts of pain mitigation at birth to assisted beef calves and determine risk factors associated with transfer of passive immunity (TPI), health, and growth. Two hundred and thirty cow-calf pairs requiring calving assistance were enrolled. Calves were randomised to receive meloxicam (0.5 mg/kg) or an equivalent volume of placebo subcutaneously at birth. Calf blood samples were collected between 1-7 days of age to determine serum immunoglobulin (IgG) concentration. Colostrum intake, treatment for disease, mortality, and weaning weights were recorded. Multilevel linear or logistic regression models were used to determine the effects of meloxicam and to identify risk factors. There was no effect of meloxicam on serum IgG concentrations, average daily gain (ADG), or risk of inadequate TPI (serum IgG concentration < 24 g/L), treatment for disease, or mortality (P > 0.05). Bottle or tube feeding calves was associated with decreased serum IgG concentrations (P = 0.01) compared to nursing. Calves with an incomplete tongue withdrawal reflex had higher odds of being treated for disease compared to those with complete withdrawal (P = 0.009). Being born meconium stained and having decreased serum IgG concentrations were associated with an increased risk of mortality (P = 0.03). Being born of a mature cow, having a higher birthweight, and increased serum IgG concentrations were associated with greater ADG to weaning (P < 0.05). Vigour assessment at birth along with good colostrum management may be important tools to improve TPI and health in high-risk calves such as those assisted at birth.

5.2 Introduction

Growing consumer interest in food production puts pressure on the beef industry to ensure practices are sustainable and welfare-friendly (Ellis et al., 2009; Wolf et al., 2016). In particular, the pain and suffering of animals are considered major concerns for the public and producers (Maria, 2006; Spooner et al., 2012; Moggy et al., 2017). Therefore, providing producers with practical knowledge and on-farm strategies to improve cattle health and welfare are important for the economic sustainability of the beef industry and the Canadian economy.

Calf health and survival are major concerns of cow-calf producers (Murray et al., 2016a). Calves assisted at birth are often compromised and experience acidemia, hypoxemia, and soft tissue trauma (Homerosky et al., 2017a; Pearson et al., 2019a). A compromised calf may be delayed in consuming colostrum and have an increased risk of inadequate transfer of passive immunity (TPI) (Waldner and Rosengren, 2009; Pearson et al., 2019a), raising their odds of pre-weaning morbidity, mortality, and reduced growth (Wittum and Perino, 1995; Sanderson and Dargatz, 2000; Dewell et al., 2006). Specifically, a difficult birth increases the risk of mortality in the first 24 hours of life (stillbirth) and in the first 30 days of life, and increases the odds of bovine respiratory disease (BRD) and calf diarrhea (PCD) in the preweaning period (Nix et al., 1998; Lombard et al., 2007).

Although the incidence of calving assistance in western Canada at birth is low, ranging from 5 to 9% (Waldner, 2014; Pearson et al., 2019b), the majority of producers assist one or more calvings each year. This means that managing compromised calves is still a required task for most cow-calf producers. Investigating risk factors associated with TPI, health, and growth are important to identify areas where management techniques could be implemented to improve calf health and welfare. Understanding the effects of an assisted calving will guide interventions for compromised calves after a difficult birth, including but not limited to the development of pain mitigation strategies for newborn calves.

In cattle, non-steroidal anti-inflammatory drugs (NSAIDs) are one of the most commonly used form of pain control and are becoming increasingly popular for use after an assisted calving (Murray et al., 2016a; Moggy et al., 2017; Pearson et al., 2019b). The NSAID class of drugs acts by inhibiting cyclooxygenase isoenzymes (COX1 and COX2) to prevent the inflammatory cascade and reduces prostaglandin synthesis (Anderson and Muir, 2005). This provides multimodal relief through analgesic, anti-inflammatory, anti-pyretic, and anti-endotoxic properties (Coetzee, 2013). Meloxicam is a COX-2 preferential inhibitor NSAID, so it causes fewer negative side effects and has high bioavailability with a prolonged half-life in comparison to other NSAIDs (Coetzee, 2013). A few studies have shown positive effects of administering an NSAID at birth to dairy calves such as improved vigour, decreased behavioral indicators of pain, and improved milk consumption (Murray et al., 2016b; Gladden et al., 2019). An intensive, small scale study showed increased growth rates within the first week of life in meloxicam-medicated beef calves after assistance at birth compared to placebo-medicated controls, but the sample size was too small to determine differences in health outcomes (Pearson et al., 2019c). Therefore, a large-scale field trial that accounts for confounding risk factors and ranch management is needed.

The objectives of the present study were to investigate the impact of administering meloxicam at birth to calves born with assistance and to investigate risk factors associated with TPI, health, and growth in preweaned beef calves. The hypothesis was that the use of meloxicam would decrease the pain and inflammation associated with an assisted birth and lead to improved TPI, a decreased risk of morbidity and mortality, and increased growth in the pre-weaning period.

5.3 Material and methods

The study was approved on January 10th, 2017, by the University of Calgary Veterinary Sciences Animal Care Committee (AC16-0209) and the Research Ethics Board (REB16-1142), and was conducted in accordance with guidelines established by the Canadian Council on Animal Care. A proposed sample size was calculated based on the likelihood of producers to intervene with colostrum administration in assisted beef calves. Based on previous research by this group showing 45% of calves assisted at birth required intervention to ensure colostrum consumption (Homerosky et al., 2017b), and using a confidence level of 95% and power of 80%, a sample size of 200 assisted calves was deemed necessary. Fifteen ranches located in southern Alberta were recruited through 2 veterinary practices to participate in the study. Ranches were selected based on willingness to participate, good record-keeping, and close proximity to the University of Calgary. To allow for attrition, 230 cow-calf pairs requiring assistance at calving were enrolled from January to June 2017.

Individual cow-calf pair information recorded at birth included: date and time of calving, dam parity (heifer or mature cow), dam body condition score, calf birth weight, sex, breed, calving difficulty, presentation (anterior or posterior), and meconium staining (present or absent). Producers were trained to assign a body condition score on the scale of 1 through 5 to dams at calving (NFACC, 2013). Calf birth weight was either estimated using a foot weight tape (Calfscale, Ames, IA) or determined using a digital scale. Calving difficulty was defined as: easy = 1 person manually pulling to deliver the calf, difficult = 2 or more people pulling to deliver the calf or mechanical extraction (i.e. calf jack), or Caesarian section (c-section).

Within 10 minutes after birth, calf vigour was assessed using the vigour parameters described by Homerosky et al. (2017a,b) that were associated with acidemia and likelihood of nursing by 4 hours after birth. These parameters included: mucous membrane colour, tongue withdrawal, and suckle reflex. Mucous membrane colour (pink or abnormal) was measured by the colour of oral mucous membranes. Tongue withdrawal (complete or incomplete) was measured by pulling the tongue from the calf's mouth and determining if it withdrew the tongue back into its mouth. Suckle reflex (strong or weak) was measured by placing a finger in the calf's mouth and feeling if it suckled the finger.

Calves were randomised to a medication group using a computer-assisted randomisation chart (Microsoft Excel, Microsoft Corporation, Redmond, WA) stratified by calving difficulty on each ranch. At birth, calves received a subcutaneous dose of meloxicam (Metacam®, 20 mg/ml, 0.5 mg/kg, Boehringer Ingelheim, Ingelheim, Germany) or an equivalent volume of placebo (0.025 ml/kg sterile saline with 1% vitamin injectable solution (Vitamaster NF, Vetoquinol, Lavaltrie, QC, Canada) to match the colour of meloxicam). Ranch personnel were blinded to the medication group. If ranch personnel were uncomfortable with an assisted calf being enrolled in the study and potentially not receiving pain mitigation, it was not enrolled.

Ranch personnel recorded the approximate time to stand within 4 categories (i.e. 0 to 30 minutes, 30 to 60 minutes, 1 to 6 hours, or required assistance) and the time to colostrum consumption within 5 categories (i.e. < 1 hour, 1-2 hours, 2-3 hours, 3-4 hours, or ≥ 4 hours). The method of colostrum consumption (i.e. nursed from dam, bottle fed, or tube fed) as well as type of colostrum (i.e. dam colostrum or colostrum replacement product) were recorded. Bottle fed and tube fed methods of colostrum consumption were later combined into one category because some producers attempted bottle feed calves first but, when unsuccessful, would then tube feed calves.

