Environmental Physiology of Livestock

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Edited by

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with **J. L. Collier**

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This book is dedicated to Dr. Amiel Berman, Professor (Emeritus) of Environmental Animal Physiology of the Faculty of Agriculture, Hebrew University, Rehovot, Israel, for his many contributions to the field of environmental physiology of domestic animals.

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Foreword

The concept for this text arose from the eighteenth Discover Conference on "Effect of the Thermal Environment on Nutrient and Management Requirements of Cattle," which was held at the Brown County Inn in Nashville, Indiana November 2 through 5, 2009. The conference was organized to address the various thermal environmental factors that influence the nutrient and management requirements for dairy and beef cattle. It became apparent during this conference that a significant amount of new data had been published in a variety of farm animal species. However, there was currently no text that summarized this information in one location. It was believed that such a text would be very useful to a variety of animal scientists and professionals such as scientists, consultants, and educators who might utilize this information. Among recent developments are: new tools to estimate heat stress loads on domestic animals, new information on environmental impacts on nutrient requirements and animal metabolism, effects of environment on gene expression and transcription, the regulation of the process of acclimation, and the impacts of environment on the various aspects of reproduction in the male and female.

Therefore, the objective of this text is to summarize this information in one location, which will provide both a reference source and a frontier view of the current state of the art on a series of new concepts that have been developed and are currently being tested in domestic animals.

Chapter 1

From Heat Tolerance to Heat Stress Relief: An Evolution of Notions in Animal Farming

Amiel Berman

Introduction

The quest for heat tolerance has gained attention with the development of dairy farming in warmer climate regions. Heat tolerance, in its narrow sense, is defined here as the maintenance of homeothermy (Bligh, 2006), i.e., thermal stability of the body in heat-stress environments. As such, it is determined by the relationship between metabolic heat production and the capacity to dissipate excess heat. Heat tolerance, in this sense, does not involve reduction of ambient heat stress or increasing heat loss by human intervention. Heat-stress relief, in contrast, consists of a means to improve animal thermal balance in stressful environments. This review attempts to present the experience of the past and its lessons for the present with a look into the near prospective. It examines the evolution of breeds in the warm climates, the attempts to create dairy breeds adapted to warm climates, and the reduction of environmental constraints on dairy productivity.

Notions on Adaptability to Warm Climate

The deleterious effect of warm climates on animal performance is well known and is not new. This awareness emerged during the course of the early attempts and failures to introduce temperate climate breeds of farm animals into the warm climates during the 1920s and 1930s. It became more evident in the endeavor to increase dairy productivity in subtropical regions during the post-WW2 period and during the development of farming in warm regions of Central and South America. During all these stages of dairy industry development, a notion prevailed that breeds endogenous to a warm climate region are endowed with capacity for heat tolerance. The following discussion examines the limits within which this notion applies. This notion

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emerged around the mid-twentieth century and is best expressed in a review of the ecology of domesticated animals (Wright, 1954) of that time: "In subtropical or tropical climates no pure-bred temperate breed of cattle is really suited." It cites from a large number of studies of crossbreeding in subtropical and tropical countries (e.g., West Indies, Philippines, Egypt, Jamaica, India, Cochin China, Cambodia, Malaysia, and East Africa) in which importing temperate zone breeds or backcrossing to temperate zone breeds were linked to regressive changes in the imported and crossbred animals. In retrospect, it is noteworthy that animals were maintained in the warm climate regions according to temperate region prevailing concepts, with the limited knowledge existent at that time of diseases caused by local ectoparasites and their prevention.

This notion probably has roots dating many decades back. It most likely dates from the formative period of modern agricultural systems in Western Europe, more than 150 years ago. During this period a multitude of cattle breeds were present; each was confined for generations to a limited ecological niche, in a specific climate, with static agricultural and socioeconomic conditions. It is likely that in such conditions a balance was reached between the specific environmental conditions of a region (i.e., climate, nutrition, disease, and management) and the genetic constitutions of animals in that region.

This balance was disturbed, however, by the advent of the mercantile society and with produce and animals shipping over great distances. Many agricultural systems in both developed and developing areas were in warm climates, in which heat stress limits animal productivity. The demand for animal products in these regions created the need to reassess the potential role of heat-tolerant breeds and heat-stress relief for increasing animal productivity in warm regions. This is carried out here for dairy cattle mostly, with only incidental reference to beef cattle, as the two are found in widely differing farming systems.

The Evolution of Warm-Climate Adapted Breeds

The nature of heat tolerance, the identity of heat-tolerant breeds, and their origins and evolution are not altogether clear. It is commonly stated that the *Bos indicus* cattle, the Zebu breeds, are better adapted to thrive in warm climates than *Bos taurus*. This notion is based on the distribution and survival of cattle types in different climates. The Zebu breeds are morphologically differentiated primarily by the presence of a thoracic or cervicothoracic hump, which is absent in taurine cattle (Epstein, 1971). Modern techniques opened new ways of examining the origin and evolution of *Bos indicus* and *Bos taurus* cattle by their paternal and maternal lineages, i.e., by their nuclear and mitochondrial DNA (mtDNA), respectively. The latter is better preserved, present in larger quantities in ancient specimens, and is therefore the main material on which ancestry is examined. The information made available by mtDNA, however, represents only about 40 mitochondrial genes, as compared to the 20,000 to 25,000 nuclear genes. The *Bos indicus* and *Bos taurus* types have been recognized as separate subspecies that evolved by speciation from wild oxen, *Bos primigenius.* Phylogeny estimation and analysis of molecular variance estimate the separation of the two mtDNA clades from the wild oxen at 200,000 years to 1 million years BCE according to one source (Loftus et al., 1994) and 1.7 to 2.0 million years ago by another source (Hiendleder et al., 2008). As domestication is thought to have occurred in approximately 10,000 BCE, ancestors of modern cattle originated in separate domestication of genetically discrete *Bos primigenius* strains (Avise et al., 1998). The *Bos indicus* subspecies that evolved in the warm areas between Pakistan and northwest India gave birth to the Asian cattle breeds. The *Bos taurus* subspecies that evolved in the Near East is the origin of both European and African cattle breed ancestors (Achilli et al., 2008;

Hiendleder et al., 2008). The *Bos indicus* subspecies is presumed to be better adapted to heat owing to its evolution in hot climates.

Cattle types most probably did not remain clearly separate and distinct of each other. Evidence was found for later introgressions of *Bos primigenius* into ancient (Mesolithic and Neolithic) domestic cattle (Stock et al., 2009). Autosomal data of *Bos taurus* cattle breeds revealed considerable introgression from *Bos indicus* cattle; this was particularly apparent in cattle populations from Iraq in the east, and declined in the populations further west toward Anatolia. The pattern of introgression suggests the introduction of zebu cattle from the region corresponding to present-day Iran and northern Pakistan. In addition, maternal and paternal markers demonstrate that the movement of cattle into and within the Near East was complex (Edwards et al., 2007). The complexity is exemplified by the presence of a *Bos indicus* admixture in the maternal but not in the paternal lineage in Damascus cattle (Edwards et al., 2007; Loftus et al., 1999), though these cattle are devoid of the typical hump characteristic for *Bos indicus* (Hirsch and Schindler, 1957). The mtDNA and casein polymorphisms data indicate existence of hybrids between taurine and indicine cattle in the Ukrainian and Central Asian zones as well as into southern and southeastern European breeds (Kantanen et al., 2009).

Breeds domesticated in the Near East and introduced in Europe during the Neolithic diffusion after 6400 BCE probably also intermixed, at least in some regions of the Mediterranean basin, with African cattle introduced by terrestrial and maritime routes (Beja-Pereira et al., 2006).

Dairy Breeds in the Americas

In North America, the initial import of European dairy breeds was followed by a rapid development of dairy farming systems, with the Holstein as the dominant breed, characterized by its high productivity. The U.S. Holstein was re-introduced into Europe, to become a dominant dairy breed in some regions. The relatively recent development of farming systems in Central and South America stimulated a renewed interest in the role of breeds in agricultural productivity in warm climates. It is there that the mixing between indicine and taurine cattle that started in ancient times continues into present times. Cattle were introduced for the first time to the Americas by Spanish conquerors traveling from the Caribbean islands in 1492. The first cattle that arrived in Brazil from Portugal and Spain (Iberia) in the early sixteenth century were the humpless taurine (*Bos taurus*). In the nineteenth century, continental European cattle and later zebu cattle (*Bos indicus*) from India were imported. In the course of a few years the cattle population spread over the continent. Currently, almost all South American countries have Creole cattle, i.e., native breed descendants of Iberian cattle mixed with indicine cattle (Dani et al., 2008).

The ancestry of the Creole cattle may be examined by its maternal lineage as well as by its paternal lineage. The matrilineage of Creole cattle throughout the American continent was analyzed in published mtDNA sequences from Creole, Iberian, and African cattle breeds. The Western European haplogroup was the most common (63.6%), followed by the African (32.4%) and the Near Eastern haplogroups (4%), none of which were found in *Bos indicus* types (Liron et al., 2006).

The paternal lineage in Creole cattle breeds was examined in a study of the geographic distribution and frequency of Y-chromosome haplotypes in *Bos taurus* and *Bos indicus*. Taurine and indicine haplotypes were detected in 85.7 and 14.3% of the males, respectively. The geographic distribution of this polymorphism suggests a male mediated pattern of zebu introgression. The highest frequencies of the Zebu Y-chromosome are found in Brazilian

populations (43–90%), in the eastern part of the continent, while absent in the southernmost breeds from Uruguay and Argentina. Bolivian breeds, at the center of the continent, exhibit intermediate values (17–41%). Differences between breeds in genetic diversity reflect the impact of modern breeding. The Creole breed consistently showed higher levels of genetic diversity among populations than the Holstein (Giovambattista et al., 2001).

In the main, aforementioned studies support the view that, with the possible exception of breeds in Pakistan and India, introgression between breeds is the rule rather than the exception. As many breeds evolved in warm climates, it may be assumed that they shared attributes of heat tolerance. The identity of these attributes is not clear, however. Neither is it clear the extent to which they constitute a relative advantage to breeds in the modern dairy-farming context. The identity of heat tolerance attributes presumably carried by indicine breeds and possibly by taurine breeds therefore is of major interest.

Elements Affecting Heat Tolerance and Their Prevalence

Heat tolerance may be defined as the ability to maintain thermal stability at warm temperatures. This definition is narrower than the earlier used, which included elements of disease and deficient nutrition. In this sense, it does not comprise resistance to ectoparasites, which would be valuable for grazing beef cattle. As such, heat tolerance is determined by the relationship between heat dissipation capacity and metabolic heat production.

