Heat stress in dairy cattle with emphasis on milk production and feed and water intake habits. Review

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Abstract:

The negative impact of heat stress (HS) in dairy cattle results in considerable economic losses at world level, as it reduces the milk production, reproductive efficiency, and productive life in the cows. In addition, the continuous genetic improvement results in highly productive cows, which are, however, less tolerant to HS because they produce greater metabolic heat. This, together with global warming, will turn HS into a hard-to-control challenge for the daily industry. In response dependent on the degree of HS, the dairy cattle carry out a series of physiological, metabolic and behavioral adjustments as thermoregulatory mechanisms for removing excess body heat and reducing the endogenous production of body heat, in order to maintain the normothermia. However, fertility and milk secretion decrease as a direct effect of hyperthermia and an indirect effect of lower dietary nutrient intake. Food and water intake are closely associated to the reduction of the productivity of dairy cattle exposed to HS. Notably, the impact of HS on productivity of dairy cattle varies among breeds, among which *Bos taurus*, particularly the Holstein breed, are less tolerant to HS. The identification of genes associated to thermotolerance utilized in selection programs using genetic markers to breed high milk-producing cows in warm climates is currently being studied. Therefore,

the purpose of this review is to carry out a comprehensive analysis of the effects of HS on milk production, activation of thermoregulatory mechanisms and feed intake behavior in dairy cattle.

Introduction

Heat stress (HS) is defined as the sum of external environmental forces that act on the animal causing an increase in body temperature, and the activation of physiological and behavioral adjustments in the first place[1]. In dairy cattle, these adjustments represent adaptation mechanisms activated to attempt of maintaining a balanced body homeostasis[2]. As global warming continues to augment, the prevalence of HS in dairy cattle will also increase in frequency, duration, and severity[3,4]. Therefore, mitigating the negative effects of HS on the productivity of dairy herds has become a challenge for the dairy industry worldwide[5].

The HS problem is higher in warm geographical areas where it can start during the late spring and extend beyond the summer, and consequently low fertility and milk production in cows can be prolonged until the fall[2,6]. The magnitude of the HS is determined by the combined effects among ambient temperature (AT), relative humidity (RH), solar radiation, and wind speed[1,2]. In the particular case of dairy cattle, the temperature-humidity index (THI) is estimated based on AT and RH, first, in order to determine the degree of HS to which the animals are exposed and, secondly, for the purpose of making herd management decisions during the hot season[1,7]. Bouraoui *et al*[5] reported that milk production diminished by 21 % when the THI increased from 68 to 78 units, or when the AT exceeded 27 °C, regardless of the age or lactation stage.

The negative impact of HS on fertility and milk production has given rise to much research in the last 50 years, and today a deep knowledge of the physiological, metabolic, endocrine, and molecular mechanisms has been attained, leading to a reduction of the productivity of the cattle resulting from HS. However, several of these mechanisms are triggered by two key factors: the reduction in feed intake and the increase in water intake[8]. In fact, milk

production is closely related to the dry matter (DM) and water intake in milk producing cows subjected to chronic HS[9]. The first physiological and intake behavior adjustments in dairy cattle are considered to be homeostatic mechanisms[8], whose main purpose is to increase evaporative heat losses (i.e., breath and sweat) and to reduce the production of endogenous heat in order to maintain normothermia[10-12]. It should be noted that the genotype plays an important role in defining the impact of HS on the dairy cattle production[13,14], among which Holstein is one of the most susceptible breeds, while the pure native cattle of warm regions, or their cross with introduced breeds, are more tolerant[15-18]. Thus, the objective of the present review is to carry out a comprehensive analysis of the effects of HS on milk production, activation of thermoregulatory mechanisms, and intake behavior of dairy cattle.

Climate change and the future of dairy production

The production of greenhouse gases such as steam, carbon dioxide, methane, and nitrous oxide, among others, alter the permeability of the atmosphere, letting the sun rays through while preventing the release of the heat radiated by the Earth's surface[19]. Thus, these gases cause global warming and, therefore, climate change, which tends to increase the amount of land surface with warm climate and, in extreme cases, desertification[20]. Studies by climatologists suggest that the AT may increase by more than 2 °C by the year 2050[19].

