Why is it important to cool drycowsand youngstock cool during hot summers: From physiology and epigenetics to economics

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Abstract

Exposure to heat stress during late gestation significantly impacts the development and health of calves, both in the short term and long term. In utero heat stress can immediately alter calf growth and immune function post-birth. Long-term effects include reduced survival rates, shortened lifespan, and decreased milk production. Furthermore, intrauterine hyperthermia affects the daughters (F1 generation) and extends to their offspring (F2 generation), highlighting multigenerational consequences. Economically, the financial losses due to in utero heat stress in the U.S. are estimated to exceed $500 million annually. Heat stress during gestation disrupts mammary gland development in offspring and induces epigenetic changes, such as organ-specific and common methylation modifications in the mammary gland and liver. These epigenetic alterations may contribute to decreased survivability and production outcomes in affected animals.

Postnatal heat stress significantly affects newborn calves during their critical developmental window before weaning. It elevates thermal stress indices, reduces feed and grain intake, and disrupts the normal development of the immune system. Environmental heat stress is detrimental to calves both before and after birth. Therefore, effective heat abatement strategies should be implemented to protect young replacement heifers and ensure their healthy development and survival in the herd.

Keywords: hyperthermia, climate change, youngstock

Introduction

Heat stress, defined by high ambient temperatures and relative humidity, is widely recognized as a significant factor negatively affecting dairy cows globally, including temperate regions. The trend of rising global temperatures poses an increasing threat to livestock production and animal welfare worldwide. NASA data indicates that the five warmest years on record have occurred since 2016, with 2020 being the warmest (NASA.gov). While the impact of heat stress on lactating cattle is well-documented and extensively studied (West et al., 2003), there is growing recognition that rising temperatures will affect dairy cattle of all ages and lactation states if heat stress prevention and mitigation strategies are not adopted. Although heat stress abatement is commonly implemented for lactating herds, non-lactating cattle (such as dry-pregnant cows and youngstock) are often not considered for such measures on farms. The dry period, coinciding with the last trimester of gestation—a phase of exponential fetal growth—renders the fetus particularly vulnerable to developmental disruptions that could affect normal intrauterine development. As a result, the fetus can be adversely impacted by maternal heat stress through changes in the intrauterine environment.

Despite increasing scientific evidence highlighting the adverse effects of heat stress on dry-pregnant cows and youngstock (as reviewed by Ouellet et al., 2020, and Dado-Senn et al., 2020a), the full extent of these impacts remains underappreciated in both research and industry. While substantial research has focused on the effects of nutritional programming on mammary gland development both pre-weaning (Soberon et al., 2012; Geiger et al., 2016) and during the pre-pubertal period (Sejrsen et al., 1982; Meyer et al., 2006), there has been limited attention to the programming effects of intrauterine conditions on mammary development and future function in unborn and pre-weaned heifers. This presentation explores how exposure to environmental heat stress during critical developmental stages—specifically hyperthermia in the last trimester of fetal development and the first two months of life—can result in suboptimal phenotypes across multiple lactations and generations compared to those gestated or raised in optimal thermal conditions. We will present new research on heat stress's short- and long-term effects during intrauterine and postnatal early-life development, including the potential physiological and molecular mechanisms behind these adverse outcomes.

Short- and long-term phenotypic effects of in utero heat stress

These effects are evidenced during pre-weaning (i.e., the first two months of life). These include lower birth weights (avg. 5 kg), lower weaning weights (avg. 8 kg), impaired innate and adaptive immune development and function (impaired apparent efficiency of IgG absorption, reduced circulating IgG and lymphocytes), and overall growth retardation (i.e., stature and head circumference). Recent studies from our group indicate that in utero hyperthermia can program cells, organs, and tissues that play crucial roles in future lactational outcomes (i.e., mammary gland growth and development), metabolism (i.e., liver), immune function (i.e., thymus and spleen), feed intake (i.e., rumen and gastrointestinal tract), and thermoregulation (i.e., sweat gland and skin characteristics). A detailed description of the short-term implications of inutero hyperthermia can be found in reviews by our group (Dahl et al., 2017; Dado-Senn et al., 2020a).