Heat dissipation is determined by relative surface area, sweating rates, external insulation, and respiratory heat loss. A larger relative body surface may transmit larger sensible and insensible heat loss from the animal's body surface to the environment. However, crossing the Jersey with the Red Sindhi did not increase the relative body surface of the daughter generation (McDowell et al., 1954).

The high sweating rate of 1.5 kg m^{-2} h^{-1}, which is typical for humans (Grucza, 1990), is a most effective means for increasing the range of tolerable environmental temperatures. Reports contrast the low sweating rate in cattle that ranges from a minimum of 0.1 to a maximum 0.6 kg m^{-2} h^{-1} in Gir and Hariana (*Bos indicus*) cattle housed indoors (Joshi et al., 1968), sun-exposed African zebu Fulani cattle (Egbunike et al., 1983), Jersey and Jersey × Red Sindhi (Pan et al., 1969), and in-shaded lactating Holstein in Israel (Berman and Morag, 1971). The sweating rates reported in association with the slick hair gene initially found in Senepol (*Bos taurus*) and Carora (mixed *Bos taurus* and *Bos indicus*) cattle and introduced into the Holstein (Dikmen et al., 2008) are in the lower range of the above reports. The absence of marked differences between cattle types in maximal sweating rates does not support a significant impact of breed type on sweating rate and, hence, on heat tolerance.

The characteristics of hair coat are a major determinant of heat loss from body periphery and have marked effects on the thermal comfort ambient temperature range (Berman, 2004). In addition, the hair cover is the interface by which incoming environmental radiation exerts it effects on the thermal balance of the animal. The absorption of short wave solar radiation (0.29 to 2.6 micron wavelength) in hair is color dependent, in contrast to the 2 to 20 micron wavelength long-wave infrared radiation, that constitutes about half of the total solar radiation. The impact of thermal radiation on skin heat balance is markedly affected by hair cover thickness, hair diameter and density, air velocity, and air velocity on hair surface. Though thermal radiation is important in grazing animals, in particular at <1 m^{-1} wind velocity

(Gebremedhin et al., 1997), it is rather unlikely that the low intensity thermal radiation present in well-designed shade structures affects the thermal balance of cattle.

Hair coat characteristics are not constant attributes, and are markedly modified by nutrition, photoperiod, and local climate. Increasing day length, warm climate, and higher nutrition levels induce the formation of a hair coat with higher heat conductance characteristics (Berman and Volcani, 1961; Gilbert and Bailey, 1991). In India, breed (e.g., Sahiwal, Tharparkar, Brown Swiss, Friesians, Jerseys) and season (i.e., hot-dry, hot-humid, and temperate) affect hair coat characteristics (Govindaiah and Nagarcenkar, 1983). A slick hair gene found in naturalized South American cattle, mentioned previously, is of particular interest as it is associated with higher heat tolerance (Dikmen et al., 2008; Olson et al., 2003). It is equivocal whether hair coat characteristics that improve heat tolerance are exclusively linked to an indicine origin of cattle, as hair coat thickness of about 1 mm prevails in well-fed high producing Holstein cattle in the warm season of a subtropical climate (Berman, 2010; Berman and Volcani, 1961). In contrast, regarding Holstein cows in Brazil, mean hair coat thickness in 939 cows was 2.5 $\pm$ 0.5 SEM, with a 1.5 to 5.3 mm range (Bertipaglia et al., 2005). There are no parallel reports on hair coat characteristics in U.S. Holstein.

Metabolic heat production is the other determinant component of heat tolerance, alongside heat dissipation capacity. Metabolic rate is composed of an approximately stable maintenance component and a highly variable milk-production dependent component. Indicine and taurine breeds differ markedly in their milk production. Indicine breeds have prevailing daily milk yields of $<$7.5 kg/d, as compared to the $>$30 kg/d common in taurine breeds, and the Holstein in particular. In a study carried out in near-natural climate conditions, which minimizes interpretation difficulties due to degree of acclimatization, such milk production difference was linked with a $\geq$2.5 rise in metabolic heat production (180 vs. 481 W/cow), which shifts by about 8°C – the thermal comfort temperature range (Berman, 1973). In a study of heat tolerance of Damascus crossed back to the Holstein for two to ten generations of crossbreeding, respiratory frequency and rectal temperature were not affected by relationship to the Damascus breed when comparisons were made at similar milk yields (Berman, 1959). In heat tolerance tests comparing European and Red Sindhi crossbreds, the tendency for higher heat tolerance in the crossbreds was attributed to their lower metabolic rate (Branton et al., 1966). A higher metabolic rate induced by higher feeding rate caused reduced heat tolerance, an effect reversed by reducing feed intake to maintenance (Yeates, 1956). In Holstein kept in a shaded subtropical climate direct and indirect evidence pointed to a summer-heat induced 10 to 20% reduction in metabolic rate (Berman, 1968; Hojman et al., 2008). In Holstein, daughters of bulls with high genetic merit for heat tolerance had lower milk yields and higher pregnancy rates than daughters of bulls with low genetic merit for heat tolerance (Bohmanova et al., 2005). Having this in mind, it is likely that: (a) the heat tolerance of indicine breeds may be attributed to their lower milk production and (b) heat tolerance comparisons between breeds should be carried out at comparable milk production. Aforementioned studies indicate that low growth rate and milk production extend heat tolerance to warmer ambient conditions. In spite of this general notion, the tentative presence of heat tolerance attributes independent of milk production may not be excluded. These data also suggest that continued selection for milk production while ignoring heat tolerance may lead to decreased heat tolerance (Ravagnolo and Misztal, 2000).

An interesting observation relates to relative dimensions of digestive tract components in Jersey, Holstein, and their crosses with the Red Sindhi (Swett et al., 1961). To mention part of these data, fore-stomach weight in crosses (e.g., 3/4 or 1/2 Holstein) are 19% less than

Holstein, intestine length is 11% less, abdominal organs weigh 8% less and thoracic organs weigh 26% less. These indicate a marked lower digestive capacity in the Red Sindhi cattle and, consequently, a lower expected production. No further observations are known for other indicine breeds and crosses.

The conclusion may thus be drawn that low growth-rate and milk production extend heat tolerance to warmer ambient conditions. These most likely are the most important elements affecting the heat tolerance of dairy cattle. Their importance is further increased in conditions in which animal survival is the predominant factor of agricultural profitability. A limited productive response to improved conditions (e.g., increased milk yield or growth rate) or its absence would indicate that low metabolic rate and growth rate are not adaptive responses to warm environments, but rather are genetically determined in an inflexible manner in heat tolerant breeds. The response of milk production to improvement of the nutritional, housing, and health environment would therefore be indicative of the extent to which a low metabolic rate is an adaptive or of an inflexible characteristic of indicine breeds. On the other hand, the productivity of temperate zone breeds in the warm climate environments would be indicative of the extent to which environmental conditions limit productivity.

Breed Productivity in Different Environments

Understanding this question may be advanced by examining the responses of animals of various breeds in warm climates, though the conditions in which these responses were recorded are not always definable. An impressive documentation of the performance of tropical dairy cattle breeds in their native environments is found in early publications (Joshi and Phillips, 1953). The data presented here address in particular the milk production of purebred and crossbred cattle in warm climates. It is, however, noteworthy that in indicine cattle and their crosses, first calving age occurs markedly later, and lactation intervals as well as dry periods are significantly longer than in Holstein cattle in temperate climates or Holstein relieved of heat stress in warm climates. Indicine cattle performance is actually rather similar to that of heat-stressed Holstein (Joshi and Phillips, 1953; Lateef, 2007; McDowell, 1985; Wright, 1954).

Indicine in India

Lactation milk yields reported during the period 1936 to 1950 for Sahiwal, Red Sindhi, Gir, and Hariana cattle on larger farms were 2,200, 1,700, 1,600, and 860 kg, respectively (Joshi and Phillips, 1953). Recent data for lactation milk yields (kg/305 d) in Zebu breeds in India were 1,942 for first lactation Sahiwal (Raja and Narula, 2007), 2,426 for Red Sindhi (Pundir et al., 2007), 1,882 for Gir cows (Bhadoria et al., 2003), and 1,429 for Hariana cows (Yadav and Rathi, 1991). The data suggest a relative stability in lactation milk yield over a 50-year period. Either environmental conditions or genetic production potential may have posed a ceiling on milk yield.

Indicine in Brazil

The 305-day yield of Guzera cows was 2,243 kg from 1985 to 1992 (Verneque et al., 2000). The yield of Gir cows in 11 herds from 1987 to 1999 was 2,746 kg (Ledic et al., 2002). From 1987 to 2004 the mean herd milk yield in 51 herds of Gir cows varied from 2,200 to 4,300 kg

(Reboucas et al., 2008), suggesting a significant response to management standard. These data suggest that indicine breeds in Brazil produced higher milk yields than in India.

Mixed Origin

The Syrian dairy cattle, the Damascus breed**,** represents a taurine breed with significant indicine introgression, estimated at 34% in the maternal lineage with no evidence of it in the paternal lineage (Edwards et al., 2007). This breed was used in the formation of the dairy herds in Israel during the first half of the twentieth century, and its 305-day milk yield from 1920 to 1940 ranged from 2,200 to 3,200 kg (Hirsch and Schindler, 1957). Mean milk yield in the Damascus cows in Israel was thus greater than in the indicine breeds in India but smaller than in the better herds in Brazil. It is not clear to what extent this represents breed differences or impact of the gross environment in Israel at that time.

Crossbreeding

The term crossbreeding may represent a number of approaches to crossing programs. It may represent an attempt to attain hybrid vigor by crossing two or more breeds, as thoroughly examined in the United States for crosses between Holstein, Brown Swiss, and Ayrshire (Rincon et al., 1982). In such crossings between temperate zone breeds, heterosis was slightly more pronounced in the warm season than in the cool season (Ruvuna et al., 1983). Crossbreeding may also represent an attempt to produce a high producing yet heat-tolerant breed, i.e., a synthetic breed, by crossing a low producing heat-tolerant *Bos indicus* breed with a high producing heat sensitive *Bos taurus* breed. It represents the presumption that by cross-breeding, the favorable genes may dominate over the unfavorable genes (McDowell et al., 1996). Crossbreeding was adopted in the early stages of dairy farming in Israel (Hirsch and Schindler, 1957), in the Southern United States (Blake et al., 1986), in India (McDowell, 1985), and in Brazil (Freitas et al., 1991). An extensive study of such crosses suggested feed availability as a major milk yield limiting factor (McDowell, 1985). Feed availability should, however, be related to milk production potential, as in both Red Sindhi crosses with Jersey or Holstein (Branton et al., 1966) and in Damascus cows (Hirsch and Schindler, 1957) – improved nutrition was associated with increased subcutaneous fat deposition. This may indicate the outcome of a feeding regimen that exceeds the milk production potential.