Research personnel visited the ranches after being notified of an enrolled calf to collect blood samples from calves between 1 and 7 days of age. Blood samples were collected from the jugular vein using a vacutainer needle (20 gauge x 1 inch; Airtite Product Co. Inc., Virginia Beach, VA) into a 6 ml coagulating tube (BD Vaccutainer®, BD, Franklin Lakes, NJ). The blood samples were placed on ice in a cooler during transport. They were then centrifuged for 20 minutes at 3000 x g (LWS M24 Combo Centrifuge, LW Scientific, Lawrenceville, GA). Serum was removed from the blood collection tubes, placed in 2 ml cryotubes, and immediately frozen at -18 °C. Once per week, samples were transferred to a -80 °C freezer until further analysis. Serum samples were analysed using an in-house radial immunodiffusion assay at the Saskatoon Colostrum Company Ltd. Quality Assurance Laboratory (Saskatoon, SK) as described by Chelack et al. (1993).

Data recorded by ranch personnel included: treatment for disease (e.g. for neonatal calf diarrhea or respiratory disease), mortality, and when possible, weaning weights. Calves that were enrolled and died prior to 6 weeks of age were submitted for necropsy examination at the University of Calgary Faculty of Veterinary Medicine's Diagnostic Services Unit to determine the cause of death and investigate any potential negative effects, such as lesions in the abomasum, colon, or kidneys, of administering an NSAID at birth.

To describe calving and colostrum management techniques of the enrolled ranches, a survey was conducted at the end of calving season at each ranch. Questions included: peri-partum management and protocols for calving and post-natal procedures.

Data were analysed with Stata 14.1 software (StataCorp LP, College Station, TX). Descriptive statistics and tests for normality were assessed on all continuous variables prior to model building. Calves with missing medication group data (n = 5) were removed from the dataset for all analysis. Additionally, calves born via c-section (n = 4) and calves from 2 farms with only 1 calf enrolled each (n = 2) were removed from the dataset for regression analysis. Multilevel linear regression models with ranch as a random effect were generated for the outcomes of serum IgG concentration and ADG to weaning. Multilevel logistic regression models with ranch as a random effect were generated for inadequate TPI (serum IgG concentration < 24 g/L), treatment for disease, and mortality. Potentially significant covariates (i.e. dam parity and BCS, calving difficulty, calf sex, presentation, meconium staining, vigour assessment, birthweight, time to stand and nurse, and method or type of colostrum consumed) were offered to the models. Serum IgG concentration was offered as a covariate to the treatment for disease, mortality, and ADG models. Univariable analysis was performed on all covariates using a P value ≤ 0.15 as the inclusion criterion for the models (Dohoo et al., 2009a). Multicollinearity was assessed using Spearman's rank correlation and parameters with a coefficient ≥ 0.7 were considered to be collinear. If collinearity occurred between variables, two different models were built including each variable and assessed using the lower AIC number to determine the best model. All models were analysed using backwards stepwise regression model-building strategies and non-significant terms were removed except the medication group, which was forced into the model because it was the variable of interest (Dohoo et al., 2009a). The significance level to be retained in the model was P ≤ 0.05. Partial F-tests were used to assess the effect of removing categorical variables from the models. Linear models were checked for assumptions by Cook-Weisberg test for heteroscedasticity and Shapiro-Wilk W test for normality. Residual-versus-fitted plots were assessed visually. Individuals that were outliers or leveraged the data were assessed using Cook's Distance and Studentized DFIT and removed.

The proportion of variance for continuous outcomes was calculated (Equation 1) and reported as percentages (Dohoo et al., 2009b).

Equation 1:
$$\frac{(\sigma_{\text{ranch-level effect}} \text{ or } \sigma_{\text{individual effect}})^2}{(\sigma_{\text{ranch-level effect}})^2 + (\sigma_{\text{individual effect}})^2}$$

The proportion of variance for categorical outcomes was calculated (Equation 2) and reported as percentages (Dohoo et al., 2009b).

Equation 2:
$$\frac{(\sigma_{\text{ranch-level effect}})^2}{(\pi^2/3) + (\sigma_{\text{ranch-level effect}})^2}$$

5.4 Results

A survey was performed to describe the calving management on each ranch. One ranch did not calve heifers during the 2017 calving season. All 15 ranches assisted calvings as necessary and the majority would intervene no later than 90 minutes after feet or an amniotic sac were observed (heifers: 71%, cows: 47%) or no progression was identified (heifers: 93%, cows: 80%) in a calving dam. Detailed information about the timing of calving intervention is described in Table 5.1. Of the 15 ranches enrolled, all used some method to determine if a calf had received colostrum (i.e. saw the calf suck from the dam, cow's udder appeared less full, calf appeared full). Various methods to ensure a calf consumed colostrum if it had not been observed to have nursed from the dam were utilized. All ranches would attempt to place the cow and calf together to encourage nursing, 11/15 ranches would restrain the cow in a chute and allow the calf to nurse, and 10/15 and 12/15 ranches would bottle feed or tube feed calves, respectively.

Of the calves enrolled, 114 received placebo and 111 received meloxicam. Overall, the mean dam body condition score was 3.6 out of 5 (SD = 0.9) with a mean of 3.6 (SD = 0.85) for placebo treated calves' dams and a mean of 3.5 (SD = 0.95) for meloxicam treated calves' dams. The majority of dams enrolled were heifers (68.9%) and the majority of calves enrolled were bull calves (66.1%) (Table 5.2). The mean birthweight of calves enrolled was 44.3 kg of body weight (SD = 6.6) with a mean birthweight of 44.7 (SD = 6.8) for placebo treated calves and a mean birthweight of 43.8 (SD = 6.6) for meloxicam treated calves. Detailed descriptions of the demographics of calves and their dams enrolled by medication group are in Table 5.2.

The majority of calves enrolled had a complete tongue withdrawal reflex (73%), strong suckle reflex (56%), and normal mucous membrane colour (64%) when assessed at birth. Detailed descriptions of vigour assessment, time to stand, and colostrum management by medication group are in Table 5.3. The mean serum IgG concentration for all calves was 35.2 g/L (SD = 17.1) with a mean of 33.2 g/L (SD = 17.8) and 37.2 (SD = 16.4) for placebo and meloxicam treated calves, respectively. Forty-nine calves had inadequate TPI (24.8%) with 28 being placebo treated calves and 21 being meloxicam treated calves.

Overall, 23 calves (10%) were treated for disease with 11 being placebo treated calves and 12 being meloxicam treated calves. Twenty-two calves (9.5%) died in the study with 11 placebo treated calves (dystocia = 1, weak calf syndrome = 1, meconium aspiration = 1, septicemia = 1, abomasal ulcer = 1, BRD = 1. PCD = 1, unknown = 3) and 11 meloxicam treated calves (dystocia = 1, congenital defects = 1, lumbar and femoral fractures = 1, septicemia = 2, unknown = 6). The mean ADG to weaning for placebo and meloxicam treated calves was 1.04 kg bodyweight (SD = 0.21) and 1.05 kg bodyweight (SD = 0.02), respectively.

There was no significant effect of administering meloxicam to assisted calves on serum IgG concentration, risk of inadequate TPI, treatment for disease, mortality, or ADG. Tables 5.4 and 5.5 describe the results for the models including the significant covariates.

When evaluating calf-level risk factors associated with the measured outcomes, calves that were bottle or tube fed had lower serum IgG concentrations than those that nursed from their dam (Table 5.4). Calves with a weak suckle reflex had lower odds of inadequate TPI than those with a strong suckle reflex (Table 5.5). Calves with an incomplete tongue withdrawal reflex had higher odds of being treated for disease in the preweaning period than those with a complete tongue withdrawal reflex (Table 5.5). Calves that were born with meconium staining and had lower serum IgG concentrations had higher odds of preweaning mortality than those that were not meconium stained at birth and had higher concentrations of serum IgG (Table 5.5). Calves that were born to a mature cow, had higher birthweights, and higher serum IgG concentrations had greater ADG to weaning (Table 5.4). The proportion of variance between ranches and individuals was calculated for each outcome and reported in Tables 5.4 and 5.5.

5.5 Discussion

Non-steroidal anti-inflammatory drugs are increasingly being used in production animals and can improve cattle welfare. Murray and colleagues (2016a) found 13% of producers reported using pain mitigation after a difficult birth, while Moggy and colleagues (2017) found 28% of producers used an NSAID in the calf after a difficult birth. More recently, 45% of surveyed western Canadian beef producers (n = 97) reported using NSAIDs after a difficult birth in the calf (Pearson et al., 2019b). Although more producers are using pain mitigation after a difficult birth, the effects of administering analgesics have not been thoroughly studied. Studies investigating physiological impacts of administering an NSAID to calves at birth have not shown an effect. Pearson et al. (2019c) found no significant effect on physiological indicators of pain and inflammation in meloxicam-treated calves in comparison to placebo-treated calves. Similarly, Gladden et al. (2018) found no significant effect of administering ketoprofen to dairy calves within 3 hours of parturition on cortisol, creatine kinase, plasma L-lactate, or total protein concentration measured 24-hr, 48 hr, or 7 days after birth. In contrast, economically relevant factors such as increased growth or feed intake have been demonstrated in NSAID treated neonatal calves (Todd et al., 2010; Murray et al., 2016b; Pearson et al., 2019c). Specifically, Murray and colleagues (2016b) found that calves treated with meloxicam at birth had greater milk intake compared to calves treated with a placebo and Pearson and colleagues (2019c) found that assisted calves administered meloxicam at birth had greater average daily gain within the first week of life compared to placebo treated calves. Although no significant effect on TPI and calf health was found in the present study, other measurements may be utilized to investigate pain and inflammation in neonates such as behavioral indicators.

