

Alternative dry cow management strategy

by

Caio Aranha Gamarra

DVM, Universidade Federal de Mato Grosso do Sul, Brazil, 2016

A THESIS

submitted in partial fulfillment of the requirements for the degree

MASTER OF SCIENCE

Department of Animal Sciences and Industry
College of Agriculture

KANSAS STATE UNIVERSITY
Manhattan, Kansas

2020

Approved by:

Major Professor
Dr. Luís G. D. Mendonça

Abstract

Poor transition from late gestation to early lactation influences postpartum performance of lactating dairy cows. Considering that increased vaginal temperature (VT) before calving is associated with reduced postpartum performance during summer, this thesis focused on investigating a novel management strategy in the dry period to improve postpartum performance during summer of cows with high temperature (HT) in late gestation. This study was conducted in three commercial dairy herds in the High Plains region during summer. Vaginal temperature was assessed from 1,603 multiparous Holstein cows with 236 to 250 of gestation, and the top 20% highest temperature were classified as HT cows. High temperature cows were randomly assigned as treatment or control. Treatment consisted of moving cows earlier to the close-up pen compared with the rest of the herd. Therefore, three groups were compared in the study: high temperature and extended days in the close-up pen (HT-TRT), high temperature and not extended days in the close-up pen (HT-CON), and low temperature and not extended days in the close-up pen (LT). Cows were followed until 90 days in milk (DIM) of the next lactation to compare postpartum performance. In a cohort of cows ($n = 201$), blood sample was collected at VT assessment to compare pregnancy-associated glycoprotein (PAG) concentration of HT and LT cows. Days spent in the close-up pen differed among treatments ($\text{HT-TRT} = 24.5 \pm 1.8$; $\text{HT-CON} = 15.9 \pm 1.8$; $\text{LT} = 20.3 \pm 1.8$). Low temperature cows had longer gestation length and decreased percentage of twinning compared with HT-CON and HT-TRT cows. Low temperature cows had and tended to have decreased percentage of stillbirth than HT-CON and HT-TRT, respectively. In addition, LT cows had decreased percentage of uterine disease in the first 21 DIM than HT-CON cows. Nonetheless, LT and HT-TRT did not differ in percentage of cows diagnosed with uterine disease. High temperature control cows had reduced percentage of cows

pregnant at first service compared with LT cows, however, no difference was detected between LT and HT-TRT cows. Pregnancy-associated glycoprotein concentration at VT assessment differed between HT and LT cows. Cows with increased VT in late gestation benefited from spending more days in the close-up pen during summer months. Differences in PAG concentrations of LT and HT cows suggest that PAG could be a potential maker to identify cows that will have postpartum problems after calving during summer months.

Table of Contents

| | |
|--|------|
| List of Figures | vi |
| List of Tables | vii |
| Acknowledgements | viii |
| Dedication | ix |
| Chapter 1 - Literature Review..... | 1 |
| Introduction..... | 1 |
| Gestation Length..... | 2 |
| Placental and Fetal Development..... | 3 |
| Hormones of Late Gestation | 5 |
| Stillbirth | 6 |
| Dry Period Duration..... | 8 |
| Dry Cow Diets | 10 |
| Heat Stress | 13 |
| Dry Cow Management Practices | 15 |
| Antibiotic Use and Public Concern | 17 |
| BIBLIOGRAPHY..... | 19 |
| Chapter 2 - Strategy to Identify Dry Cows More Susceptible to Heat Stress, Reduce Antimicrobial Treatments, and Improve Performance After Calving. | 30 |
| INTRODUCTION | 30 |
| MATERIALS AND METHODS..... | 31 |
| Animals and Facilities..... | 31 |
| Vaginal Temperature Assessment, Treatments, and Temperature-Humidity Index..... | 31 |
| Antimicrobial Treatments, Disease Definitions, and Culling | 32 |
| Body Condition Score and Milk Yield | 33 |
| Blood Sampling | 33 |
| Statistical Analyses | 34 |
| RESULTS | 35 |
| DISCUSSION | 38 |
| BIBLIOGRAPHY..... | 48 |

| | |
|---------------------------------------|----|
| Chapter 3 - General Conclusions | 60 |
|---------------------------------------|----|

List of Figures

| | |
|--|----|
| Figure 1 Milk yield during the first 13 wk of lactation of cows classified as low temperature (LT), high temperature treatment (HT-TRT), or high temperature control (HT-CON). (A) Primiparous cows (overall mean \pm SEM): LT = 41.7 ± 0.8 ; HT-TRT 39.4 ± 1.1 ; HT-CON = 39.7 ± 1.1 kg/d. (B) Multiparous cows (overall mean \pm SEM): LT = 44.4 ± 0.7 ; HT-TRT = 45.4 ± 1.1 ; HT-CON = 42.3 ± 1.1 kg/d..... | 58 |
| Figure 2 Plasma concentration of bovine pregnancy-associated glycoprotein (PAG) in Holstein cows classified as high or low temperature based on vaginal temperature before calving. High temperature cows had greater ($P = 0.02$) PAG concentration compared with low temperature cows (4.11 ± 0.13 vs. 3.74 ± 0.15 ng/mL). | 59 |

List of Tables

| | |
|--|----|
| Table 1 Prepartum descriptive data (mean \pm SEM) of cows classified as high temperature treatment (HT-TRT), high temperature control (HT-CON), and low temperature (LT) before calving | 56 |
| Table 2 Incidence of antimicrobial treatment and culling risk during the first 60 days postpartum, and reproductive efficiency of cows classified as high temperature treatment (HT-TRT), high temperature control (HT-CON) and low temperature (LT) | 57 |

Acknowledgements

To the only one who is the reason of all things: my Savior, my God.

To my brothers and their unconditional love.

To my parents for all their sacrifice and tears because of me. For every night that they prayed, surrendering their own will to make mine possible. For the unconditional love among us that neither seas nor distance can separate or diminish.

To the new family that God gave me. A woman who never left my side. For all that she has done to me and for me. For the emotional support, advice, and trust in whom I am. Especially for my young boy and his little smile, his sweet presence, and his pure heart.

To Dr. Luis Mendonça, my great friend, mentor, and advisor. For all his effort to shape my professional character.

Dr. Jeffrey Stevenson and Dr. Kenneth Odde as members of my committee.

To the true friends that believed in me, supported, and never forgot the value of our memories.

To Kansas State University staff and employees.

Dedication

“For from him and through him and to him are all things. To him be glory forever. Amen.”

Romans 11:36

Chapter 1 - Literature Review

Introduction

Postpartum performance of dairy cows is directly associated with the ability of the cow to cope with changes during the transition from late gestation to early lactation. Because of the increased nutritional challenges and physiological changes during the transition period, adoption of specific management practices during this period is important for cows to overcome some of these challenges in order to improve postpartum health and productive life (Arnold and Becker, 1936; Drackley, 1999). Appropriate nutritional strategies and management protocols, such as altering nutrient density of the diet and implementation of a non-lactating or dry period, can reduce the biological and physiological imbalances of the transition cow (Grummer, 1995; Capuco et al., 1997).

Numerous prepartum management practices are implemented based on the expected parturition date and their effectiveness relies on the accuracy of predicting calving. Several factors are reported to affect duration of gestation of dairy cows, and therefore, compromise the efficacy of strategies adopted (Norman et al., 2009; Tomasek et al., 2017). Cows with shortened or extended gestation length (GL) have decreased postpartum performance and increased incidence of postpartum disorders after calving (Vieira-Neto et al., 2017). Scanavez et al. (2017) demonstrated that deviations from the average GL of the population is also associated with prepartum core body temperature (CBT). Considering that the associations described in these reports evaluated cows exposed to similar management practices under the same environment, it is likely that a single management strategy may not be appropriate for the entire herd.

The focus of this review of literature is to provide an overview of relevant aspects of pregnancy development and describe prepartum factors that may impact performance of the dam

in the subsequent lactation. This thesis focused on exploring a novel management strategy to improve postpartum health of cows susceptible to have postpartum health disorders.

Gestation Length

Gestation length, which is the period between conception and subsequent parturition, has changed during the past decades in dairy cows. In the 1950s, it was reported that the average GL of Holstein cows was 280 days (Andersen and Plum, 1965). A report published in the 1990s evaluated changes of GL of dairy cows during five decades (Silva et al., 1992). This report demonstrated that GL decreased 0.08 days yearly, which represents a decrease of 4 days during 50 years. One of the possible reasons for this change in GL is genetics. It is possible that genetic selection for greater milk production was associated with shorter GL.

Other factors not related to genetics or breed may have also contributed to changes in GL of the modern dairy cow. The fetal-maternal interaction, fetal characteristics, number of calves, exposure to heat stress during late gestation, and season of calving are some of the intrinsic and extrinsic factors that have been shown to be associated with GL (Nogalski and Piwczyński, 2012; Norman et al., 2009; Tomasek et al., 2017). Mechanisms that trigger the parturition process may be delayed or hastened by metabolic or physical stressors, and consequently, altering GL. Exposure to heat stress or poor nutritional status during late gestation can negatively affect the morphological adaptations of the placental epithelium. Therefore, metabolic function of placental cells may be compromised and lead to a nutritional restriction to the fetus and hypoxia (Fowden and Moore, 2012; Tao and Dahl, 2013). Impairment of placental function results in a premature initiation of parturition mediated by fetal-secreted cortisol or dam-induced fetal stress. Calf gender affects GL because male calves have longer development of the

hypothalamic-pituitary-adrenal axis, which delays the initiation of the parturition process, resulting in increased GL (Matthews and Challis, 1996).

Deviations from the expected GL in dairy cows also is associated with occurrence of postpartum diseases and compromised milk production and reproductive performance (Jenkins et al., 2016; Vieira-Neto et al., 2017). It was demonstrated by Vieira-Neto et al. (2017) that longer GL had a negative impact in multiparous cows, but this association was not observed in primiparous cows. Nevertheless, negative effects of shorter GL were observed in both primiparous and multiparous cows (Vieira-Neto et al., 2017). Besides the negative impact on the dam, reports have demonstrated negative carryover effects of GL on the offspring (Jenkins et al., 2016; Vieira-Neto et al., 2017). Female calves born to dams with shorter or longer GL had reduced reproductive performance and decreased survival compared with calves born from dams with normal GL.

Because the reports that investigated the impact of GL on performance are observational studies, it is not possible to isolate other factors that led to decreased postpartum performance of cows with shorter GL. Nevertheless, it is plausible that a multifactorial etiology, involving nutrition, metabolic status, pregnancy characteristics, and environmental conditions, affects GL and subsequent postpartum performance.

Placental and Fetal Development

In ruminants, the interaction between conceptus and dam during gestation is mediated via the placenta, which is responsible for maintaining fetal viability and providing nutrients to the conceptus until term. Because of the unique features of migratory fetal chorionic binucleate cells (BNC) through the chorionic tight junction and fusing with uterine epithelial cells, the placenta of ruminants is classified as synepitheliochorial (Wooding, 1992). Development of the placenta

during the first weeks of gestation is critical for its secretory and subsequent regulatory activities. Factors limiting the early placental development, such as hypoxia and dietary restriction, can impair placental function, and consequently, fetal development (Penniga and Longo, 1998). In addition, impairment of early placental development impacts structural and functional maturation of fetal tissues near term, which affects the calving process and calf survival (Fowden et al., 1998). Increased concentration of fetal glucocorticoids near parturition is critical for final conceptus development of lung, liver, gut, and vital tissues (Fowden et al., 1998). Furthermore, the increase of glucocorticoid plays an important role in the expression of placental steroidogenic enzymes, ultimately increasing myometrial activity and labor (Jenkin and Young, 2004).

Towards the end of gestation, fetus and maternal tissues reach maximal growth rates (Prior and Laster, 1979). The utero-placental tissues utilize a substantial proportion of maternal nutrients, which result in a maternal-fetal conflict over allocation of requirements (Van Saun, 1991). To fulfill the considerable nutritional demand, the placenta undergoes morphological and structural changes to optimize nutrient distribution. Placental changes, such as increase in surface area and decrease of barrier thickness, are associated with greater blood flow and altered transplacental concentration gradient, which improves nutrient diffusion to cope with fetal demand (Fowden and Moore, 2012). Despite direct and indirect placental adaptations to supply increased requirements during late gestation, potential lack of nutrients diverted to the fetus may negatively affect calf viability and performance of the dam after calving. The burden of increased nutrient requirements and diminished dam reserves may contribute to increased risk of postpartum health disorders or premature delivery (Van Saun, 1991; Fowden and Moore, 2012).

Hormones of Late Gestation

In many mammalian species, the placenta has an important role in maintenance of gestation by producing steroid hormones. In cattle, synthesis and site of action of placental hormones are not fully understood. Estergreen et al. (1967) demonstrated an extraovarian participation source of progesterone (P4) late in gestation, however, not sufficient to maintain pregnancy in ovariectomized cows. Further, placental contribution to P4 synthesis was demonstrated by Gross and Williams (1988). The same authors showed that fetal villi BNC are the major site of P4 production in the placenta. In addition, the paracrine activity of placental steroid hormones on expression of local estradiol and progesterone receptors suggests an important activity for controlling caruncular growth and function (Hoffmann and Schuler, 2002). Different than other species in which the placenta contributes solely to maintaining gestation, it is suggested that placenta steroid hormones are involved with parturition process and detachment of fetal membranes (Williams et al., 1987).

Bovine placental lactogen (bPL), a 200-amino acid protein produced by BNC, plays a pivotal role in regulating and coordinating fetal growth and metabolism. During the first half of gestation, PL exerts growth-promoting effects that act directly in fetal tissues. Binding to receptors with similar affinity to growth hormone (GH), PL stimulates fetal development at the time of maximal fetal linear growth (Chan et al., 1976). From the second half of gestation until term, the metabolic role of PL is involved in modification of uterine epithelium. In association with leptin, both placental hormones ensure an optimal nutrient supply for the fetus, which assists on partitioning nutrients between dam and fetus (Handwerger, 1991; Ravelich et al., 2004). Placental lactogen also is described to have structural and functional similarity with bovine prolactin and somatotropin. Binding to its receptor, PL acts as a weak somatotropin

agonist displaying lactogenic activity, altering the mammary gland and furthering milk production (Byatt et al., 1992).

Direct and indirect alterations in placental hormonal synthesis during late gestation can have detrimental effects on both calf and dam performance. Reducing the period of exposure to placental hormones or reduced receptor expression affects the function and morphology of placenta. Decreased or impaired activity of the placenta may negatively impact fetal development and maternal performance traits by increasing the risk of incomplete detachment of fetal membranes after parturition. Furthermore, it is not fully understood how placental hormones influence the mammary gland tissue, however, it is speculated that it is involved in its development and subsequent lactogenesis.