Similar developments seem to occur in Central and South America. Around the 1940s Brazilian farmers began to cross the Gir (an imported *Bos indicus* breed) with the Holstein. Milk yields of Holstein × Gir crosses were 2,574 kg per 305 days in 4,805 lactation records (Faco et al., 2008), higher than the 1,600 kg produced by Gir in India (Joshi and Phillips, 1953), and increased with proximity to the Holstein from 1/2 to 7/8 (Barbosa et al., 2008). However, increasing proximity to the Holstein improved milk production only in herds with higher nutrition regimen (Faco et al., 2002). In 1989 standards were set for the Girolando synthetic breed to be 5/8 Holstein and 3/8 Gir. According to breeder reports the Girolando first calve at about 30 months, and mean calving interval is 410 d (The Cattle Site, 2009). These performance indicators are closer to the Gir than to the Holstein.

Finally, backcrossing a low producing local breed to a high producing breed also allows a farming system to gradually adapt to the requirements of a high producing breed. This occurred in Israel in which Damascus was backcrossed to the Holstein in an attempt to produce a synthetic Damascus × Holstein breed. This occurred concurrent with development

of milk recording, feeding regimen, veterinary care, milking systems improvement and initial steps of progeny testing. These gradually changed over a 30-year period and were accompanied by a gradual increase in mean herd milk production from 3,700 kg in 1934 to 5,400 kg in 1959 (Hojman et al., 2008). The changes in the farming system took place before the advent of genetic progress induced by progeny testing of sires, and before the introduction of heat-stress relief measures. The marked increase in productivity during this period may therefore be attributed mostly to farming system improvement.

Holsteins in Warm Countries

On a Pakistan dairy farm from 1990 to 1992 Holstein cows produced an estimated 3,200 kg/305 d (Farooq, 2003). The 305-day yield of Holstein either imported (n = 66) or born on the farm (n = 204) of the Livestock Experiment Station of the Research Institute for Animal Reproduction in Punjab during the 1986 to 2001 period was 4,028 and 3,164, respectively (Lateef, 2007).

In Brazil, the 305-day milk yield in 77,360 Holstein cows calving from 1987 to 1992 was 6,054 kg (Torres et al., 2000). In the later data when complete lactation records of 49,676 Holsteins from 1992 to 2003 were examined, 305-day milk yield varied among production units from 7,336 to 8,617 kg (de Paula et al., 2009).

In Israel, in 1959, it was recognized that proximity to the Damascus breed does not convey adaptation to environmental heat at similar milk yields (Berman, 1959). The use of crossbred sires was then discontinued and Holstein sires were used exclusively, concurrent with massive importation of pregnant Holstein heifers. Later, forced ventilation and combined forced ventilation and coat wetting were introduced in 1975 and 1983, respectively (Flamenbaum et al., 1984; Folman et al., 1979). Mean herd milk production reached 6,833 and 8,734 kg/305 d in 1975 and 1983, respectively (Hojman et al., 2008). The continued use of progeny testing, importing semen from superior Holstein sires, improvements in feeding and housing, the country-wide acceptance of heat-stress relief measures, along with the interaction between research, extension service, and farmers, led to a mean herd milk yield of 11,500 kg in 2008 (Hojman et al., 2008).

The contrast between performance of dairy herds in Pakistan on one side, and Brazil and Israel on the other side is exemplified by noteworthy increases in production over time. This large increase in production over time in the latter countries possibly reflects the effects of a marked improvement in gross environment conditions over those periods. The gross environment comprises the climate, its modification by housing systems, the use of heat-stress relief means, a nutrition that supports the genetic production potential, the veterinary care, and adequate breeding programs. These data, collectively taken, strongly suggest that a high productivity of Holstein in warm climates is feasible, dependent on the overall quality of the farming system.

Heat-Stress Relief Means

Heat tolerance, in its narrow sense, was defined here as the maintenance of homeothermy. This definition does not imply absence of diurnal fluctuations in body temperature. It rather implies a fluctuation of limited range (Bligh, 2006). Heat-stress relief thus refers to the attenuation of environmental factors that affect the maintenance of homeothermy. The main element that

daily disrupts thermal stability in animals without access to shade is the repeated input of solar radiation heat. The second element is made up of ambient temperature and air humidity.

Radiant Heat Exchange

The total midday incoming radiation (direct and diffuse components) on a horizontal surface in the lower latitudes is of the order of 1,000 W/m^2 (Monteith, 1973). This compares to the 85 or 174 W/m^2 heat production of a cow yielding 10 or 35 kg milk/d, when heat production is calculated according to the National Research Council (NRC, 2001), and updated equations are used for body surface, tissue, and external insulation (Berman, 2003, 2004). This demonstrates the large heat quantity potentially added by solar radiation to the thermal balance. Therefore, in all farming systems, provision of shade, even by simplest means, is the primary means for reduction of ambient heat stress.

The incoming radiation is intersected by the shading material and splits into three components: radiation absorbed, radiation reflected, and radiation emitted. The heat of the radiation absorbed raises the temperature of the body absorbing it and thus increases the infrared radiation emitted by that body. The energy emitted is 5.67×10^{-8} Wm^{-2}K^{-4} (Monteith, 1973), e.g., 480, 620, and 700 W/m^2 for bodies at 30, 50, and 60°C, respectively. The three examples of radiant heat intensity represent green vegetation covered ground, unshaded corral ground, and manure cover, respectively. They indicate the tentative relative impact of environment quality on heat balance. A shaded ground would normally be close to air temperature. The surface temperature of animals exposed to radiation would vary between 30 and 50°C, according to air velocity and orientation relative to the radiation source (Clapperton et al., 1965). An animal would gain or lose heat by thermal radiation exchange with surrounding bodies, according to their respective temperatures and their relative proportion in the surroundings of the animal. The spherical approach to thermal radiation is the most efficient approach for its analysis (Kelly et al., 1950). Provision of shade would reduce radiant heat load from the upper hemisphere by 30 to 70%, depending on shade quality. The radiant heat incoming from the lower hemisphere depends on the temperature of surfaces composing it and their relative magnitudes.

In contrast to thermal balance or nutrition, where criteria are present for recommendation of requirements, shade allowances are based on common usage. Recommended shade allowance in the United States varies: 1.8 to 2.5 m^2/cow (Hahn, 1981) used in the drier southern United States (Keister et al., 2002), 3.5 to 4.5 m^2/cow (Armstrong, 1994), and 4.2 to 5.6 m^2/cow in the more humid southeast (Buffington et al., 1983). A recent study indicated that 9.6 m^2/cow shade is preferred over smaller shaded areas, thereby reducing aggressive encounters between cows and increasing time spent lying down (Schütz et al., 2010). In Israel, the incidental observation in 1975 of cows sheltered in the large shaded area of an open shed provided with a high roof drew attention to its potential benefits and led to the adoption of this shelter type since 1980 as the dominant dairy cattle shed in the country (Berman and Wolfenson, 1992). Its characteristics are a large shaded area per animal (∼16 to 22 m^2/cow), and a high roof (∼11 m at its center) with ∼5 m high eaves. The large surface per cow has a number of effects. Excreta water evaporates from soil surface and does not penetrate the ground. The impact of radiant heat emanating from bodies of neighboring cows is reduced, which lessens the thermal radiation received from them and markedly reduces the large between-cow interference with air flow (Gebremedhin and Wu, 2003). This effect by itself may reduce thermal radiation impinging on a cow's surface by about 40 W/m^2.

A higher roof is exposed to higher air velocities, which reduce its temperature and, consequently, radiation from its lower surface to the animals. The height of the roof also increases exposure of animals to cooler parts of the sky, namely those between the solar beam and the hot ground. Clear skies may have a low radiant temperature, 5 to −30°C, depending upon local conditions. Clear skies emit about 200 to 339 W/m^2, while a body at 30°C emits 480 W/m^2. Exposure to the cool sky would therefore increase heat loss as radiant heat by 140 to 280 W/m^2. This rather simplified description of a complex radiant energy exchange situation is supported by the fact that animals exhibit marked preference for higher roof sheds (Kelly et al., 1950). Stanchions located at 0.8 to 0.85 m from each other, to allow air movement between animals, led to a 3 to 6°C decrease in air temperature adjacent to cow surface versus a 0.7 m distance between stanchions (Berman, unpublished data). The combination of these elements creates a shaded area with lower radiant load, a space open to prevailing wind, in which animals may find exposure to the cool sky. Feed supply in the shaded central alley and animal cooling means along the feed bunk enhance feeding stimulus.

Heat-Stress Relief Implementation

The adoption of heat-stress relief interventions, in addition to provision of shade, depends upon the intensity of the heat to which animals are subjected. Heat stress varies according to local climate conditions and according to milk production. A commensurate use of heat-stress relief requires, therefore, an assessment of the extent of heat and the periods in which it is present. The lower limit of the thermal comfort temperature range for cows producing 20 to 30 kg/d was estimated in climate chamber studies as −10 and −40°C, respectively, which precludes the possibility of even moderate milk yield production in the subtropics (Hamada, 1971; Webster, 1974). The discrepancy between climate chamber estimates and dairy performance in the subtropics is probably due to exposure to constant temperature and the absence of adequate acclimatization (Berman, 2004, 2005). A rational application of heat-stress relief requires the determination of the periods at which heat occurs and its extent in the near natural conditions in which animals produce.

This approach was implemented in Israel by the study of diurnal and seasonal cycles in thermoregulatory responses to farm conditions in heifers and cows fed at two levels of intake (Berman, 1967, 1968; Berman et al., 1963), and in lactating cows (Berman and Morag, 1971). The data produced by these studies were used to estimate the ambient temperatures critical for thermal comfort as a function of milk production (Berman and Meltzer, 1973). The estimates, supported by milk yield changes with ambient temperature in farm conditions (Igono et al., 1992), served for assessing feasibility of heat-stress relief means. Forced ventilation for improving thermal balance of dairy cows was introduced on this basis (Berman et al., 1985; Folman et al., 1979). Thermal balance model simulations were used to assess impact of air velocity and animal posture on thermal balance (Berman, 2004, 2005). Forced ventilation was not sufficient however to alleviate thermal strain with rising milk production, as reflected in the seasonal decline in conception rate (Flamenbaum and Ezra, 2003). An additional means of coupling animal surface wetting with forced ventilation to extract heat by forced evaporation was introduced (Flamenbaum et al., 1984). This proved highly efficient in alleviation of heat stress (Flamenbaum and Ezra, 2007), although it is sensitive to vasomotor responses (Berman, 2010). The approach was based on incorporation of heat-stress relief in existing farming systems and its use according to need. It contrasts the approach for heat-stress relief by evaporative cooling (Ryan et al., 1992). In the latter, a confined or semi-confined environment is created in which air temperature is reduced by water evaporation. Evaporative cooling has

best results in hot dry climates, in which air temperature reductions of ~15°C may be attained. Its use is limited however by ambient humidity and the maximal humidity in the confined space compatible with animal comfort and welfare. Available data suggest this limit is at about 70 to 75% RH (relative humidity; Berman, 2009).