Behavioral indicators of pain and inflammation are important tools for assessing pain (Millman, 2013). Murray et al. (2016b) found calves that received meloxicam at <6 hrs of age had greater improvements in vigour from birth to 1 day of age than those receiving a placebo. Gladden and colleagues (2019) randomised calves by calving assistance (unassisted versus assisted) to receive ketoprofen or placebo treatment within 3 hours of parturition and found that calves receiving ketoprofen had increased play behaviour and spent less time in lateral recumbency than those receiving a placebo. Although behavioral indicators of pain and inflammation were not measured in this study, these previous studies indicate that administering an NSAID at birth to calves may improve calf welfare.

Vigour assessment has been used to predict outcomes of neonatal vitality in many different species (Apgar, 1953; Randall, 1971; Veronesi et al., 2005, 2009). Risk factors for poor vigour in calves include acidemia, trauma, assistance at calving, being born to young or very old dams, being born a bull calf, or being born during very cold temperatures (Riley et al., 2004; Barrier et al., 2012b; Homerosky et al., 2017a; Pearson et al., 2019a). Poor vigour can have negative outcomes for a calf such as resulting in taking longer to stand and inadequate intake or timely consumption of colostrum (Diesch et al., 2004; Vasseur et al., 2009; Homerosky et al., 2017b). In this study, vigour was an important predictor of TPI and calf health. Specifically, calves with a weak suckle reflex had lower odds of inadequate TPI than those with a strong suckle reflex. In contrast to the findings of the present study, previous work conducted by our research group has shown that calves with a weak suckle reflex were less likely to nurse from their dam by 4 hours after birth (Homerosky et al., 2017b) and had lower concentrations of serum IgG (Pearson et al., 2019a) compared to those with a strong suckle reflex. Producers involved in the present study were aware of the associations between suckle reflex and colostrum consumption and it is speculated that this knowledge influenced their colostrum intervention strategies.

In this study, calves with an incomplete tongue withdrawal reflex had higher odds of being treated for disease in the preweaning period than those with a complete tongue withdrawal reflex. This may be due to the relationship between acidemia and inadequate TPI in less vigorous calves (Boyd, 1989; Besser et al., 1990). Specifically, an incomplete tongue withdrawal reflex is associated with neonatal acidemia and inadequate TPI (Homerosky et al., 2017a; Pearson et al., 2019a), and acidemia has been associated with increased risk of inadequate TPI (Boyd, 1989). Acidemia and inadequate TPI are associated with higher morbidity in preweaned calves (Szenci, 1985; Schuijt and Taverne, 1994;Wittum and Perino, 1995; Dewell et al., 2006), therefore, this may explain the relationship found between an incomplete tongue withdrawal and increased risk of treatment for disease.

Calves that were born to a mature cow, had higher birthweights, and higher serum IgG concentrations had greater ADG to weaning. Higher serum IgG concentrations have been associated with greater ADG to weaning (Dewell et al., 2006). Older dams produce higher immunoglobulin concentrations in colostrum (Waldner and Rosengren, 2009; Morin et al., 2001, Conneely et al., 2013) and greater volumes of colostrum and milk (Butson et al., 1980), which may explain why older parity dams weaned calves with better growth.

Colostrum management is an important tool to help improve TPI in high risk calves (Godden, 2008). Due to the syndesmochorial structure of the bovine placenta, transfer of maternal antibodies across the placenta is not possible (Barrington and Parish, 2001). Therefore, the calf must ingest enough good quality colostrum in a timely fashion for absorption of immunoglobulins and TPI (Godden, 2008). Timely consumption of good quality colostrum decreases the risk of failed TPI and subsequent risks of morbidity and mortality (Barrington and Parish, 2001; Filteau et al., 2003; Dewell et al., 2006; Waldner and Rosengren, 2009). In this study, the method of colostrum consumption (nursed from dam) was associated with higher serum IgG concentrations than calves that were bottle or tube fed colostrum. In contrast, Filteau et al. (2003) found beef calves who were bottle fed had a lower risk of failed TPI than those who were left with their dam or led to the udder. This may be due to different management techniques and housing of animals in that study, where cow-calf pairs housed in stanchion barns were at higher risk of failed TPI. In the current study, all ranches calved outside in small paddocks or larger pastures. Furthermore, all producers checked for consumption of colostrum in calves and intervened with colostrum ingestion if the calf was not observed to have consumed colostrum.

The relationship between calves nursing from dams and having higher serum IgG concentrations may be due to a difference in colostrum quality, which was not evaluated in this study, rather than the method of colostrum consumption per se. Priestley et al. (2013) found that calves that received maternal colostrum had higher serum total protein and serum IgG concentrations and were more likely to have adequate TPI compared to those fed plasma or colostrum derived colostrum replacer products. Calves fed maternal colostrum also had higher weaning weights and ADG, and lower morbidity and mortality. Maternal colostrum is generally considered to be superior to a replacement product, but if the maternal colostrum quality is poor (e.g. low IgG concentration, high bacterial count, possible transmission of diseases) then a replacement product may be the better option (Godden, 2008). Therefore, the type and quality of colostrum may have more of an effect than the method. In the current study, calves that nursed from their dam always received maternal colostrum but those that were bottle or tube fed may have received colostrum replacement product or maternal colostrum. Type and method of colostrum administration had high collinearity and so therefore were not offered to the model simultaneously.

Being born with meconium staining and having lower serum IgG concentrations increased the odds of preweaning mortality in assisted calves in this study. This is consistent with other studies where higher serum IgG concentrations were associated with a lower risk of mortality (Dewell et al., 2006; Waldner and Rosengren, 2009). Ranch personnel involved in this study always checked to make sure a calf consumed colostrum, and if not, they intervened with various colostrum management techniques, which may explain high serum IgG concentrations in this population. Similar colostrum management practices have been reported on western Canadian cow-calf operations (Murray et al., 2016a; Pearson et al., 2019b).

Meconium staining occurs when the fetus experiences intrauterine hypoxia and meconium is expelled into the amniotic sac causing a yellowish-brown staining of the skin and hair. Aspiration and inhalation of meconium can lead to partial airway obstruction, ventilation-perfusion mismatch, chemical pneumonitis, and disruption of surfactant function (Poulsen and McGuirk, 2009). Hypoxia and meconium aspiration have both been associated with a higher risk of mortality in multiple neonatal species including humans, piglets, and calves (Lopez et al., 1992; Alonso-Spilsbury et al., 2005).

Timely intervention to assist a calving when necessary has been shown to be an important management tool to reduce the impacts of a prolonged or difficult birth on calf survival and vigour, as well as the risk of cow recumbency (Nix et al., 1998; Mee, 2004; Lombard et al., 2007). The ranches enrolled in this study intervened with calving assistance in a timely fashion and conducted management decisions similar to current management decisions as described in a benchmarking study investigating calving management practices on western Canadian cow-calf operations (Pearson et al., 2019b).

The majority of the proportion of variance accounted for in these models was at the individual level rather than the ranch level. These findings indicate that ranch-level factors had minimal impact on the outcomes and that most of the variance in the models was at the individual calf level. For treatment for disease, half of the variance was due to ranch-level influences, which may be explained by differences in treatment intervention protocols by ranch.

A potential bias of this study was that producers had the option to not enroll difficult assisted calves. Because all the ranches enrolled were working cow-calf operations, producers were allowed to not enroll a calf if they were uncomfortable with the possibility that a calf might receive a placebo, as many already had pain mitigation strategies in place. Although it is unknown the number of calves on each ranch that were not enrolled in the study, this may have biased our sampled population to calves that had less traumatic deliveries or were apparently less compromised at birth. An effect of meloxicam on calf health may not have been seen due to this selection bias. Another potential bias was that ranches selected to be enrolled in this study were well managed ranches, intervening with calving assistance early and administering colostrum to calves who were not observed to consume colostrum on their own, which may have lessened the impacts of a difficult calving on calf health and growth.