Stillbirth

The most commonly accepted definition of stillbirth was described by Philipsson et al. (1979), who characterized stillbirth as the presence of a dead calf before, during, or by the first 48 h after parturition. Stillbirth is commonly used benchmark of herd performance because of the economic impact of replacing a dead calf. It has been shown that the economic impact of stillbirth in the dairy industry annually exceeds \$125 million (Meyer et al., 2001). The impact on profitability of dairy operations does not rest solely on calf losses but on decreased performance of dairy cows throughout lactation. Stillbirth is considered a risk factor for postpartum health disorders, such as retained fetal membranes and metritis (Correa and Scarlett, 1993). Characteristics such as oversized fetus, twinning, and elevated calf weight during pregnancy are associated with dystocia and stillbirth in dairy cows (Johanson and Berger, 2003). As a

consequence of stillbirth, the compromised uterine wall is susceptible to bacterial infections, which may lead to further clinical diseases (Markusfeld, 1987).

Poor health status and increased incidence of clinical diseases during the first postpartum weeks have a major impact on milk production and reproductive performance of dairy cows. Berry et al. (2007) demonstrated that cows giving birth to a stillborn calf had reduced peak milk yield and cumulative milk production during the first 60 days in milk (DIM) compared with cows delivering a live calf. Similar findings were reported by Bicalho et al. (2008). A stillbirth event was associated with reduced milk production during the first weeks after parturition (Bicalho et al., 2008). In addition, cows with a stillbirth event had increased days open and poorer reproductive efficiency compared with control cows. Furthermore, cows that had a stillbirth event were more likely to have increased mortality and culling compared with cows giving birth to a live calf (Bicalho et al., 2007).

The genetic component associated with breed and heterosis was speculated to be one of the main drivers of calf mortality during the first 24 h after birth. Hansen et al. (2004) demonstrated that genes related to increased calf weight, smaller dam size, twinning, and gestation length are predisposing factors for stillbirth events. Smaller pelvic size is the main risk factor for heifers and first-lactation cows to have dystocia and stillbirth compared with mature cows (Meyer et al., 2001; Johanson and Berger, 2003). Therefore, parity of the dam is one of the main effects to predispose a stillbirth event (Berry et al., 2007). In addition, shorter GL is another factor associated with stillbirth (Meyer et al., 2001; Vieira-Neto et al., 2017). In spite of evidence that GL impacts stillbirth, contradictory results were obtained by Hansen et al. (2004), who reported a weak correlation between GL and stillbirth.

Another important aspect to be considered is the nutritional status of the dam, which can affect the newborn calf. Chebel et al. (2018) demonstrated that cows with shorter dry periods and excessive body condition score (BCS) loss had a greater proportion of dead calves during the first 24 h after birth compared with cows that did not have reduced dry periods or excessive BCS loss. Nonetheless, Berry et al. (2007) reported no association between BCS loss during the prepartum period and stillbirth incidence. Heat stress during late gestation may predispose cows to have stillborn calves (Meyer et al., 2001). On the other hand, contradictory results were reported by Johanson and Berger (2003), who demonstrated an increased incidence of stillbirth during winter compared with summer.

Many factors related to the dam and fetus affect mortality of calves during the first 24 h after calving. Indeed, strategies focused on decreasing incidence of stillbirth in dairy herds are still lacking and would be valuable to improve cow performance and herd profitability.

Dry Period Duration

A non-lactating or dry period between lactations is commonly used in dairy herds as a management practice. Arnold and Becker (1936) described advantages and disadvantages when implementing dry period durations varying from 10 days up to 10 weeks on subsequent cow performance.

The non-lactating period between lactations is necessary for reasons not just related to nutrition but physiological factors (Capuco et al., 1997; Collier et al., 2004). The biological and morphological changes of the mammary gland during the dry period were observed by Capuco et al. (1997). Capuco et al. (1997) reported a necessary replacement of the damaged senescent epithelial cells before the subsequent lactation. In addition, the process involving the proliferation and turnover of mammary cell tissue before parturition seems to be critical for

increased milk production during the next lactation. Collier et al. (2004) described a series of physiological adaptations involving most of the body tissues and nutrient classes during the transition from pregnancy to lactation. Changes in the absorption, synthesis, and mobilization of bones, muscle, and organs are fundamental for the body to achieve homeostasis during the transition period (period of 3 weeks before and after parturition).

Considering the necessary adaptations occurring during the transition period, several studies evaluated diverse durations of the dry period. Grummer and Rastani (2004) recommended a non-lactating period of 40 to 60 days. Nonetheless, it is possible that an optimal dry period duration may vary among individual cows in order to maximize performance of each animal.

The process of mammary gland differentiation in preparation for a new lactation is critical for subsequent productive performance. Shortening or omitting the non-lactating period has been demonstrated to have a negative impact on the physiological and morphological changes of the mammary gland (Capuco et al., 1997). During the dry period, the mammary gland undergoes a remodeling process characterized by involution, proliferation, and differentiation. The process includes changes that dictate milk production potential during the subsequent lactation. Apoptosis, programmed cell death, occurs during the involution state immediately after milk cessation and can occur up to 25 days after dry-off (Collier et al., 2004). Characterized by the activation of proteases, the lobular-alveolar structure of the gland is destroyed by degrading the extracellular matrix and basement membrane, including the loss of alveolar cells (Capuco and Akers, 1999). After involution, mammary epithelial cells increase proliferation throughout the remainder of the dry period to replace old tissue and initiate mammary development. Old mammary cells from a previous lactation have reduced capacity of proliferation and secretion

compared with new cells, and consequently, influences milk production in the upcoming lactation (Capuco and Akers, 1999). The processes of degradation and regeneration promote renewal of the mammary gland, increasing milk production potential after calving. During the last week of gestation, cell proliferation is greatest and is characterized by differentiation into a secretory phenotype promoting the final preparation for subsequent lactation (Akers, 2002).

Despite the possible negative effects of decreasing the duration of the dry period on mammary gland development, studies reported a positive effect of a shorter period (4 weeks) on health and milk production (Watters et al., 2008). The shorter dry period might decrease the effects of negative energy balance during the transition period, and consequently, reduce the incidence of health disorders (Watters et al., 2008; Andree O'Hara et al., 2019). In addition, other known factors, such as heat stress and elevated CBT, impact dry period duration and subsequent lactation performance (Tao et al., 2011; Scanavez et al., 2017). Besides all the physiological and hormonal changes during the dry period, several management practices occur during this period, such as vaccinations, pen movements, preventive treatments, and diet changes with the goal to optimize performance in the subsequent lactation. Therefore, dry period duration is an important factor to be considered in the lifecycle of the cow. Nonetheless, the optimal duration of a dry period is debatable, and more research must be conducted in this area.

Dry Cow Diets

Nutritional strategies can be used during the dry period to improve postpartum health and increase milk production in the subsequent lactation. Rations offered to dry cows should meet the nutritional requirements associated with mammary gland development and fetal growth (Van Saun, 1991). In addition, nutritional strategies used in the dry period impact the early postpartum period of dairy cows. Drackley (1999) suggested that the last 3 weeks of gestation and the first 3

weeks of lactation is the most critical phase in the production cycle of dairy cow. The early postpartum period, which is influenced by the dry period, is characterized by elevated nutritional requirement and decreased dry matter intake (DMI), inducing cows to undergo a state of negative energy balance. An inadequate nutritional strategy during the prepartum or postpartum period can lead to excessive BCS loss during this phase, a surge of metabolic diseases, and lastly, impaired milk production and reproductive efficiency.

Nutritional strategies have been used to improve the energy balance during the periparturient period, and therefore, reducing fat mobilization, body weight loss, and consequently, reducing metabolic and clinical diseases (Drackley, 1999). Drackley (1999) suggested that diets balanced for prepartum cows should maximize DMI. Nonetheless, decrease in DMI before calving is inevitable because of physiological and behavioral changes (Grummer, 1995; Luchterhand et al., 2016). The strategy to formulate 2 separate diets with different energy content for the early (far-off dry period) and late (close-up dry period) dry periods is commonly used by dairy nutritionists. It has been demonstrated that high-energy diets at the beginning of the dry period results in reduced postpartum DMI and increased metabolic disorders (Dann et al., 2006). Reduced postpartum DMI exacerbates negative energy balance and fat mobilization, leading to elevated levels of nonesterified fatty acids (NEFA) and β -hydroxybutyrate (BHBA). These metabolites have been shown to be associated with increased incidence of postpartum metabolic and clinical diseases (Ospina et al., 2010). In contrast, cows fed low-energy diets during the far-off dry period had increased DMI and adequate energy balance after calving. In consequence of decreased fat mobilization, reduced serum concentrations of NEFA and BHBA after calving were observed (Dann et al., 2006).

Feeding strategies based on high-energy density during entire dry period led to increased body weight and BCS, and more pronounced negative energy balance after calving (Grummer et al., 2004). Over-conditioned cows have elevated NEFA and BHBA and increased risk of hyperketonemia, displacement of the abomasum, metritis, and other health events (McArt et al., 2013). Cows with elevated BCS at dry-off tended to have moderate to excessive BCS loss during the dry period, which was associated with reduced reproductive and productive performance after calving (Chebel et al., 2018). Therefore, a controlled-energy diet during dry period minimizes postpartum diseases and improves postpartum performance of the subsequent lactation (Drackley et al., 1999; Dann et al., 2006).

Another feeding strategy to improve postpartum health status is the use of acidogenic salts in prepartum diets or reduce the dietary cation-anion difference (DCAD) of rations. During the last 3 weeks of gestation, a substantial proportion of dairy cows undergo an imbalance of calcium homeostasis because of colostrum and milk syntheses (Littledike, 1976). Because of the inability to maintain blood calcium concentrations through intestinal absorption or bone resorption, some cows develop clinical hypocalcemia. Martinez et al. (2014) reported that hypocalcemia alters energy metabolism and immune function. Hypocalcemia is associated with other metabolic disorders, increased postpartum diseases, and reduced reproductive performance. To reduce imbalance of calcium homeostasis, diets with a negative DCAD can be used as a nutritional strategy (Block, 1984). Prepartum diets with a negative DCAD can be created by adding acidogenic salts. Diets with negative DCAD result in a metabolic acidosis in the prepartum cow, stimulating target tissue responsiveness to parathyroid hormone (PTH; Goff et al., 2004). Mediated by responsiveness to PTH, osteoclasts activity along bone surfaces leads to enhanced bone resorption and intestinal calcium absorption (Goff et al., 2004; Block et al.,

1994). In consequence, blood calcium concentration is increased, decreasing the likelihood of cows developing hypocalcemia.

A recent study performed by Lopera et al. (2018) demonstrated that not just the level of DCAD but the duration that the diet was fed can impact performance of postpartum cows and their metabolism. Increasing the number of days on the DCAD diet negatively impacted milk production and reproductive efficiency of cows after calving. In addition, reducing DCAD levels decreased postpartum DMI. Observational studies have demonstrated that reduced periods on prepartum diets impacted performance of cows, but gestation length is a confounder in these experiments (Scanavez et al., 2017; Vieira-Neto et al., 2017). More research studies are needed to evaluate the impact of increasing or decreasing the length of feeding negative DCAD diets during the prepartum period on postpartum health and performance.

Heat Stress

As previously described, management strategies implemented during the dry period influence the subsequent lactation of dairy cows. In addition to physiological challenges during late gestation, external factors such as elevated temperature negatively impact postpartum performance (Tao and Dahl, 2013). Dry cows exposed to more pronounced heat stress had decreased milk production after calving compared with cows provided heat abatement in the dry period (do Amaral et al., 2009; Tao and Dahl 2013; Tao et al., 2018). Heat stress occurs when a combination of factors elevates environmental temperature above the cow's thermoneutral zone. To evaluate the degree of heat stress, the temperature-humidity index (THI) is used commonly. Wiersma (1990) developed a chart to estimate the severity of heat stress based on ambient temperature and relative humidity. The index indicated that performance of dairy cows can be

impaired when THI exceeds 72. Nonetheless, the assessment performed by Berman (2005) demonstrated a reduction of the THI threshold for high-producing dairy cows. Considering the constant genetic selection for high yield dairy cows, modern dairy cows will continue to be susceptible to heat stress. Most recent studies demonstrate that reduced performance was observed at THI as low as 68 (Zimbelman et al., 2009; Bernabucci et al., 2010).

Heat abatement can reduce the effects of heat stress on dairy cows. Active cooling in the dry period may reduce body temperature and improve subsequent milk and fat yield after calving compared with non-cooled cows (Tao and Dahl, 2013; do Amaral et al., 2011). In a study in which mammary biopsies were performed in cows exposed or not to heat abatement during the dry period, demonstrated no difference on cell apoptosis; however, cows exposed to heat abatement had decreased cell proliferation compared with cows with no heat abatement (Tao et al., 2011). These findings indicate that heat stress impacts mammary gland development, which may compromise subsequent milk production. Even though the mechanisms involved in altered mammary gland development of dry cows exposed to heat stress are not completely understood, hormonal synthesis and nutrient availability may be impacted, which also may affect development and function of the mammary gland (do Amaral et al., 2009; Tao et al., 2011).

Reproductive performance of lactating dairy cows is reduced in warmer months compared with cooler months. Decreased capacity of oocyte development is one of the factors that impacts fertility of heat-stressed cows (Ferreira et al., 2011). In addition, evidence supports that compromised embryonic development is another factor that influences fertility of cows during warm months (Sartori et al., 2002). Furthermore, hormonal changes during warmer months in lactating dairy cows influences expression of estrus (Stevenson et al., 1984). Even though sufficient information in the literature demonstrated the negative impact of heat stress on

fertility, limited studies have explored the effects of heat stress during the dry period on reproductive performance after calving. Studies conducted in Florida demonstrated that cows dried-off during warmer months had reduced reproductive efficiency compared with cows dried-off during cooler months (Thompson and Dahl, 2012). Thompson and Dahl (2012) suggested that heat stress during the dry period had a negative carry-over effect on reproductive performance. On the other hand, Avedaño-Reyes et al. (2006) did not observe an association between heat stress in late gestation and reproductive performance in the subsequent lactation.

Increased ambient temperature impacts immune responses of dairy cows. Elevated temperature during late gestation can impair both specific and nonspecific immune responses. Do Amaral et al. (2011) demonstrated that neutrophil function in the periparturient period is reduced in dry cows not exposed to heat abatement compared with cows exposed to heat abatement. Neutrophil function was determined by evaluating capacity of phagocytosis and oxidative burst of blood cells. Humoral response, involved in production of antibodies against an antigen, also was impaired during late gestation of dry heat-stressed cows when compared with cooled dry cows (do Amaral et al., 2011). Periparturient immunosuppression associated with heat stress may result in increased susceptibility to postpartum diseases, therefore, increasing the probability of cows being treated with antimicrobials after calving.

Dry Cow Management Practices

In addition to nutritional strategies used during the dry period, other adopted practices aimed to maximize performance in the subsequent lactation. These additional strategies involve reducing microbial infections, and improvement of immune responses and overall health of the mammary gland.