Today, the profitability of the dairy industry is endangered by the climate change, which has reduced the availability of natural resources, pasturelands, and production of grains and fodder, while it has favored the cattle losses due to natural disasters, as well as the prevalence of parasites and unforeseen diseases[2,21]. The increase of agroecological areas with high AT as a result of climate change has also decreased milk production and increased production costs[8,22]. In fact, HS is expected to increase in severity, duration, and presence in the near future[21]. In the United States of America, economic losses in the dairy industry due to HS were estimated in 897 million dollars[22], and they recently projected economic losses of 0.4 and 1.2 % by 2050 and 2100, respectively, in the dairy basin in the northeast of that country[21]. In Mexico, there are no reports of losses generated by HS in dairy cattle; however, such losses are evident, based on the seasonality of the milk production of dairy basins in warm weather[6,23]. It is worth mentioning that the world food safety is jeopardized by climate change, considering that the demand of meat and milk will increase by 73 and 58 %, respectively, by 2050 in relation to the 2010 production levels[24].

Thermoregulation and metabolic heat production in dairy cattle

Bovines, like any other farm animal, are homeothermal and, therefore, have the ability to maintain a relatively stable internal body temperature regardless of the environmental conditions of their surroundings[25]. In absence of thermal insults or in presence of fever, the body temperature of the dairy cattle ranges between 38.0 and 38.5 °C and is the combined reflex of the balance between environmental heat gains and metabolic heat production in a homeostasis state[1]. In fact, in a thermoneutral environment and without milk production, cows can maintain their normothermia because they use mainly non-evaporative means (conduction, convection, and radiation), which do not entail an increase in the energetic cost associated to thermoregulation[26]. If the rectal temperature (RT) is ≥42 °C, the body homeostasis balance can be disrupted, resulting in the death of the animal[22].

It should be noted that the body temperature is not stable and exhibits a circadian rhythm which varies by approximately 1°C between maximum and minimum temperatures registered through the day[1]. The body temperature reaches its maximum peak between 8 and 10 h after the AT has reached its maximum level; however, dairy cows can adapt to changes in AT and RH throughout the year[27,28]. This is because its thermoneutral zone is very broad, ranging between -0.5 and 20.0 °C[1,2,10]. According to certain studies, the maximum critical AT at which the Holstein cattle can maintain a stable body temperature in the range between 24 and 27° C[29].

On the other hand, the milk synthesis in mammary gland of cows demands a great amount of metabolic activity, and therefore, the endogenous heat production increases in proportion to the level of milk production[25,27]. It should be noted that the genetic improvement of dairy cattle has focused on increasing the milk production parameters, which has turn cows into metabolic heat producing machines, making them highly susceptible to warm climates[17,30,31]. Cows that produce 18 to 31 L/day generate 28 to 48 % more metabolic heat than dry cows[32]. A cow weighing 700 kg and producing 60 kg/d of milk generates approximately 44,171 kcal of heat per day; the same cow produces 25,782 kcal of heat per day at the end of the lactation period (20 kg/d)[27]. Dairy cows that convert feed into milk more efficiently produce less metabolic heat and have a lower skin temperature[33]. Thus, cows with a high milk production will have to make a greater effort in order to regulate their internal temperature under thermoneutral conditions, while under AT conditions they will be less tolerant to HS.

Physiological thermoregulation of dairy cattle under heat stress

High AT´s combined with a high percentage of RH further limit the ability of dairy cows to dissipate heat, and, in consequence, they experience HS and the activation of physiological thermoregulation mechanisms for dispelling the heat load[2,5,26]. Certain climate indexes have been developed in order to predict the level of HS in dairy cattle; however, the THI proposed by Hahn[34] is the most commonly used worldwide. This index combines the climate values of AT and RH into an equation (THI = [0.81 × AT] + [RH / 100] * [AT − 14.4] + 46.4), and dairy cows are considered to begin to suffer from HS when they exhibit 72 units[1]. Armstrong[35] classified HS into three types according to the THI: mild (72 to 78 units), moderate (79 to 89 units), and severe (90 to 98 units) (Figure 1).