Although a few studies have investigated the effects of administering an NSAID to neonatal calves, none have reported pathological side effects (Todd et al., 2010; Murray et al., 2016b; Gladden et al, 2018; Gladden et al., 2019; Pearson et al., 2019c). Several studies have investigated the negative side effects of NSAIDs in neonatal foals, indicating repeated and higher doses of flunixin meglumine associated with stomach ulcerations, and petechiations of the cecum and colon (Carrick et al., 1989), but no side effects were found with daily administration of meloxicam in 2-3 day old foals (Raidal et al., 2013). Drug clearance has also been demonstrated to be different in neonatal foals in comparison to adult horses (Semrad et al., 1993; Crisman et al.,1996; Raidal et al., 2013). However, these studies were performed in healthy foals and NSAIDs in neonates that are dehydrated, have poor tissue perfusion, or are hypovolemic may be at greater risk of negative side effects, and require further investigation.

5.6 Conclusions

This study identified several factors that can be identified at birth that were associated with an increased risk of inadequate TPI, treatment for disease, mortality, and reduced growth. Although there was no effect of giving an NSAID at birth to assisted calves on TPI, health, and growth, assessing vigour at birth and ensuring good colostrum management may be important tools to improve TPI and health in high risk calves such as those that are assisted at birth.

Table 5.1. Calving management strategies on 15 cow-calf ranches located in southern Alberta during the 2017 calving season.

Management Practice	Number of ranches: Heifers (n = 14)[a]	Number of ranches: Cows (n = 15)
Frequency check dams during daylight hours		
Every 1-2 hours	7	4
3-6 times a day	5	9
Twice a day	2	2
Frequency check dams during night hours		
Every 1-2 hours	5	2
3-6 times at night	3	4
Twice at night	5	6
Do not check dams at night	1	3
Time to intervene after dam water bag or feet showed		
30-60 minutes	4	4
60-90 minutes	6	3
90-120 minutes	1	2
>120 minutes	3	6
Time to intervene after dam is not showing progression with labor		
30-60 minutes	11	9
60-90 minutes	2	3
90-120 minutes	0	1
>120 minutes	1	2

[a]One ranch did not calve heifers during the 2017 calving season.

Table 5.2. Demographics of 225 beef calves by medication group. Calves were administered a dose of either subcutaneous meloxicam (Metacam®, 20 mg/ml, 0.5 mg/kg body weight, Boehringer Ingelheim, Ingelheim, Germany) or placebo (0.025 ml/kg) at birth. All parameters are presented as counts and percentages.

	Placebo (n = 114)		Meloxicam (n = 111)		Total (n = 225)	
Demographic	**Count**	**Percentage**	**Count**	**Percentage**	**Count**	**Percentage**
Parity of dam						
Heifer	74	66.7%	77	71.3%	151	68.9%
Cow	37	33.3%	31	28.7%	68	31.1%
Sex of calf						
Heifer	42	36.8%	33	30.8%	75	33.9%
Bull	72	63.2%	74	69.2%	146	66.1%
Twin						
No	108	97.3%	105	97.2%	213	97.3%
yes	3	2.7%	3	2.8%	6	2.7%
Calving difficulty						
Easy assist	50	44.6%	58	54.2%	108	49.3%
Difficult assist	59	52.7%	48	44.9%	107	48.9%
Caesarian Section	3	2.7%	1	0.9%	4	1.8%
Presentation of calf						
Anterior	92	90.2%	91	88.3%	183	89.3%
Posterior	10	9.8%	12	11.7%	22	10.7%
Meconium staining						
No	81	84.4%	81	84.4%	96	50.0%
Yes	15	15.6%	15	15.6%	96	50.0%

Table 5.3. Vigour assessment and colostrum management for 225 beef calves by medication group. Calves were administered a dose of either subcutaneous meloxicam (Metacam®, 20 mg/ml, 0.5 mg/kg body weight, Boehringer Ingelheim, Ingelheim, Germany) or placebo (0.025 ml/kg) at birth. All variables are presented as a count and percentage (%).

	Placebo (n = 114)		Meloxicam (n = 111)		Total (n = 225)	
Variable	**Count**	**Percentage**	**Count**	**Percentage**	**Count**	**Percentage**
Tongue pinch withdrawal						
Complete	76	71.0%	78	75.7%	154	73.3%
Incomplete	31	29.0%	25	24.3%	56	26.7%
Suckle reflex						
Strong	59	57.3%	56	55.4%	115	56.4%
Weak	44	42.7%	45	44.6%	89	43.6%
Mucous membrane colour						
Normal	70	65.4%	64	62.1%	134	63.8%
Abnormal	37	34.6%	39	37.9%	76	36.2%
Time to stand						
0-30 min	20	22.7%	20	24.1%	40	23.5%
30-60 min	36	40.9%	27	32.6%	63	36.8%
1-6 hrs	28	31.8%	30	36.1%	58	33.9%
Required assistance	4	4.6%	6	7.2%	10	5.8%
Method of colostrum consumption						
Nursed from dam	79	78.2%	73	78.5%	152	78.4%
Bottle- or tube-fed	22	21.8%	20	21.5%	42	21.6%
Type of colostrum consumed						
Dam's colostrum	88	83.8%	82	86.3%	170	85.0%
Replacer product	17	16.2%	13	13.7%	30	15.0%
Calf nursed from the dam						
Yes	80	83.3%	79	88.8%	159	86.4%
No	15	16.7%	10	11.2%	25	13.6%
Time to consume colostrum						
<1 hr	20	19.8%	19	19.6%	39	19.7%
1-2 hrs	22	21.8%	21	21.6%	43	21.7%
2-3 hrs	27	26.7%	28	28.9%	55	27.8%
3-4 hrs	19	18.8%	22	22.7%	41	20.7%
4+ hrs	13	12.9%	7	7.2%	20	10.1%

Table 5.4. Multilevel linear regression models of serum immunoglobulin G (IgG) concentrations and average daily gain to weaning in 219 beef calves assisted at birth and medicated with subcutaneous meloxicam (Metacam®, 20 mg/ml, 0.5 mg/kg body weight, Boehringer Ingelheim, Ingelheim, Germany) or placebo (0.025 ml/kg) while adjusting for covariates and clustering by ranch.

	Coefficient	Standard Error	P Value	Proportion of Variance (%)	
				Individual Level	Ranch Level
Serum IgG concentration, g/L				>99%	<1%
Medication group					
Placebo	Referent	-			
Meloxicam	3.6	2.6	0.2		
Method of colostrum consumption					
Nursed from Cow	Referent	-			
Bottle- or tube-fed	-8.5	3.2	0.008		
Average daily gain to weaning, kg/day				96.8%	3.2%
Medication group					
Placebo	Referent	-			
Meloxicam	0.02	0.03	0.4		
Dam parity					
Mature cow	Referent	-			
Heifer	-0.1	0.04	0.02		
Birthweight, kg	0.009	0.002	<0.0005		
Serum IgG concentration, g/L	0.002	0.0008	0.008		

Table 5.5. Multilevel logistic regression models of transfer of passive immunity, treatment for disease, and mortality in calves assisted at birth and medicated with subcutaneous meloxicam (Metacam®, 20 mg/ml, 0.5 mg/kg body weight, Boehringer Ingelheim, Ingelheim, Germany) or placebo (0.025 ml/kg) while adjusting for covariates and clustering by ranch.

	Odds Ratio	Standard Error	P Value	Proportion of Variance	
				Individual Level	Ranch Level
Inadequate transfer of passive immunity (<24 g/L IgG)				>99%	<1%
Medication group					
Placebo	Referent	-			
Meloxicam	0.6	0.2	0.2		
Suckle reflex					
Strong	Referent	-			
Weak	0.5	0.2	0.05		
Treatment for disease				46%	54%
Medication group					
Placebo	Referent	-			
Meloxicam	1.7	1.0	0.4		
Tongue withdrawal reflex					
Complete	Referent	-			
Incomplete	5.8	3.9	0.009		
Mortality				97.6%	2.4%
Medication group					
Placebo	Referent	-			
Meloxicam	2.0	1.4	0.3		
Meconium staining					
No	Referent	-			
Yes	5.4	3.8	0.02		
Serum IgG concentration, g/L	0.95	0.02	0.03		

CHAPTER 6 – GENERAL CONCLUSIONS AND DISCUSSION

6.1. Thesis background

Calves assisted at birth are often compromised due to trauma and oxygen deprivation (Bellows et al., 1987; Homerosky et al., 2017a). This can lead to poor vigour causing prolonged latency to stand and nurse from the dam (Barrier et al., 2012b; Homerosky et al., 2017a,b). Weak, compromised, and less vigorous calves are more likely to have inadequate transfer of passive immunity (Mellor and Stafford, 2004), which is associated with an increased risk of morbidity and mortality in the preweaning period (Wittum and Perino, 1995; Dewell et al., 2006; Waldner and Rosengren, 2009). Therefore, assisted calves represent a high-risk group that may require intensive intervention strategies to improve calf health and wellbeing.