Dry cow therapy is a widespread practice used at the beginning of the dry period. Dry cow therapy may involve administration of intramammary antibiotics, internal teat sealant, or both. The goal of treating cows with antibiotics is to cure existing infections and prevent further infections. Internal teat sealant acts as a physical barrier against environmental pathogens, thereby reducing potential infections during the dry period. Smith et al. (1968) demonstrated that quarters infected during the dry period produced less milk during the subsequent lactation, which is expected to impact profitability. Mammary gland infections are more likely to occur during the initial phase or the involution stage of the dry period (Bradley and Green, 2004). With the cessation of milking, a flush of bacteria from the streak canal is diminished, and protective effects from immunoglobulins and intramammary lactoferrin is delayed (Bradley and Green, 2004). Therefore, after cessation of milking, susceptibility to new infections is increased.

Because blanket dry cow treatment with antimicrobials results in treatment of the entire herd at dry-off, adoption of different strategies to reduce susceptibility to infections and antimicrobial use are needed. Researchers have proposed a selective treatment approach instead of blanket treatment in order to reduce the number of cows treated with antimicrobial (Cameron et al., 2014; Scherpenzeel et al., 2018). Selective dry cow treatment programs must use selection criteria to target therapy for specific subgroups of cows, therefore, decreasing the number of treatments (Cameron et al., 2014)

Another common strategy used during the dry period is vaccination programs in order to mount an immune response against potential infections. Because mastitis is extremely prevalent in dairy herds, vaccination programs have been developed to reduce the severity of clinical signs of gram-negative bacteremia. Bradley and Green (2000) demonstrated that 52% of clinical mastitis cases from gram-negative agents occurring during the first 100 DIM originate from

infections during the dry period. Vaccination programs focusing on reducing cases of toxic clinical mastitis have the goal of increasing antibodies against lipopolysaccharide-core antigens. This strategy has been demonstrated to diminish clinical symptoms caused by bacterial toxin, despite no difference on infection rates (Hogan et al., 1992).

Modulation of the immune system with vaccines during dry period also may affect the offspring through passive transfer of antibodies found in colostrum feeding. Vaccinating cows during the dry period stimulates humoral and cellular-mediated immune responses and increases titers in serum and colostrum (Wileman et al., 2011; Smith et al., 2014). Increased titers in calves fed colostrum from immunized cows compared with calves fed colostrum from non-immunized cows demonstrates the efficacy of passive transfer of immunoglobulins (Foster et al., 2019). Vaccination programs during the dry period are designed based on the expected day of calving. Cows with shorter or longer dry periods may not be immunized as planned. Therefore, colostrum of these cows may not contain large quantities of immunoglobulins and cows may bear greater risk of developing certain disorders after calving. It is possible that vaccination programs for dry cows are not effective for the entire herd considering the large variation in gestation length and other factors not discussed in this thesis.

Antibiotic Use and Public Concern

Use of antibiotics in food animal production allows our farming systems to maximize production and reduce animal morbidity and mortality. Preventive or therapeutic antimicrobial treatments of animals with clinical and subclinical diseases allow livestock producers to control disease outbreaks and improve health status of animals. Considering that a substantial number of antibiotics used in human medicine also are used for livestock production, public concern exists about potential residues and antibiotic resistance. Nonetheless, evidence exists demonstrating

that antibiotic use in adult dairy cows does not increase resistance of veterinary pathogens to antimicrobials (Oliver et al., 2011). Moreover, a 7-year study revealed no change in bacterial isolates susceptibility of pathogens involved with mastitis infections (Erskine et al., 2002). In the future, food production agriculture should focus on understanding how antimicrobials currently used impact multi-drug resistance and public health (Shea et al., 2003; Oliver et al., 2011).

Similar to antibiotic use, animal welfare is another aspect that animal agriculture must address. The focus should not be limited to the absence of injuries or illnesses of animals, but evaluating how management practices and animal behavior is perceived by the public. Besides concerns about inhumane treatment of animals, the livestock industry should be ready to discuss issues related to water and carbon footprint. Conversations about these topics should be addressed correctly to avoid damaging brands and consumption of rich-nutrient animal products. Surveys conducted with U.S. consumers demonstrate that the general public is highly concerned about indiscriminate use of antibiotics (Wolf et al., 2016). Because of the growing concern of the public about animal agriculture, novel strategies to reduce the use of antimicrobials and improve health of animals must be considered to address the expectation of consumers, and hopefully, improve public perception of animal agriculture.

BIBLIOGRAPHY

- Akers, R. M. 2002. Lactation and the Mammary Gland. R. M. Akers, ed. Iowa State Press, Ames, USA.
- Andersen, H., and M. Plum. 1965. Gestation length and birth weight in cattle and buffaloes: A Review. *J. Dairy Sci.* 48:1224–1235. doi:10.3168/jds.S0022-0302(65)88431-4.
- Andrée O’Hara, E., R. Båge, U. Emanuelson, and K. Holtenius. 2019. Effects of dry period length on metabolic status, fertility, udder health, and colostrum production in 2 cow breeds. *J. Dairy Sci.* 102:595–606. doi:10.3168/jds.2018-14873.
- Arnold, P. T. D., and R. B. Becker. 1936. Influence of preceding dry period and of mineral supplement on lactation. *J. Dairy Sci.* 19:257–266. doi:10.3168/jds.S0022-0302(36)93061-8.
- Avendaño-Reyes, L., F. D. Alvarez-Valenzuela, A. Correa-Calderón, J.S. Saucedo-Quintero, P. H. Robinson, and J. G. Fadel. 2006. Effect of cooling Holstein cows during the dry period on postpartum performance under heat stress conditions. *Livest. Sci.* 105:198–206. doi:10.1016/j.livsci.2006.06.009.
- Berman, A. 2005. Estimates of heat stress relief needs for Holstein dairy cows. *J. Anim. Sci.* 83:1377–1384. doi:10.2527/2005.8361377x.
- Bernabucci, U., N. Lacetera, L. H. Baumgard, R. P. Rhoads, B. Ronchi, and A. Nardone. 2010. Metabolic and hormonal acclimation to heat stress in domesticated ruminants. *Animal* 4:1167–1183. doi:10.1017/S175173111000090X.
- Berry, D. P., J. M. Lee, K. A. Macdonald, and J. R. Roche. 2007. Body condition score and body weight effects on dystocia and stillbirths and consequent effects on postcalving performance. *J. Dairy Sci.* 90:4201–4211. doi:10.3168/JDS.2007-0023.

- Bicalho, R. C., K. N. Galvão, S. H. Cheong, R. O. Gilbert, L. D. Warnick, and C. L. Guard. 2007. Effect of stillbirths on dam survival and reproduction performance in Holstein dairy cows. *J. Dairy Sci.* 90:2797–2803. doi:10.3168/JDS.2006-504.
- Bicalho, R. C., K. N. Galvão, L. D. Warnick, and C. L. Guard. 2008. Stillbirth parturition reduces milk production in Holstein cows. *Prev. Vet. Med.* 84:112–120. doi:10.1016/J.PREVETMED.2007.11.006.
- Block, E. 1984. Manipulating dietary anions and cations for prepartum dairy cows to reduce incidence of milk fever. *J. Dairy Sci.* doi:10.3168/jds.S0022-0302(84)81657-4.
- Block, E. 1994. Manipulation of dietary cation-anion difference on nutritionally related production diseases, productivity, and metabolic responses of dairy cows. *J. Dairy Sci.* 77:1437–1450. doi:10.3168/jds.S0022-0302(94)77082-X.
- Bradley, A. J., and M. J. Green. 2000. A study of the incidence and significance of intramammary enterobacterial infections acquired during the dry period. *J. Dairy Sci.* 83:1957–1965. doi:10.3168/JDS.S0022-0302(00)75072-7.
- Bradley, A. J., and M. J. Green. 2004. The importance of the nonlactating period in the epidemiology of intramammary infection and strategies for prevention. *Vet. Clin. North Am. - Food Anim. Pract.* 20:547–568. doi:10.1016/j.cvfa.2004.06.010.
- Byatt, J. C., P. J. Eppard, L. Munyakazi, R. H. Sorbet, J. J. Veenhuizen, D. F. Curran, and R. J. Collier. 1992. Stimulation of milk yield and feed intake by bovine placental lactogen in the dairy cow. *J. Dairy Sci.* 75:1216–1223. doi:10.3168/jds.S0022-0302(92)77870-9.
- Cameron, M., S. L. McKenna, K. A. MacDonald, I. R. Dohoo, J. P. Roy, and G. P. Keefe. 2014. Evaluation of selective dry cow treatment following on-farm culture: Risk of postcalving intramammary infection and clinical mastitis in the subsequent lactation. *J. Dairy Sci.*

- 97:270–284. doi:10.3168/jds.2013-7060.
- Capuco, A. V., and R. M. Akers. 1999. Mammary involution in dairy animals. *J. Mammary Gland Biol. Neoplasia* 4:137–144. doi:10.1023/A:1018769022990.
- Capuco, A. V., R. M. Akers, and J. J. Smith. 1997. Mammary growth in Holstein cows during the dry period: quantification of nucleic acids and histology. *J. Dairy Sci.* 80:477–487. doi:10.3168/jds.S0022-0302(97)75960-5.
- Chan, J. S. D., M. J. Robertson, and H. G. Friesen. 1976. The purification and characterization of ovine placental lactogen. *Endocrinology* 98(1):65–76. doi:10.1210/endo-98-1-65.
- Chebel, R. C., L. G. D. Mendonça, and P. S. Baruselli. 2018. Association between body condition score change during the dry period and postpartum health and performance. *J. Dairy Sci.* 101:4595–4614. doi:10.3168/jds.2017-13732.
- Collier, R. J., E. L. Annen, and A. C. Fitzgerald. 2004. Prospects for zero days dry. *Vet. Clin. North Am. - Food Anim. Pract.* 20:687–701. doi:10.1016/j.cvfa.2004.06.009.
- Correa, M. T., H. Erb, and J. Scarlett. 1993. Path analysis for seven postpartum disorders of Holstein cows. *J. Dairy Sci.* 76:1305–1312. doi:10.3168/JDS.S0022-0302(93)77461-5.
- Dann, H. M., N. B. Litherland, J. P. Underwood, M. Bionaz, A. D’Angelo, J. W. McFadden, and J. K. Drackley. 2006. Diets during far-off and close-up dry periods affect periparturient metabolism and lactation in multiparous cows. *J. Dairy Sci.* 89:3563–3577. doi:10.3168/jds.S0022-0302(06)72396-7.
- do Amaral, B. C., E. E. Connor, S. Tao, J. Hayen, J. Bubolz, and G. E. Dahl. 2009. Heat-stress abatement during the dry period: does cooling improve transition into lactation?. *J. Dairy Sci.* 92:5988–5999. doi:10.3168/jds.2009-2343.
- do Amaral, B. C., E. E. Connor, S. Tao, M. J. Hayen, J. W. Bubolz, and G. E. Dahl. 2011. Heat

- stress abatement during the dry period influences metabolic gene expression and improves immune status in the transition period of dairy cows. *J. Dairy Sci.* 94:86–96.
doi:10.3168/jds.2009-3004.
- Drackley, J. K. 1999. Biology of dairy cows during the transition period: the final frontier?. *J. Dairy Sci.* 82:2259–2273. doi:10.3168/jds.s0022-0302(99)75474-3.
- Erskine, R. J., R. D. Walker, C. A. Bolin, P. C. Bartlett, and D. G. White. 2002. Trends in antibacterial susceptibility of mastitis pathogens during a seven-year period. *J. Dairy Sci.* 85:1111–1118. doi:10.3168/jds.S0022-0302(02)74172-6.
- Estergreen, V. L., O. L. Frost, W. R. Gomes, R. E. Erb, and J. F. Bullard. 1967. Effect of ovariectomy on pregnancy maintenance and parturition in dairy cows. *J. Dairy Sci.* 50:1293–1295. doi:10.3168/jds.S0022-0302(67)87615-X.
- Ferreira, R. M., H. Ayres, M. R. Chiaratti, M. L. Ferraz, A. B. Araújo, C. A. Rodrigues, Y. F. Watanabe, A. A. Vireque, D. C. Joaquim, L. C. Smith, F. V. Meirelles, and P. S. Baruselli. 2011. The low fertility of repeat-breeder cows during summer heat stress is related to a low oocyte competence to develop into blastocysts. *J. Dairy Sci.* 94:2383–2392.
doi:10.3168/jds.2010-3904.
- Foster, D., M. Jacob, D. Stowe, and G. Smith. 2019. Exploratory cohort study to determine if dry cow vaccination with a *Salmonella* Newport bacterin can protect dairy calves against oral *Salmonella* challenge. *J. Vet. Intern. Med.* 33:1796–1806. doi:10.1111/jvim.15529.
- Fowden, A. L., J. Li, and A. J. Forhead. 1998. Glucocorticoids and the preparation for life after birth: are there long-term consequences of the life insurance?. *Proc. Nutr. Soc.* 57:113–122.
doi:10.1079/pns19980017.
- Fowden, A. L., and T. Moore. 2012. Maternal-fetal resource allocation: co-operation and

- conflict. *Placenta* 33:e11–e15. doi:10.1016/J.PLACENTA.2012.05.002.
- Goff, J. P., R. Ruiz, and R. L. Horst. 2004. Relative acidifying activity of anionic salts commonly used to prevent milk fever. *J. Dairy Sci.* 87:1245–1255. doi:10.3168/jds.S0022-0302(04)73275-0.
- Gross, T. S., and W. F. Williams. 1988. In vitro-steroid synthesis by the placenta of cows in late gestation and at parturition. *J. Reprod. Fertil.* 83:565–573. doi:10.1530/jrf.0.0830565.
- Grummer, R. R. 1995. Impact of changes in organic nutrient metabolism on feeding the transition dairy cow. *J. Anim. Sci.* 73:2820–2833. doi:10.2527/1995.7392820x.
- Grummer, R. R., D. G. Mashek, and A. Hayirli. 2004. Dry matter intake and energy balance in the transition period. *Vet. Clin. North Am. - Food Anim. Pract.* 20:447–470. doi:10.1016/j.cvfa.2004.06.013.
- Grummer, R. R., and R. R. Rastani. 2004. Why reevaluate dry period length?. *J. Dairy Sci.* 87:E77–E85. doi:10.3168/jds.S0022-0302(04)70063-6.
- Handwerger, S. H. 1991. Clinical counterpoint: The physiology of placental lactogen in human pregnancy. *Endocr. Rev.* 12:329–336. doi:10.1210/edrv-12-4-329.
- Hansen, M., M. S. Lund, J. Pedersen, and L. G. Christensen. 2004. Gestation length in Danish Holsteins has weak genetic associations with stillbirth, calving difficulty, and calf size. *Livest. Prod. Sci.* 91:23–33. doi:10.1016/j.livprodsci.2004.06.007.
- Hoffmann, B., and G. Schuler. 2002. The bovine placenta; a source and target of steroid hormones: Observations during the second half of gestation. *Domest. Anim. Endocrinol.* 23:309–320. doi:10.1016/S0739-7240(02)00166-2.
- Hogan, J. S., K. L. Smith, D. A. Todhunter, and P. S. Schoenberger. 1992. Field trial to determine efficacy of an *Escherichia coli* J5 mastitis vaccine. *J. Dairy Sci.* 75:78–84.

doi:10.3168/jds.S0022-0302(92)77741-8.

