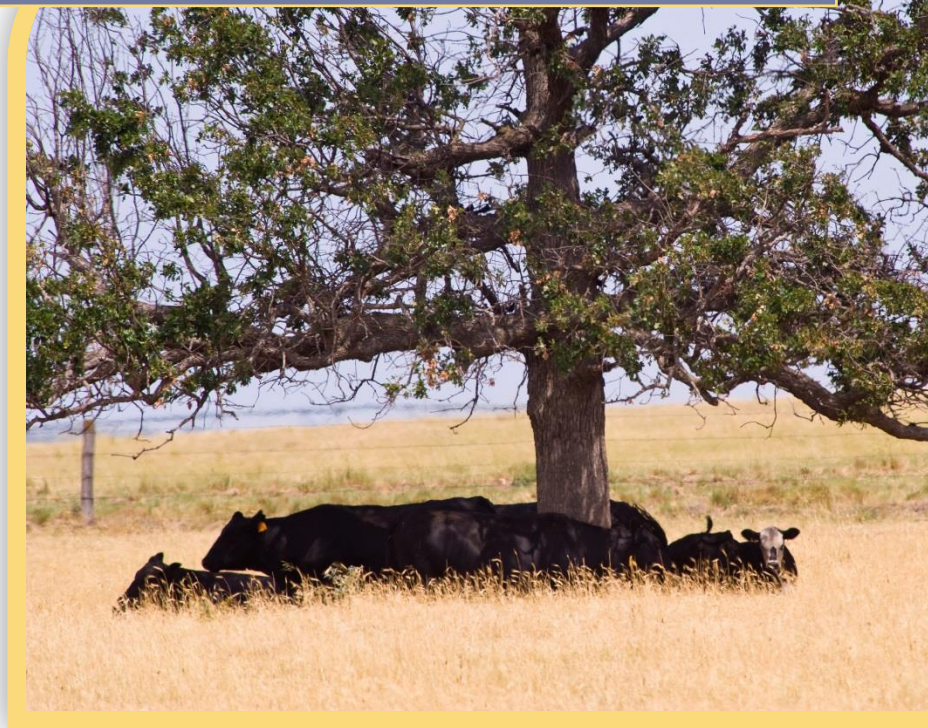# Genetic Basis for Heat Tolerance in Cattle

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Summary

❖ Heat stress is a challenge the beef industry should be prepared to address due to productivity losses and concern for animal well-being

❖ Heat stress will likely become more prevalent over the next few decades as predicted changes in climate could cause increases in severity of weather events and warmer average temperatures

❖ Management changes in confined feeding settings can address many of these challenges for cattle in a feedlot, but are more difficult to implement in pasture settings

❖ In warmer climates, genetic selection for heat tolerance offers one possible solution for simultaneously improving animal well-being and productivity

Introduction

Heat stress is a condition caused by an animal's inability to dissipate body heat effectively to maintain normal body temperature, a vital process known as thermoregulation. Cattle not only gain heat from the environment through solar radiation (exposure to sunlight), high ambient temperatures, and humidity, they also produce additional heat internally through fermentation in the rumen during digestion. Within the beef industry, there has been a tremendous focus on management interventions for heat stress in feedlot cattle as a result of large death losses induced by extreme weather events (Busby and Loy 1997; Mader 2014). Heat stress in beef cows has received considerably less scrutiny. Presumably because beef cows are managed in extensive production systems, less heat stress data has been collected on beef cows relative to feedlot cattle and dairy cows. Furthermore, beef cows often have access to natural types of mitigation (i.e. shade from trees). Regardless of the production system, animal well-being is just as vital in the cowherd as in later stages of production. Consequently, it is important that all options available are considered to improve the well-being of beef cows on pasture. Thus, this paper includes a discussion of the basic premise of heat stress, presents a brief overview of the literature related to management interventions for heat stress, and reviews genetics research that may illuminate new approaches aimed at mitigating heat stress in beef cows.

Overview of Heat Stress

Heat stress results from a negative balance between the net amount of energy flowing from the animal to its surrounding environment, and the amount of heat energy produced and absorbed by the animal. Essentially, cattle that are producing and absorbing more heat from the environment than they can dissipate will experience heat stress. While cattle can acclimatize to hotter conditions, an individual animal's adjustment period encompasses anywhere from 2-7 weeks (Blackshaw and Blackshaw 1994). Additionally, animals exhibiting higher levels of performance tend to generate more heat due to their inherently higher levels of productivity, hence, they experience more heat stress (West 1994). As emphasis on productivity continues to mount, heat stress mitigation will likely receive even greater attention in the beef industry.