Current calving and colostrum management techniques on western Canadian cow-calf operations have not been adequately described. Doing so could provide producers and veterinarians with benchmarks to use as guidelines to improve management techniques and production on cow-calf operations. A major component of cow-calf operations is managing calvings and the calves after they are assisted at birth. Calves that have a difficult birth may experience trauma, which has previously only been reported by performing post-mortem examinations of stillborn calves (Ferguson et al., 1990; Waldner et al., 2010). Quantifying the amount of subclinical trauma by different degrees of calving difficulty has not been evaluated prior to this thesis, nor has the use of pain mitigation for trauma experienced by a difficult calving been investigated in assisted beef calves. Although risk factors, such as calving assistance, are known for calf morbidity and mortality, specific, individual calf factors for assisted beef calves have not been previously investigated and may help develop management tools to reduce calf morbidity and mortality, and improve production in high risk calves.

Therefore, the overall aim of this thesis was to investigate management factors and the impacts of a difficult calving on calf wellbeing.

6.2 Summary of results

In Chapter 2, the objectives were to describe current calving management practices on western Canadian cow-calf operations and to investigate associations between herd demographics and herd-level incidence of calving assistance, morbidity, mortality, and the use of calving and colostrum management practices. Herds that started calving dams earlier in the spring had higher herd-level incidences of calving assistance, morbidity, mortality, and used more hands-on calving and colostrum management techniques compared to herds that started calving in later months. This suggests that herds calving in earlier months are more intensively managed than herds that started calving later and that herd demographics are important to consider when investigating factors associated with management strategies, health, and production. The average herd-level incidence of assisted calvings within the surveyed group was 4.9%, yet greater than 90% of producers assisted at least 1 calving, indicating that although calving assistance incidence may be low, the majority of producers are providing calving assistance to some dams each year. These results suggest that managing high-risk calves at birth is still important for the majority of cow-calf operations.

Forty-five percent of producers surveyed also administered nonsteroidal anti-inflammatory drugs (NSAIDs) at birth to the cow and calf after a difficult calving despite the lack of scientific evidence for this off-label use. This suggested that studies investigating trauma associated with difficult assisted births and the clinical impacts of administering an NSAID to assisted beef calves are needed to better understand its impacts on calf wellbeing.

In Chapter 3, the objective was to quantify subclinical trauma and its association with calving difficulty, calf vigour, and transfer of passive immunity. Calves experiencing a difficult assisted calving had evidence of subclinical trauma, were less vigorous, and had increased odds of inadequate transfer of passive immunity (TPI). Elevated levels of biomarkers for subclinical trauma were associated with poor vigour in calves. Poor vigour was associated with increased odds of inadequate TPI. Understanding the impacts of a traumatic birth may aid in the development of management strategies, such as pain mitigation, for compromised newborn beef calves.

In Chapter 4, the objective was to investigate the impacts of administering an NSAID (meloxicam) to assisted beef calves on physiological indicators of pain and inflammation, TPI, health, and growth. Meloxicam-treated calves had significantly greater average daily gain (ADG) to 7-10 days of age compared to placebo-treated calves. There was no significant effect of meloxicam on physiological indicators of pain and inflammation, time to stand, time to nurse, TPI, health, or ADG to weaning. This study indicated that meloxicam increased growth in assisted calves, yet due to the small sample size, a larger field trial was necessary to investigate the effects of pain mitigation on calf health and production.

In Chapter 5, the objectives were to investigate the impact of administering an NSAID (meloxicam) to assisted beef calves and to determine risk factors associated with TPI, health, and growth. There were no effects of administering meloxicam to assisted calves on serum immunoglobulin G (IgG) concentrations, ADG to weaning, or risk of inadequate TPI, treatment for disease, or mortality. Calves that nursed from their dam had higher serum IgG concentrations compared to those that were bottle or tube fed colostrum. Calves with an incomplete tongue withdrawal had a higher risk of being treated for disease compared to those with a complete withdrawal, and calves with meconium staining at birth and decreased serum IgG concentrations had an increased risk of mortality. Calves born to a mature cow, who were born with higher birthweights, or had increased serum IgG concentrations had higher ADG to weaning. Vigour assessment as well as good colostrum management are important tools identified to improve TPI, health, and growth in high-risk calves such as those assisted at birth.

6.3 Study limitations

As with all field studies, the most significant limitation is the lack of consistency and control over variables in the environment and potential unmeasured confounders that exist on owner-operated cow-calf ranches. However, this inconsistency in management is replaced with the increased external validity that results from using such ranches compared to a research facility.

Misclassification bias was a potential concern in Chapters 3, 4, and 5. The degree of calving difficulty was a subjective classification based on the number of people pulling or the use of a calf jack. This classification does not take into consideration individual producer experience and preference on ways to deliver calves (e.g. some prefer to use a calf jack over multiple people pulling to deliver a calf). It was decided to use calving ease score as a way to estimate the degree of calving difficulty to allow for inclusion of calving difficulty as a covariate into the models because the direct measurement of the amount of force used to deliver a calf was unattainable at that time.

Potential selection bias occurred in Chapters 3 and 5. In Chapter 3, it was not feasible to select at random the animals enrolled in the study. Dams were enrolled based on a purposive sampling scheme of those calving within a 24-day period and that could be handled without injury to the animal handlers or excessive stress to the cow. This sampling scheme allowed for cow-calf pairs to be enrolled who required different degrees of calving difficulty to compare the effects of calving difficulty on subclinical trauma, calf vigour, and TPI. Calves enrolled in Chapter 5 were those requiring assistance at birth, yet producers had the option of not enrolling an assisted calf if they were concerned that it may not receive pain mitigation and would receive a placebo due to the randomisation of treatments. Although the number of assisted calves not enrolled was unknown, this may have decreased the likelihood of finding a significant impact of pain mitigation on calves experiencing the most traumatic births.

Neonatal physiology is complicated and relationships between hypoxemia, acidemia, perfusion, trauma, and tissue damage at birth are not well understood. A potential confounder of this thesis is the lack of measurement of pO2, pCO2, and pH at birth to determine the degree of hypoxemia and acidemia in assisted calves in association with muscle damage. In addition to trauma, calves with elevated levels of hypoxemia and acidemia may also have delayed reflexes and decreased vigour (Barrier, et al., 2012b; Homerosky et al., 2017a; Pearson et al., 2019a). It is important to recognize that NSAIDs are unlikely to improve hypoxemia and acidemia in neonates. Future studies should investigate the complicated relationships among acidemia, hypoxemia, trauma, and muscle damage, and its impact on neonatal calves to better develop management protocols for compromised calves at birth. For example, ventilation and oxygenation may be necessary to correct hypoxemia and acidemia in addition to managing the pain associated with trauma. Interestingly, in premature human infants with a persistent ductus arteriosus (PDA) causing respiratory distress syndrome, NSAIDs (indomethacin and ibuprofen) are used to close a delayed or enlarged ductus arteriosus (Pacifici, 2014). Although the frequency and risk of PDAs in calves is rare, the impact of prostaglandins on neonates transitioning from an intra-uterus to extra-uterus environment may be important to understand.

This thesis measured many different physiological and neuroendocrine indicators of pain and inflammation, and associations between pain mitigation and pain and inflammatory mediators were not detected. Previous research investigating the effects of pain mitigation at the time of painful procedures (e.g. castration, dehorning) have shown positive effects of decreasing pain and inflammation in older calves by administering NSAIDs (Heinrich et al., 2009; Allen et al., 2013; Coetzee, 2013; Melendez et al., 2017). However, pain in neonates is not well understood and indicators used for older calves may not be appropriate for neonates. Differences in pain responses between premature and newborn human infants as well as alternations in development of nerve pathways and the stress response in infants experiencing pain early in life have been shown (Johnston et al., 1994; Grunau et al., 2013). This suggests that age of the neonate and early exposure to pain may influence their future response to pain.

The studies in this thesis did not investigate behavioral indicators of pain and inflammation because of producer intervention strategies that could have confounded the results (e.g. assisting a calf to stand, separation of the cow and calf after birth, etc.). Behavioral indicators of pain and inflammation are important aspects of identifying pain in cattle and have been found to be influenced by pain mitigation in other neonatal calf studies (Murray et al., 2016b; Gladden et al., 2019) and should be investigated in future research.