Jenkin, G., and I. Young. 2004. Mechanisms responsible for parturition; the use of experimental models. *Anim. Reprod. Sci.* 82–83:567–581. doi:10.1016/J.ANIREPROSCI.2004.05.010

Jenkins, G. M., P. Amer, K. Stachowicz, and S. Meier. 2016. Phenotypic associations between gestation length and production, fertility, survival, and calf traits. *J. Dairy Sci.* 99:418–426. doi:10.3168/jds.2015-9934.

Johanson, J. M., and P. J. Berger. 2003. Birth weight as a predictor of calving ease and perinatal mortality in Holstein cattle. *J. Dairy Sci.* 86:3745–3755. doi:10.3168/JDS.S0022-0302(03)73981-2.

Littledike, E. T. 1976. Relationship of milk secretion to hypocalcemia in the dairy cow. *J. Dairy Sci.* 59:1947–1953. doi:10.3168/jds.S0022-0302(76)84466-9.

Lopera, C., R. Zimpel, A. Vieira-Neto, F. R. Lopes, W. Ortiz, M. Poindexter, B. N. Faria, M. L. Gambarini, E. Block, C. D. Nelson, and J. E. P. Santos. 2018. Effects of level of dietary cation-anion difference and duration of prepartum feeding on performance and metabolism of dairy cows. *J. Dairy Sci.* 101:7907–7929. doi:10.3168/jds.2018-14580.

Luchterhand, K. M., P. R. B. Silva, R. C. Chebel, and M. I. Endres. 2016. Association between prepartum feeding behavior and periparturient health disorders in dairy cows. *Front. Vet. Sci.* 3:1–8. doi:10.3389/fvets.2016.00065.

Markusfeld, O. 1987. Periparturient traits in seven high dairy herds. Incidence rates, association with parity, and interrelationships among traits. *J. Dairy Sci.* 70:158–166. doi:10.3168/JDS.S0022-0302(87)79990-1.

Martinez, N., L. D. P. Sinedino, R. S. Bisinotto, E. S. Ribeiro, G. C. Gomes, F. S. Lima, L. F. Greco, C. A. Risco, K. N. Galvão, D. Taylor-Rodriguez, J. P. Driver, W. W. Thatcher, and

- J. E. P. Santos. 2014. Effect of induced subclinical hypocalcemia on physiological responses and neutrophil function in dairy cows. *J. Dairy Sci.* 97:874–887.
doi:10.3168/jds.2013-7408.
- Matthews, S. G., and J. R. G. Challis. 1996. Regulation of the hypothalamo-pituitary-adrenocortical axis in fetal sheep. *Trends Endocrinol. Metab.* 7:239–246.
doi:10.1016/S1043-2760(96)00126-9.
- McArt, J. A. A., D. V. Nydam, G. R. Oetzel, T. R. Overton, and P. A. Ospina. 2013. Elevated non-esterified fatty acids and β -hydroxybutyrate and their association with transition dairy cow performance. Elsevier Ltd.
- Meyer, C. L., P. J. Berger, K. J. Koehler, J. R. Thompson, and C. G. Sattler. 2001. Phenotypic trends in incidence of stillbirth for Holsteins in the United States. *J. Dairy Sci.* 84:515–523.
doi:10.3168/JDS.S0022-0302(01)74502-X.
- Nogalski, Z., and D. Piwczyński. 2012. Association of length of pregnancy with other reproductive traits in dairy cattle. *Asian-Australasian J. Anim. Sci.* 25:22–27.
doi:10.5713/ajas.2011.11084.
- Norman, H. D., J. R. Wright, M. T. Kuhn, S. M. Hubbard, J. B. Cole, and P. M. VanRaden. 2009. Genetic and environmental factors that affect gestation length in dairy cattle. *J. Dairy Sci.* 92:2259–2269. doi:10.3168/jds.2007-0982.
- Oliver, S. P., S. E. Murinda, and B. M. Jayarao. 2011. Impact of antibiotic use in adult dairy cows on antimicrobial resistance of veterinary and human pathogens: a comprehensive review. *Foodborne Pathog. Dis.* 8:337–355. doi:10.1089/fpd.2010.0730.
- Ospina, P. A., D. V. Nydam, T. Stokol, and T. R. Overton. 2010. Evaluation of nonesterified fatty acids and β -hydroxybutyrate in transition dairy cattle in the northeastern United States:

- Critical thresholds for prediction of clinical diseases. *J. Dairy Sci.* 93:546–554.
doi:10.3168/jds.2009-2277.
- Penninga, L., and L. D. Longo. 1998. Ovine placentome morphology: effect of high altitude, long-term hypoxia. *Placenta* 19:187–193. doi:10.1016/S0143-4004(98)90008-X.
- Philipsson, J., J. Foulley, J. Lederer, T. Liboriussen, and A. Osinga. 1979. Sire evaluation standards and breeding strategies for limiting dystocia and stillbirth. Report of an E.E.C./E.A.A.P. working group. *Livest. Prod. Sci.* 6:111–127. doi:10.1016/0301-6226(79)90013-7.
- Prior, R. L., and D. B. Laster. 1979. Development of the Bovine Fetus. *J. Anim. Sci.* 48(6):1546–1553. doi:10.2527/jas1979.4861546x.
- Ravelich, S. R., A. N. Shelling, A. Ramachandran, S. Reddy, J. A. Keelan, D. N. Wells, A. J. Peterson, R. S. F. Lee, and B. H. Breier. 2004. Altered placental lactogen and leptin expression in placentomes from bovine nuclear transfer pregnancies. *Biol. Reprod.* 71:1862–1869. doi:10.1095/biolreprod.104.032201.
- Sartori, R., R. Sartor-Bergfelt, S. A. Mertens, J. N. Guenther, J. J. Parrish, and M. C. Wiltbank. 2002. Fertilization and early embryonic development in heifers and lactating cows in summer and lactating and dry cows in winter. *J. Dairy Sci.* 85:2803–2812.
doi:10.3168/jds.S0022-0302(02)74367-1.
- Scanavez, A. L. A., B. Fragomeni, L. Rocha, B. E. Voelz, L. E. Hulbert, and L. G. D. Mendonça. 2017. Association between 4-day vaginal temperature assessment during the dry period and performance in the subsequent lactation of dairy cows during the warm season. *J. Anim. Sci.* 95:5208–5217. doi:10.2527/jas2017.1620.
- Scherpenzeel, C. G. M., H. Hogeveen, L. Maas, and T. J. G. M. Lam. 2018. Economic

- optimization of selective dry cow treatment. *J. Dairy Sci.* 101:1530–1539.
doi:10.3168/jds.2017-13076.
- Shea, K. M. 2003. Antibiotic resistance: What is the impact of agricultural uses of antibiotics on children's health?. *Pediatrics* 112:253–258.
- Silva, H. M., C. J. Wilcox, W. W. Thatcher, R. B. Becker, and D. Morse. 1992. Factors affecting days open, gestation length, and calving interval in Florida dairy cattle. *J. Dairy Sci.* 75:288–293. doi:10.3168/jds.S0022-0302(92)77764-9.
- Smith, A., F. H. Dodd, and F. K. Neave. 1968. The effect of intramammary infection during the dry period on the milk production of the affected quarter at the start of the succeeding lactation. *J. Dairy Res.* 35:287–290. doi:10.1017/S0022029900018999.
- Smith, G. W., M. L. Alley, D. M. Foster, F. Smith, and B. W. Wileman. 2014. Passive immunity stimulated by vaccination of dry cows with a *Salmonella* bacterial extract. *J. Vet. Intern. Med.* 28:1602–1605. doi:10.1111/jvim.12396.
- Stevenson, J. S., M. K. Schmidt, and E. P. Call. 1984. Stage of estrous cycle, time of insemination, and seasonal effects on estrus and fertility of Holstein heifers after prostaglandin F_{2α}. *J. Dairy Sci.* 67:1798–1805. doi:10.3168/jds.S0022-0302(84)81507-6.
- Tao, S., J. W. Bubolz, B. C. do Amaral, I. M. Thompson, M. J. Hayen, S. E. Johnson, and G. E. Dahl. 2011. Effect of heat stress during the dry period on mammary gland development. *J. Dairy Sci.* 94:5976–5986. doi:10.3168/jds.2011-4329.
- Tao, S., and G. E. Dahl. 2013. Invited review: heat stress effects during late gestation on dry cows and their calves. *J. Dairy Sci.* 96:4079–4093. doi:10.3168/jds.2012-6278.
- Tao, S., R. M. Orellana, X. Weng, T. N. Marins, G. E. Dahl, and J. K. Bernard. 2018. Symposium review: the influences of heat stress on bovine mammary gland function 1. *J.*

- Dairy Sci. 101:5642–5654. doi:10.3168/jds.2017-13727.
- Thompson, I. M., and G. E. Dahl. 2012. Dry-period seasonal effects on the subsequent lactation. Prof. Anim. Sci. 28:628–631. doi:10.15232/S1080-7446(15)30421-6.
- Tomasek, R., P. Rezac, and Z. Havlicek. 2017. Environmental and animal factors associated with gestation length in Holstein cows and heifers in two herds in the Czech Republic. Theriogenology 87:100–107. doi:10.1016/j.theriogenology.2016.08.009.
- Van Saun, R.J. 1991. Dry cow nutrition. The key to improving fresh cow performance. Vet. Clin. North Am. Food Anim. Pract. 7:599–620. doi:10.1016/S0749-0720(15)30785-4.
- Vieira-Neto, A., K. N. Galvão, W. W. Thatcher, and J. E. P. Santos. 2017. Association among gestation length and health, production, and reproduction in Holstein cows and implications for their offspring. J. Dairy Sci. 100:3166–3181. doi:10.3168/jds.2016-11867.
- Watters, R. D., J. N. Guenther, A. E. Brickner, R. R. Rastani, P. M. Crump, P. W. Clark, and R. R. Grummer. 2008. Effects of dry period length on milk production and health of dairy cattle. J. Dairy Sci. 91:2595–2603. doi:10.3168/jds.2007-0615.
- Wiersma, F., 1990. THI for Dairy Cows. Department of Agricultural Engineer, The University of Arizona, Tucson, AZ.
- Wileman, B. W., D. U. Thomson, K. C. Olson, J. R. Jaeger, L. A. Pacheco, J. Bolte, D. T. Burkhardt, D. A. Emery, and D. Straub. 2011. Escherichia coli O157:H7 shedding in vaccinated beef calves born to cows vaccinated prepartum with Escherichia coli O157:H7 SRP vaccine. J. Food Prot. 74:1599–1604. doi:10.4315/0362-028X.JFP-11-034.
- Williams, W. F., M. J. Margolis, J. Manspeaker, L. W. Douglass, and J. P. Davidson. 1987. Peripartum changes in the bovine placenta related to fetal membrane retention. Theriogenology 28:213–223. doi:10.1016/0093-691X(87)90268-8.

- Wolf, C. A., G. T. Tonsor, M. G. S. McKendree, D. U. Thomson, and J. C. Swanson. 2016. Public and farmer perceptions of dairy cattle welfare in the United States. *J. Dairy Sci.* 99:5892–5903. doi:10.3168/jds.2015-10619.
- Wooding, F. B. P. 1992. The synepitheliochorial placenta of ruminants: Binucleate cell fusions and hormone production. *Placenta* 13:101–113. doi:10.1016/0143-4004(92)90025-O.
- Zimbelman, R. B., R. P. Rhoads, R. J. Collier, and G. C. Duff. 2009. A re-evaluation of the impact of temperature humidity index (THI) and black globe humidity index (BGHI) on milk production in high producing dairy cows. Pages 158–168 in *Proc. Southwest Nutr. Man. Conf.*, Tempe, AZ. Univ. Arizona, Tucson.

Chapter 2 - Strategy to Identify Dry Cows More Susceptible to Heat Stress, Reduce Antimicrobial Treatments, and Improve Performance After Calving.

C.A. Gamarra, A. L. A. Scanavez, J.G.N. Moraes, J.A. Green, H. Taguchi, R.S.S. Oliveira and
L.G. D. Mendonça.

INTRODUCTION

Antibiotic use in food animal production has elicited societal concerns because of potential public health issues (Landers et al., 2012). Because antimicrobials are fundamental for treating diseases and minimizing economic losses of dairy operations (Stevens et al., 2016; Lhermie et al., 2018), banning use of antibiotics in dairy herds is unreasonable. Nonetheless, development of strategies to reduce use of antibiotics may be an alternative to address consumer concerns. One possible strategy is to identify subpopulation of cows more susceptible to be treated with antimicrobials and implement practices to improve their health.

Summer months often present a challenging environment to dairy cows because of heat stress. In a recent study conducted with heat-stressed cows, incidence of health disorders during the first 60 days in milk (DIM) was greater for cows with high vaginal temperature (VT) before calving compared with cows with low VT (Scanavez et al., 2017). In addition, VT was associated with twinning and shorter gestation lengths (SGL; Scanavez et al., 2018), which are risk factors for postpartum diseases and antimicrobial treatments (Chebel et al., 2018). Considering that exposure to heat stress during late gestation compromises postpartum health, implementation of strategies to minimize antibiotic treatments in a subpopulation of cows during the summer may reduce overall use of antimicrobials in dairy farms.

We hypothesized that: (1) heat-stressed dairy cows with high VT in the prepartum pen have greater incidence of antimicrobial treatments than low VT cows; and (2) number of days spent in the prepartum pen would be associated with postpartum treatments and health status of high VT cows during summer. The objectives of the study were to: (1) identify a subpopulation of heat-stressed cows more susceptible to develop postpartum disorders; and (2) evaluate a management strategy to reduce antibiotic treatment and improve postpartum health of dairy cows.

MATERIALS AND METHODS

Animals and Facilities

This experiment was conducted in three commercial dairy herds. Two herds were located in Kansas (Dairy A and Dairy C) and one in Oklahoma (Dairy B). Dry cows from the three herds were housed in dry-lot corrals with shaded areas. Lactating cows from dairy A and B were milked twice daily and housed in dry-lot corrals with shade. Lactating cows from Dairy C were milked thrice daily and housed in free-stall barns equipped with fans and sprinklers, with access to a dirt exercise lot adjacent to the free-stall barn. Lactating and dry cows were fed a total mixed ration to meet or exceed NRC (2001) twice or once daily, respectively. In the prepartum pens, cows were fed with acidogenic salts.