However, recent studies[11,36] have reported that a THI of 68 is already a critical value at which dairy cows will begin to exhibit symptoms of HS. Another study[37] found HS symptoms in highly producing dairy cows when the daily average THI was above 68 units or when the minimum THI was above 65 units. The climate in which the dairy cattle develop also plays an important role in defining the onset of HS based on the THI, given that under tropical conditions the negative effects of HS began at a THI > 70 units[1], and at a THI >60 under temperate conditions[9]. This suggests that the pressure caused by genetic selection to improve dairy production counters tolerance to HS in dairy cattle[17].

An imminent response to presence of HS in dairy cattle is an increase in the RT due to excessive body heat accumulation from the environment. This activates body heat losses through both evaporative and non-evaporative means[6,10,26]. However, the activation sequence of physiological thermoregulation mechanisms will depend upon the HS type (acute or chronic) and degree (slight, moderate, or severe)[11]. A more severe or more chronic HS will determine the reduction of body heat loss through non-evaporative means, while evaporative heat losses due to sweat and panting will increase considerably[8]. Maia et al[26] observed 85 % body heat losses due to skin evaporation, and only 15 % through the respiratory tract in Holstein cows exposed to AT >30 ℃.

Figure 1: Classification of heat stress according to the temperature-humidity index (THI) in dairy cattle (based on Armstrong, 1994).
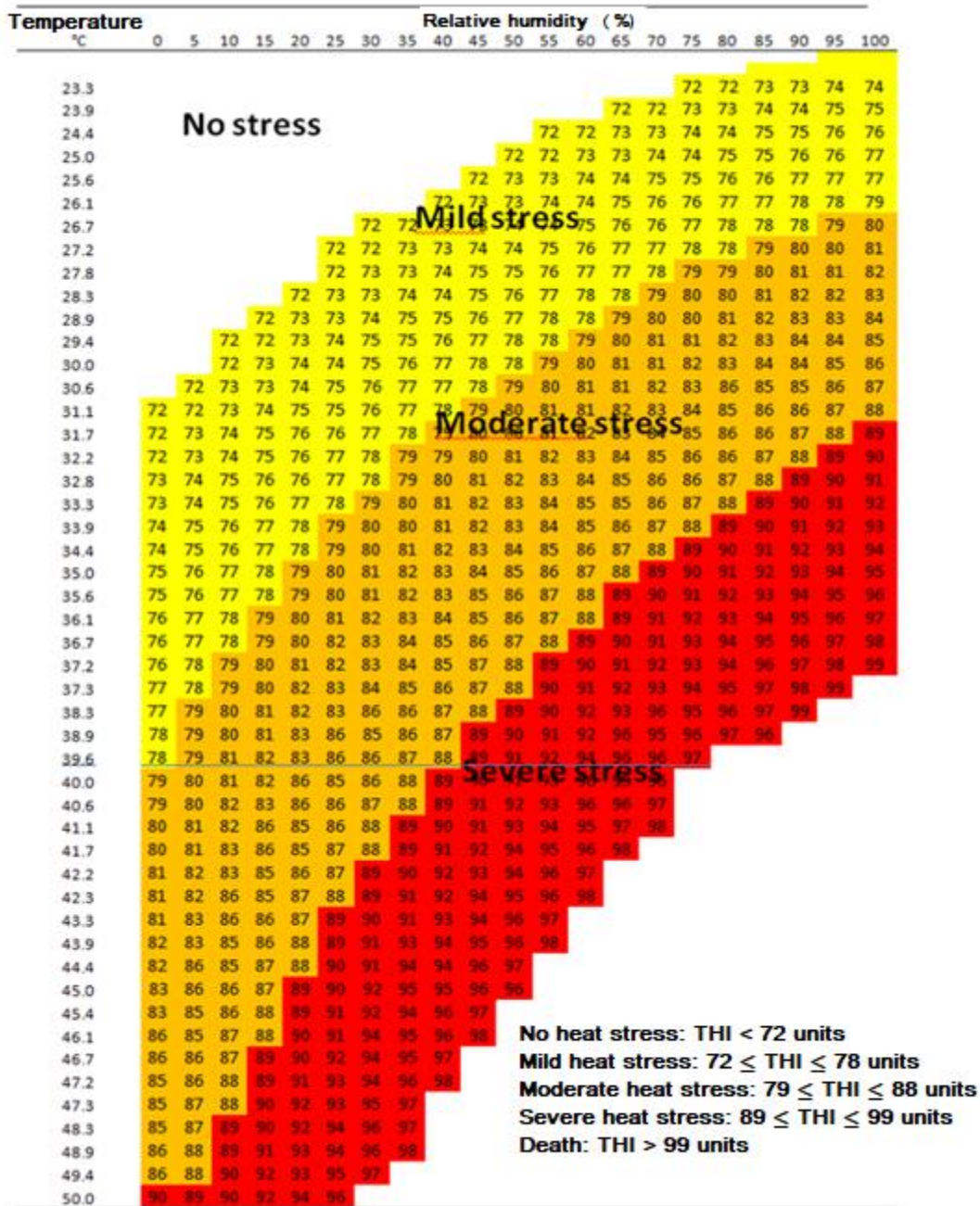
A high RH reduces the effectiveness of body heat losses through evaporative means[10]. The results obtained by Bonmanova *et al*[7] showed that RH was the limiting factor for HS in humid climates, while in dry climates the limiting factor was AT. Furthermore, the activation of these evaporative thermoregulatory mechanisms entails additional energy expenditure unlike with non-evaporative mechanisms, whereby there is a greater energetic expenditure for maintenance in heat-stressed dairy cows. An increased respiratory frequency (RF)