6.4 Future research

As demonstrated by this thesis, calves experiencing a difficult birth had evidence of subclinical trauma and were less vigorous at birth. Although difficult births are considered extremely painful for the cow and calf (Huxley and Whay, 2006; Barrier et al., 2012a), the relationship between calving difficulty and pain and inflammation has not been well described in cows or calves (Mainau and Manteca, 2011). Pain and inflammation are commonly measured using physiological, neuroendocrine, behavioural, and production related changes (Coetzee, 2013; Millman, 2013). This thesis measured pain and inflammation by physiological, neuroendocrine, and production related changes, but behavioural indicators of pain were not measured. Although not reported in Chapter 5, producers did perceive a beneficial effect of administering meloxicam to calves despite being blinded to the medication group. Producers reported that calves that received product A (meloxicam) "seemed to get up and get going faster, mothered up faster, and cow-calf pairs were kicked out of the barn sooner". The impact of pain mitigation on the cow and is limited to a few clinically-relevant publications (Laven et al., 2012; Gladden et al., 2018) and the impact of pain mitigation on cow-calf bonding has not been investigated.

Cow-calf bonding is an important post-calving act influenced by hormonal and learned behaviours. The bond is initiated within the first few hours after birth and involves the cow and calf learning to recognise each other as well as the cow committing to caring for and protecting its calf. Disruptions in formation of the bond can be caused by stress, painful or traumatic calving events, inexperience (i.e. females calving for the first time), and weak or less vigorous calves (von Keyserlingk and Weary, 2007). Although the incidence of mismothering is low (Pearson et al., 2019c), many producers spend a considerable amount of time and various techniques to initiate a cow-calf bond. Future studies should investigate the physiological and behavioural impacts of pain mitigation in the cow and calf after a difficult calving and its effect on improving the cow-calf bond, as was perceived by producers.

Another area of future research should involve investigating the pharmacokinetics and potential pathological side effects of NSAIDs in compromised neonates. Studies have been performed in neonatal calves investigating the effects of administrating an NSAID and none have reported negative clinical effects (Todd et al., 2010; Murray et al., 2016b; Gladden et al, 2018; Gladden et al., 2019; Pearson et al., 2019b). Use of NSAIDs in neonates is increasing to minimize the pain and inflammation caused by a difficult birth but specific doses and risk of side effects have not been well studied in large animals. In neonatal foals, daily administration of flunixin meglumine was associated with stomach ulcerations, and petechiation of the cecum and colon (Carrick et al., 1989). Other reports have found that neonatal clearance of flunixin meglumine was lower and drug disposition was longer in 24-48 hour old foals compared to 1 month old foals, indicating dose and frequency of NSAIDs administered to neonates in the first 1-2 days differs from older foals (Semrad et al., 1993; Crisman et al., 1996) When investigating the use of meloxicam in neonatal foals ranging in age from 2-23 days, more rapid clearance of meloxicam was found in younger foals in comparison to adult horses but no difference in time to maximum plasma concentration was found (Raidal et al., 2013). In addition, no negative side effects were reported in 2-3 day old foals given meloxicam twice daily at higher doses. Unfortunately, these studies were performed on healthy foals and side effects in compromised neonates that are dehydrated, have poor perfusion, or are hypovolemic may still be a risk. This indicates that further investigation into the concentration, frequency, and potential side effects of administering NSAIDs to compromised neonates is warranted. In addition to investigating the side effects of NSAIDs in neonates, it is plausible that the current labeled dose and frequency of NSAIDs in neonatal calves is not appropriate for pain mitigation. Future studies investigating the pharmacokinetics in neonates or investigating other analgesics may improve pain mitigation, yet pharmacokinetic studies are still necessary as other classes of analgesics may cause negative side effects, such as bradycardia and sedation, which can be detrimental in a neonate. It is also important to mention that meloxicam, while licensed in Canada for use in calves, is not labeled for pain associated with dystocia in neonatal calves, so appropriate veterinary-client-patient relationships and good communication with producers about extra-label drug use should occur.

The studies in this thesis also focused on trauma caused by a difficult birth and did not investigate the relationship between trauma, hypoxia, acidemia, and poor perfusion in assisted calves. It is unknown how these factors interact with each other in a compromised neonate and there are no easy calf-side diagnostic tests to determine if a calf is less vigorous at birth due to trauma, acidemia, hypoxemia, or a combination thereof. Therefore, future research to investigate the varying degrees of severity or combinations of these factors and their impacts on calf health are necessary. Furthermore, developing calf-side diagnostic tests to identify compromised neonates would aid in the decisions about appropriate treatment.

6.5 Contribution to new knowledge

This thesis is the first study to investigate the impacts of a difficult calving and implications of pain mitigation and management of assisted beef calves on transfer of passive immunity, health, and growth. The findings are relevant to the beef industry shareholders, producers, and veterinarians.

The studies in this thesis provided novel benchmarking information for the beef industry by providing current calving and colostrum management techniques being used on western Canadian cow-calf ranches. This information can be used to describe current practices and fill the gap in knowledge of current calving and colostrum management practices as well as the relationships between herd demographics and calf health. Specifically, Chapter 2 found interesting relationships between herd demographics and incidence of assistance, morbidity, mortality, and calving and colostrum management strategies, indicating that herd demographics are important to consider when investigating factors associated with management strategies, health, and productivity in cow-calf herds.

Although it may seem intuitive that more difficult calvings cause greater trauma, the amount of subclinical trauma experienced by these calves had not been previously described, nor had the associations among subclinical trauma, calf vigour, and TPI been investigated. Findings from Chapter 3 provided important information for producers and veterinarians to better understand the effects of a difficult calving on calf vigour and TPI, and to suggest further research investigating intervention strategies, such as pain mitigation, to improve calf health.

Chapters 4 and 5 are the first studies to investigate pain mitigation strategies in beef calves after calving assistance. These studies provided producers and veterinarians with the knowledge of potential beneficial effects of administering an NSAID at birth to assisted calves to improve calf growth in the first week of life. Concerns for the welfare of assisted beef calves were addressed through this thesis investigating pain, inflammation, and pain mitigation in assisted calves. Although only ADG to one week of age was improved by calves receiving meloxicam, other publications suggests potential benefits of pain mitigation on behavioural indicators of pain. Producer perception and use of pain mitigation after a difficult birth also suggest potential benefits yet require further investigation.

Results reported within this thesis repeatedly demonstrated the association between calf vigour and colostrum management and improvements in TPI, health, and production in assisted beef calves. These associations may lead to development of calf-side tools that producers and veterinarians can use to assess assisted calves at birth and intervene with different management practices as necessary to improve calf health and growth.

6.6 Conclusions

Overall, this thesis found that although the incidence of assisted calvings appear to be decreasing, producers are still managing compromised neonates assisted at birth. Calves experiencing a difficult birth have increased subclinical trauma that effects calf vigour and TPI. There may be improvements in calf wellbeing in calves medicated with an NSAID, as indicated by increase in ADG in the first week of life, yet investigation of behavioural indicators of pain and inflammation are required to better understand these improvements. Associations of vigour assessment parameters and good colostrum management with calf health and growth were repeatedly highlighted, indicating these important tools should be used to improve the wellbeing of assisted beef calves.

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APPENDIX A: CALVING MANAGEMENT QUESTIONNAIRE

Western Canadian Cow-Calf Surveillance Network Survey

Calving Management and Practices in Cow-Calf Herds

THIS QUESTIONNAIRE IS PART OF THE RESEARCH FOR THE BCRC-FUNDED DISEASE SURVEILLANCE NETWORK THAT IS BEING CONDUCTED BY RESEARCHERS AT THE UNIVERSITY OF CALGARY FACULTY OF VETERINARY MEDICINE AND THE WESTERN COLLEGE OF VETERINARY MEDICINE.

Your participation is voluntary. All of your responses will be kept confidential. Return of our questionnaire by mail will indicate your consent to participate in the survey and have your responses summarized in the final report.

- **Please answer each question in the survey.**
- **Please return the survey in the provided stamped envelope.**
- **Pages have questions on both sides.**
- **Please send back each page of the survey.**
- **Answer each question as best as you can; If something else should have been asked or included, please write us a note to explain.**

Please enter your name: _______________________________date:_____________

If you have any questions regarding the survey, feel free to email:

Dr. Jennifer Pearson at the University of Calgary, Faculty of Veterinary Medicine;

jennifer.pearson@ucalgary.ca

Production information for your herd for the 2016 year

A. 2016 Calving Season:

1) How many **seasonal workers** performed ranch work during the **calving season**?

____

2) How many **full time workers** performed ranch work **year-round**? (e.g. worked >10 months/year) ________________

3) Does your operation have **both a spring and fall calving herd**? (*Circle ONE answer that best applies)* Yes or No

Note: If your operation has both a spring and fall calving herd, use the ***SPRING calving group*** *to answer the following section.*

4) When was the **2nd full term** calf born to a female in the 2016 calving season? (e.g. Mar 1st, 2016)

Heifers: _____________ Cows: _____________

5) When was the **last calf** born to a female in the 2016 calving season?

Heifers: _____________ Cows: _____________

6) How many **bred females** were assisted (not by c-section) in delivering their calf during the 2016 calving season?