Vaginal Temperature Assessment, Treatments, and Temperature-Humidity Index

Vaginal temperature of 607 primiparous and 996 multiparous dry Holstein cows (Dairy A = 516; Dairy B = 590; Dairy C = 497) at 243 ± 7 d of gestation was assessed once using a calibrated accurate digital thermometer (Fisherbrand™ Traceable™ Platinum Ultra-Accurate Digital Thermometer) by study personnel in order to classify cows into high (HT) and low (LT) temperature. Vaginal temperature was assessed once weekly for 10 weeks in each dairy at the

far-off pen between 1900 and 2100 h. Each day, immediately after VT assessment, 20% of the cows with the greatest VT evaluated each day were blocked by projected 305-d mature equivalent milk yield and DIM at dry-off. The experiment was a completely randomized design in which HT cows were assigned as control (HT-CON) or treatment (HT-TRT) using a coin toss (head and tail representing HT-CON and HT-TRT, respectively). Cows designated as HT-TRT were moved earlier to the close-up pen 7 d before the date stipulated by the dairy's standard operating procedure (SOP), whereas the HT-CON cows were moved per each dairy's SOP. Control cows, the remaining 80% of cows classified as LT, were assigned to be moved to the close-up pen, once a week, according to the dairy's SOP. The SOP for moving cows to the close-up pen were the following days of gestation: >249, >245, and >250, dairy A, B, and C, respectively.

From VT assessment to calving, ambient temperature and humidity were recorded every 5 min from the far-off pens by temperature loggers (HOBO U23 Pro v2; Onset Computer Corp., Pocasset, MA). Loggers were placed approximately 3 m above ground level under the shade structure in the far-off pen. To calculate temperature-humidity index (THI), the following equation was used: $THI = T - (0.55 - 0.55 RH/100) \times (T - 58)$, where T and RH are dry bulb temperature (°F) and relative humidity, respectively (NOAA, 1976).

Antimicrobial Treatments, Disease Definitions, and Culling

Calving-related events, such as calving date, calf gender, stillbirth, and number of calves, were extracted from the on-farm management software (DairyComp; Valley Agricultural Software, Tulare, CA). In addition, health outcomes associated with antibiotic treatments, and sold and death events recorded during the first 60 DIM also were collected from the dairy software. Diagnoses of health problems and treatments with antibiotic were performed by trained

farm personnel under the supervision of a veterinarian. Health events associated with treatments occurring during the first 60 DIM were uterine diseases (UTD; retained fetal membranes or metritis), mastitis, and digestive, respiratory and locomotor problems. Retained fetal membranes (RFM) was defined as failure to expel fetal membranes by 24 h postpartum. Metritis was characterized by the presence of fetid and red or brown uterine discharge during the first 21 DIM. Mastitis was characterized as the presence of abnormal milk (i.e., clots or distinct coloration), inflammation of the mammary gland, or both. Digestive problems consisted of alterations in consistency and color of feces. Respiratory problems were defined as increased respiratory frequency and presence of fever (rectal temperature $> 39.5^{\circ}\text{C}$). Lastly, clinically lame cows were considered to have a locomotor disorder. Date of sold and death events were used to calculate DIM at culling from the herd.

Body Condition Score and Milk Yield

Body condition score (BCS) was assessed on a scale 1 (severe underconditioned) to 5 (obese) with quarter-points increments (Ferguson et al., 1994) at enrollment and after calving (4 ± 3 DIM). Individual daily milk yield was recorded using a parlor management software (DairyPlan C21; GEA Farm Technologies, Naperville, IL) and weekly milk calculated by the on-farm computer software (DairyComp) was extracted.

Blood Sampling

In a subgroup of cows ($n = 201$), a blood sample was collected from a coccygeal vessel into evacuated tubes containing K2 EDTA (Becton Dickinson Vacutainer Systems, Franklin Lakes, NJ) for later evaluation of pregnancy-associated glycoproteins (PAG). Blood sample tubes were placed on ice until centrifugation for plasma separation ($1,200 \times g$ for 15 min at 4°C). Plasma samples were frozen and stored at -20°C until analysis.

Statistical Analyses

The difference between calving and previous conception dates was used to calculate gestation duration, and dry date and close-up pen move date were used to days dry, and days in the close-up pen, respectively. Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). Dichotomous variables were analyzed by logistic regression and continuous variables were analyzed by ANOVA using the GLIMMIX procedure. The MIXED procedure was used to analyze the milk yield data as repeated measures. Models used in the statistical analyses included VT treatments (HT-CON vs. HT-TRT vs. LT), parity (primiparous vs. multiparous), and the interaction between VT treatments and parity. In the repeated-measure analyses, the following independent nuisance variables also were included in the model: week of lactation and the interactions between week of lactation and VT treatments, week of lactation and parity, and week of lactation, VT treatments and parity. Interactions were removed from the model in instances that *P* value was > 0.10 . Orthogonal contrasts (C) were used to evaluate the associations between outcomes of interest and classifying cows into VT treatments, moving HT cows earlier to the close-up pen, or both (C1: HT-CON + HT-TRT vs. LT; C2 = HT-CON vs. HT-TRT; C3 = HT-TRT vs. LT; C4 = HT-CON vs. LT).

Because distribution of PAG residuals were not normally distributed, PAG values were log-transformed before statistical analysis. In addition, because blood samples were collected at enrollment (before applying the management strategy to HT-TRT cows), the fixed effect of VT treatment in the model consisted of 2 factors (HT vs. LT) rather than 3 (HT-CON vs. HT-TRT vs. LT). In addition, pregnancy type (singleton vs. twins) was included in the model that evaluated the association between PAG concentration and variables of interest. Dairy was

included as a random effect in all the models. Statistical significance was defined as $P \leq 0.05$ and statistical tendencies as $0.05 < P \leq 0.10$.

RESULTS

Eight cows were removed from the study and were not included in the statistical analyses. Of these cows, one was not moved to the close-up pen according to the dairy's SOP because of a health disorder and seven cows were diagnosed not pregnant after 300 days of gestation.

Temperature-Humidity Index

Average daily THI during the period cows were in the close-up pen was 73.6, 72.0, and 73.7 for dairies A, B, and C, respectively. Furthermore, average daily maximum and minimum THI were 85.1 and 64.3 (dairy A), 81.5 and 62.4 (dairy B), and 83.7 and 64.8 (dairy C). Average daily temperature and relative humidity for dairies A, B, and C were 26.5 °C and 61.6%, 25.9 °C and 53.3%, and 26.3 °C and 61.9%, respectively.

Vaginal Temperature and Prepartum Descriptive Data

Proportion of primiparous cows enrolled in the study did not ($P = 0.87$) differ between HT-TRT and HT-CON. In contrast, fewer ($P < 0.01$) primiparous cows were in the LT compared with HT (35.1 vs. 49.5%) treatments. Cows classified as HT had greater VT ($P < 0.01$), incidence of twinning ($P < 0.01$), and proportion s of male calves ($P = 0.02$) than LT cows (Table 1).

Previous projected 305-d mature equivalent milk yield, DIM at dry-off, and BCS change from enrollment to parturition did not differ among treatments. Cows classified as HT had reduced ($P < 0.01$) gestation and dry period length than LT cows. Cows classified as HT-CON spent fewer ($P < 0.01$) days in the close-up pen than HT-TRT and LT cows. As a consequence of

the management strategy evaluated in this study, days spent in the close-up pen also differed ($P < 0.01$) between HT-TRT and LT cows (Table 1).

Stillbirth and Antimicrobial Treatments

High temperature cows had greater ($P < 0.01$) incidence of stillbirth compared with LT cows (Table 2). Parity and the interaction between VT treatment and parity were not associated ($P \geq 0.21$) with incidence of stillbirth. Cows classified as HT were more likely ($P = 0.03$) to be treated with antimicrobials for RFM compared with LT cows. Nonetheless, no difference ($P = 0.16$) was detected in proportion of cows treated with antimicrobials between HT-TRT and LT. Proportion of cows treated for metritis did not differ ($P = 0.18$) between HT and LT cows; however, a tendency ($P = 0.08$) was detected for more HT-CON cows to be treated compared with LT cows. Low temperature cows tended ($P = 0.06$) to have fewer treatments for uterine disease than HT cows during the first 21 DIM (RFM or metritis), but no differences were detected between HT-TRT and LT cows (Table 2). Proportion of cows treated for mastitis during the first 60 DIM was not associated ($P \geq 0.56$) with VT treatment. Considering all antimicrobial treatments during the first 60 DIM, HT cows tended ($P = 0.08$) to be more likely to be treated than LT cows. The interaction between VT treatment and parity was not associated with stillbirth or any antimicrobial treatments.

Culling Risk

Proportion of cows that died during the first 60 DIM differed ($P = 0.01$) between LT and HT-CON cows (Table 2), but no difference ($P = 0.11$) was detected between HT-TRT and HT-CON cows. The interaction between VT treatment and parity was not ($P = 0.74$) associated with the proportion of dead cows. Proportion of cows sold during the first 60 DIM was not ($P \geq 0.39$) associated with VT treatment, but was associated ($P = 0.04$) with interaction of VT treatment and

parity. Considering both proportion of dead and sold cows during the first 60 DIM, HT-CON had increased ($P = 0.02$) culling risk than LT cows (Table 2). Nonetheless, no difference ($P = 0.13$) was detected between HT-CON and HT-TRT cows. The interaction between VT treatment and parity tended ($P = 0.07$) to be associated with culling during the first 60 DIM.

Milk Yield

Cows classified as HT had decreased ($P < 0.01$) milk yield compared with LT cows. Nonetheless, milk yield did not differ ($P < 0.01$) between HT-TRT and LT cows. The interaction between week of lactation, parity, and VT treatment was not associated ($P = 0.56$) with milk yield during the first 90 DIM. The interaction between week of lactation and parity affected ($P = 0.05$) milk yield. In addition, the interaction between week of lactation and VT treatment tended ($P = 0.07$) to affect milk yield (Figure 1A and 1B).

First-Service Reproductive Performance

Proportion of cows submitted to first service differed between HT and LT cows ($P = 0.04$) and HT-CON and LT cows ($P < 0.01$; Table 2). Nonetheless, no differences were observed between HT-TRT and LT cows ($P = 0.51$) and HT-TRT and HT-CON cows ($P = 0.18$). Similar findings were observed for the proportion of cows pregnant to first service (Table 2).

Plasma Pregnancy-Associated Glycoprotein (PAG) Concentration

Plasma concentration of PAG was cows greater ($P = 0.02$) for HT compared with LT cows (Figure 2). Primiparous cows had greater ($P = 0.01$) PAG concentration than multiparous cows (4.13 ± 0.16 vs. 3.72 ± 0.12 ng/mL). In addition, cows bearing twins had greater ($P < 0.01$) PAG concentration than cows carrying singletons (4.31 ± 0.22 vs. 3.54 ± 0.08 ng/mL). The interaction between VT treatment and parity did not ($P = 0.73$) affect plasma concentration of PAG.

DISCUSSION

Approximately 75% of health disorders that affect dairy cows occur during the first few weeks after parturition (LeBlanc et al., 2006). Several of these disorders require treatments that include use of antimicrobials. Besides affecting well-being and culling of dairy cows, occurrence of health disorders early in lactation negatively impacts milk yield (Duffield et al., 2009; Dubuc et al., 2011; Moussavi et al., 2012). Identification of dairy cows more prone to have postpartum health disorders before calving allows implementation of targeted interventions tailored to prevent postpartum problems, which may potentially reduce antimicrobial usage and improve milk yield of dairy cows after parturition. Recent observational studies demonstrated that VT approximately 3 wk before calving is associated with postpartum health and productive performance during the subsequent lactation of heat-stressed dairy cows (Scanavez et al., 2017; 2019). In these studies, VT was assessed in dry cows from herds that provided (Scanavez et al., 2019) or did not provide (Scanavez et al., 2017) evaporative cooling to alleviate heat stress during the dry period. In both studies, elevated VT assessed at 250 to 260 days of gestation was associated with a greater occurrence of health disorders during the first 60 DIM of the subsequent lactation (Scanavez et al., 2017; 2019). In addition, Scanavez et al. (2017; 2019) indicated that cows classified as having high VT during the dry period had reduced milk yield after calving compared with cows classified as having low VT.

Consistency in the findings observed in these studies indicate that VT may be used to identify dry cows that are more likely to present health disorders and have reduced milk yield after parturition during periods of heat stress. Nonetheless, the method used to evaluate VT by Scanavez et al. (2017; 2018; 2019) may not be practical for implementation in commercial dairy herds because it requires specialized temperature loggers and is highly time consuming. In

pursuance of a more practical approach to identify HT and LT cows at the farm level, the authors of the current experiment used an ultra-accurate thermometer to assess a single measurement of VT of dry cows. Furthermore, the authors investigated whether moving cows earlier to the close-up pen would improve postpartum health, milk yield, and reproductive performance of cows that presented greater VT during the dry period. Ultimately, the main goal of the current experiment was to test a management practice targeted to cows presenting HT during the dry period in order to reduce the proportion of cows treated with antimicrobials after calving.

Authors of the present study hypothesized that HT cows would be more likely to have postpartum health disorders and be treated with antimicrobials than their LT counterparts. Recent studies demonstrated that short GL is a risk factor for postpartum health disorders and consequent treatment with antimicrobials in dairy cows (Vieira-Neto et al., 2017; Chebel et al., 2018). In the current study, GL was shorter for HT compared with LT cows, which agrees with findings reported by others (Scanavez et al., 2017; 2018; 2019). In addition, twinning is a significant risk factor for several postpartum health disorders such as RFM and metritis in dairy cattle (Vieira-Neto et al., 2017; Chebel et al., 2018). Twinning incidence in the present study was approximately 3-fold greater for HT cows compared with LT cows, which corroborates results reported by Scanavez et al. (2019), in which incidence of twinning was 19.7 and 4.2% for cows classified as having high or low VT during the dry period, respectively. Because GL is shorter in cows bearing twins compared with cows carrying singletons (Echternkamp and Gregory, 1999; Vieira-Neto et al., 2017), it is likely that greater twinning incidence in HT cows partially explains the reduced GL observed in this cohort compared with LT cows. Furthermore, both shorter GL and twinning are associated with increased risk of stillbirth (Olson et al., 2009; Chebel et al., 2018). Findings reported in the current study confirm the association between

shorter GL and twinning with occurrence of stillbirth, given that HT cows were more likely to have stillbirth than LT cows. Nonetheless, stillbirth incidence was smaller in the current study than previously reported (Meyer et al., 2001). Overall, multiple characteristics differed between cows classified as having HT or LT during the dry period (e.g., GL, and twinning, and stillbirth incidence), which likely increased the risk of HT cows to have more postpartum health disorders, therefore, requiring more antimicrobial treatments compared with the LT counterparts. Further research must be conducted to determine whether HT and LT cows have different genetic characteristics.