Socioeconomic Considerations

Seen from the viewpoint of heat tolerance, the suitability of a breed to a specific climatic region is determined by the capacity of the particular breed to maintain thermal balance at the desired milk production. The suitability of a breed for a climatic region cannot be dissociated from the quality of the local farming system, however. The latter is generally, but not obligatorily, related to the socioeconomic nature of the region at large.

In a familial type of farm, one at subsistence level or close to it, a milk yield not far above that needed for consumption on the farm poses the least amount of difficulties. Producing in excess of this amount necessitates additional animal feed, either from farm resources or by its purchase, and milk surplus handling means. The capital required for these usually is beyond that available to a subsistence-type farm. Under these conditions, a breed in which the genetic potential for milk production is about 1,200 to 1,800 kg per year (e.g., *Bos indicus* or African mixed breeds) would be an adequate choice. Local climate would have little impact on these animals. This estimate is lower than the 1,800 to 2,200 kg suggested as sustainable on tropical grasses and crop residues (McDowell, 1985). Such an approach would reduce the incidence of under-nutrition and related deficiencies when production is significantly higher than supportable by the farming system. It would provide marked nutrition improvement, with little if any credit need. At such production level, thermal balance may be maintained even at relatively high temperatures, if protection from solar radiation during hot hours is available.

The choice of a higher producing breed may depend upon cost and availability of factors like long-term credit, surplus marketing organizations, manpower, pollution treatment, veterinary care, mastitis control, heat-stress relief, as well as technical support. Cooperation may enable higher producing animals purchase, milk surplus collection and marketing, feed purchase at lower costs, feed mixing, nutrition, veterinary and management support and artificial insemination. In many cases it seems to be the only possibility for a step increment in production concurrent with social structure maintenance. In Israel, cooperation led to creation of 2 to 3 joint-family operations that enabled the creation of larger, economically more efficient production units. In the latter case, milk yields >11,000 in Holstein cows were attained in joint dairy herds of 100 to 200 lactating cows. Such larger production units, still of family farm structure, were economically advantageous owing to credit opportunities, cooperative feed production, feed purchase, mixing and distribution, AI services, milk collection, and marketing.

The suitability of a particular breed is, however, not always related to the nature of the surrounding agricultural community. Available capital may respond to urban demand for milk and milk products by the acquisition of technologies needed for high milk production breeds irrespective of, and independent of, the status of the farming sector.

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Chapter 2

Physiological Basics of Temperature Regulation in Domestic Animals

Donald E. Spiers

Introduction

Domestic animals inhabit many different thermal environments around the world, and in every situation they must utilize physiological mechanisms to balance heat flow into and out of the body. In the extreme cold of polar regions, the animal's primary challenge is to limit or reduce the outflow of metabolic heat from the body and increase the inflow of heat from the ambient. Animals that live in desert regions must reverse these processes by augmenting the environment of metabolic heat and minimizing the influx of thermal energy from an environment with a heat content level that possibly surpasses that in the animal's body. The classic example of an animal that is able to rapidly shift between these thermal extremes is the camel (Schmidt-Nielsen et al., 1956), which utilizes simultaneous shifts in thermal and water balance to raise and lower body heat. The difficulty in understanding these processes begins with a basic misunderstanding of the key elements in the thermal environment – heat and temperature.

The Definitions of Heat and Temperature

Any material with molecular movement possesses kinetic energy in the form of heat. Every object in our typical environment has a temperature above absolute zero and therefore contains some level of heat. A more appropriate appreciation of the value of heat in the universe and, more importantly to living animals, is derived from a consideration of the First and Second Laws of Thermodynamics. In summary, the First Law states that we have all the energy in the universe today that has ever existed. The total amount has neither increased nor decreased over time. Therefore, energy is never created but only transferred from one form to another. Heat represents the bottom level of energy transformation, which leads to the Second Law. Simply

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put – this law states that all order goes toward disorder. We have less organized energy in the universe today than we had yesterday, with the result being the ultimate release of energy in its lowest form (i.e., heat). There are reversals of this breakdown in organization, in which energy can be assimilated into a more organized form (e.g., growth, development). However, these periods are only temporary. Ultimately, animals age and die, with breakdown of this short-term organization and release of energy back to the universe.

The Second Law of Thermodynamics becomes important in defining heat flow. The statement that all order moves toward disorder can be rephrased as heat always flows downhill from hot to cold objects. This process does not occur in reverse, without adding energy to the system. For example, opening the door to your home in the winter results in heat flowing passively downhill along a temperature gradient from warm to cold environments. Newton proposed in his Law of Cooling that the rate of change in the temperature of an object is directly proportional to the temperature difference between the object and its surroundings, or the change in object temperature over time. Kleiber (1975) noted that Newton was unaware of heat flow and incorrectly considered temperature to be the object that flowed. He also suggested that it is inappropriate to use this law to explain heat loss in homeotherms since they are not inanimate objects that cool, but instead are constantly generating heat to maintain homeothermy. A more appropriate expression of heat transfer in living birds and mammals is Fourier's Law of Heat Flow. This Law, which accounts for the influence of thermal gradients, states that the rate of heat flow by conduction within a system is equal to: 1) the thermal conductivity of the conducting material; 2) the area across which the heat flows and insulator thickness; and 3) the thermal gradient between the exchange regions. Each of these physical parameters affect an animal's ability to regulate its core body temperature in different thermal environments.

There are several unique facts about temperature that make it essential for thermoregulation. First, it determines the direction of heat flow. Both Newton's and Fourier's Laws have the temperature gradient as a central physical component in the determination of cooling and heat flow, respectively. Birds utilize a large thermal gradient to regulate body temperature. In general, they have a higher internal body temperature (i.e., $>40^{\circ}C$) than mammals (i.e., $<39^{\circ}C$) under thermoneutral conditions. This elevated temperature provides them with an advantage in the heat, in that the thermal gradient between animal and environment is increased, facilitating heat loss from the bird and maintenance of homeothermy. Second, temperature is an indicator of the heat intensity within a system. Animals have specific neurosensors located throughout the body, both peripherally and centrally, which detect temperature and not heat. Therefore, an animal's judgment that an object or environment is "hot" or "cold" is based on temperature and not on heat content. Likewise, there are numerous physiological and behavioral activities that depend on detection of temperature and not heat. Onsets of shivering activity in the cold and panting activity in the heat are directly related to temperature of the environment and, in turn, the skin site where the thermoreceptors are located.

Thermal conductivity, which is another physical component of Fourier's Law, also alters the perception of temperature (i.e., hot versus cold) and potentially many of the physiological responses to the thermal environment. Most people agree that humid cold air feels colder than dry air. The question is why? Initial consideration of this question concerning thermal comfort produces the obvious answer that an increase in the water content of air increases its thermal conductivity and results in greater heat loss from the animal. In fact, this is incorrect. A phase shift in water from solid to liquid to gaseous states produces a large change in thermal conductivity. Water vapor has a lower thermal conductivity than dry air. Therefore, adding water vapor to air, by using misters and foggers, slightly insulates the animal, in addition to

reducing the vapor pressure gradient for evaporative heat loss to the environment. In reality, this alteration in thermal conductivity is very small given that there can only be about 2% water in the air under these extremely humid conditions created by these devices. Adams (1992) answered this question by making a distinction between thermal perception and actual thermal strain on the animal. He noted that we could feel colder, in the absence of altered thermal strain, as a result of an increase in the water content of the tissue surrounding the thermoreceptors (i.e., deep below skin surface). This region (i.e., stratum corneum) readily absorbs water under humid conditions, which increases its thermal conductivity as a result of increased liquid content. With this increase, there is a drop in the temperature of the region containing the thermoreceptors toward the level of the skin surface. The receptors will signal that it is colder, even though the level of thermal stress is essentially unchanged. Exposure to a dry, cold environment will reduce the hydration and thermal conductivity of the stratum corneum, with less reduction in the temperature of the receptors in this region. As a result, the individual feels warmer. The combination of skin hydration and thermal conductivity levels is very important in determining how we perceive our environment and its temperature.

The effect of skin hydration on cold perception works in a similar manner on heat perception, albeit in the opposite direction. Under extremely hot conditions, skin surface temperature may exceed skin thermoreceptor temperature. As in the cold, an increase in skin hydration will increase thermal conductivity of this region and cause the temperatures of these regions to approach each other. In this case, thermoreceptor temperature will rise to give the perception of an increase in heat stress. Again, actual heat stress remains essentially unchanged. However, the perception of heat stress is real. As a result, this environment is often termed "steamy" or "muggy," and there is usually a reduction in performance.

Although the terms temperature and heat are often used to explain behavioral and physiological events related to thermoregulation and, as shown, are in many ways "linked" to each other, they are distinctly different concepts that should never be used interchangeably. A similar problem arises in the use of the terms stress and strain as they refer to the impact of the environment on biological systems.

Stress of the Environment versus Strain on the System

The term "stress" is a part of every discussion of the immediate effects of the environment on an animal, and adaptation to these effectors. In fact, it is often used interchangeably with "strain" in describing animal-environment interactions. A short definition of stress or stressor is any condition or agent that alters the resting state of a system (physiological or biological; Fregly, 1996) and ultimately results in an adaptive response (Curtis, 1983). The displacement from base level of the system due to stressor impact is defined as the "strain" on the system (Fregly, 1996). This system shift can be due to internal or external stressors, and must be a measurable property, such as intensity, duration, frequency, or variability (Fregly, 1996).

One reason for confusion in using the terms "stress" and "strain" is that many agents can be classified as either, depending on the system or pathway in question. Any integrative physiological analysis faces this dilemma. For example, a change in the external thermal environment (i.e., stressor) may cause shifts in skin or core body temperatures (i.e., strains). However, body temperature (now the stressor) will elicit a series of physiological responses or strains, such as redirection of blood flow, altered respiratory rate, or shift in metabolic heat production. This term confusion can be eliminated by simply defining the analyzed system in terms of its components.