Heifers: _____________ Cows: _____________

7) How many **bred females** were assisted **by c-section** in delivering their calf during the 2016 calving season?

Heifers: _____________ Cows: _____________

8) How many calves were **born in total** during in the 2016 calving season?
(These are calves that were full term and includes full term calves born dead)

Heifers: ____________ Cows: ____________

9) How many calves were delivered dead and were not full term (aborted)?

Heifers: ____________ Cows: ____________

10) How many full term live calves were born?

Heifers: ____________ Cows: ____________

11) How many full term calves were delivered dead or died before 24 hours of age (stillborn)?

Heifers: ____________ Cows: ____________

12) How many calves died from 1-7 days of age?

Heifers: ____________ Cows: ____________

13) How many calves died from 7-30 days of age?

Heifers: ____________ Cows: ____________

14) How many calves died from 30 days of age to weaning?

Heifers: ____________ Cows: ____________

15) How many calves were treated for the following diseases during 2016?

Scours: ________ Pneumonia: ________ Other diseases: ________

Please fill in the number of animals in each of the following categories that you owned during the 2015-2016 production cycle.

16) How many **breeding females** were **pregnant at fall preg check (2015) but did not calve** during the 2016 calving season?

Heifers: ____________ Cows: ____________

17) How many **breeding females calved** during the 2016 calving season?

Heifers: ____________ Cows: ____________

18) How many **breeding females** had **twins** during the 2016 calving season?

Heifers: ____________ Cows: ____________

19) How many **breeding females died between** fall 2015 and calving 2016?

Heifers: ____________ Cows: ____________

20) How many **breeding females died during** the 2016 calving season?

Heifers: ___________ Cows: ____________

21) How many **bred females** did you manage for mismothering in the 2016 calving season?

Heifers: ____________ Cows: ____________

22) How many calves were fostered onto a new heifer or cow due to **mismothering** during the 2016 calving season? ___________

23) How many calves were fostered onto a new heifer or cow due to **twinning** during the 2016 calving season? ___________

24) How many calves were fostered onto a new heifer or cow due to **mortality of their dam** during the 2016 calving season? ___________

Do you have any other questions or comments that you would like to share with us?

Thank you so much for taking the time to complete this survey. Your responses will provide valuable information of value to the Canadian beef industry!

This questionnaire will ONLY focus on your management for the 2016 calving season, the management leading up to calving for those cows and heifers that calved in 2016, and the management of the calves born in 2016.

B. Pregnant Cow Management:

Please answer the following question regarding ***bred/pregnant cow management practices*** *in terms of how the* ***MAJORITY*** *of either* ***heifers or cows*** *in your herd were housed prior to the start of calving season during the 2015-2016 production cycle. Please select only* ***one option*** *per questions.*

Definitions:

Extensive Grazing: Cattle are housed on large land areas with a relatively large number of acres per animal and the main feed source being grazing or green feed

Small Pasture: Cattle are housed on a small land area with a relatively low number of acres per animal with supplemental feed and/or grains provided as the main feed source either on the ground or in a feeder or feedbunk

Dry lot Confinement: Cattle are housed in a cattle-dense dry lot (feedlot) with all feed and/or grains provided in a feeder or feedbunk

25) How were bred/pregnant animals housed? (*Please check the box with an "X")*

	A) Heifers			**B) Cows**		
	Extensive Grazing	**Small Pasture**	**Dry lot**	**Extensive Grazing**	**Small Pasture**	**Dry lot**
i. Breeding to Preg Check						
ii. Overwintering period						
iii. Two months prior to the start of calving season						

C. Calving Management:

*Please answer each of the following questions regarding **pre-calving management practices** in terms of how the **MAJORITY** of either **heifers or cows** in your herd were managed during the 2015-2017 production cycle. Please select only **one option** per question.*

26) When were animals moved to the calving area prior to the start of the expected 2017 calving season? *(Check only one box for heifers and one for cows)*

	Heifers	Cows
Calving occurs on the same area as overwintering	☐	☐
>6 weeks	☐	☐
3-6 weeks	☐	☐
1-3 weeks	☐	☐
<1 week	☐	☐

27) When (if at all) were animals **most likely** to be moved into the barn during calving? *(Check only one box for heifers and one for cows)*

	Heifers	Cows
When signs suggest she will calve within 24hrs (e.g. bagged up/loose tailhead)	☐	☐
When signs of active calving were present (e.g. water bag/feet out)	☐	☐
I bring my animals into the barn to calve only if they need assistance with calving	☐	☐
I do not move my animals into a barn to calve	☐	☐

28) When (if at all) did you move cow-calf pairs into the barn after calving? *(Check all that apply)*

	Heifers	Cows
Cold weather	☐	☐
Mismothering	☐	☐
Bad udder	☐	☐
Cross-fostering	☐	☐
Other (please explain):	☐	☐

____

____

29) When (if at all) were cow-calf pairs **most likely** to be **moved out** of the calving area? *(Check only one box for heifers and one for cows)*

	Heifers	Cows
I moved individual pairs as soon as possible after calving	☐	☐
I moved batches of cow-calf pairs once every 24 hours	☐	☐
I moved cow-calf pairs at greater than 24 hours but less than 1 week	☐	☐
I moved cow-calf pairs every 1-2 weeks	☐	☐
All animals remained in the calving pasture until after the end of calving season	☐	☐
Pairs stay where they calved and cows/heifers yet to calve get moved to a new pasture (i.e. the sandhill calving system)	☐	☐
Other (please explain):	☐	☐

____

____

30) If cows/heifers yet to calve get moved from the calving pasture to a fresh pasture, how often do you move those animals? *(Circle ONE answer that best applies)*

Weekly   2 weeks   3 weeks   >3 weeks

31) How often do you check **heifers** in the calving pasture during **daylight** hours? *(Circle ONE answer that best applies)*

At least hourly   Every 1-2 hours   3-6 times/day   Twice daily   Once daily

Other (please explain): ____

32) How often do you check **cows** in the calving pasture during **daylight** hours? *(Circle ONE answer that best applies)*

At least hourly   Every 1-2 hours   3-6 times/day   Twice daily   Once daily

Other (please explain): ____

33) How often do you check **heifers** in the calving pasture during **night-time** hours? *(Circle ONE answer that best applies)*

At least hourly   Every 1-2 hours   3-6 times/day   Twice daily   Once daily

Other (please explain): ____

34) How often do you check **cows** in the calving pasture during **night-time** hours? (*Circle ONE answer that best applies*)

At least hourly   Every 1-2 hours   3-6 times/day   Twice daily   Once daily

Other (please explain): ____

35) Which of the following criteria do you use to decide to assist an animal with delivering her calf? (*Please check all that apply)*

☐ Water bag/feet showing for **heifers** *(Circle the amount of time you TYPICALLY wait before assisting)*

30 minutes 30-60 min 60-90 min 90-120 min 120-180 min >180 min

☐ Water bag/feet showing for **cows** *(Circle the amount of time you TYPICALLY wait before assisting)*

30 minutes 30-60 min 60-90 min 90-120 min 120-180 min >180 min

☐ **Heifer** appears to be in labor with no progression *(Circle the amount of time you TYPICALLY wait)*

30 minutes 30-60 min 60-90 min 90-120 min 120-180 min >180 min

☐ **Cow** appears to be in labor with no progression *(Circle the amount of time you TYPICALLY wait)*

30 minutes 30-60 min 60-90 min 90-120 min 120-180 min >180 min

☐ Calf appears to be backwards

☐ Calf appears to be malpositioned (e.g. one foot, only a head, etc.)