Incidence of antimicrobial treatments for UTD in the present study tended to be greater for cows classified as HT during the dry period compared with LT cows. This finding partly supports our initial hypothesis that dry cows with HT would be more likely to be treated with antimicrobials than LT cows. In line with our findings, Scanavez et al. (2017) reported that cows classified during the dry period as having high VT were more likely to be treated for uterine disorders (e.g., RFM and metritis) during the first 3 wk of lactation than cows that had low VT. As previously described, HT cows had shorter GL and increased incidence of twinning than LT cows, which are important risk factors for RFM and metritis (Echterkamp and Gregory, 1999; Vieira-Neto et al., 2017; Chebel et al., 2018). Prepartum feeding time and DMI are reduced in cows that develop RFM and metritis after parturition compared with cows that do not develop uterine diseases (Huzzey et al., 2007; Luchterhand et al., 2016). In studies that compared the effects of cooling dry cows during the summer on postpartum productive performance, it has been suggested that prepartum DMI is reduced in heat-stressed dry cows (Adin et al., 2009; Tao et al., 2011; Karimi et al., 2015). Considering that HT cows were more severely affected by heat stress than their LT counterparts, as indicated by greater VT, we speculate that DMI may have

been lesser for HT than LT cows in the current experiment. Because the current study was conducted in large commercial dairy herds, individual DMI could not be evaluated. In contrast to UTD, proportion of cows treated for mastitis during the first 60 DIM was not associated with VT group. This finding is in agreement with results reported by Scanavez et al. (2017; 2019), in which no associations were detected between occurrence of mastitis after parturition and dry-period VT as a categorical or continuous predictor.

Findings from a previous experiment indicated that providing cooling to dry cows during summer improves immune function during early lactation (Thompson et al., 2014), which may lead to greater ability of cows to cope with intra-mammary infections, such as mastitis. In the study conducted by Thompson et al. (2014), however, all intra-mammary infections were induced artificially, which prevents evaluation of mastitis incidence and direct comparisons with results described herein. Nonetheless, increased incidence of antimicrobial treatments in HT compared with LT cows indicates the method adopted to classify cows based on VT during the dry period was useful to identify cows more prone to have health disorders after parturition. In an observational study conducted in two large commercial dairy herds, Chebel et al. (2018) suggested that BCS loss during the dry period greatly increases the likelihood of dairy cows to be treated with antimicrobials after parturition. In the current study, BCS change did not differ among VT treatments. Thus, the underlying mechanisms accounting for differences in incidence of treatments with antimicrobials between HT and LT cows seem to be independent of BCS changes during the dry period.

Because prepartum-identified HT cows are more susceptible to postpartum health disorders, an intervention was tested as an attempt to optimize health, and productive and reproductive performance after parturition. Based on results reported by Scanavez et al. (2017;

2018; 2019) the authors expected GL to be shorter for HT cows, which would ultimately reduce the number of days spent in the close-up pen for this cohort of cows compared with their LT counterparts. Prepartum diets with anionic salts reduce incidence of postpartum hypocalcemia (Ender et al., 1971; Block, 1984) which, in turn, is a risk factor for several postpartum health disorders (Chapinal et al., 2011; Martinez et al., 2012). Despite the lack of controlled experiments to determine the ideal duration of exposure of cows to transition diets in the close-up pen, observational studies suggest that productive and reproductive performance are impaired in cows that spend less than 2 or 3 wk receiving a prepartum transition diet containing anionic salts (DeGaris et al., 2008; 2010). As demonstrated by Scanavez et al. (2017; 2019) and confirmed in the current study, cows with increased VT during the dry period have shorter GL and spend fewer days in the close-up pen than cows with low VT. Thus, the authors hypothesized that increasing the number of days spent in the prepartum pen would optimize health and reduce antimicrobial treatments in HT-TRT compared with HT-CON cows. Our results partly confirm our initial hypothesis because proportion of cows treated with antimicrobial did not differ between HT-TRT and LT cows, but were greater for HT-CON than for LT cows. This finding suggests that antimicrobial treatment for uterine diseases was reduced for HT-TRT. The authors contend, however, that incidence of uterine disorders in cows with high VT was considerably reduced in the current than in previous studies (Scanavez et al., 2017; 2019). Therefore, it is possible that lack of statistical power to detect a lesser incidence of UTD in the present study may have prevented detection of a statistical difference between HT-CON and HT-TRT cows. Nevertheless, it seems that moving cows earlier to the close-up pen did not reduce the overall use of antimicrobial treatments during the first 60 DIM.

Milk yield during the first 13 wk of lactation was greater for LT compared with HT cows. This finding further indicates that the method used to assess VT in the present study was useful to identify dry cows expected to have reduced milk production after parturition. Moreover, this finding agrees with previous results (Scanavez et al., 2017; 2019), who reported that cows with increased VT during the dry period have reduced milk yield early in lactation compared with cows that presented lower VT before calving. It has been suggested that mammary cell proliferation is negatively impacted in dry cows exposed to heat stress, which ultimately results in reduced milk yield after parturition (Adin et al., 2009; Tao et al., 2011). The authors speculate that mammary cell proliferation may have been impacted negatively in HT cows, impairing milk yield after parturition compared with LT cows. Increased number of days spent in the prepartum pen increased postpartum milk yield in HT-TRT compared with HT-CON in multiparous cows. Several authors reported that supplementation with acidogenic salts during the last few weeks before parturition increases postpartum milk yield (DeGroot et al., 2010; Lean et al., 2019). It has been suggested that exposure to anionic diets for approximately 25 d increases milk yield in the subsequent lactation (DeGaris et al., 2008). In the current study, HT-TRT cows spent approximately 25 d in the close-up pen. The authors contend, however, that the design of this study does not allow one to determine whether longer exposure to the prepartum diet was the main factor for increased milk yield of HT-TRT compared with HT-CON cows. We speculate that other factors associated with the far-off and close-up pens, such as stocking density, played a role in increasing milk yield after parturition. Nutrient partitioning towards growth in primiparous cows may explain the lack of effect of extending duration in the prepartum pen on milk production of HT-TRT cows.

Reduced milk yield is one of the main reasons for culling in dairy herds (Pinedo et al., 2010). Even though culling during the first 60 DIM did not differ between LT and HT cows, culling risk was greater for HT-CON compared with LT cows. Increased culling risk of HT-CON cows occurred mostly because of greater mortality by 60 DIM compared with cows classified as LT. Several studies suggested that death loss is the number one reason for removal during the first 60 to 100 DIM (Dechow and Goodling, 2008; Pinedo et al., 2010). In addition, mortality of lactating dairy cows is increased during warm months of the year (Pinedo et al., 2010), suggesting a relationship between early lactation mortality and heat stress. Heat stress negatively affects the immune status of dairy cows during the periparturient period (do Amaral et al., 2011), which may increase susceptibility of cows to develop postpartum health disorders. Cows that deliver twins are more likely to be culled during the first 90 DIM than cows carrying singletons (Andreu-Vazquez et al., 2012). Therefore, it is possible that greater incidence of twinning may be one of the factors influencing the increase in culling risk for HT-CON compared with LT cows. Moreover, because reduced exposure to transition diets increases culling risk in dairy cows (DeGaris et al., 2010), we speculate that greater culling was observed in HT-CON because they spent fewer days in the close-up pen than HT-TRT and LT cows.

Besides affecting culling dynamics, twinning is associated with impaired reproductive performance in dairy cows (Andreu-Vasquez et al., 2012; Vieira-Neto et al., 2017). Because of the extensive evidence of carry-over effects of heat stress on reproductive traits (Roth et al., 2001; Al-Katanani et al., 2002; Torres-Júnior et al., 2008), one of the objectives in the current study was to investigate whether VT before calving was associated with reproductive performance in the subsequent lactation. Despite the vast literature focused on the effects of heat stress during the lactating period on reproductive performance (Flamenbaum and Galon, 2010;

Schüller et al., 2014; Ortiz et al., 2015), very limited data are available regarding the association between exposure to heat stress during the dry period and subsequent reproductive performance after parturition. In the present study, a smaller proportion of HT cows were inseminated after parturition than their LT counterparts, likely because of greater culling risk by 60 DIM in the HT-CON cohort. Furthermore, pregnancy at first service was greater for LT compared with HT cows. These results differ from those reported by Scanavez et al. (2017; 2019) that indicated that pregnancy at first service was similar between cows classified during the dry period as having high or low VT. Those studies (Scanavez et al., 2017; 2019), however, used a considerably smaller number of experimental units than the current experiment. Furthermore, authors of the current study decided to classify cows as HT only the ones with the 20% highest VT, whereas Scanavez et al. (2017; 2019) considered cows with the 50% highest VT. The classification method used herein may have selected the most heat-susceptible cows, which ultimately resulted in differences in pregnancy at first service between HT and LT cows. In a prospective cohort study, DeGaris et al. (2010) reported increased pregnancy risk when cows were exposed longer to prepartum transition diets was increased. Because no difference in proportion of pregnant cows at first service was detected between LT and HT-TRT cows, it is unlikely that increasing days in the prepartum pen improved reproductive efficiency after calving.

Similar to Scanavez et al. (2019), the present study demonstrated increased plasma concentration of PAG in HT compared with LT cows in late gestation. Limited data exist in the literature regarding PAG profile during late gestation, which prevents direct comparisons with findings from the current study. In lactating dairy cows, milk yield, number of lactations, and heat stress have a negative association with PAG concentrations (Thompson et al., 2013; Ricci et al., 2015). Furthermore, PAG concentration in blood can indicate fetal viability (Giordano et al.,

2012; Pohler et al., 2013), and have a positive association with number of fetuses and calf birth weight (Patel et al., 1995; Giordano et al., 2012). Cows bearing twins present greater PAG concentration than cows pregnant with singletons (Serrano et al., 2009), likely because of the presence of two placentas (Patel et al., 1997). Thus, it is possible that the increased PAG concentration in plasma of HT cows may be partially explained by the greater twinning incidence observed compared with LT cows. Notwithstanding, HT cows bearing singletons also had increased PAG concentration compared with LT cows, suggesting that factors other than twinning also are involved in the association between VT category and PAG concentration. Patel et al. (1997) demonstrated that PAG concentration profile during late gestation can be used as indicator of fetal-placental viability. In sheep, Penninga and Longo (1998) described compromised placental development in presence of stressors such as hypoxia and dietary restriction. Furthermore, these events can lead to an increased concentration of circulating corticoids, also observed in cows with increased rectal temperature resulting from thermal stress (Jain, 1976; Wegner et al., 1973). Ward et al. (2002) demonstrated that increased circulating cortisol in ewes decreased the number of binuclear cells (BNC) in the placenta, likely because of increased rate of BNC placental migration. The migratory event of BNC on fetal-maternal syncytium precedes the exocytosis of the cellular granules containing glycoproteins (Wooding, 1992) and its release into maternal circulation. The authors of that study speculated that stressors such as hyperthermia during late gestation can play an important role on placental function and its secretory activity, ultimately affecting PAG concentrations in plasma. More research is warranted to evaluate mechanisms of PAG secretory patterns during late gestation and its association with late gestation stressors. Nevertheless, because HT cows had greater PAG concentration, greater risk of being treated with antimicrobials early in lactation, and produced

less milk than LT cows, we speculate that late gestation PAG concentration may be used as indicator of increased susceptibility of postpartum health disorders and treatment with antimicrobials, and subpar productive performance in the subsequent lactation.

In conclusion, a single VT assessment during the dry period was useful to identify cows more likely to be treated with antimicrobials, have reduced milk yield, and decreased reproductive performance after parturition. Although the proposed strategy of increasing days in the close-up pen reduced antimicrobial treatments for uterine diseases in HT cows, proportion of cows treated for any antimicrobial treatment during the first 60 DIM was not reduced. Nonetheless, the management strategy evaluated in this study increased milk yield of multiparous HT cows. The authors contend that this study was not designed to evaluate specific prepartum diets. Instead, our focus was to evaluate the use of a management practice (e.g., extending days in the close-up pen) and its responses on postpartum outcomes. Therefore, based on our findings, the authors cannot precisely identify the factors that improved performance of cows after calving, limiting our conclusions to moving HT cows earlier to the close-up pen benefited dairy cows. Nonetheless, findings reported herein have the potential to greatly improve productive performance of dairy cows exposed to heat stress during the dry period in commercial dairy operations and limit the use of antimicrobial treatment for uterine diseases.

BIBLIOGRAPHY

- Adin, G., A. Gelman, R. Solomon, I. Flamenbaum, M. Nikbachat, E. Yosef, A. Zenou, A. Shamay, Y. Feuermann, S. J. Mabjeesh, and J. Miron. 2009. Effects of cooling dry cows under heat load conditions on mammary gland enzymatic activity, intake of food, water, and performance during the dry period and after parturition. *Livestock. Sci.* 124:189-195. doi:10.1016/j.livsci.2009.01.014.
- Al-Katanani, Y. M., F. F. Paula-Lopes, and P. J. Hansen. 2002. Effect of season and exposure to heat stress on oocyte competence in Holstein cows. *J. Dairy Sci.* 85:390–396.
- Andreu-Vázquez, C., I. Garcia-Ispuerto, S. Ganau, P. M. Fricke, and F. López-Gatius. 2012. Effects of twinning on the subsequent reproductive performance and productive lifespan of high-producing dairy cows. *Theriogenology* 78:2061–2070. doi:10.1016/j.theriogenology.2012.07.027.
- Block, E. 1984. Manipulating dietary anions and cations for prepartum dairy cows to reduce incidence of milk fever. *J. Dairy Sci.* doi:10.3168/jds.S0022-0302(84)81657-4.
- Chapinal, N., M. Carson, T. F. Duffield, M. Capel, S. Godden, M. Overton, J. E. P. Santos, and S. J. LeBlanc. 2011. The association of serum metabolites with clinical disease during the transition period. *J. Dairy Sci.* 94:4897–4903. <https://doi.org/10.3168/jds.2010-4075>.
- Chebel, R. C., L. G. D. Mendonça, and P. S. Baruselli. 2018. Association between body condition score change during the dry period and postpartum health and performance. *J. Dairy Sci.* 101:4595–4614. doi:10.3168/jds.2017-13732.
- Dechow, C. D., and R. C. Goodling. 2008. Mortality, culling by sixty days in milk, and production profiles in high- and low-survival Pennsylvania herds. *J. Dairy Sci.* 91:4630–4639.