Potter (1971) used stressor terminology to define the ideal environment and adaptation. His proposal was that extremely low or high levels of stress result in the lowest levels of performance, and that there is a requirement for a certain level of stress in our daily lives to obtain the optimum level of function and survival. Potter summarized that our culture should provide "systematic challenges by physical and mental tasks" at specific periods of life to induce expression of our full genetic potential and adaptation. It is likely that similar levels of challenge at appropriate times would improve performance of domestic animals as well.

The British physicist Thomas Young is credited with the discovery in 1807 of an inherent property of any material that predicts the strain in the material that results from a known stressor (i.e., Young's Modulus of Elasticity; stress/strain). Fregly (1996) suggested that this concept might be utilized to identify an animal's ability to adapt to a particular stressor and characterize different components of the acclimation process (e.g., duration, frequency, and magnitude of response). Environmental stressors can impact an object in one of two ways. The object can be deformed or moved from its location. Isotonic contraction of skeletal muscle is a good example of this, where tension remains unchanged but there is a shortening of muscle length and movement (Sherwood et al., 2005). In contrast, an object could respond with an increase in tension and no deviation in location. This would be characteristic of isometric contraction where there is not shortening of the skeletal muscle but a rise in strain (Sherwood et al., 2005). Fregly (1996) expands the Modulus concept beyond inanimate objects to include animals by explaining that its reciprocal (i.e., strain/stress) represents the adaptive compliance of an animal in response to a stressor and might be referred to as an "index of acclimation." He notes that such an index could be used to 1) measure the degree of acclimation following a specific period of exposure, 2) determine the completion time for acclimation, and 3) compare levels of acclimation across species. Quantification of the stressor is relatively easy and would center on measurements of thermal input. A greater challenge is the quantification of the strain to the animal's cells, organs, or systems. An additional, and often neglected, factor is the temporal component that must be incorporated into any strain/stress index of both acclimation and de-acclimation for a given situation.

Homeostasis and Maintenance of a Constant State

All living organisms are in a constant state of dynamic change. Initially, this idea might appear to be a contradiction, because the terms "constant state" and "change" are used. In fact, this is not the case. *Constant state* refers to the organization that occurs within the body systems, and *change* identifies the movement that must occur around this organization in order to maintain a steady-state environment. For example, core body temperature of many adult birds and mammals is maintained at a relatively constant level through the continuous flow of heat into and out of the body. The fact that systems within living animals continuously function to maintain a constant internal environment or minimize changes due to the external environment (i.e., *la fixité du milieu intérieur*) was initially presented by the French physiologist Claude Bernard (1878). He stated that this constant state is a requirement for any living organism to maintain an existence that is independent of its environment. The next significant step in the evolution of the concept of self-sustaining organization occurred when Harvard physiologist Walter B. Cannon (1932) proposed the term homeostasis. He realized that living organisms utilize complex coordinated physiological reactions to reduce systemic disturbances in different external environments. Homeostasis united all physico-chemical interactions within a living animal under the goal of maintaining a constant internal environment. Physiologists agree that this

is one of the most important concepts in physiology. A common misconception, however, is that Cannon intended to use this term to define the maintenance of constant states within the body, along the path of Bernard's original proposal. In fact, his aim was not to define a static constancy, but one that is dynamic and moving with variation around a maintained value. More recently there has been a tendency to forget that this fluidity was a component of the original concept of constant state.

Although there are a wide variety of models associated with life functions and homeostasis, most have several basic characteristics in common. Each has a central pool that is maintained at a theoretical constant level under normal conditions by balanced input and output of energy. In the thermoregulatory system, the pool is usually body heat content that is determined by the inflow and outflow of heat from the body. Using the concept of balance, the inflow can occur from the environment with exposure to air temperature above skin temperature or electromagnetic radiation that actually penetrates the body surface. Heat can also be contributed to the central pool as a result of generation within the body (e.g., shivering thermogenesis). Exchanges within the body are additional determinants of the pool size. These include the incorporation of material into other compounds, as well as storage of the pool material throughout the body. In the case of the thermoregulatory system, there are deposits of large quantities of heat in different regions, such as brown adipose tissue found in many neonates or skeletal muscle during shivering or exercise. On the outflow side, products in the pool can be broken down or metabolized and released from the body. Returning to the thermoregulatory system, we know that heat is the lowest energy state and so cannot be converted into other forms. However, it is certainly released from the body and under normal conditions balances the inflow.

Any system in the body can be evaluated and classified by placement in one of three states: 1) output greater than input (negative balance); 2) input greater than output (positive balance); and 3) input equals output (stable state or homeostasis). These states can be easily visualized for the thermoregulatory system if one thinks of the system as a balance, weighing heat loss against heat gain. Using this scenario, a negative balance would produce hypothermia, a positive balance would result in hyperthermia, and the balance of input and output would result in homeothermy. "Homeothermy" is defined as the balance of heat production and heat loss (IUPS Thermal Commission, 2001) to maintain body-heat content relatively constant in different thermal environments. The term was used, not many years after "homeostasis" was introduced by Cannon to describe the development of thermoregulation in young rats (Brody, 1943).

The development of models around the concepts of homeostasis and maintenance of a constant state was originally used as a simplified approach to understand complex physiological processes, such as thermoregulation and homeothermy. They were simple in that they consisted of a selected variable, such as body heat content, that served as a black box with input and output activities. The benefit of this approach is its simplicity and ease of visualization. It remains to be determined if it is sufficient for evaluation of stress in production environments. Another concern is that this simplistic approach does not allow for prediction of an output, such as thermal status. In addition, it does not provide a mechanism that allows for integration of multiple systems, which more likely approximates the true thermoregulatory system.

Control of the Thermoregulatory System

Animal models are simple constructs that do not duplicate, but approximate biological systems (Horton and Bicak, 1987). These artificial creations allow researchers to study normal

and pathological events across different animal species and also to conceptualize complex processes. More importantly, these creations provide the ability to test specific components of a system in order to better understand physiological activities and their interactions under different conditions. This is especially true for the thermoregulatory system, with its numerous theories to explain and predict the control of body temperature. Such models run the gamut from the sub-cellular level to the interaction of the animal with its environment. In addition, there are old and new concepts in the literature that have been used as general models to understand the effects of stress on physiological systems. Initially, the idea of homeostasis was used to describe how different physiological activities maintain important variables (e.g., core temperature, osmotic concentration) within a constant range, even during exposure to environmental stressors. Control theory was integrated into this concept as a means to understand how a stable state could be created and maintained through the use of feedback mechanisms. This concept has evolved over the decades to incorporate change into our view of physiological regulation and now includes the theories of rheostasis (Mrosovsky, 1990), homeorhesis (Waddington, 1940), and allostasis (Eyer, 1975; Eyer and Sterling, 1977).

Despite the wide variety of models associated with life functions and homeostasis, most have several basic characteristics in common. Each has a theoretical central pool that is maintained at a constant level under normal conditions by balanced input and output of energy. In the case of the thermoregulatory system, the pool is usually body heat content that is determined by the inflow and outflow of heat from the body. Using the concept of balance, the inflow is usually from the environment with exposure to air temperature above skin temperature or electromagnetic radiation that actually penetrates the body surface. Heat can also be generated within the body (e.g., shivering thermogenesis) and contribute to the central pool. Exchanges within the body are additional determinants of the pool size. These include the incorporation of material into other compounds, as well as, storage of the pool material throughout the body. Within the thermoregulatory system, there are deposits of large quantities of heat in different regions, such as brown adipose tissue found in many neonates or skeletal muscle during shivering or exercise activities. The heat deposit locations shift with the thermal environment and status of the animal. During cold stress, the chief deposit location is the thermal core in the center of the body. In contrast, the deposit locations are spread more evenly throughout the body (Aschoff and Wever, 1958) during heat stress.

Interest in the use of a control system approach or engineering concepts of regulation have existed for most of the twentieth century. The initial idea likely emerged with Barbour's demonstration (1912) that the hypothalamus acted as a thermostat in temperature control. In spite of the early emergence of control system terminology, there was no major advancement of this idea until mid-century, when studies using thermodes to examine the control characteristics of the preoptic anterior hypothalamus emerged (Hammel et al., 1960). Wiener (1961) first emphasized the use of animal/machine analogies and noted that the maintenance of homeostasis is achieved through negative feedback control. The concept was originally borrowed from engineers in an attempt to compartmentalize and, in turn, simplify complex physiological processes and systems. "A control system can be viewed as a set of communication channels interconnecting subsystems that process information" (Houk, 1988). The advantage of using this approach for the analysis of a problem is that the input and output at each level of a model can be controlled and measured to identify components of a physiological system. An animal's potential for maintenance of homeostasis is dependent on its ability to sense and respond to changes in its internal and external environments.

The general model for a control system, as it relates to the thermoregulatory system, has several basic components with different levels of complexity and controversy. The components

include setpoint, controller, error signal, effector, receptor, and afferent signal. Physiological control systems, in the absence of environmental stress, usually exist within a dead zone. In this region, controlled processes are unaffected by change in stressor input (e.g., shifts in air temperature). Dependent variables such as core body temperature may fluctuate within the dead zone with no shift in the controlled output. Core temperature of many adult domestic animals is unresponsive to changes in air temperature below 25°C and above 10 to 15°C. This is one reason why it is difficult to give a single normal core temperature for any species. Instead, one refers to a temperature range. The range of core temperature for mammals and birds is 36.4 to 40.1°C and 40.6 to 43.0°C, respectively (Reece, 1997). An additional reason why it is a challenge to identify a single normal core temperature is that interior temperature is different throughout the body. Ruminal temperature in cattle is approximately 1 to 2°C higher than rectal temperature at thermoneutrality (Beatty et al., 2008).