☐ I do not assist my **heifers** with calving

☐ I do not assist my **cows** with calving

☐ Other (please explain): ____

36) If a heifer or cow is having difficulties at calving, when do you decide to call a vet? (*Select the ONE answer that best applies*)

☐ As soon as I discover something is abnormal

☐ After I have attempted to correct the problem and was not successful

☐ Only if surgery is needed (e.g. C-section or cutting out a dead calf)

☐ I don't call a vet for calvings

☐ Other (please explain):

D. Colostrum Management:

37) What criteria do you use to verify if a calf has received colostrum? (*Check all that apply*)

☐ Saw the calf suck

☐ Cow's udder does not appear full, appears to have been sucked

☐ Calf looks full

☐ I do not check to see if calves consume colostrum

☐ Other (please explain):

38) **Rank** the following techniques you would **typically** use to ensure calves receive colostrum when it appears the calf has not sucked from the cow and you decide to intervene? (*Rank only those that apply starting with 1. Use the same number for options that are tied in rank)*

____Put the cow and calf together in a stall to monitor

____Restrain the cow and help the calf to suck

____Bottle feed the calf

____Tube feed the calf

____I do not intervene if calf has not sucked from the cow

____Other (*please specify*): ____

39) **Rank** the source of colostrum you **typically** use when assisting a calf in colostrum consumption (*Rank only those that apply starting with 1. Use the same number for options that are tied in rank)*

____Milk from the calf's mother

____Colostrum Replacement/supplement product

Please list product: ______________________________________

____Frozen colostrum collected from our cows

____Dairy colostrum

____Other *(please specify)*: ____

E) Calving Protocols:

40) **Rank** the following techniques you **typically** use to resuscitate a calf? (*Rank only those that apply starting with 1. Use the same number for options that are tied in rank)*

___Rub vigorously

___Hang over a fence or gate (lift hind end so fluid drains out)

___Pour cold water in its ear

___Poke straw or a finger in its nose

___Other (*please specify):* ____

41) Which of the following do you record at calving? *(Check all that apply)*

- ☐ Date of birth
- ☐ Identification number
- ☐ Calving difficulty score
- ☐ Birth weight
- ☐ I do not record any information at birth
- ☐ Other (*please specify):* ____

42) How do you record calving information? *(Select the ONE answer that best applies)*

- ☐ Calving notebook or paper record only
- ☐ On paper then transfer to computer record later
- ☐ Directly into smartphone or other electronic device
- ☐ Other (*please specify*): ____

43) What do you administer to the **MAJORITY** of **cows or heifers** that had **a difficult delivery**? *(Check all that apply)*

- ☐ Non-Steroidal Anti-Inflammatory Drug (NSAID) (e.g. Banamine, Metacam, Anafen)
  Please list product: ____
- ☐ Lidocaine epidural
- ☐ Vitamins or minerals
- ☐ Oxytocin
- ☐ Antibiotics
  Please list product: ____
- ☐ I do not administer any drugs to the cow when assisted at birth
- ☐ Other____

44) What do you administer to the **MAJORITY** of **calves that were born by a difficult delivery**? (*Check all that apply*)

- ☐ Non-Steroidal Anti-Inflammatory Drug (NSAID) (e.g. Banamine, Metacam, Anafen)
  Please list product:____
- ☐ Vitamins ADE
- ☐ Selenium +/- Vitamin E
- ☐ Antibiotics
  Please list product: ____
- ☐ Dip navel
- ☐ I do not administer any drugs to the calf when assisted at birth
- ☐ Other____

45) Which of the following do you perform/administer to calves within the first week of life:
(Check all that apply)

☐ Visual identification (ear tags)
☐ Castration
☐ Vitamins ADE
☐ Selenium +/- Vitamin E
☐ Antibiotics
Please list product: ____
☐ Navel disinfectant
☐ I do not administer anything to calves within the first week of life
☐ *Other (please specify):* ____

G) Mismothering *(Definition: Cow demonstrates poor mothering ability or lack of mothering behavior by rejecting her calf after birth, refusing to let it nurse, not interacting with it, and/or showing aggression towards it, etc.)*

46) What are the most common behaviors you see that result in mismothering? (*Rank only those that apply starting with 1. Use the same number for options that are tied in rank)*

___Cow/heifer abandons calf

___Cow/heifer is aggressive towards calf

___Cow/heifer does not allow calf to nurse

___Cow/heifer had twins and rejected one or both calves

___I do not observe mismothering behaviors

___Other (*please specify):* ____

47) What are the most common procedures you **typically** perform to deal with mismothering? (*Rank only those that apply starting with 1. Use the same number for options that are tied in rank)*

___House cow and calf together in a box stall for 24 hours or longer

___Separate cow and calf but keep them close in a confined area (e.g. box stall)

___ Restrain cow in chute and assist calf to nurse

___ Sedate cow with a drug (e.g. acepromazine)

___ Cross-foster the calf onto another cow

___ Other *(please specify):* ____

48) When a heifer or cow exhibits mismothering behaviors, what is the **one most common** management approach you take? *(Select the ONE answer that best applies)*

	Heifers	Cows
Cull the animal	☐	☐
Give the animal one more chance	☐	☐
Close monitoring at calving next season	☐	☐
Nothing different	☐	☐
Other *(please explain):*	☐	☐

____

____

49) **Rank** the procedures you **typically** use to foster a calf onto a new heifer/cow? (*Rank only those that apply starting with 1. Use the same number for options that are tied in rank)*

___Place cow and calf together in a box stall

___Place placenta from foster heifer or cow on foster calf

___Place dead calf's hide on foster calf

___Place scent masking powder on foster calf *(e.g. Calf Claim, Orphan-No-More)*

___Place grain on foster calf

___Sedate foster heifer or cow and place foster calf with her

___I do not foster calves onto foster heifers or cows

___ Other *(please specify):* ____

H) Breeding Management:

50) Please check **the one most important** trait you considered when you selected a bull for your **heifers** during the 2016 breeding season to calve in the 2017 calving season *(Select the ONE answer that best applies)*

- ☐ Bull birthweight
- ☐ Breed reputation for calving ease
- ☐ Bulls EPD for calving ease
- ☐ Physical appearance
- ☐ Pedigree
- ☐ Price
- ☐ Other *(please specify):* ____

51) How likely are you to cull a cow or heifer from the herd for each of the following reasons?*(Please check the box with an X)*

	Very Unlikely	**Unlikely**	**Possible**	**Likely**	**Very Likely**
Aggressive behavior towards people					
Bad foot conformation					
Bad udder conformation					
Dead calf at birth					
Lameness					
Mismothering behaviors					
Open (not pregnant) at fall preg check					
Poor body condition					

APPENDIX B -SUPPLEMENTAL DATA FOR CHAPTER 4

Table 4.6. Description of mean (SD) blood parameters and physical examination findings associated with pain or inflammation in 33 beef calves assisted at birth and medicated with subcutaneous meloxicam (0.5 mg/kg) or placebo (0.025 ml/kg) at different times after birth by medication group.

	Birth	1 hour	4 hour	24 hour	7-10 day
Cortisol, ng/ml					
Placebo	83.4 (25.4)	68.9 (25.8)	37.9 (24.9-76.0)[1]	19.1 (9.2-33.4)[1]	-
Meloxicam	77.7 (25.5)	68.9 (25.8)	49.9 (22.7-59.3)[1]	13.4 (9.0-20.2)[1]	-
Corticosterone, ng/ml					
Placebo	2.1(1.5-2.9)[1]	1.7 (0.99-2.2)[1]	0.6 (0.2-1.8)[1]	0.5 (0.2-0.8)[1]	-
Meloxicam	1.8 (1.5-2.2)[1]	1.7 (1.4-2.3)[1]	0.6 (0.4-1.3)[1]	0.3 (0.3-0.5)[1]	-
Substance P, pg/ml					
Placebo	187.8 (56.5)	156.1 (130.8-188.6)[1]	336.2 (190.9-654.5)[1]	401.1 (272.3-558.6)[1]	-
Meloxicam	191.5 (64.7)	150.5 (129.9-196.7)[1]	297.1 (149.5-382.5)[1]	543.9 (410.2-623.1)[1]	-
Heart Rate, bpm					
Placebo	145.6 (18.9)	167.0 (25.1)	160.0 (150-170)[1]	147.5 (21.8)	-
Meloxicam	144.7 (22.7)	160.6 (23.3)	160.0 (130.0-160.0)[1]	141.6 (20.5)	-
Respiratory Rate, bpm					
Placebo	59.8 (17.1)	53.1 (11.3)	50.6 (1.2)	52.8 (13.7)	-
Meloxicam	54.7 (21.8)	48.8 (13.2)	50.0 (10.0)	54.8 (10.1)	-
Rectal Temperature, C°					
Placebo	39.6 (0.4)	39.3 (38.9-39.6)[1]	38.8 (38.1-39.1)[1]	38.7 (38.5-39.0)[1]	-
Meloxicam	39.7 (0.5)	39.3 (38.7-39.6)[1]	39.2 (38.7-39.5)[1]	38.8 (38.6-38.9)[1]	-
L-Lactate, mmol/L					
Placebo	9.1 (3.3)	-	-	2.8 (1.8-3.4)[1]	-
Meloxicam	10.0 (3.0)	-	-	2.7 (2.2-4.1)[1]	-
Haptoglobin, g/L					
Placebo	0.13(0.13-0.14)[1]	-	-	0.15 (0.14-0.16)[1]	0.16 (0.14-0.41)[1]
Meloxicam	0.14 (0.12-0.16)[1]	-	-	0.15 (0.13-0.17)[1]	0.17 (0.13-0.26)[1]

[1]Denotes median and interquartile range

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Dr. M. Claire Windeyer, BSc, DVM, DVSc
Associate professor in beef cattle health and welfare
Department of Production Animal Health

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Elizabeth Homerosky, DVM, MSc., DABVP (Beef cattle)

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