- DeGaris, P. J., I. J. Lean, A. R. Rabiee, and C. Heuer. 2008. Effects of increasing days of exposure to prepartum transition diets on milk production and milk composition in dairy cows. *Aust. Vet. J.* 86:341–351. doi:10.1111/j.1751-0813.2008.00335.x.
- DeGaris, P. J., I. J. Lean, A. R. Rabiee, and M. A. Stevenson. 2010. Effects of increasing days of exposure to prepartum diets on the concentration of certain blood metabolites in dairy cows. *Aust. Vet. J.* 88:137–145. doi:10.1111/j.1751-0813.2009.00530.x.
- DeGroot, M. A., E. Block, and P. D. French. 2010. Effect of prepartum anionic supplementation on periparturient feed intake, health, and milk production. *J. Dairy Sci.* 93:5268–5279. doi:10.3168/jds.2010-3092.
- do Amaral, B. C., E. E. Connor, S. Tao, M. J. Hayen, J. W. Bubolz, and G. E. Dahl. 2011. Heat stress abatement during the dry period influences metabolic gene expression and improves immune status in the transition period of dairy cows. *J. Dairy Sci.* 94:86–96. doi:10.3168/jds.2009-3004.
- Dubuc, J., T. F. Duffield, K. E. Leslie, J. S. Walton, and S. J. LeBlanc. 2011. Effects of postpartum uterine diseases on milk production and culling in dairy cows. *J. Dairy Sci.* 94:1339–1346. doi:10.3168/jds.2010-3758.
- Duffield, T. F., K. D. Lissemore, B. W. McBride, and K. E. Leslie. 2009. Impact of hyperketonemia in early lactation dairy cows on health and production. *J. Dairy Sci.* 92:571–580. doi:10.3168/jds.2008-1507.
- Echternkamp, S. E., and K. E. Gregory. 1999. Effects of twinning on gestation length, retained placenta, and dystocia. *J. Anim. Sci.* 77:39–47. doi:10.2527/1999.77139x.
- Ender, F., I. W. Dishington, and A. Helgebostad. 1971. Calcium balance studies in dairy cows under experimental induction and prevention of hypocalcaemic paresis puerperalis.

- Zeitschrift für Tierphysiologie Tierernährung und Futtermittelkd. 28:233–256.
doi:10.1111/j.1439-0396.1971.tb01573.x.
- Ferguson, J. O., D. T. Galligan, and N. Thomsen. 1994. Principal descriptors of body condition score in Holstein cows. *J. Dairy Sci.* 77:2695–2703. doi:10.3168/jds.S0022-0302(94)77212-X
- Flamenbaum, I., and N. Galon. 2010. Management of heat stress to improve fertility in dairy cows in Israel. *J. Rep. Dev. Suppl.* 56:36-41.
- Giordano, J. O., J. N. Guenther, G. Lopes, and P. M. Fricke. 2012. Changes in serum pregnancy-associated glycoprotein, pregnancy-specific protein B, and progesterone concentrations before and after induction of pregnancy loss in lactating dairy cows. *J. Dairy Sci.* 95:683–697. doi:10.3168/jds.2011-4609.
- Huzzey, J. M., D. M. Veira, D. M. Weary, and M. A. G. von Keyserlingk. 2007. Prepartum behavior and dry matter intake identify dairy cows at risk for metritis. *J. Dairy Sci.* 90:3220-3233. doi:10.3168/jds.2006-807.
- Jain, N. C. 1976. Neutrophil leukocytes and inflammation of the bovine mammary gland. *Theriogenology* 6:153–173. doi:10.1016/0093-691X(76)90011-X.
- Karimi, M. T., G. R. Ghorbani, S. Kargar, and J. K. Drackley. 2015. Late-gestation heat stress abatement on performance and behavior of Holstein dairy cows. *J. Dairy Sci.* 98:6865–6875. doi:10.3168/JDS.2014-9281.
- Landers, T. F. 2012. A Review of Antibiotic Use in Food Animals: Perspective, Policy, and Potential. *Public Heal. Rep.* 127.
- Lean, I. J., J. E. P. Santos, E. Block, and H. M. Golder. 2019. Effects of prepartum dietary cation-anion difference intake on production and health of dairy cows: A meta-analysis. *J.*

- Dairy Sci. 102:2103–2133. doi:10.3168/jds.2018-14769.
- LeBlanc, S. J., K. D. Lissemore, D. F. Kelton, T. F. Duffield, and K. E. Leslie. 2006. Major advances in disease prevention in dairy cattle. *J. Dairy Sci.* 89:1267–1279. doi:10.3168/jds.S0022-0302(06)72195-6.
- Lhermie, G., L. W. Tauer, and Y. T. Gröhn. 2018. The farm cost of decreasing antimicrobial use in dairy production. *PLoS One* 13:1–18. doi:10.1371/journal.pone.0194832.
- Luchterhand, K. M., P. R. B. Silva, R. C. Chebel, and M. I. Endres. 2016. Association between prepartum feeding behavior and periparturient health disorders in dairy cows. *Front. Vet. Sci.* 3:1–8. doi:10.3389/fvets.2016.00065.
- Martinez, N., C. A. Risco, F. S. Lima, R. S. Bisinotto, L. F. Greco, E. S. Ribeiro, F. Maunsell, K. Galvão, and J. E. P. Santos. 2012. Evaluation of periparturient calcium status, energetic profile, and neutrophil function in dairy cows at low or high risk of developing uterine disease. *J. Dairy Sci.* 95:7158–7172. doi:10.3168/jds.2012-5812.
- Meyer, C. L., P. J. Berger, K. J. Koehler, J. R. Thompson, and C. G. Sattler. 2001. Phenotypic Trends in Incidence of Stillbirth for Holsteins in the United States. *J. Dairy Sci.* 84:515–523. doi:10.3168/JDS.S0022-0302(01)74502-X.
- Moussavi, A. H., M. D. Mesgaran, and R. O. Gilbert. 2012. Effect of mastitis during the first lactation on production and reproduction performance of Holstein cows. *Trop. Anim. Health Prod.* 44:1567–1573. doi:10.1007/s11250-012-0107-3.
- NOAA. 1976. Livestock hot weather stress. Operations manual letter 1976; C-31-76. NOAA, Kansas City, MO.
- NRC. 2001. Nutrient Requirements of Dairy Cattle. 7th rev. ed. Natl. Acad. Press, Washington, DC.

- Olson, K. M., B. G. Cassell, A. J. McAllister, and S. P. Washburn. 2009. Dystocia, stillbirth, gestation length, and birth weight in Holstein, Jersey, and reciprocal crosses from a planned experiment. *J. Dairy Sci.* 92:6167–6175. doi:10.3168/jds.2009-2260.
- Ortiz, X. A., J. F. Smith, F. Villar, L. Hall, J. Allen, A. Oddy, A. al Haddad, P. Lyle, and R. J. Collier. 2015. A comparison of 2 evaporative cooling systems on a commercial dairy farm in Saudi Arabia. *J. Dairy Sci.* 98:8710-8722.
- Patel, O. V., I. Domeki, N. Sasaki, T. Takahashi, M. Hirako, R. G. Sasser, and P. Humblot. 1995. Effect of fetal mass, number and stage of gestation on pregnancy-specific protein B concentrations in the bovine. *Theriogenology* 44:827–833. doi:10.1016/0093-691X(95)00268-D.
- Patel, O. V., J. Sulon, J. F. Beckers, T. Takahashi, M. Hirako, N. Sasaki, and I. Domeki. 1997. Plasma bovine pregnancy-associated glycoprotein concentrations throughout gestation in relationship to fetal number in the cow. *Eur. J. Endocrinol.* 137:423-438.
- Penninga, L., and L. D. Longo. 1998. Ovine placentome morphology: Effect of high altitude, long-term hypoxia. *Placenta* 19:187–193. doi:10.1016/S0143-4004(98)90008-X.
- Pinedo, P. J., A. De Vries, and D. W. Webb. 2010. Dynamics of culling risk with disposal codes reported by Dairy Herd Improvement dairy herds. *J. Dairy Sci.* 93:2250–2261. doi:10.3168/jds.2009-2572.
- Pohler, K. G., T. W. Geary, C. L. Johnson, J. A. Atkins, E. M. Jenkins, D. C. Busch, J. A. Green, M. D. MacNeil, and M. F. Smith. 2013. Circulating bovine pregnancy associated glycoproteins are associated with late embryonic/fetal survival but not ovulatory follicle size in suckled beef cows. *J. Anim. Sci.* 91:4158–4167. doi:10.2527/jas2013-6348.
- Ricci, A., P. D. Carvalho, M. C. Amundson, R. H. Fourdraine, L. Vincenti, and P. M. Fricke.

2015. Factors associated with pregnancy-associated glycoprotein (PAG) levels in plasma and milk of Holstein cows during early pregnancy and their effect on the accuracy of pregnancy diagnosis. *J. Dairy Sci.* 98:2502–2514. doi:10.3168/jds.2014-8974.
- Roth, Z., A. Arav, A. Bor, Y. Zeron, R. Braw-Tal, and D. Wolfenson. 2001. Improvement of quality of oocytes collected in the autumn by enhanced removal of impaired follicles from previously heat-stressed cows. *Reproduction.* 122:737-744.
- Scanavez, A. L. A., B. Fragomeni, and L. G. D. Mendonça. 2018. Animal factors associated with core body temperature of nonlactating dairy cows during summer. *J. Anim. Sci.* 96:5000-5009. doi:10.1093/jas/sky353.
- Scanavez, A. L. A., B. Fragomeni, L. Rocha, B. E. Voelz, L. E. Hulbert, and L. G. D. Mendonça. 2017. Association between 4-day vaginal temperature assessment during the dry period and performance in the subsequent lactation of dairy cows during the warm season. *J. Anim. Sci.* 95:5208–5217. doi:10.2527/jas2017.1620.
- Scanavez, A. L. A., B. E. Voelz, J. G. N. Moraes, J. A. Green, and L. G. D. Mendonça. 2019. Physiological, health, lactation and reproductive traits of cooled dairy cows classified as having high or low core body temperature during the dry period. *J. Anim. Sci.* doi:10.1093/jas/skz345. In press.
- Schüller, L. K., O. Burfeind, and W. Heuwieser. 2014. Impact of heat stress on conception rate of dairy cows in the moderate climate considering different temperature-humidity index thresholds, periods relative to breeding, and heat load indices. *Theriogenology* 81:1050–1057. doi:10.1016/j.theriogenology.2014.01.029.
- Serrano, B., F. López-Gatius, P. Santolaria, S. Almería, I. García-Ispuerto, G. Bech-Sabat, J. Sulon, N. M. de Sousa, J. F. Beckers, and J. L. Yániz. 2009. Factors affecting plasma

- pregnancy- associated glycoprotein 1 concentrations throughout gestation in high-producing dairy cows. *Reprod. Dom. Anim.* 44:600-605. doi:10.1111/j.1439-0531.2007.01025.x.
- Stevens, M., S. Piepers, K. Supré, J. Dewulf, and S. de Vliegher. 2016. Quantification of antimicrobial consumption in adult cattle on dairy herds in Flanders, Belgium, and associations with udder health, milk quality, and production performance. *J. Dairy Sci.* 99:2118–2130. doi:10.3168/jds.2015-10199.
- Tao, S., J. W. Bubolz, B. C. do Amaral, I. M. Thompson, M. J. Hayen, S. E. Johnson, and G. E. Dahl. 2011. Effect of heat stress during the dry period on mammary gland development. *J. Dairy Sci.* 94:5976–5986. doi:10.3168/jds.2011-4329.
- Thompson, I. M., S. Tao, J. Branen, A. D. Ealy, and G. E. Dahl. 2013. Environmental regulation of pregnancy-specific protein B concentrations during late pregnancy in dairy cattle. *J. Anim. Sci.* 91:168–173. doi:10.2527/jas.2012-5730.
- Thompson, I. M. T., S. Tao, A. P. Monteiro, K. C. Jeong, and G. E. Dahl. 2014. Effect of cooling during the dry period on immune response after *Streptococcus uberis* intramammary infection challenge of dairy cows. *J. Dairy Sci.* 97:7426–7436.
- Torres-Júnior, J. R. de S., M. de F. A. Pires, W. F. de Sá, A. de M. Ferreira, J. H. M. Viana, L. S. A. Camargo, A. A. Ramos, I. M. Folhadella, J. Polisseni, C. de Freitas, C. A. A. Clemente, M. F. de Sá Filho, F. F. Paula-Lopes, and P. S. Baruselli. 2008. Effect of maternal heat-stress on follicular growth and oocyte competence in *Bos indicus* cattle. *Theriogenology*. 69:155-166.
- Vieira-Neto, A., K. N. Galvão, W. W. Thatcher, and J. E. P. Santos. 2017. Association among gestation length and health, production, and reproduction in Holstein cows and implications for their offspring. *J. Dairy Sci.* 100:3166–3181. doi:10.3168/jds.2016-11867.

- Ward, J. W., F. B. P. Wooding, and A. L. Fowden. 2002. The Effects of Cortisol on the Binucleate Cell Population in the Ovine Placenta During Late Gestation. *Placenta* 23:451–458. doi:10.1053/PLAC.2002.0834.
- Wegner, T. N., D. E. Ray, C. D. Lox, and G. H. Stott. 1973. Effect of Stress on Serum Zinc and Plasma Corticoid in Dairy Cattle. *J. Dairy Sci.* 56:748–752. doi:10.3168/jds.S0022-0302(73)85245-2.
- Wooding, F. B. P. 1992. The synepitheliochorial placenta of ruminants: Binucleate cell fusions and hormone production. *Placenta* 13:101–113. doi:10.1016/0143-4004(92)90025-O.

Table 1 Prepartum descriptive data (mean \pm SEM) of cows classified as high temperature treatment (HT-TRT), high temperature control (HT-CON), and low temperature (LT) before calving

| Item | Treatment ¹ | | | P-value ² | | | |
|---|------------------------|--------------|--------------|----------------------|-------|-------|-------|
| | LT | HT-TRT | HT-CON | C1 | C2 | C3 | C4 |
| Number of cows | 1,277 | 160 | 159 | - | - | - | - |
| Average vaginal temperature, °C | 39.13 (0.06) | 39.71 (0.07) | 39.70 (0.07) | <0.01 | 0.72 | <0.01 | <0.01 |
| Days of gestation at enrollment | 242.3 (0.7) | 243.0 (0.7) | 242.7 (0.7) | <0.01 | 0.26 | <0.01 | 0.05 |
| Body condition score ³ at enrollment | 3.39 (0.05) | 3.33 (0.06) | 3.31 (0.06) | 0.02 | 0.68 | 0.13 | 0.04 |
| Body condition score at parturition | 3.13 (0.01) | 3.07 (0.03) | 3.02 (0.03) | <0.01 | 0.27 | 0.10 | <0.01 |
| Body condition score change ⁴ | -0.58 (0.25) | -0.43 (0.30) | -0.68 (0.30) | 0.85 | 0.29 | 0.39 | 0.59 |
| Dry period duration, d | 54.3 (2.3) | 53.1 (2.4) | 51.0 (2.4) | <0.01 | 0.03 | 0.08 | <0.01 |
| Days spent in close-up pen, d | 20.3 (1.78) | 24.5 (1.84) | 15.9 (1.84) | 0.75 | <0.01 | <0.01 | <0.01 |
| Gestation duration, d | 274.1 (0.5) | 271.5 (0.7) | 270.6 (0.7) | <0.01 | 0.16 | <0.01 | <0.01 |
| P305 ME ⁵ , kg | 15,541 (414) | 15,341 (472) | 15,203 (473) | 0.16 | 0.69 | 0.44 | 0.19 |
| Days in milk at dry-off, d | 320.8 (3.7) | 317.2 (5.1) | 316.6 (5.1) | 0.18 | 0.91 | 0.35 | 0.28 |
| Twinning, % | 5.6 | 15.4 | 18.2 | <0.01 | 0.51 | <0.01 | <0.01 |
| Female calves born, % | 49.8 | 44.7 | 38.9 | 0.02 | 0.35 | 0.27 | 0.02 |

¹ Low temperature (LT), high temperature treatment (HT-TRT), and high temperature control (HT-CON).

