HEAT STRESS EFFECTS ON IMMUNE FUNCTION IN DAIRY CATTLE

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Environmental factors, particularly heat stress, present challenges to dairy cow productivity and health. In the absence of active cooling, exposure to elevated temperatures and humidity significantly reduce dry matter intake during lactation, and subsequent declines in milk yield can approach 25% depending on the severity and duration of the heat stress (reviewed by West, 2003). Lactating cows make metabolic adaptations which repartition additional energy away from productive purposes such that the actual decline in production exceeds what would be expected based on the lower DMI (Rhoads et al., 2009). Similarly, when dry cows are exposed to heat stress they produce less milk than cooled dry cows in the next lactation, even when both groups are cooled after calving (reviewed in Tao and Dahl, 2013). Dry cows under heat stress consume less feed than cooled cows, but the metabolic adaptations observed in lactating cows are not present (Tao et al., 2012). Despite the significant losses associated with productivity under heat stress, additional negative impacts on the overall health of lactating and dry cows and their calves accrue with exposure to high temperatures and humidity, and those outcomes are the focus of this paper.

Udder health is one of the first considerations with heat stress. Heat stress negatively impacts leukocyte migration into the mammary gland after a chemotactic challenge in lactating cows (Elvinger et al., 1992). When lactating cows were subjected to graded increases in temperature and humidity (i.e. Temperature Humidity Index [THI]), leukocyte numbers declined as did circulating cytokines, including TNF-alpha and IL-10, further evidence of a broad effect of heat stress to depress immune status (Zhang et al., 2014). Lactating ewes under heat stress had reduced leukocyte counts versus those provided shade, and had elevated mastitis pathogen loads in their milk relative to shaded flock mates (Sevi et al, 2001). Milk SCC, however, was unaffected by heat stress in ewes, but that may reflect a lack of power to detect differences. In general, heat stress reduces the cow's immune competence.

When ambient temperature and humidity rise, a cow will experience significant shifts in endocrine systems to accommodate to the need to increase heat loss. In particular, cortisol and prolactin, both hormones known to affect the immune system, increase with heat stress (reviewed in Collier et al., 2008). Collier et al. (2008) reviewed evidence that prolactin and cortisol exert influences over genes associated with immune responses, notably the heat shock proteins (HSP's) that act to limit the negative effect of excessive temperatures at the cellular level. Thus, it follows that heat stress would affect immune function at the interface of the endocrine and immune systems.

Heat stress has direct effects on immune function in cows during the dry period, and those impacts linger after calving. For example, adaptive immune function, as measured by the proliferative capacity of lymphocytes, is directly suppressed with exposure to heat stress (do Amaral et al, 2011, 2012). Further negative impacts on adaptive immunity were noted when cows' antibody production was assessed to a foreign antigen in the form of chicken ovalbumin, an innocuous non-self protein that elicits an immune reaction. No difference was observed in antibody production to cows at dry off, but after two weeks exposure to heat stress, antibody production in response to a booster of ovalbumin was reduced relative to that in cooled dry cows (do Amaral et al., 2011). This differential response persisted through the dry period but disappeared after calving when all cows were cooled, further evidence that heat stress directly depressed antibody production. Because many dry cow management protocols include vaccination against mastitis causing pathogens, it is important to consider heat stress abatement as an additional approach to improve health and immune function as the cow transitions into lactation.

One concern regarding dry cow cooling is the observation that the higher milk yield drives greater bodyweight loss in early lactation, and that is associated with greater circulating NEFA and BHBA concentrations as well (do Amaral et al., 2009). Elevated NEFA and BHBA have been associated with reduced immune status, so it is possible that dry cow cooling would lead to reduced immune function after calving. However, we have observed that like milk yield, there is a positive carryover effect of dry cow cooling on innate immune function, as cooled dry cows have more robust neutrophil action relative to those that were heat stressed, despite elevated NEFA and BHBA (do Amaral et al., 2011; Thompson et al, 2014). There is also evidence that pathogen mediated disease incidence is lower in cows that were dry during cool seasons compared with hotter periods (Thompson and Dahl, 2012), further support for the concept of a positive effect of dry cow cooling on subsequent health.

Heat stress can also affect the immune status of the developing fetus, with significant carryover effects after birth. Calves born to heat stressed dams are lighter at birth and typically born 4 to 5 days earlier than those from cooled dams (Tao et al., 2012). In utero heat stress reduces the calves circulating immunoglobulin concentrations during the first month of life, which is negatively associated with health and survival (Tao et al., 2012). A series of studies indicate that the observed reduction in IgG concentrations results from poorer absorption of IgG from colostrum, regardless of the source and quality of that colostrum (Monteiro et al., 2014). Thus, it appears that in utero heat stress alters the calf's ability to absorb IgG. Recent work supports the concept that gut closure is accelerated in heat stressed calves, such that IgG absorption is reduced (Ahmed et al, 2015). As the calf matures, in utero heat stress is associated with higher numbers leaving the herd before completing the first lactation compared with calves from cooled dams, which is consistent with poorer immune status in early life compromising later health (Monteiro et al., 2016).