Cattle respond to environmental conditions differently than humans, and are more sensitive to environments with high temperature and humidity (Webster 1973). Therefore, cattle are more susceptible to heat stress than humans under the same environmental conditions. Core body temperature of cattle is typically higher than ambient temperature (see Figure 1), which helps ensure that heat from the animal flows to the environment (Collier et al. 2006). As with all animals, cattle can dissipate heat to the environment through radiation (such as the infrared radiation emitted by animals that can be seen with infrared cameras), conduction (transfer of heat between objects in physical contact), and convection (transfer of heat between an object and the environment), but these cooling methods become less effective as ambient temperature rises. When temperature and humidity are high, the primary means by which cattle dissipate heat is by evaporation (West 2003; Blackshaw and Blackshaw 1994).
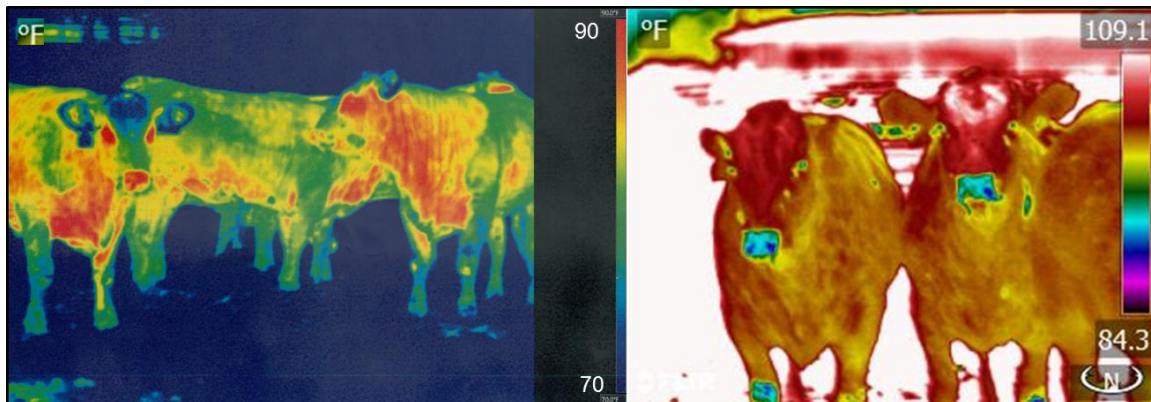
Figure 1: Thermal images showing cattle that are warmer than the surrounding environment (left panel), so the environment serves as a heat sink for cooling the cattle contrasted with cattle that are in a very hot environment (right panel) where it will be very difficult for them to dissipate heat and maintain their body temperatures. Temperature scales are provided on the right side of each image.

Because evaporative cooling (such as sweating and panting) is essential to maintain body temperatures during heat-related events, open-mouthed breathing and panting are some of the most obvious signs of heat stress. This is often accompanied by seeking shade, excessive salivation, and foaming around the mouth. When humidity is high, evaporative cooling is compromised, and even these heat stress-related behaviors may not effectively prevent a rise in body temperature (West 2003). Ideally, heat stress should be identified and mitigated before the onset of conditions that would initiate heat stress. Planning ahead for heat stress mitigation and making necessary adjustments before the onset of symptoms can improve both the performance and well-being of the animal.

Risk Factors for Heat Stress

Ambient temperature and humidity are environmental conditions that collectively impact heat stress, and they are often combined into one metric called the temperature humidity index (THI). The THI has been shown to be a reliable indicator of heat stress in cattle (Dikmen and Hansen 2009). Animals can often endure higher temperatures if humidity is low, and the risk for heat stress increases dramatically as humidity increases, even at lower ambient temperatures. Adjusting the THI for wind speed and solar radiation increases predictability of heat stress (Mader et al. 2006). In addition to these daytime conditions, nighttime conditions (minimum

wind speed, minimum solar radiation, and minimum THI) also impact heat stress in cattle (Mader et al. 2006), because cattle can often dissipate significant heat during the night if temperatures are lower.

Characteristics of individual animals can also position them at higher risk for heat stress. Hide color is a well-known risk factor because dark hair has lower reflectance values (da Silva et al. 2003) and dark skin absorbs a greater proportion of solar radiation (93% thermal absorption for black skin vs 43% for non-pigmented skin; da Silva et al. 2003). Predictably, animals with black hides spend significantly more time in the shade (89% for black hides and 55% for white; Gebremedhin et al. 2011). Dark-hided cattle are 25% more stressed at temperatures above 25 degrees Celsius when compared to light-hided cattle (Brown-Brandl et al. 2006) and exhibit 5.7x higher mortality risk in the feedlot (Hungerford et al. 2000). A study by Brown-Brandl et al. (2006) also identified other risk factors for heat stress aside from hide color, including history of respiratory pneumonia, level of fatness, and temperament. In this study, cattle that were one body condition score (BCS) category higher (i.e. moving from a BCS 6 to a 7) were 10% more stressed than the animals with 1 BCS lower.   Brown-Brandl et al. (2006) also established that excitable animals were 3.2% more stressed than their calm counterparts and the calm animals gained 5% more. Treatment history for respiratory pneumonia increased heat stress by 10.5% while conversely reducing average daily gain (ADG) by 8%.

Impact of Heat Stress on the Beef Industry

The most obvious potential for economic losses to the industry due to heat stress results from decreases in animal performance.   A study by St. Pierre et al. (2003) quantified economic losses due to decreased performance, including reduced feed intake, growth and reproduction, as well as increased mortality for beef cows and finishing calves. They concluded that annual losses to the beef industry averaged approximately $369 million. At today's market prices, this amount would likely be even higher.