The basic elements of any control system are shown in Figure 2.1. Millions of thermosensors, or receptors, in the body shell are located in the cutaneous region, where they consist of free endings of afferent nerves (Boulant, 2001). Receptors in the core are found in the preoptic anterior hypothalamus (PO/AH), spinal cord, gastrointestinal tract, brain stem, and other central regions (Zeisberger, 2001). The basic neuronal response to an increase or decrease in body temperature is an increase in firing rate. Cutaneous information is transmitted through the central nervous system to the ventrobasal thalamus and then relayed to the somatosensory region of the cerebral cortex. Combined processing of thermal and tactile inputs by the thalamus and cortex allows for precise determination of thermal stimuli at the skin. Separate information passes through the reticular formation to the PO/AH where it is processed and integrated to represent larger cutaneous regions than for sensory stimuli (Boulant, 2001). The PO/AH itself is thermosensitive. However, its neuronal activity may be altered by afferent signals from other regions of the body. It is this comparison at the PO/AH level of multiple afferent inputs from different regions of the body with the thermal status of the PO/AH, and possibly a setpoint value, that results in an error signal to thermoregulatory effectors. Examples of effectors would include skeletal muscle and peripheral vasculature with controlled processes being shivering and vasodilator activities, respectively. The resulting increase in heat production (i.e., shivering thermogenesis) and heat loss (i.e., convective heat transfer) would result in concomitant shifts in central or peripheral heat content. Environmental input or influence on the thermal status of

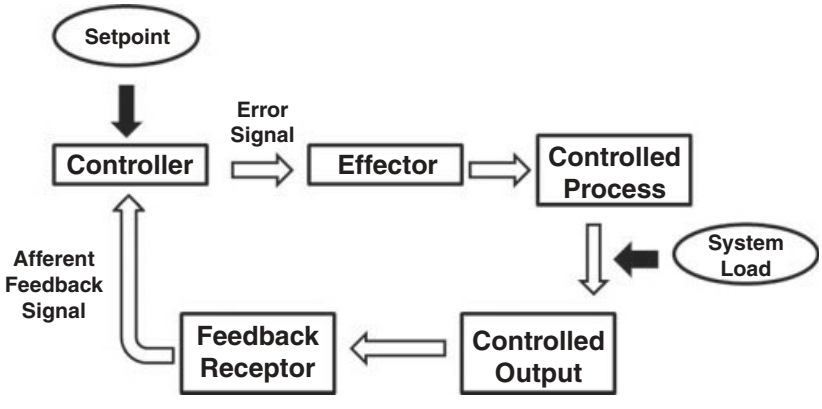

Figure 2.1. The classical control system showing the basic elements and entry points for the setpoint into the controller and environmental stress or system load.

the animal occurs between the controlled processes and output event in the form of a system load. For example, the same level of cutaneous vasodilation in mild heat would result in greater heat loss than in severe heat due to the differences in the tissue to air thermal gradient between the two environments. The lower heat content in the former example would result in a lower tissue temperature than in severe heat. Thermosensors (i.e., feedback receptors) respond to the rate of change in local temperature with a high level of sensitivity to a few thousandths of a degree. The result of this stimulation is an increased firing rate as the information returns through a feedback signal into the central nervous system. Additional comparisons occur at this point with system reevaluation and a new error signal.

Control systems can be positive or negative in structure. Negative systems are regulatory in that they attempt to minimize the shifts in body temperature. The generation of an error signal in the previous example produces an effector response that moves the controlled output in the opposite direction that, in turn, diminishes the error value. This opposite response is referred to as negative action. Other control systems may be positive or feed-forward systems and are nonregulatory (Houk, 1988). In this case, a signal generated by the central nervous system in response to incoming afferent information (i.e., input) amplifies the output and moves the body forward in a certain direction. A thermoregulatory example would be the sensing of a cold burst of air by cutaneous thermoreceptors that initiate shivering activity even before there is a change in core temperature. The approaching cold is anticipated and defensive action taken to potentially reduce strain on the system.

There are two types of control that are key components of the thermoregulatory system. They are proportional and differential controls. Of the two, proportional control is the most common. It is referred to as proportional because the magnitude of the output signal is directly related to the magnitude of the input signal. Acute sweating and shivering intensities are typically proportional to the thermal loads once the animal is above or below critical body temperatures, respectively. Differential control systems are more complex in nature. Basically, the magnitude of the output response is determined by the rate of change in the input signal. The response of cutaneous thermosensors is characteristic of differential control. Rapid exposure to hot or cold ambient temperatures will produce a greater perception of these temperatures than slow exposure. An example of differential control and heat perception is rapid versus gradual entry into a hot bath. The bath temperature is the same in both situations, but the perception of heat is very different. It is thought that differential control provides a feed-forward, anticipatory response to an approaching stress and allows the animal an opportunity to prepare for strain.

A basic characteristic of a physiological control system is the element of gain. This is the change in the output of any component of a system based on input. It often occurs at the level of the controller or central nervous system. The gain of a system can be either high or low. Figure 2.2 shows the three types of gain: 1) normal where output is equal to input; 2) low when output is less than input; and 3) high when output is greater than the input.

An example of a high-gain situation is the release during cold stress of thyroid hormones, which have a permissive, potentiating effect on thermogenesis mediated by the sympathetic nervous system (Silva, 1995). On the opposite end, anesthesia reduces the gain of a control system to thermal stimulation. Injection of an anesthetic directly into a local cutaneous region will reduce the activity of thermal receptors in that region and transmission to the central nervous system. The result is less sensation of change in the thermal environment. General anesthesia results from action at the level of the brain with inhalation or injection of an anesthetic directly into a vein. In this case, the perception of temperature and output of the PO/AH is reduced to widen the zone of body temperature control. The effect of alcohol on

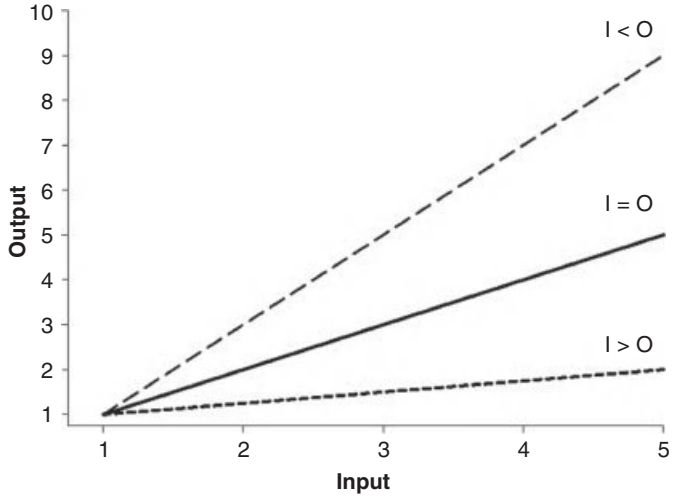

Figure 2.2. System output (O) as a function of input (I) for normal, low, and high levels of performance.

thermoregulatory ability is a good example. Alcohol intake effectively lowers the precision of thermoregulatory control by reducing metabolic rate and heat production in the cold with a resulting drop in core temperature, and a reduction in heat loss capabilities in the hot environment to increase hyperthermia (Spiers, 1995). The result is an increased fluctuation in core temperature with less control.

Cassel and Casselman (1990) noted that although temperature is a measure of intensity or magnitude of heat, it is not directly related to quantity or amount of heat. Body temperature and heat content can change independently of each other. These differences are due primarily to heat capacity and specific heat. In order to understand these concepts, it is important to use standard definitions. The more recent and acceptable definitions were issued by IUPS (2001). Heat capacity (kcal/°C) is the product of body mass and specific heat, and heat content (kcal) is the product of body temperature, specific heat, and mass. As a result, a steer can absorb much more heat than a calf before there is a change in body temperature. Specific heat (kcal/kg/°C) is defined as the amount of heat needed to raise the temperature of a unit mass of material by 1°C. Different materials have different specific heats. For example, the specific heat of water is 1 kcal/kg/°C, whereas moist and dry animal tissues average 0.83 and 0.40 kcal/kg/°C, respectively. The result is that hydrated tissue can absorb more than twice the heat of dehydrated tissue before there is a change in temperature. Since thermosensors detect body temperature and not heat content, these physical characteristics become important determinants of the thermoregulatory control system performance at a location between the controlled output and receptors. This independence of body temperature and heat content means that body heat is often exchanged without a change of body temperature or an effect on the thermoregulatory control system. Body temperature is not an accurate representation of stored heat until the upper limit of thermal capacitance is reached. These relationship differences instill in the animal a delay and offset in the thermal response to hot and cold stress conditions. This also means that the thermal core of an animal may remain stable during exposure to different thermal environments, while there is a shift in the thermal shell temperature. During cold stress, the thermal core of a large domestic animal may be unchanged in heat content and

temperature. However, the heat content of the thermal shell may be reduced along with the peripheral temperature. As a result, total body heat content is decreased and the reduction in temperature of this region could affect the controlled system.

The traditional view of the thermoregulatory control system as a tight set of feedback and error signals is inappropriate, considering there are shifts in gain and thermal capacitance throughout the system. Regional body temperature alone is certainly not a conclusive determinant of body heat content. In addition, there is current controversy regarding the validity of setpoint theory and questions as to the need for a control system approach to explain thermoregulation. Kobayashi et al. (2006) have questioned the receptor idea as presented in the model of a thermoregulatory control system. The dogma is that temperature alters the firing rate of thermosensors as signals sent to the brain. In reality, a thermosensor alone cannot detect a temperature without decoding at the level of the brain. Likewise, thermosensors respond to other stimuli (e.g., osmotic pressure, chemicals) that could alter the firing rate in response to thermal stimulation. This would result in an inaccurate measurement that becomes an unreliable component of the system. Instead, Kobayashi et al. (2006) proposed that thermosensors are comparators at the level of the detection site that do not require the transfer of information directly to the brain. The suggestion is that the thermal comparators evaluate the sensed temperature against its own reference signal. Once the comparator is activated by a threshold signal, it may send a signal to other regions that include the brain for thermosensation. Along this same line of thought, Werner (2010) proposed that neither a setpoint nor a comparison of signals at the level of the central nervous system is necessary to explain the thermoregulatory control system. He noted that to regulate a variable within a control system model requires an input signal, with the difference between the afferent input and the setpoint used to generate an error signal. Werner and Romanovsky (2007) argued that a setpoint is a misleading and unnecessary concept. Werner (2010) made the point that a steady-state, homeostatic condition, by definition, can only be achieved if the afferent input to the controller becomes a zero value and there is no evidence for this. Likewise, proportional control does not acknowledge the steady-state condition when the error signal is at zero level, but effector output is still required for everyday activities. Such a condition cannot exist. Although there are current debates on the existence of an actual setpoint or direct afferent input into the brain, the classical control system concept is still a useful means to conceptualize the thermoregulatory system and test theoretical components of the system.