The most common method of cooling cows during the dry period is consistent with that of lactation cooling, i.e. shade, fans, and soakers to provide active cooling (Collier et al., 2006). In the University of Florida facilities, soakers are positioned over the feedline and fans are over the free stalls. When the ambient temperature exceeds 21.1 °C, fans automatically turn on and the soakers are activated for 1.5 min at 5 min intervals. Using this system, we consistently observe reductions in rectal temperatures of 0.4 to 0.5 °C, and normalization of respiration rate from over 70 breaths/min in heat stressed cows to less than 45 breaths/min in the cooled cows. Most important is the need to cool cows for the entire dry period rather than just the close-up or latter stages. In a recent study we observed a negative impact of heat stress imposed at any time during the dry period on subsequent yield (Fabris et al., 2017a); it is likely that similar negative outcomes occur with regard to immune function.

There may also be nutritional management approaches to ameliorate some of the negative effects of heat stress. Ingredients that improve skin surface exchange of heat through vasodilation, such as niacin, have met with some success in reducing body temperature under heat stress. Supplementation of encapsulated niacin reduced rectal temperatures in lactating cows under heat stress, as a result of greater evaporative heat loss (Zimbelman et al., 2010). However, Lohölter et al. (2013) did not observe an effect of niacin on rectal temperatures, although the form of the niacin or level of heat stress may have affected the response. Indeed, skin temperature increased, but rectal temperature was unaffected in lactating cows supplemented with nicotinic acid (DiCostanzo et al., 1997). Betaine, a natural osmolyte, increased milk yield in lactating cows under thermoneutral conditions but not under heat stress (Hall, et al., 2016). However, betaine did alter heat shock protein (HSP) 27 and HSP 70 expression in leukocytes, with an inverse shift, i.e. decreased HSP 27 and increased HSP 70 following heat stress. Betaine also improved subsequent milk yield when fed to dry cows for the entire dry period (Monteiro et al., 2017). Limited information, however, is available with regard to nutritional modulators of immune status, especially with heat stress.

Feeding one immunomodulatory compound, however, has shown consistent reductions in rectal temperature and respiration rate in heat stressed cows. OmniGen-AF fed at the recommended rate has reduced the rectal temperature of lactating (Lieva et al., 2017), transition (Brandão et al., 2016), and dry cows (Fabris et al., 2017) when animals are housed under heat stress. Whereas the reduction in rectal temperature in dry cows is not as great as that observed with active cooling, there is a substantial lowering of respiration rate as well, and OmniGen-AF feeding before, during and after the dry period to heat stressed cows increased subsequent milk yield (Fabris et al., 2017b).

In addition to the effect on rectal temperatures, OmniGen-AF feeding to lactating cows reduced circulating cortisol during heat stress relative to cows not receiving OmniGen-AF (McBride et al., 2016). As expected, the lower cortisol with OmniGen-AF feeding was associated with improved immune function during heat stress. To further tease out the mechanism of lower cortisol, cows were challenged with corticotropin releasing hormone (CRH) and adrenocorticotropin (ACTH), two of the normal upstream stimulators of cortisol release. During heat stress, responses to CRH and ACTH were lower in OmniGen-AF fed cows relative to controls. Because cortisol is negatively associated with immune function, the reduction in responsiveness to its physiological stimulators is likely a factor in the immunomodulatory effect of OmniGen-AF.

Consistent with the impact on rectal temperature and respiration rate, OmniGen-AF feeding also positively affected the immune status of heat stressed dry cows. We have hypothesized that immune status early in the dry period is critically important to successful and full involution of the mammary gland and subsequent regeneration of secretory cells for the next lactation (Fabris et al., 2017c). OmniGen-AF feeding in late lactation improved neutrophil function and the expression of L-selectin, which suggest a greater capacity for immune response at dry off. Coupled with the observation that mammary restructuring was altered by OmniGen-AF feeding, and the improved milk yield, this suggests that better immune status early in the dry period may lead to more complete involution and greater regeneration of functional mammary tissue.

In summary, heat stress reduces immune status in lactating and dry cows, and many of these effects are mediated via the immune system that links to altered metabolism and production. Cooling cows throughout the production cycle is critical to optimize health and productivity, and is easily achieved through facilities improvements. Dietary measures may further enhance the positive effects of cooling on lactating and dry cows.

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