 Today's consumers have begun to take a greater interest in how their food is produced and how animals are raised, including actively pursuing this information through technology and social media (Lyles and Calvo-Lorenzo 2014). Although it can require different tools to study and quantify, concern for animal well-being has become not a secondary effect, but an equally strong motivator to understand and mitigate the effects of heat stress (Silanikove 2000; Lyles and Calvo-Lorenzo 2014). When animals are not confined, they are wholly subjected to the environment where management interventions for heat stress can be difficult. Animals raised in confinement are typically viewed less favorably by consumers, but confined systems can offer easy access for implementation of management interventions to mitigate heat stress (i.e. sprinkler systems, water cooling strategies, etc.). Generating creative solutions for the mitigation of heat stress in extensive beef cow herd systems may involve thinking beyond management interventions to discover viable solutions to decrease animal well-being concerns related to heat stress for extensive beef production systems.

Management Interventions

There are a variety of management interventions that work well for heat stress abatement. In brief, these include:

Shade: Shade provided by trees, buildings, or sunshades provides animals with the means to reduce solar radiation by providing a shield from direct sunlight, and can reduce the radiant heat load by 30% or more (Blackshaw and Blackshaw 1994). Shading feed and water can also be beneficial, especially for British and European breeds of cattle (Blackshaw and Blackshaw 1994).

Air Flow: In the dairy industry, fans are often utilized to enhance evaporative cooling by increasing airflow.   While fans can be effective mitigation tools by themselves, Seath and Miller (1948) showed that wetting cows combined with air movement from fans increased cooling even further. Air flow can also be effectively utilized by being cognizant of air flow when cattle group around feed and water sources, shelter within barns or other buildings, and gather underneath shade structures when space is limited.

Drinking Water: When hot conditions are present, availability of high-quality water (Finch 1985) and adequate bunk space becomes critical to ensure that cattle consume enough water to facilitate evaporative cooling (Mader 2003). The bunk space requirement for water may increase by a factor of three during extreme heat episodes (Mader et al. 1997). Increased consumption (Lofgreen et al. 1975) and decreased performance can occur when water temperatures are elevated (Ittner et al. 1954; Bond and McDowell 1972), and increased water temperature can affect the ability of animals to thermoregulate (Beede and Collier 1986). When considering water sources for the cowherd, the availability of high-quality water can sometimes become more challenging during drought conditions. Animals that are provided low-quality water sources can exhibit decreased performance, likely due to decreased water palatability and water intake (Lardner et al. 2005).

Sprinkling/misting: Wetting an animal's hide is a management tool that can enhance evaporative cooling (Morrison et al. 1973). Misting of animals has been shown to decrease rectal temperatures and lower respiration rates, both of which can be used to evaluate heat stress (Mitlohner et al. 2001). However, Mitlohner et al. (2001) concluded that shade was more effective in mitigating the negative impacts of heat stress on performance and misting was largely ineffective in achieving these goals. Sprinkling may be more effective than misting, because misting can add to humidity, whereas the larger water droplet size from sprinkling makes contact with animal's skin and enhances evaporative cooling. Sprinkling the ground can also be effective at mitigating heat stress by reducing the temperature of the floor in which cattle are in constant contact (via standing or lying) (Davis et al. 2002; Mader 2003).

Transportation: Whenever possible, the transportation of cattle during periods of high heat should be avoided. If they must be transported, it should occur in the evening or early morning when it is cooler. Heat can build up very rapidly inside a stationary trailer, so cattle should be loaded and unloaded promptly to avoid long periods of time in a stationary vehicle (Ag Guide, 2010).

Processing: Processing cattle should be avoided during periods of intense heat. When it is hot outside, it is best to work cattle in the early morning when they are the coolest. Avoid processing during the day or evening hours, because it can elevate body temperature by as much as three degrees (Osborne 2003).

Feeding Strategies: Numerous studies have evaluated the effectiveness of different feeding strategies to cope with heat stress in animals. These strategies included restricted feeding regimens, shifting feeding times, or alteration of diet content (such as increasing levels of roughage in the diet). In all of these studies, the goal is to decrease metabolic heat load or to shift intake times so that the peak metabolic heat load does not occur at the same time as the peak climatic heat load (Mader 2003).
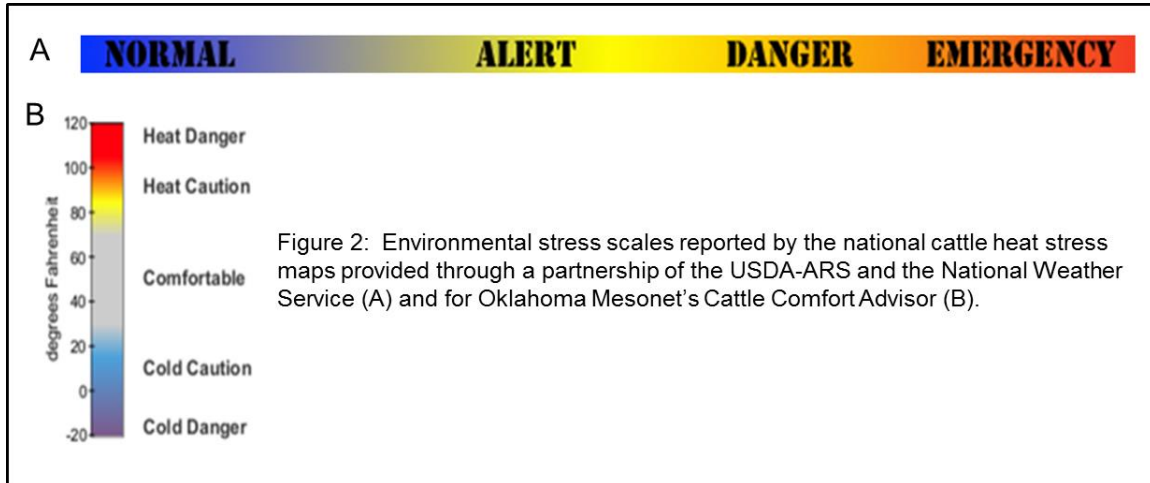
Decision support tools: At the current time, there are a variety of decision support tools available to help identify environmental conditions when management interventions to mitigate heat stress should be initiated. The Oklahoma Mesonet publishes the Cattle Comfort Index, which can be reached through this link, but is currently only available for producers within Oklahoma. Thermal stress level categories for the Mesonet Cattle Comfort Advisor are reported as degrees Fahrenheit; however, the values do not represent exact temperatures. They do represent the approximate temperature an animal is experiencing physiologically. Table 1 outlines the cattle comfort categories utilized in the tool, which are based on the Comprehensive Climate Index categories outlined by Mader et al. (2010).