requires an additional energy expenditure of 7 to 25 % due to movement of the muscles of the respiratory tract[38], and the water vaporization process through the skin and respiratory tract demands an energy expenditure of 2.43 J/ml of evaporated water[1]. For this reason, the activation of heat losses through evaporative means is an option for the animal when non-evaporative losses are unable to release the body heat load under HS. In this sense, the RF increases with a THI above 73 units, while the RT increases with a THI >80 units[39].

On the other hand, diurnal variations in climatic conditions and the changes in animal behavior improve the physiological thermoregulatory capacity of heat-stressed dairy cattle. An AT ≤21°C during the nighttime, with a duration of 3 to 6 h, favors the total body heat loss accumulated in the daytime, as the animal promotes a redistribution of blood flow toward the skin, allowing an efficient release of the body heat load throughout non-evaporative means (radiation and convection)[40]. A wind speed between 1.8 and 2.8 m/s also promotes body heat losses through the skin[28]. Likewise, cows adopt a standing position in order to reduce the body area exposed to sun rays and the heat gain from contact with the ground[41]. When under HS, they also reduce their feed intake per day and eat at those times of the day when AT is lowest[8]. This allows their daily water intake to increase[42].

Heat stress and feed intake

The reduction in milk production by heat stressed dairy cattle has traditionally been associated to a reduction in feed intake[8], and the degree at which it diminishes depends on the duration and severity of the prevalent HS, as well as on the adaptation level of the breed[14,18,25]. Thus, the AT has an inverse relationship with DM intake under chronic HS, while, under acute HS, feedd intake is rapidly reduced one day after the exposure[43]. In fact, feed intake begins to decline at an AT of 26 °C in lactating cows[1], and its reduction can reach up to 40 % at an AT≥40 °C[44].

Given that the presence of HS is determined based on the estimation of THI in dairy cattle and that this climatic parameter is easier to obtain than a daily measurement of feed intake, certain researchers opted to establish the association between them, and results showed a reduction of 0.51 kg in DM intake per unit which increases THI within the range of 72 to 84 units[8]. Another study found that the variation in minimum THI has a greater association with the changes in feed intake than the variation in maximum THI[45].