² Contrasts: C1 = LT vs. HT-TRT + HT-CON; C2 = HT-TRT vs. HT-CON; C3 = LT vs. HT-TRT; C4 = LT vs. HT-CON.

³ Body condition score on a scale 1 (severe underconditioned) to 5 (obese).

⁴ Body condition score change from enrollment to parturition.

⁵ P305 ME: Previous projected 305-d mature equivalent milk yield.

Table 2 Incidence of antimicrobial treatment and culling risk during the first 60 days postpartum, and reproductive efficiency of cows classified as high temperature treatment (HT-TRT), high temperature control (HT-CON) and low temperature (LT)

| Item | Treatment ¹ | | | P-value ² | | | |
|--|------------------------|--------|--------|----------------------|------|------|--------|
| | LT | HT-TRT | HT-CON | C1 | C2 | C3 | C4 |
| Stillbirth, % | 4.1 | 6.9 | 8.3 | < 0.01 | 0.65 | 0.08 | 0.01 |
| Retained fetal membranes, % | 7.8 | 10.7 | 12.1 | 0.03 | 0.70 | 0.16 | 0.05 |
| Metritis, % | 2.9 | 3.3 | 5.4 | 0.18 | 0.39 | 0.68 | 0.08 |
| Treatment of uterine diseases ³ , % | 9.6 | 11.9 | 14.0 | 0.06 | 0.59 | 0.29 | 0.07 |
| Mastitis, % | 12.3 | 13.3 | 11.2 | 0.70 | 0.56 | 0.48 | 0.93 |
| All disorders, % | 23.8 | 26.1 | 28.2 | 0.08 | 0.69 | 0.29 | 0.11 |
| Died by 60 DIM, % | 2.8 | 2.5 | 6.3 | 0.16 | 0.11 | 0.98 | 0.01 |
| Sold by 60 DIM, % | 5.6 | 4.4 | 5.7 | 0.64 | 0.50 | 0.94 | 0.39 |
| Culled by 60 DIM, % | 8.3 | 6.9 | 12.0 | 0.11 | 0.13 | 0.80 | 0.02 |
| Inseminated, % | 89.7 | 89.4 | 84.3 | 0.04 | 0.18 | 0.51 | < 0.01 |
| Pregnant at first AI, % | 41.4 | 37.0 | 33.9 | 0.03 | 0.56 | 0.20 | 0.05 |

¹ Low temperature (LT), high temperature treatment (HT-TRT), and high temperature control (HT-CON).

² Contrasts: C1 = LT vs. HT-TRT + HT-CON; C2 = HT-TRT vs. HT-CON; C3 = LT vs. HT-TRT; C4 = LT vs. HT-CON.

³ Uterine diseases: cows treated with antimicrobials for retained fetal membranes or metritis.

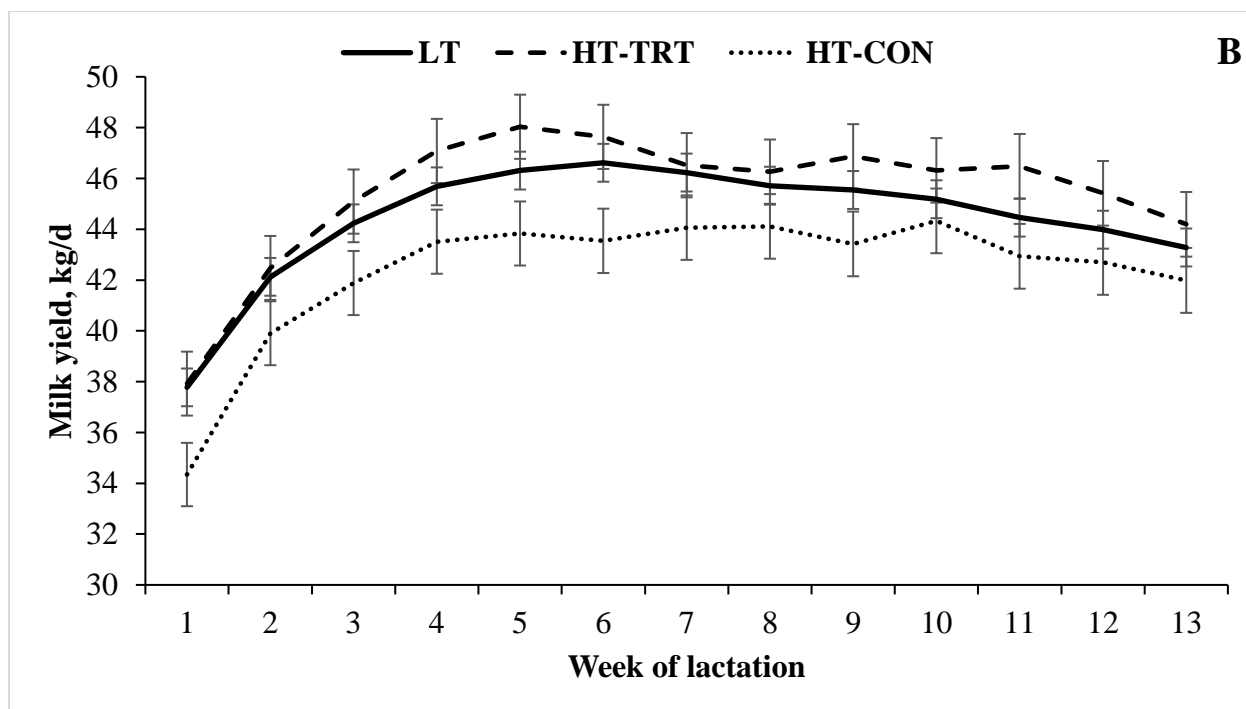
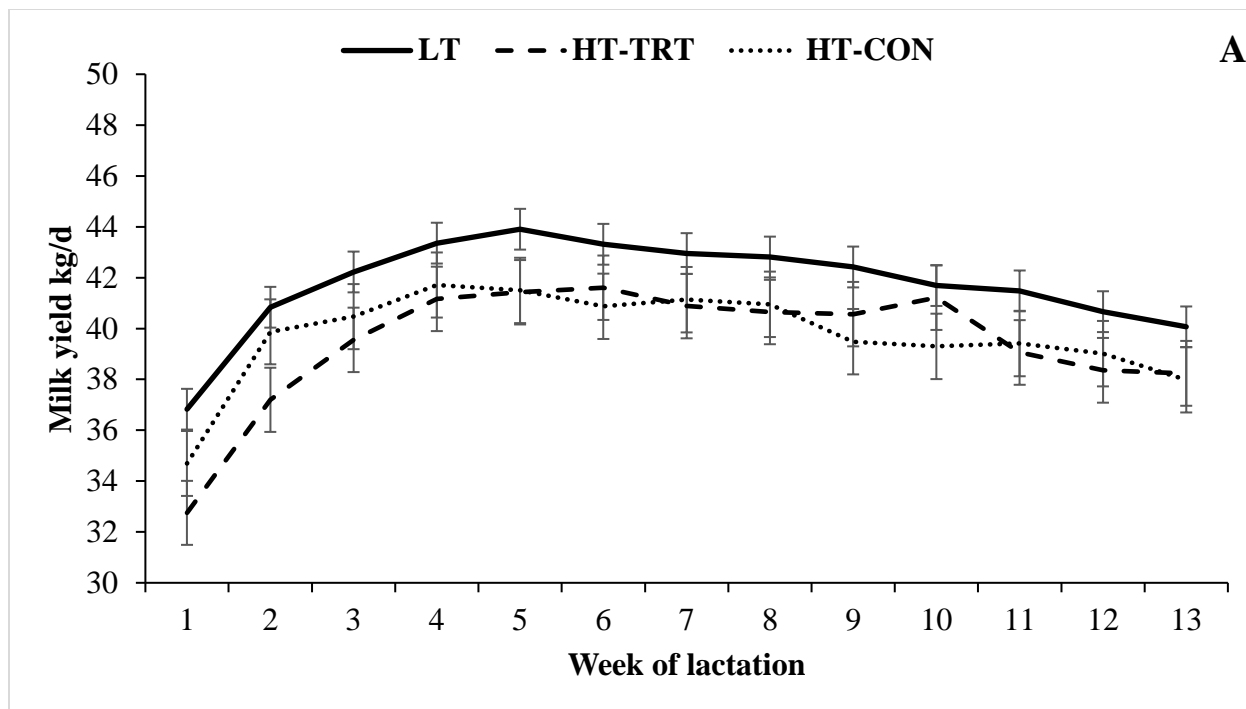


Figure 1 Milk yield during the first 13 wk of lactation of cows classified as low temperature (LT), high temperature treatment (HT-TRT), or high temperature control (HT-CON). (A) Primiparous cows (overall mean \pm SEM): LT = 41.7 ± 0.8 ; HT-TRT 39.4 ± 1.1 ; HT-CON = 39.7 ± 1.1 kg/d. (B) Multiparous cows (overall mean \pm SEM): LT = 44.4 ± 0.7 ; HT-TRT = 45.4 ± 1.1 ; HT-CON = 42.3 ± 1.1 kg/d.

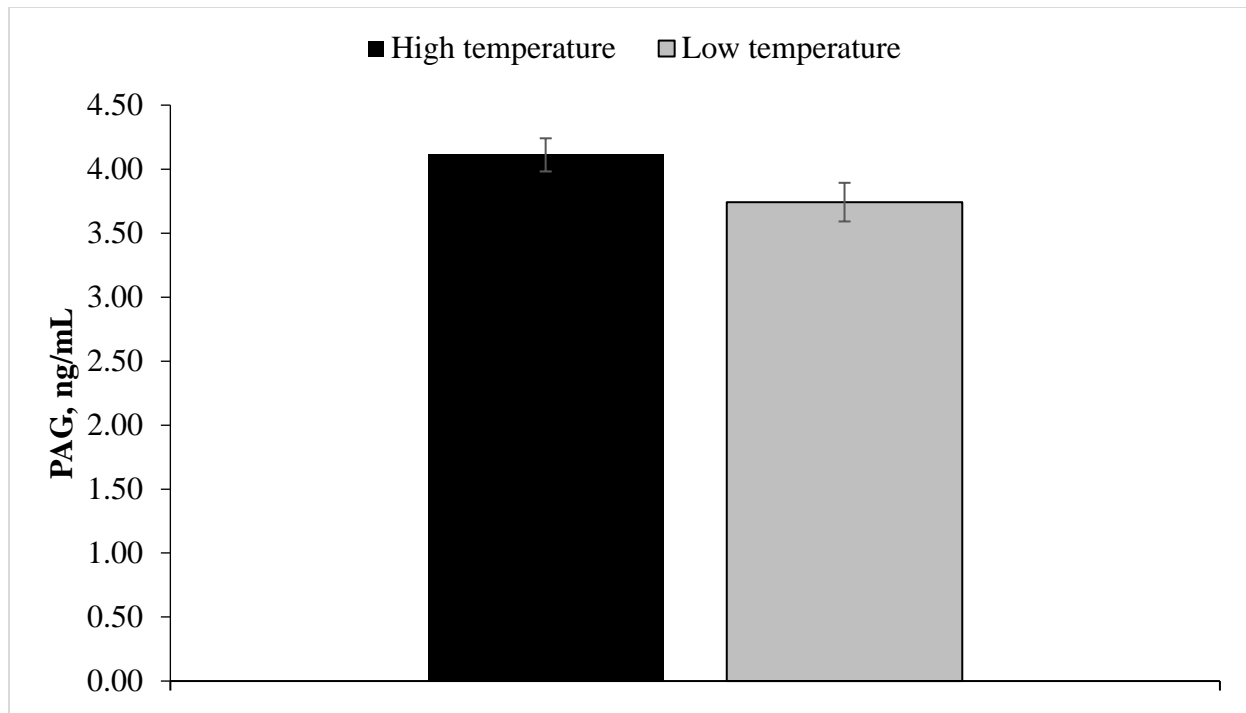


Figure 2 Plasma concentration of bovine pregnancy-associated glycoprotein (PAG) in Holstein cows classified as high or low temperature based on vaginal temperature before calving. High temperature cows had greater ($P = 0.02$) PAG concentration compared with low temperature cows (4.11 ± 0.13 vs. 3.74 ± 0.15 ng/mL).

Chapter 3 - General Conclusions

During the past decades several researchers have demonstrated the impact of poor transition from late gestation to lactation on performance of dairy cows after calving. As discussed in this thesis, several factors may affect cows on late gestation, resulting in a detrimental effect on health, milk production, reproductive efficiency, and culling dynamics after calving. Previous studies have demonstrated that heat-stressed dry cows that will have poor performance after calving can be identified during the early dry period (Scanavez et al., 2017, 2019). Some characteristics of these cows are shortened GL, reduced days in prepartum pen, increased proportion of twinning, and increased VT during late gestation. Chapter 2 of this thesis highlights results of a study that used a new approach to identify heat-stressed dry cows more susceptible to have issues after calving. This innovative approach involved assessing VT once in the early dry period, which resulted in accurate identification of a cohort of cows with increased susceptibility for postpartum disorders. In addition, findings from this study demonstrated that concentration of PAG in late gestation has the potential to be used as a biomarker to identify cows with high VT, which is the cohort of cows more susceptible to be treated for postpartum diseases after calving. These findings should assist other researchers interested in further understanding the role of PAG in ruminants.

In order to improve transition performance of cows more susceptible to have poor performance after calving, implementation of a management practice was adopted. The goal of the management practice was to extend the days in the prepartum pen (close-up pen) for cows susceptible to have health problems after calving (high-temperature cows) in order to reduce the use of antimicrobials and improve overall performance after calving. The strategy evaluated was reported in Chapter 2 partly confirmed our initial hypothesis. High temperature cows that were

moved earlier to the close-up pen had similar proportion of cows treated with antimicrobials for uterine disorders than LT cows. Nonetheless, HT cows that the management strategy was not utilized tended to be more likely to be treated for uterine disease than LT cows. Although benefits of implementing the management strategy were observed for cows developing uterine disease, no differences were observed in overall antimicrobial treatments during the first 60 DIM. Nevertheless, the new management strategy resulted in increased milk yield during the first 90 DIM.

This thesis highlights that dairy producers can be more efficient with the potential to reduce use of antimicrobials for specific disorders by targeting management strategies to cows more susceptible to have problems after calving. Because reducing the number of antimicrobial treatments in livestock is a pressing issue to address societal concerns, other strategies must be explored to target cows more prone to have disorders after calving. Lastly, further research is warranted to understand the mechanism involved in cows having increased VT before calving.