Table 1. The Oklahoma Mesonet Cattle Comfort Advisor cattle comfort categories.

Mesonet Cattle Comfort Categories	Comprehensive Climate Index Categories[a]	Impacts	Cattle Comfort Index (˚C)	Cattle Comfort Index (˚F)
Heat Danger	Hot conditions: Extreme danger	Animal deaths may exceed 5%	>40	>105
Heat Caution	Hot conditions: Moderate to Severe	Decreased production, 20% or more Reduced conception, as low as 0%	30 to 40	85 to 105
Comfortable	Mild conditions		-10 to 30	15 to 85
Cold Caution	Cold conditions: Moderate to Severe	18-36% increase in dry matter intake	-10 to -30	15 to -20
Cold Danger	Cold conditions: Extreme danger		<-30	<-20

[a]based on Mader et al. 2010

National cattle heat stress forecasts can also be obtained through this site, which are produced as a partnership of USDA-ARS and the National Weather Service (Figure 2).

Figure 2: Environmental stress scales reported by the national cattle heat stress maps provided through a partnership of the USDA-ARS and the National Weather Service (A) and for Oklahoma Mesonet's Cattle Comfort Advisor (B).

Addressing Heat Stress in the Cowherd

Genetic selection tools have been utilized to make tremendous changes in the performance of beef cattle in the past few decades. The exploitation of genetics to improve heat tolerance is one potential solution to improve the well-being of beef cows. The majority of heat stress genetics research that has been conducted in cattle utilizes dairy cattle rather than beef cattle, likely because of the abundance of production records and accessibility of phenotypic data relative to beef cattle. Most of the heat stress studies in beef cattle have been performed in the feedlot, where animals are in a more confined setting. While heat stress is typically less for grazing cattle due to the inherent availability of shade (commonly from trees) and lower heat load in grassy areas as compared to the darker colored dirt floor of feedlot pens, there are still opportunities to increase the ability of cattle on pasture to cope with heat stress through genetics. The use of genetics to improve thermotolerance in the cowherd would have the added benefit of producing heat tolerant animals which, later in the beef value chain, would also benefit stocker and feedlot operators. There are three primary areas where research has examined the impact of genetics on heat tolerance in the cowherd: mating systems, evaluation of plasticity in response to environment (commonly called genetic by environment interactions, or GxE), and the identification of animals that are resilient and/or adaptable to particular environments through either traditional genetic approaches or utilization of genomic technologies.

Mating Systems

Bos taurus cattle (which includes all the major British and European cattle breeds utilized in the US) and *Bos taurus* x *Bos indicus* cattle perform better than *Bos indicus* cattle under ideal climates and nutritional planes (Frisch and Vercoe 1977). That relationship can change when the environment becomes less ideal, and it is a well-known fact that *Bos indicus* cattle are adapted to environments with high heat and humidity. *Bos indicus* cattle produce less heat

internally (Gaughan et al. 1999), likely because of their lower metabolic rates due to slower growth rates and lower levels of milk production (Hansen 2004). They also have an increased capacity for heat loss to the environment (Hansen 2004), which is aided by the properties of their skin (size and abundance of sweat glands). Additionally, they have lower maintenance (Reid et al. 1991) and lower visceral organ mass (Swett et al. 1961). These advantages in response to heat stress can be seen in a variety of ways. A study by Gaughan et al. (1999) showed that rectal temperatures of Hereford animals were initially higher and that temperature increased steadily throughout the day (the THI was between 75 and 84) as compared to Brahman animals, whose temperatures were lower initially and actually decreased throughout the day. The same study also revealed a higher sweating rate for Brahman as compared to Hereford during mid-day. One of the most important differences is in embryo development, which can affect reproductive rate. Short-term exposure of embryos to elevated temperatures has been shown to cause severe reductions in development for Angus and Holstein as compared to Brahman and Romosinuano embryos (Paula-Lopes et al. 2003; Hernandez-Ceron et al. 2004).