Besides the reduction in feed intake, heat stressed cows also modify their feed intake schedules in order to reduce their endogenous heat production during the hottest hours of the day. Metabolic heat associated to ruminal fermentation represents 3 to 8 % of the total

endogenous heat produced by bovines, depending on the dietary fiber level[12]. Dairy cows have a daily natural feed consumption pattern, being high after receiving fresh diet, as well as in the afternoon and evening[46,47]. However, dairy cattle under HS prefer to eat very early in the morning and at nightfall, as digestion and metabolic heat production reach their peak 3 to 4 hours after feed intake, just before the hottest period of the day[32]. It is worth noting that HS in dairy cattle also impacts the ruminal kinetic of the ingested feed, as it decreases the motility of the gastrointestinal tract, changes the patterns of fermentation and production of volatile fatty acids, and increases the retention time of feed in rumen and its digestibility[38,47].

In order to mitigate the reduction of DM intake and sustain milk production during the warm season of the year, certain cattle breeders modify the dietary chemical composition to increase the energy level, which involves increasing the content of grains and reducing the amount of dietary fiber[12,39]. This nutritional strategy benefits the cattle by allowing them to meet their nutritional requirements with a lower feed intake. However, the modification in the dietary ingredients can have negative consequences if too many adjustments are made; for instance, a high blood urea concentration due to a high protein digestion in rumen increases the RT[48], or a high concentrate diet can contribute to potentiate the acidosis issue generated by HS in cows[12].

Heat stress and water intake

An insufficient availability of drinking water has adverse effects on the productivity and welfare of dairy cattle under any environmental conditions, but it becomes more critical at high AT[42]. Regardless of the climate, lactating cows require larger amounts of water, as both the body and the milk are composed of more than 90 % water[38,49]. Nevertheless, these cows can vary their water intake according to the amount of DM consumed in the diet and daily kilograms of milk produced[50]. A restriction in water intake can reduce milk production by up to 26%, and this reduction can be even greater in HS conditions[51].

Dairy cows satisfy their water requirements from three sources: direct water intake, water from foods, and water derived from the tissue oxidative metabolism[42]. However, the main source of water for cattle is direct intake under any climate condition (83 %)[49]. Water intake is affected by such factors as: DM intake, milk production, and intake of potassium, sodium, and nitrogen[52]. Cows under thermoneutral conditions can consume 14 to 171 kg/d of water, with a daily average of 82 kg, and, based on the milk production and dietary sodium intake, water intake is estimated to be 4 to 4.5 L/kg of milk produced[42]. On the other hand, a water intake of 146 g per gram of ingested sodium[52] was found in absence of a thermal insult. In

dry cows without heat stress, water intake is significantly lower (15 to 61 L/d)[53], but increases by 27 % with the onset of milk production during the early lactation[54].

Dairy cows can experience severe dehydration when they lose 12 % of their body weight due to lack of water intake; such dehydration can be lethal if the total body water loss reaches approximately 20 %[55]. Given that HS increases water loss in ruminants considerably, its intake at adequate levels becomes critical for dairy cows[54]. In warm areas, water intake can increase between 10 and 20 % during the summer, when even a cow classified as low producing can drink more than 100 L/d[32]. A recent study reported that the water intake can increase by up to 50 % as the THI approaches 80 units [56]. A cow is estimated to increase its water intake by 1.52 kg for each Celsius degree that the AT increases[42]. Furthermore, the time devoted every day to water intake increases from 0.26 to 0.5 h as the THI changes from 56.2 to 73.8 units[57] or the AT increases from 15 to 33 °C[58]. The greater water intake under HS conditions is attributed to an increase in the urine volume (25 %), evaporation through the respiratory tract (panting), and sweating[1], which are thermoregulatory mechanisms that help dissipate excess body heat load in this type of environments[59].

On the other hand, as previously stated, water intakes in dairy cattle are very high under thermoneutral conditions and even higher under HS, which leads this species to have different water intake behaviors compared to other species. Under thermoneutral conditions, Holstein cows with a medium milk production drink water approximately eight times a day, consuming an average of 12.9 L on each occasion[60], while high producing Holstein cows drink water more frequently (12 to 16 times) but consume a smaller amount (5.4 to 6.0 L) on each occasion[61]. In the absence of HS, these cows prefer to drink 97 % of their total daily intake during the daytime, rather than at night[60]. Conversely, when under HS, the water intake behavior among these animals becomes highly variable at AT above 30 °C[62]. This may be due to individual differences in tolerance to heat and, therefore, in milk production. In general, heat stressed cows resort to the water trough more frequently than unstressed cows, but they prefer to drink water at times when solar radiation is at its lowest or absent[63]. The reason for this low water intake behavior during the daytime, particularly during the hottest hours of the day (on three to five occasions), is that cows prefer to remain motionless, rather than gaining heat by seeking this nutrient. Therefore, the construction design of pens or grazing areas is crucial for the cow's decision to taken a drink of water under hot weather.