Long-term phenotypic effects of in utero heat stress

These effects areevidenced post-weaning and beyond). These includereduced stature and body weight until 12 months of age. Still, the most notable long-term phenotypic effect is that heifers gestated under in utero hyperthermia produce less milk (~ 4.5 kg/d) in their first lactation. This was initially demonstrated by a retrospective study summarizing 5-years of experiments at the University of Florida (Monteiro et al., 2016).Yet, amore extensive research study summarizing a 10-year data set led by our group (Laporta et al., 2020) revealed that late-gestation heat stress impacts daughters' survivability and productivity across not only one but multiple lactations. More specifically, the average dairy cow born to a heat-stressed dam in the United States would have a 5-month shorter productive life and lose 120 kg of milk per year for three consecutive lactations compared to a cow born to a cooled dam. Significantly more nulliparous heifers born to a heat-stressed dam would leave the herd before they reach first lactation, and the overall lifespan would be reduced by approximately 11 months. A detailed description of the short-term implications of inutero hyperthermia can be found in Ouellet et al. (2020).

Long-term multigenerational effects

Multigenerational (also referred to as intergenerational) effects can occur when a pregnant dam (the maternal generation, F_0) is exposed to a stressor (i.e., any factor that disrupts homeostasis) that can have direct effects on the developing fetus (F1) and the germ line of the fetus (that will give rise to the F2), leading to altered phenotypes of the resulting offspring. Yet, a true transgenerational will be revealed in the F_3 generation - the first "unexposed transgenerational offspring" (Skinner, 2008). The conjunct analysis of 10 controlled heat stress studies by Laporta et al. (2020) allowed us to follow the records of granddaughters (F2, born to F1 daughters of the dam exposed to heat stress). This study revealed adverse carryover effects on the F2's survival and milk production, including reduced survival through puberty and decreased milk yield during their first lactation. However, it remains unknown if these effects are transgenerational as we lack information on the F3 generation, which would be the first unexposed transgenerational offspring.

Financial Implications on Late-gestation Heat Stress on Dam and F_1 Offspring

It is undeniable that the severity of heat stress in the southeastern U.S. is more significant than that in the midwestern and northeastern regions. For instance, not only does Florida experience over 200 heat stress days a year compared with Wisconsin's, Minnesota's, and New York's average of 60 days of heat stress, but also levels and patterns of heat stress differ significantly. Southeast U.S. is considered a humid subtropical environment where chronic periods of high ambient temperature and relative humidity carry over into the evening and sometimes night hours with little respite (West et al. 2003). In contrast, the Midwestern and northeastern regions can be considered temperate or humid continental climates with temperatures that vary significantly from summer to winter and cooler evening diurnal patterns (NOAA Climate Zones 2020). Despite these apparent differences in climatic conditions, the average U.S dairy cow experiences an average of 96 days of heat stress a year, according to Ferreira et al. (2016). These authors estimated the annual economic loss from dry cows' heat stress exposure (i.e., if they do not receive adequate heat stress abatement) at $ 810 million. Yet, these estimations do not account for the subsequent losses in the progeny. We sought to estimate the financial losses from intrauterine hyperthermia impacting the progeny postnatally. Thus, accounting for the increased heifer costs, reductions in productive life, and milk loss in the first, second, and third lactations reported by our group in Florida (Laporta et al., 2020), the repercussions on the United States dairy sector profitability are estimated to be around $600 million annually. Collectively in the U.S, the total loss to late-gestation heat stress could increase to $1.4 billion if the direct losses in subsequent milk production of the dam are combined with the indirect financial damage from in utero carry-over effects of heat stress on daughter lactational performance. Taken together, the economic loss arising from heat stress in lactating cattle and the financial loss of dry period heat stress are comparable when including the indirect loss from the progeny.