One possible way to capitalize on the superiority of *Bos indicus* cattle or tropically-adapted taurine cattle is to utilize crossbred cows within the cowherd. Research in feedlot steers indicates that Brahman x English crossbred animals and straightbred Brahman animals perform similarly (and superior to straightbred Angus) with regard to panting scores, even when the heat load is very high (Gaughan 2009). Adapted breed genetics can be incorporated into the cowherd and terminal sires can be utilized to ensure that marketed feeder cattle meet market targets for growth and quality grade. The added bonus of this scenario is the ability to capitalize on maternal heterosis in the cowherd, which can provide dramatic improvements in lowly-heritable traits including fertility (Cundiff 1970). A review paper by Thrift et al. (2010) summarizes carcass performance in feeder calves with a variety of adapted and non-adapted sire breeds. Many studies showed similarities between the percent of choice carcasses or marbling score between the different sire breeds. Some studies did indicate significant differences between the two sire breeds, but this effect may have been exacerbated because some of the cowherds were comprised of high-percentage adapted-breed cows. The percentage of adapted breed influence that confers significant heat tolerance benefits is unknown and likely varies between regions and environmental conditions, but it is likely that utilizing some percentage of adapted-breed genetics in crossbred females for the cowherd would still provide some of the advantages of heat tolerance and heterosis while still maintaining acceptable carcass performance in feeder calves.

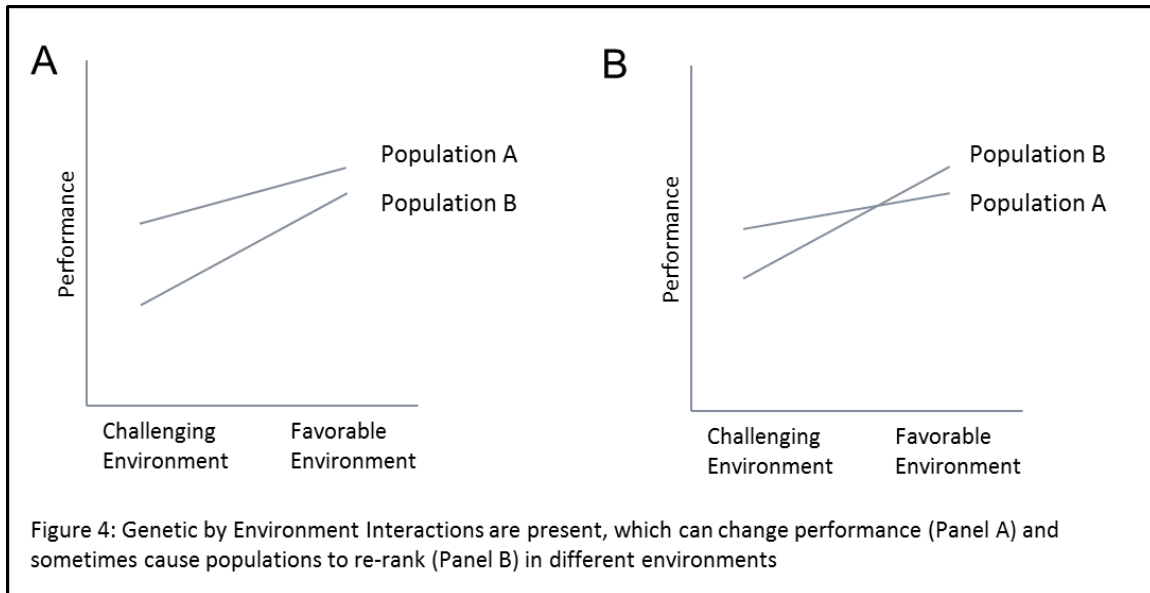## Genetic by Environment Interactions

Any phenotype, or any level of performance for an animal, is a result of both genetics and environment. However, genetics and phenotype can also interact with each other to result in changes in the value of a particular genotype (or breed or population of animals) within different environments. In the classical model of phenotypes, there is no interaction between the genotype and the environment, which is the scenario that we see in Figure 3. In this figure, there are two populations, A and B, which are utilized in two different environments. The genotype effect (in green) shows that population A is superior in performance to population B,

Figure 3: No Genetic by Environment Interactions
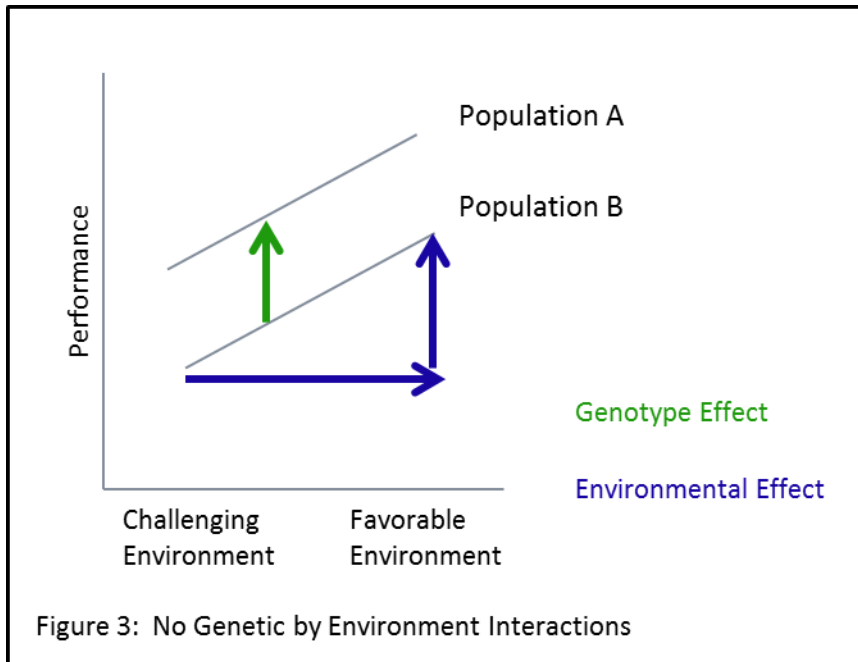
regardless of the environment (in blue). There is no GxE because the relationship between population A vs. B is the same in both environments (the effect of genotype is the same). In contrast, Figure 4 (Panel A) shows a genetic by environment interaction. Population B is sensitive to the environment, and as the environment improves, the performance in population B improves dramatically. Population A is less sensitive to the environment, and performance improves as the environment becomes more favorable, but not to the same degree as population B. This interaction between genetics and environment does not change the superiority of population A in all environments, but does change the degree of that superiority, or the scale, as the environment becomes more favorable. In some cases, the GxE will be large enough to result in a re-ranking between two different populations when the environment changes, as is shown in panel B of Figure 4. Population A is superior in the challenging environment, but is less sensitive to the environment, while population B, which is very sensitive to the increase in favorable characteristics in the environment, performs the best within the favorable environment. In this case, there is a change in both the scale of the difference between the two populations and the rank due to GxE.