The water troughs located at a large distance from the feed troughs, particularly when these have no shade, causes that heat stressed cows have to choose whether to move toward the shaded area or toward the water trough after eating[56]. So, it is recommended to strategically distribute water troughs both in pasturelands and pens in order to prevent cows having to walk more than 250 m[32]; likewise, these animals prefer high and long water troughs[64]. The cleanliness and temperature of the water are factors that largely determine intake in sufficient amounts by cows exposed to high AT. Like any other species, dairy cattle avoids drinking

foul-smelling water, being necessary to continually wash the water troughs under any climate[60]. Cows also prefer to drink their warm water (≥24 ºC), rather than cool (15 a 20 ºC) or cold (≤10 ºC), under both thermoneutral[65] and HS[66] conditions. It is noteworthy that this preference of heat stressed cows to drink warm rather than cold water is contradictory, as it has been proven that the cold or cool water intake reduces both RT and RF[67]. Given the importance of this nutrient, it is essential to measure the water intake of dairy cattle, whether heat stressed or not, in order to maintain an optimal milk production and the good health of cows[42,50].

Impact of heat stress on milk production

Dairy cows reach their optimal milk production at a temperature range of 5 to 25 °C, which is considered as the comfort zone for lactating cows[1]. Exposure of cows to ATs above the upper limit of this comfort zone may reduce milk production by 10 to 40 %[38]. However, the impact of HS on milk production depends on the stage of lactation, intensity of the heat, and cow's genetic potential to synthesize milk. Thus, in presence of HS, high producing dairy cows experience a greater reduction in milk production than medium or low producing cows[12,25]. Medium-lactation dairy cows decrease their milk production by 35 % in response to HS, while early-lactation cows reduce it only by 14 %[25]. High-producing dairy cows tend to exhibit a larger bone structure and gastrointestinal tract capacity, which allows them to ingest and digest more food; however, metabolic heat production also increases and reduces their ability to maintain normothermia under HS conditions[1]. In fact, an increase in milk production from 35 to 45 kg/day reduces by 5 °C the AT at which HS begins[68].

Milk production starts to diminish at an AT of 27 °C, regardless of the cow's age or lactation stage[1]; this negative effect becomes evident 24 to 48 h after the onset of any type of HS[43]. A study carried out on Israeli Holstein cows of 3rd and 4th lactation found a reduction of 0.38 kg/cow/day in milk production for every Celsius degree that the AT increased during the summer[69]. As expected, there is a close negative association (r= - 0.76) between the THI and milk production[5]; the same applies to the AT. Therefore, this production parameter decreases by 0.41 kg/cow/day for every unit of THI above 68[40]. Nevertheless, there are studies reporting a lower reduction in milk production (0.2 kg/cow/d) per unit of THI above 72[70]. Variations in milk production level and AT may explain this discrepancy between studies.

Reduction in milk production occurs by direct and indirect effect of HS. Direct effects include adjustments in energy and protein metabolism in order to prioritize the availability of nutrients for the cows' thermoregulation processes instead of sending them to the mammary

gland for milk synthesis[71]. Likewise, HS increases the presence of oxidative stress, which alters the cellular metabolic and molecular activity in the mammary secretory tissue, reducing the cellular efficiency for synthesis of milk components[30]. Indirectly, the mechanism is associated with a reduction in DM intake, since maintenance energy requirements increase as a result of the activation of physiological thermoregulation mechanisms in a scenario where availability of body nutrients is limited due to low feed intake[3,38]. A reduction in the efficiency of energy use for milk production by 30 to 50 % has been reported for dairy cows in warm climates[1].