Molecular Signature of Late-Gestation Heat Stress on Offspring

Our research focuses on understanding how in utero hyperthermia affects mammary gland development and function, reducing milk production in adulthood. Milk yield depends on the number of mammary cells and their metabolic activity (Capuco et al., 2010). An increase in cell number would likely have a lasting effect, while changes in metabolism (e.g., gene and protein expression) might be more temporary. Epigenetics, particularly DNA methylation, is a key mechanism by which environmental factors can cause long-term changes in gene expression (Skinner et al., 2011). We evaluated the effects of intrauterine hyperthermia on mammary tissue structure and methylation patterns during the first lactation compared to those gestated under thermoneutral conditions (F_1 daughters) and in their respective daughters (F_2).

Tissue Microstructure. We collected serial mammary biopsies during early and peak lactation (21 and 42 days in milk) from first-lactation heifers that were either heat-stressed or cooled in utero: *F1 daughters*. Histological analysis showed that heifers exposed to heat stress in utero had mammary glands with smaller alveolar luminal areas (50% smaller) and fewer secretory cells despite having a similar number of alveoli as the cooled group. There was also more stromal connective tissue, fewer proliferating cells, and more apoptotic cells in the heat-stressed group, suggesting these changes could impair lactational performance (Skibiel et al., 2018a).

Epigenetic Changes. We examined DNA methylation in mammary tissues of heifers during their first lactation (21 days in milk) to understand prenatal programming effects. In utero heat stress led to 135 differentially methylated genes in the mammary gland, including PRKG1 and PTK2, and 50 genes shared with liver tissues. This indicates that in utero heat stress can induce specific and shared epigenetic changes across different tissues and may impact multiple aspects of physiology critical for lactation. These findings suggest numerous candidate genes for further investigation into the multigenerational effects of heat stress (Skibiel et al., 2018b).

Heat Stress in Pre-weaned Dairy Calves

Elevated temperatures trigger elevated respiration rates and increase core body temperature, and sweating in young calves affects their growth, development, and overall health. When dairy calves are exposed to high temperatures and humidity, two primary physiological and developmental processes are disrupted, along with a disruption of behavioral patterns.

Growth and feed intake**:** Heat stress reduces feed intake and nutrient absorption in calves, leading to lower growth rates. Calves under heat stress often have reduced body weight gain, which affects their development and future productivity (See: Dado-Senn et al., 2020b).

Behavior*:* Environmental heat stress impacts preweaning dairy calves' behavioral responses and activity patterns. Specifically, calves under heat stress (average daily Temperature Humidity Index > 77) increase the time they lie laterally and reduce the time lying sternally in a tucked position during night hours. Calves under heat stress stand for more extended periods across the day, particularly overnight(See: Dado-Senn et al., 2021)

Immune function**:** Heat stress can weaken the immune system in calves, making them more susceptible to diseases and infections. The stress response can lead to increased levels of stress hormones like cortisol, which can suppress immune function (See:Marrero et al., 2021).

Overall, heat stress represents a significant challenge for dairy calves, necessitating effective management strategies to mitigate its effects and protect the health and productivity of future dairy cows. Our group continues to actively investigate the molecular signature of intrauterine hyperthermia in mammary gland development and function across developmental stages and generations.

Conclusions

Maternal exposure to elevated temperature and humidity during late gestation causes intrauterine hyperthermia, reducing postnatal daughter longevity, productive life, and overall productivity (milk yield) for up to 3 lactations. Annual losses for the U.S dairy sector arising from in utero heat stress are estimated at $600 million. Alterations in mammary gland microstructure and cell turnover, along with epigenetic changes, such as DNA methylation introduced in utero, appear responsible for the long-lasting observed phenotypic outcomes. Heat stress also negatively affects young dairy claves when exposed during the pre-weaning vulnerable life stage, delaying growth and immune development. Providing efficient heat abetment methods to dry-pregnant cows and calves in early life ensures optimal survivability and productivity for multiple generations.

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