When one refers to GxE in a single animal, it is sometimes called plasticity (Pigliucci 2005), which is defined as the sensitivity of an animal to a particular environment. Practical evaluation of environmental sensitivity is possible through the use of reaction norms (Kolmodin and Bjima 2004). Reaction norms employ regression lines to evaluate the level of production (the intercept) and the responsiveness (slope) of an animal to an environment (Schaeffer 2004). Environments can be evaluated and ranked according to the THI, elevation, and/or average herd production levels (Schaeffer 2004). A single animal could be evaluated for performance in many different environments, but a simpler approach is to evaluate a sire utilizing progeny data collected from many different environments and herds (Maricle 2008; Hayes et al. 2009).

Figure 4: Genetic by Environment Interactions are present, which can change performance (Panel A) and sometimes cause populations to re-rank (Panel B) in different environments

This approach has been utilized in both beef and dairy studies. Hayes et al. (2009) demonstrated that there were inherent differences between dairy sires when examined over a scale of THI or herd average daily milk production levels. The sire that was most sensitive to the environment showed a 3 kg decrease in average daily milk production of daughters as the THI increased from 60 to 90, whereas the least sensitive remained very stable across all THI values. The authors also reported that sires re-ranked in terms of average daily milk yield of daughters within herds with different management (as reflected by ranking the average daily milk production values). Their results showed that some sires superior in herds with low average daily milk production and less sensitive to the environment were outperformed by other sires in herds where the average daily milk production was high (similar to Figure 4 Panel B). Another study (Maricle 2008) utilized reaction norms to investigate the sensitivity of animals across environments in Angus cattle and found that bulls differ in progeny performance across different environments (in this case, herd average performance). They also concluded that reaction norms might be a useful tool to rank bulls that will be utilized across diverse environments and diverse management systems. In addition, breeding values can be estimated using this information (Maricle 2008), presenting a means for producers to gauge this variability. It can also be useful in genomic analyses (Hayes et al. 2009), which paves the way for this information to enhance EPD prediction through the use of genomic-enhanced EPDs. Given the fact that, currently, most national cattle evaluations are performed within an entire breed where data is collected on cattle within a wide variety of environments, there is potential to identify sires that are very stable across environments (have a regression line with a flat slope) so that they can be employed in herds with less intensive management or a more unfavorable THI.

Genetic Selection for Heat Tolerance

The goal of any selection program for heat tolerance must be to develop cattle that can perform in challenging environments while maintaining high levels of productivity and carcass performance (Scharf et al. 2010). Simulated dairy production data has suggested that it may be

more effective to select for heat tolerance within a high milk-producing breed than it would be to select for high milk production within a breed that is highly adapted to hot climates, due to the increased number of generations for the adapted breed to reach comparable levels of milk production (Nardone and Valenti 2000). Although this result may be influenced by the fact that milk production heritability estimates are generally lower than estimates of heritability for heat tolerance, it does indicate that selection for heat tolerance could be an efficient way to increase adaptability and resilience in high producing animals.

Heat tolerance is a heritable trait (Ravagnolo and Misztal 2000), so genetic selection can be utilized to increase heat tolerance, provided that the phenotypes and tools exist to make these selection decisions. As with any genetics study, it is important to accurately define phenotypes. Two common phenotypes in the literature include respiration rate, measured as breaths per minute, and body temperature regulation. Heritability estimates of respiration rate range from approximately 0.76 to 0.84 (Seath and Miller 1947). Because respiration rate is fairly labor intensive to collect, body temperature regulation has been the preferred method for studies of heat tolerance. Body temperature regulation heritability estimates range from 0.11 to 0.68 (Burrow 2001; Da Silva 1973; Dikmen et al. 2012; Mackinnon et al. 1991; Seath and Miller 1947; Turner 1983; Howard et al. 2014). These phenotypes can be collected using body temperature probes either in the ear (tympanic), rectally, or intravaginally, through surface body temperatures, or internal body temperatures collected utilizing rumen temperature boluses.