The HS negatively affects not only milk production but also its composition[56]. A reduction in fat and protein content combined with an increase in somatic cell count (SCC) are results commonly associated to HS[5]. The results of a study contrasting spring thermoneutral conditions *versus* severe summer HS showed that fat (3.58 %) and protein (2.96 %) contents in milk decreased by 30 and 23 %, respectively, during the summer[5]. The same study detected an increase in SCC by 110 % due to summer HS. Another study reported a 40 % decrease in milk fat content of Holstein cows under moderate to severe HS, as well as a 17 % decrease in protein content[1]. Bernabucci *et al*[72] observed a slightly lower casein concentration in milk during the summer compared to winter (2.18 *vs* 2.58 %). The reduction in the casein percentage may account the low cheese production during that season[73].

Adaptive responses of dairy breeds to heat stress

Holstein cattle is the genotype par excellence for the global dairy industry; however, they have little resistance to HS. Genetic improvement programs for this breed have focused on selecting traits associated to increase milk quality and production, whose effects are contrary to their ability to tolerate high AT´s[28]. Thus, the heritability index for milk production in Holstein cows can diminish due to HS and, consequently, the selection response based on this trait may not be as expected in warm climates[17]. In spite of this, Holstein cattle continues to be used in warm regions because it maintains a larger average milk production than other genotypes adapted to the region, mainly in technified and semi-technified production systems[13,18].

Although Holstein cattle has proven to maintain a higher milk production than such breeds as Simmental (20.4 *vs* 28.1 L)[13] and Jersey (26.6 *vs* 34.2 L)[16] under tropical HS conditions, their milk is characterized by having a high SCC and low fat and protein content. In addition, the reduction in milk production as a result of HS is more pronounced in Holstein cows; this is an unmistakable symptom of lower tolerance to high AT´s[13,18]. Therefore, the use of the Holstein breed in warm climates, particularly in tropical and subtropical regions, cannot be

justified based on the milk production level, given that HS conditions reduce the quality of this product and compromise the health and welfare of cows.

The use of animal genetic resources of the region, including native and introduced cattle breeds that are highly adapted to the warm-humid climate[31,74], is recommended for milk production in tropical climates. Some studies also suggest crossbreeding between the Holstein and zebu breeds in order to generate cattle with a dairy genotype tolerant to warm climates[10,15]. Thus, dairy cattle breeds adapted to HS exhibit greater tolerance to these environmental conditions because, phenotypically, they have thinner and less dense hair, as well as a higher density of sweat glands in the skin, which allows them to more easily release their body heat load by convection and radiation[14,75]. In addition, this type of cattle under HS relatively maintain their feed intake and thyroid gland activity, which explains the lower variation in milk production compared to non-adapted cattle[75]. The main breeds used in the Mexican tropics for milk production are Brown Swiss, Jersey, Holstein, Gyr, and Brahman, as well as their crosses; however, other management and feeding factors, along with the climate conditions, lead to a low productive and reproductive efficiency[76].

On the other hand, the cells of HS-adapted cattle activate heat shock transcription factors to coordinate protective mechanisms in response to the thermal insult, including expression of genes, activation of heat shock proteins (HSP), and carbohydrate metabolism[77]. In HS tolerant bovines (*Bos indicus*) compared to HS intolerant cattle (*Bos taurus*), cells exhibit a greater HSP expression (mainly of 70 kDa[78] and 90 kDa[79]) in response to HS, which improves their viability and immune activity[80]. However, it has been proven that dairy cattle mononuclear cells may exhibit an HSP-72 overexpression in response to hyperthermia, which is counter-productive for their immune response and tolerance to heat[81]. This became evident in a study in which mononuclear cells of Holstein and Brown Swiss cattle were cultivated *in vitro* at 39 (normal), 40, 41, 42, and 43 ºC, and results showed that hyperthermia conditions triggered excessive mRNA production for HSP-72 and low DNA synthesis in Brown Swiss cattle compared to Holstein[81]. Contrary to the predictions, these findings suggest that Holstein cattle resists better hyperthermia than Brown Swiss cattle, although the latter can maintain an adequate productive efficiency under HS as long as their thermoregulatory capacity is not compromised and the core temperature does not rise above 40 ºC[81].