Modes of Heat Exchange and the Thermoregulatory Profile

An understanding of thermoregulation, and particularly the physiological responses to heat stress, requires basic knowledge of heat production and the avenues of heat exchange. Discussions of the sources of animal heat occurred as early as the time of Plato and Aristotle (Goodfield, 1960; Mendelsohn, 1964), with the current theories not developing until the 1800s. In contrast, heat exchange and heat loss to the environment did not receive serious examination until the end of the 1800s and the early part of the twentieth century, with principles borrowed from physics and engineering. Rubner (1902) concentrated on the use of calorimetry to measure heat production primarily in dogs and humans, and addressed heat exchange by conduction, convection, evaporative, and radiant exchange. However, it was not until the combined work of physiologists and engineers in the 1930s that major advancement occurred in partitional calorimetry (Winslow et al., 1936). There are several comprehensive reviews of the avenues of heat exchange that have been recently published (Gagge and Gonzalez,

1996; Werner, 1998; Adams, 2001; Hillman, 2009). Each avenue has unique differences and similarities that are important for their interaction within the framework of the thermoregulatory system.

Heat Exchange

Core body temperature is considered to be the outcome of a balance between heat inflow or production (i.e., metabolic rate) and heat outflow. As discussed earlier, body temperature is an expression of body heat content and therefore the traditional calculation is for the storage of total body heat or change in body heat content (S; kcal; kJ):

$$S = M + W + C + K + R - E \text{ (IUPS, 2001; Adams, 2001)} \quad (2.1)$$

Where:

S = storage of body heat or change in total body heat content (kcal; kJ)
M = metabolic heat gain or metabolic rate (Btu/h; watts)
W = work rate (positive for useful work; negative for mechanical power absorbed by body; Btu/h; watts)
C = convective heat transfer or exchange (Btu/h; watts)
K = conductive heat transfer or exchange (Btu/h; watts)
R = radiant heat exchange or exchange (Btu/h; watts)
E = evaporative heat loss (Btu/h; watts)

An increase in total body heat storage will in turn increase core body temperature, and a decrease will reduce the core body temperature. Metabolic rate is the primary source of heat gain for the living animal due to the Second Law of Thermodynamics, as noted earlier. The majority of energy released from biological reactions in the resting living animal is heat (Rhoades and Tanner, 1995), or a by-product of metabolism.

Heat transfer into and out of a living animal is complex and occurs by four pathways: conduction, convection, radiant exchange, and evaporation. The magnitude of heat transfer by the first three avenues is highly dependent on the temperature differences between the exchange objects in the environment. Conduction occurs when two stationary objects are in contact with each other. Other determinants of the magnitude of conductive heat transfer include the surface area of contact, thickness of the conducting materials, and thermal conductivity of the conducting objects (i.e., an intrinsic property). The thermal conductivity of objects in contact with the animal is also an important component of thermal perception. For example, a metal surface with high thermal conductivity will conduct heat rapidly from the skin where the thermal receptors are located. In contrast, a wood surface with lower thermal conductivity would conduct heat from the skin at a slower rate. As a result, a metal surface will feel cooler than a wooden one even at the same temperature.

Convective heat transfer occurs when objects of different temperatures flow by each other. The dependence on the area of contact and a thermal gradient is the same as for conduction. Likewise, the convective heat transfer coefficient of the material is important. Thickness of the exchange materials, however, is not a determinant. The two mechanisms for convective heat transfer are passive and forced. Passive exchange occurs when air near the skin surface microenvironment is heated to result in a reduction in air density and movement up from the surface. This produces small currents of air that may result in significant heat loss under resting conditions. Forced convection occurs when external energy is used to move one material over

another. This mode of transfer is very important for internal heat movement, using blood flow and air movement in the respiratory system. Likewise, external movement of gas and fluid over the animal surface is an effective means for heat dissipation from the body when the temperature of the medium is below skin surface temperature. However, circulation of air or water over the animal surface at a temperature higher than skin temperature will actually add heat content and increase internal body temperature.

Radiant energy exchange relies on several factors that are the same for conductive and convective exchanges. They include the temperature of the transmitting objects, the thermal gradient, and the exchange surface areas. The reliance of these exchange routes, which are collectively classified as dry or sensible heat loss avenues (see Fig. 2.3), on a thermal gradient, also makes these routes less effective as environmental temperature approaches skin temperature.

There are, however, several differences between radiant exchange and the other sensible avenues. Radiant exchange is the only heat loss process that occurs at the speed of light (299,792 km/sec) and in a vacuum. In fact, exchange by this route cannot occur if there is fluid in the space between the emitters. The rate of radiant exchange between emitters is also dependent on the emissivity of the objects in the environment. Emissivity is defined as "the ratio of the total radiant energy emitted by a full radiator at the same temperature" (IUPS, 2001). A full radiator is an ideal emitter (maximum obtainable) of radiant energy from all parts of the electromagnetic spectrum. Usually this is a dull, non-shiny black surface that is

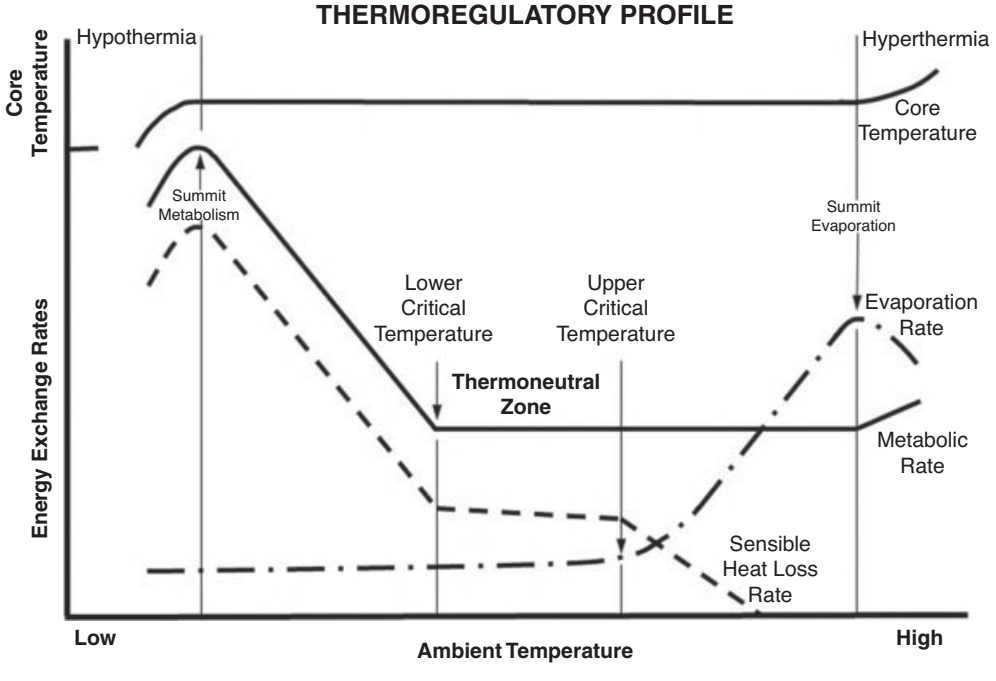

Figure 2.3. The thermoregulatory profile schematic showing both core temperature and energy exchange routes as functions of ambient temperature. Limits of homeothermy are identified with summit metabolic and evaporation rates. The thermoneutral zone is displayed by lower and upper critical temperatures (adapted from Mount, 1974).

referred to as a black body. The emissivity of a full radiator is one, and approaches zero for a shiny surface. Therefore, reflectance of an object's surface (shiny versus dull) is an important determinant of emissivity and absorptance. Both the emissivity and temperature of a surface determine the magnitude of electromagnetic energy emitted from an object and absorbed by it. In fact, this characteristic of an object is even more important than the color of an object's surface in affecting its capacity to absorb radiation, especially in a shaded environment or at night.

Any object with a temperature above absolute zero emits electromagnetic radiation. On average, the total radiant energy from the sun at the edge of our atmosphere is approximately 1.35 kW/m^2, and at least half of this energy is in the infrared region of the electromagnetic spectrum (Moss et al., 1982). More importantly nearly all-radiant exchange between living animals is in this region. The color of an object is an important factor during exposure to direct sunlight, with dark objects absorbing more energy in the visible portion of the spectrum than light objects. However, infrared exchange is the primary avenue in the absence of sunlight, and the color of an object is not a factor (Heppner, 1970). A dark-colored object will absorb and emit radiation equal to a light-colored object in the absence of visible solar radiation. The more important factor for radiant exchange, on average, is the nature of the surface (i.e., dull or shiny; rough/smooth hair or feather coat).

Evaporation is the fourth avenue for heat loss from an animal. Adams (2001) noted that "evaporation of a liquid is not an avenue of heat exchange (gain or loss); it is only a way to lose heat." Thermal energy is put into a liquid to produce a phase change to a gaseous state. When water evaporates from a surface, there is a loss of approximately 580 cal g^{-1} at a skin temperature of 30°C (Morimoto, 2001). The important point is that the water must evaporate from the surface (e.g., skin, respiratory mucosa) for heat loss to occur. If it does not change to a gaseous state due to high humidity, or if it drips off the animal, there is essentially no heat dissipation.

There are similarities and differences between evaporative loss and the other avenues of heat exchange. As noted for conduction, convection, and radiant exchange, the exposed exchange surface area is an important factor that determines the rate of heat loss by evaporation. In this case, it needs to be the wet surface. Likewise, air velocity across the wet surface is a determinant, as is true for convective exchange. At this point, the similarities end with notation of a characteristic of evaporative heat loss that makes it extremely useful in very hot environments. It is the only avenue that does not require a thermal gradient for heat loss. There is a reduction in heat loss by conductive, convective, and radiant avenues, as the temperature of the surrounding medium comes closer to skin temperature. This is the major reason why animals have reduced heat loss and overheat in hot environments. In contrast, evaporative heat loss increases above the upper critical temperature (IUPS, 2001; see Fig. 2.3) with commencement of active evaporative heat loss (e.g., panting, gular fluttering, sweating). The magnitude of heat loss via this avenue, and the driving force for evaporation, is the water vapor pressure gradient between the exchange surfaces and the environment. An increase in the water vapor pressure of the environment with a rise in humidity can severely limit heat dissipation to result in a greater level of hyperthermia.

All animals experience passive evaporative heat loss from both skin and respiratory surfaces (Hillman, 2009). Blood flows to all of these regions and hydrates the tissue at each site. If there is a water vapor pressure gradient for heat loss, then this will continuously occur at these surfaces and exhibit a slight increase with air temperature prior to active evaporation (see Fig. 2.3). Birds actually rely on passive evaporation from the skin, since they are devoid of sweat glands.