A study completed by Ravagnolo and Misztal (2000) in dairy cattle separated additive genetic variance (the type of genetic variance we select for when we use EPDs) into generic additive genetic variance and additive genetic variation for heat tolerance. The variance attributable to heat tolerance was zero when THI was approximately 72, but increased as the THI increased, until it was approximately equal to the generic additive variance at THI of 88-92. These results demonstrate that producers could select for heat tolerance, especially in environments where the THI is high. Ravagnolo and Misztal (2000) also showed that the genetic correlations between breeding values (a breeding value is the EPDx2) were 1 (meaning perfect concordance) at THI 68-74. As the THI increased beyond 74, the genetic correlation between the breeding value at low THI vs. the breeding value estimated at a higher THI dropped steadily until it reached a correlation of approximately 0.6 when the THI was 92. This indicates that genetic merit of sires exhibited re-ranking as the THI increased, and production records produced at low THI were less accurate for prediction of genetic merit in environments with high THI.

Given the implications of decreased EPD accuracy in environments with varying THI, it is logical to explore selection tools that can be utilized in conjunction with EPDs to identify animals that are particularly well-adapted to an environment. Cattle that have short, sleek hair coats can regulate their body temperatures better during periods of heat stress (Dikmen et al. 2008). A study by Gray et al. (2011) examined use of hair shedding scores to evaluate whether the ability of a cow to shed its winter hair coat influences productivity in warm environments. Hair shedding has been shown to be a heritable trait, with estimates ranging from 0.35 to 0.63 (Turner and Schleger 1960; Gray et al. 2011). Gray et al. (2011) showed that hair shedding impacts 205 day adjusted weaning weights, and lower scoring cows (meaning they had shed

greater than 50% of their hair coat before June 1) produced calves which weighed approximately 11 kg more at weaning than those cows that did not shed their coat as quickly. The earlier coats were shed (with March as the first month in the analysis), the higher the adjusted weaning weights. Shedding scores exhibit a moderate genetic correlation with 205 day adjusted weaning weights (-0.58; Gray et al. 2011), indicating that as cattle shed their hair more readily, weaning weight tends to increase. Hair shedding has not been shown to effect body condition scores in cows (Gray et al. 2011).

Genes Involved in Heat Stress Responses

Thermotolerance appears to be a quantitative trait influenced by many regions of the genome, and genomics studies have identified regions of the genome that appear to be important for regulation of body temperature in both beef and dairy cattle (Dikmen et al. 2013; Howard et al. 2014; Hayes et al. 2009). Additionally, some breeds may be segregating for genes of large effect on heat tolerance. One study in Senepol has mapped a "slick hair gene" to chromosome 20 (Mariasegaram et al. 2007) that appears to be present in Spanish criollo breeds (Olson et al. 2003) and has been introgressed into other breeds like Holstein through crossbreeding (Dikmen et al. 2008).   Howard et al. (2014) showed that only a small number of the most influential (top 5%) genomic regions involved in predicting body temperature regulation during the summer and winter were shared between both traits (9%), which means that advancements in selection for both heat and cold tolerance traits is possible while not necessarily sacrificing performance in either trait. The genes and/or pathways and functions identified in genome-wide association studies are outlined in Table 2 below. As with any association analysis, it is important to verify these associations and results with additional studies. Another way to increase confidence in associations of genomic regions with phenotypes is to examine their connections with biological pathways that impact cell function.

While we typically think of heat stress in the beef industry on the level of the whole animal, it may be helpful to also consider the impacts of heat stress on a cellular level. While the basis for thermotolerance has not been elucidated on a molecular basis, many of the direct effects on cells appear to be caused by heat shock (Hansen 2014). While there are undoubtedly many factors and pathways that influence thermotolerance in beef cattle, several factors that have been implicated in cellular processes regulating thermotolerance include peroxisome proliferator-activated receptor alpha (PPARα; Fang et al. 2014), heat shock proteins (Hansen 1999; 2014), glutathione (Hansen 1999), and the insulin-like growth factor 1 system (Hansen 2014). While space does not permit discussing each protein product individually, heat shock proteins have been moderately well-studied in the context of bovine embryo development because reproduction is very easily disrupted by heat stress (Hansen 2014), so their function will be reviewed briefly below.

Table 2. List of pathways and/or genes that have been identified in genomic studies as potential candidate genes for body temperature regulation.

Pathway/Function	Gene(s)	Publication
Cellular response to stress	STAC, WRNIP1, MLH1, RIPK1, SMC6, GEM1	Howard et al. 2014
Response to heat	STAC	Howard et al. 2014
Gap junction	TUBB2A, TUBB2B	Howard et al. 2014
Cellular response to stress	CCNG, TNRC6A	Howard et al. 2014
Apoptosis	FGD3, G2E3, RASA1, CSTB, DAPK1, MLH1, RIPK1, SERPINB9, HMGB1	Howard et al. 2014
Ion transport	CACNG3, CLCN4, PRKCB, TRPC5, KCNS3, SLC22A23, TRPC4	Howard et al. 2014
Thyriod hormone regulation	DIO2	Howard et al. 2014
Body weight and feed intake	NBEA	Howard et al. 2014
Heat shock protein response	HSPH1, TRAP1	Howard et al. 2014
Respiration	ITGA9	Howard et al. 2014
Calcium ion and protein binding	NCAD	Dikmen et al. 2012
Protein ubiquitination	RFWD12, KBTBD2	Dikmen et al. 2012
	CEP170, PLD5	Dikmen et al. 2012
Thyriod hormone regulation	SLCO1C1	Dikmen et al. 2012
Insulin signaling	PDE3A	Dikmen et al. 2012
RNA metabolism	LSM5, SNORD14, SNORA19, U1, SCARNA3	Dikmen et al. 2012
Transaminase activity	GOT1	Dikmen et al. 2012
Apoptosis, cell signaling	FGF4	Hayes et al., 2009
	XM_865508 (G3PD-like)	Hayes et al., 2009