Genetic markers associated to thermotolerance in dairy cattle

A large number of studies have focused on identifying the gene expression associated to thermotolerance in HS-adapted dairy cattle, and this information is being utilized to establish

marker-assisted genetic selection programs[82]. Likewise, work is being carried out to identify males expressing thermotolerance genes, which are then selected as sires in order to transmit these characteristics to their offspring[28]. Special attention is being given to the search for these genes in high-producing dairy cattle, given the interest of the dairy industry in having HS tolerant genotypes that will produce large volumes of high quality milk.

In Mexico, there is little research on the identification of genes linked to thermotolerance in dairy cattle. Hernández-Corderos *et al*[83] identified seven genes (*AVPR1A*, Furin, *IGFBP5, IGFBP6, PMCH, PRLR*, and *STAT5B*) associated with milk production in heat-stressed Holstein cattle reared in the Yaqui Valley, Sonora; specifically, a single-nucleotide polymorphism (SNP) within each gene related to the prolactin and somatotropin pathway. Another study[84] reported the identification of six genes associated with milk production and its fat and protein contents (*SFXN1, LOC781028, ANKRD31, LOC100296562, LOC107131388,* and *WDR41*) in a genome-wide association analysis conducted in Holstein cattle reared in the desert region of Mexicali, Baja California, Mexico. Further studies of Mexican Holstein cattle located in warm climate are required to identify other genes that may be directly associated with thermoregulatory traits, which, in combination with those already known to be related to milk production, may serve as genetic markers to recognize HS tolerant cattle.

In the United States, a recent study[82] identified three genomic regions (BTA5, BTA14, and BTA15) which account a large part of the variation in milk production of heat-stressed Holstein cows. Ten genes were identified within these regions as associated to thermotolerance, given that they are involved in various cellular processes in response to HS, such as activation of HSP (*PEX16, HSF1, EEF1D,* and *VPS28*), reduction of oxidative stress, modulation of the apoptosis process (*MAPK81P1, CREB3L1*), DNA maintenance (*TONSL*), and thermotolerance (*CRY2*). Other genomic regions associated with the presence of thermotolerance genes in American Holstein cattle are BTA-24[85] and BTA-26[86], which are related to RT and milk production, respectively. Regarding the Chinese Holstein cattle, there is also evidence that they carry SNPs associated to thermotolerance genes such as *ATP1A1*[87], *HSP90AA1*[88], *HSF1, HSP70A1A*, and *HSPB1*[28].

Certain HS-thermotolerant genes have also been identified in other dairy cattle breeds. The SLICK haplotype gene has been identified in Senepol cattle and has been introduced into the Holstein breed with positive results for HS tolerance without compromising milk production[89]. The genes *HSP90AB1* and HSPB8 have been found in Sahiwal dairy cattle, native breed to India[90]. It is worth noting that, seemingly, dairy breeds of the Mexican tropic have not been typified to detect genes associated with thermotolerance at high AT´s; this, therefore, remains a topic for future research.

Conclusions and implications

Heat stress is a key factor that conditions the milk production level in cattle, being more noticeable in those breeds that are sensitive to high AT´s. Dairy cattle start to experience HS when environmental conditions promote a THI of 72 units, although high-producing dairy breeds can begin to experience it at 68 units. Facing the HS environment, the cattle make physiological and metabolic adjustments to reduce endogenous heat production while releasing excess body heat load; however, the activation of thermoregulation mechanisms decreases the capacity of milk synthesis and secretion of cows. At least 40 % of the reduction in milk production is associated with low DM intake, and the rest, with direct effects on the general metabolism and cellular thermo-resistance. Today, the high pressure to select traits associated to milk production has resulted in cattle with a lower tolerance to HS; this genetic improvement strategy must therefore be modified by taking into account the presence of thermotolerant genes. In this sense, research on HS in dairy cattle must focus mainly on HS mitigation strategies that help reduce the energetic cost resulting from the activation of thermoregulatory mechanisms, as well as increase the daily feed intake.

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