Because most diagrams illustrating DNA and proteins are usually 2D, it is easy to forget that all of these molecules operate in a 3-dimensional space, and their structure, which facilitates how they interact with other molecules, is vitally important. High temperatures and other stresses inhibit proteins from forming the appropriate structure and sometimes denature, or unfold, the structures of proteins that have already formed. The unfolding of proteins can expose areas that would not normally interact, which results in them interacting with each other and aggregating, which can ultimately kill a cell. When a cell undergoes thermal stress, the expression of heat shock proteins increases in an effort to stabilize proteins and repair proteins that have denatured. They also act as chaperones, which can help transport proteins to the correct location in the cell. Heat shock proteins are sometimes called stress proteins, and they are found in all organisms and all types of cells within an organism (Li and Srivastava 2004). They are a vital player in protecting cells against cell death (known as apoptosis, see Table 2) and stress (Li and Srivastava 2004). It has been noted that thermotolerance can be induced by exposing cells to a mild heat shock that will induce production of heat shock proteins and other cellular products that can then protect cells from a subsequent severe heat shock (Al-Katanani and Hansen 2002). An extensive list of heat shock protein genes and their products in humans and mice can be found in Li and Srivastava (2004). Although many studies have been performed that examine the role of heat shock proteins in bovine embryo development, considerably less work has been done to determine the role of these classes of proteins in other types of cells and how they may affect beef cattle production and thermotolerance.

If the genes and process involved in conferring heat tolerance in beef cattle are identified, three different approaches could be taken to confer their benefits within a population: selection for favorable variation in those genes within a breed or population, direct introduction of those genes through crossbreeding, or, in the future, direct editing of the genome.

Genetic Antagonisms

Genetic antagonisms exist between many economically important production traits, and can be generally defined as undesirable genetic relationships between traits. The genetic relationship between traits is commonly described by the genetic correlation, which can be any value between -1 and 1, with a value of 0 indicating that they are not correlated, or have no relationship. The sign (- or +) does not describe whether the relationship is favorable or not, but simply describes the relationship between the two traits. Therefore, unfavorable genetic correlations, or genetic antagonisms, can exist when genetic correlations are positive (as weaning weight increases, birth weight tends to increase) or negative (as birth weight goes up, calving ease tends to go down).

While few studies have looked at genetic antagonisms with production traits and heat tolerance in beef cattle, these relationships have been the focus of several dairy studies. Ravagnolo and Misztal (2000) showed that the genetic correlation between milk production and heat tolerance in dairy cattle is approximately -0.3. Another study (Ravagnolo and Misztal 2002) indicated that the genetic correlation for non-return rate at 90 days (a measure of fertility) and heat tolerance is even greater (-0.95). These genetic correlations indicate that as animals are selected for higher performance in milk production or especially reproduction, their heat tolerance is reduced. However, these relationships are not completely antagonistic (-1), and the correlation appears to be fairly small in some cases (milk production), which indicates that we can effectively select for improvements in both traits if we consider both traits in selection decisions.

It is highly probable that similar types of unfavorable genetic correlations exist within beef cattle populations. These genetic antagonisms complicate selection for desirable traits, because selection for desirable performance in one trait can lead to unintended negative consequences in other traits. Data in dairy cattle would suggest that continued selection for increased performance without regard to environmental adaptability actually reduces heat tolerance (Ravagnolo and Misztal 2000; Dikmen et al. 2012). Because of these antagonisms, one of the most viable tools for selection on overall genetic merit, while increasing or maintaining heat tolerance, would likely be a selection index. A selection index would allow incorporation of measures on heat tolerance and also traits of interest in production systems (even those that may have unfavorable genetic correlations) with the proper weighting for each trait. The end product would facilitate multi-trait selection decisions with the potential to improve both heat tolerance and economically important production traits.

Conclusions

Heat stress is a multi-faceted challenge that can be mitigated utilizing a variety of available tools and resources. Heat stress not only causes production losses, but is also an important animal well-being issue that merits consideration in management and breeding programs. Management interventions should be utilized wherever possible, but may be arduous within the cowherd when compared to animals in later stages of the production cycle. One solution for beef producers is to consider genetic approaches for improving heat tolerance in cows including utilizing mating systems and selection for novel phenotypes, such as hair shedding. Scientific research demonstrates that heat tolerance is heritable and is a significant factor in re-ranking of individuals between environments. Because of this, genetic variation could be exploited to further increase thermotolerance within the beef industry and expand the set of tools available to producers who operate in adverse environments.   The broadest challenge with utilization of genetic selection will be defining heat tolerance phenotypes that can be regularly and easily collected within the industry.

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