Active cutaneous evaporation occurs at the sweat glands. A comprehensive review of sweat glands (Folk and Semken, 1991), notes that there are sebaceous, apocrine (epitrichial), and eccrine (atrichial) glands in the skin. Apocrine glands are larger than eccrine and associated with hair follicles. They release fluid with adrenergic stimulation, while the eccrine glands rely on cholinergic pathways (Robertshaw, 1977). In humans, the apocrine glands are situated deep in the dermis and located in the pubic, anal, and axilla regions, with little involvement in thermoregulation (Folk and Semken, 1991). Instead, humans rely primarily on eccrine glands for evaporative heat loss associated with thermoregulation. These glands are located closer to the surface, and found in largest numbers on the palms and soles of the feet. In contrast, cows, sheep, and horses have only apocrine glands and effectively use these for evaporative cooling. The distribution of these glands in cattle varies greatly with region, with larger numbers in the trunk and neck, and fewer in the legs and ventral region (Hillman, 2009). These differences in numbers across regions result in large differences in sweat rate during heat stress (Scharf et al., 2008). Dogs and cats have few sweat glands and they are primarily located on the paws. As a result, these animals must rely on other mechanisms for evaporative cooling, such as panting. Pigs likewise have only a few sweat glands, and these are nonfunctional. Instead, they spread moisture on the skin that evaporates for cooling. Birds do not have sweat glands, and must depend on passive diffusion of moisture through the skin or use of the respiratory system for evaporation.

The respiratory tract is an important region for active evaporative heat loss in birds and mammals. Evaporation occurs primarily in the upper region of the tract where there are the largest thermal and vapor pressure gradients. In every animal, there is increased frequency of breathing above the upper critical temperature to increase heat dissipation. Mount (1979) noted that respiratory minute volume increases 10-, 12-, 15-, and 23-fold with panting in the ox, sheep, rabbit, and dog, respectively. This effectively increases evaporative heat loss, but reduces tidal volume for gas exchange in the lungs (Richards, 1970). Many birds combine panting with high frequency movement of the gular pouch to augment water evaporation during heat stress.

Thermoregulatory Profile

The complex balance between metabolic heat production, evaporative heat loss, and sensible heat exchange in determining core body temperature can be summarized using the thermoregulatory profile diagram (see Fig. 2.3). The extreme boundaries of the profile are those points outside of homeothermic maintenance, where core body temperature exhibits either a major reduction (i.e., hypothermia) beyond summit metabolism or an increase (i.e., hyperthermia) beyond the limit of summit evaporation. Although the theoretical basis of the profile predicts no change in core body temperature prior to reaching these limitations, there are significant shifts in temperature associated with circadian rhythm (Piccione and Refinetti, 2003; Bitman et al., 1984) and exposure to air temperature above the upper critical temperature. The upper and lower critical temperatures represent the inner, and generally more useful, borders of the thermoregulatory profile. They identify the range of the thermoneutral zone, where the animal expends the least amount of energy for thermoregulation. This zone is, by definition, the region where the animal has available the largest amount of energy for growth and production. For this reason, its identification is extremely important.

The lower critical temperature is the easier to define, as it is the ambient temperature below which the animal must increase its metabolic heat production to maintain a relatively constant

core body temperature. This temperature is stable in many large domestic animals far below the lower critical temperature simply due to their large body mass and small surface-area-to-volume ratio, which increases the capacity to store body heat. Although there is general agreement on the definition of lower critical temperature, this is not the case for the upper critical temperature or the upper limit of the thermoneutral zone. The official definition issued by the IUPS Thermal Commission (2001) is that it is "the ambient temperature above which the animal must increase evaporative heat loss rate to maintain thermal balance." Others define the upper critical temperature as the ambient temperature above which metabolic heat production increases as the animal augments heat loss activities (Curtis, 1983; Yousef, 1985). Mount (1979) notes that heat loss increases prior to this rise in metabolism, with increases in panting and sweating activities. Therefore, the region between the two points of increase in metabolism does not define the range of ambient temperature where the animal expends the least thermoregulatory effort. Metabolic rate increases during extreme heat stress due to the Q_{10} effect (Bligh, 1985) associated with the increase in core body temperature, which results from the animal reaching the limit of homeothermic control (see Fig. 2.3). Therefore, the latter definition of the upper critical temperature overextends the inner, more appropriate zone. The range and location of the thermoneutral zone changes as a function of species, age, and thermal adaptation (Yousef, 1985). For example, the newborn piglet has a lower critical temperature of 31°C compared to a lower critical temperature of 3°C for the lactating sow (Yousef, 1985). A reduction in thermal insulation with hair loss during summer months may shift both upper and lower critical temperatures upward in many animals (Bligh, 1985). Shifts in the thermoneutral zone can be useful in assessing the impact of an environmental stressor on animal performance, if other potential influences are controlled or identified as a part of the evaluation.

The last important component of the thermoregulatory profile is the change in sensible or non-evaporative heat loss rate as a function of air temperature (see Fig. 2.3). This value combines the avenues of heat exchange that depend on a thermal gradient (i.e., conduction, convection, and radiant exchange). Beginning at the point of summit metabolism, sensible heat loss is just below metabolic heat product and remains at this point up to the lower critical temperature. The sum of sensible and evaporative (i.e., insensible) heat losses should equal metabolic heat production, if core body temperature is to remain constant throughout this period. Sensible heat loss increases at a regular rate with a decrease in ambient temperature below the lower critical temperature because this is by definition the limit of animal adjustment in thermal insulation. Therefore, the progressive increase in the thermal gradient between body and ambient temperatures below the lower critical temperature (remember thermal insulation has reached its limit) must be accompanied by a rise in sensible heat loss that is matched by an increase in heat production. This explains the parallel nature of heat production and sensible heat loss during this period. The rate of decline in sensible heat loss is minimal within the thermoneutral zone because the animal is adjusting thermal insulation through behavioral (e.g., huddling) and physiological processes (e.g., peripheral vasodilation) to alter the body to an ambient thermal gradient. The upper critical temperature marks not only the initiation of active evaporative processes, but also a limit of the animal's adjustment of thermal insulation (e.g., maximally vasodilated). Sensible heat loss continues to decrease, with a matching increase in evaporative heat loss, beyond the upper critical temperature and eventually reaches zero when the ambient temperature equals the exchange surface temperature of the animal (usually skin temperature). At this point, evaporative heat loss must equal metabolic heat production to maintain homeothermy.

Although the thermoregulatory profile schematic does not show the detailed shifts in any of these variables in response to thermal stress, it has been repeatedly proven useful (Mount, 1979; Curtis, 1983; Bligh, 1985; Yousef, 1985; Spiers et al., 2005; Hillman, 2009) for illustrating basic principles that are the framework of the thermoregulatory system.

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Chapter 3

Heat Stress and Evaporative Cooling

Kifle G. Gebremedhin

Economic Loss

In the summer of 2006, the heat wave (with temperatures reaching above 38°C) in California killed 25,000 dairy cows (AFP, 2006). This loss was equivalent to $1,500 to $2,500 per head or between 37.5 and 62.5 million dollars total. The same news release reported that milk production in central California was down by 400,000 gallons (1.1 million liters) per day. In July 1995, a heat wave in Iowa caused dairy cow deaths and performance losses in the amount of 28 million dollars (Smiley, 1996). Although the California and Iowa heat waves were news-worthy, the impact of summer heat stress on dairy and feedlot cows has been an ongoing problem. It has been estimated that the U.S. dairy industry alone loses up to nearly 900 million dollars annually due to heat stress (St-Pierre et al., 2003).

Animals and Stress

Stress is the force or influence exerted on an object from the environment. The force can be physical or emotional. An intrinsic characteristic of living creatures is their ability to maintain internal stability (e.g., temperature, composition of blood, etc.). The natural environment is constantly changing at daily and seasonal paces, and the magnitude of environmental variations is large. Therefore, the optimal conditions under which the least effort (i.e., metabolic energy) is required to regulate body temperature seldom occurs and animals are coping with stress throughout most of their lifetime.

Animals living in the wild have been well adapted to their natural habitats and local climate; however, in modern animal production, domestic animals are confined in enclosed structures where they have limited mobility. Also the genetic makeup of many domestic animals has been modified to increase production, leading to increased metabolism that makes animals more vulnerable to stressors. Closely monitoring and assessing the thermal stress exerted by

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the thermal environment on animals is a basic and necessary operating routine for animal producers. Animal producers need to monitor the thermal status of their herds.

Biological Optimum Temperature

It would be useful to have an indicator that would allow comparison of animals' abilities to cope efficiently within a given housing or environmental condition. Unfortunately, when attempting to apply this simple concept to a complex biological organism, there is no time of least thermoregulatory effort, because studies have not found a wide range of ambient temperature where metabolism is at a constant minimum (Nichelmann, 1983). The term, "biological optimum temperature" has been proposed as an ambient temperature where the animal is, on average, under the least amount of thermal stress, with respect to such factors as health, growth, production performance, and so on. Each of these factors has optimum temperatures that usually differ from one another. Integrating these factors yields an optimum temperature, which can be described as the ambient temperature where core body temperature is at a minimum. Biological optimum temperature is not a constant value, but it varies with respect to factors as the state of acclimation, age, breed, size, or microclimatic conditions. Therefore, in order to meaningfully characterize the point of minimum thermal stress for a farm animal, one must know the breed, age, sex, health, thermal history, environmental settings, nutritional status, and microclimatic conditions – all of which can change the biological optimum temperature (Hillman, 2009).

Animal-Environment Interactions

The components of thermal environment include air temperature, relative humidity, radiation (solar and thermal), and wind speed. Living objects interact with these environmental conditions in complex ways. Physiological responses – observed or measured – when animals are exposed to thermal stress include body core temperature, skin temperature, sweating rate, respiration rate, feed intake, and production performance (e.g., egg yield, milk yield, body weight gain, conception success rate). The immune systems and behaviors of animals also change under thermal stress (Hillman, 2009). Since the thermal environmental components can be easily measured, and the physiological indicators as well as immune functionality and animal behaviors are either difficult or tedious to measure and quantify, finding linkages between the thermal environmental conditions and animal reactions becomes important when assessing animal comfort.

Various behavioral and autonomic thermoregulatory mechanisms are utilized by cattle to relieve heat stress. A distressed animal may seek shade, change its orientation to the sun, and increase water intake (Blackshaw and Blackshaw, 1994). Sweating and panting are two of the primary autonomic responses exhibited by an animal under heat stress. Sweating leads to evaporative heat loss from the skin surface, whereas in panting, sensible heat is used to heat the water vapor and remove heat in the form of vaporized moisture from the lungs.

Thermal Stress Indicators

Respiration rate and rectal temperature are easily measurable indicators of heat stress in dairy or feedlot cows. Stowell (2000) suggested that a respiration rate of 80 to 90 breaths/min was a clear indication of a cow experiencing heat stress. Armstrong (1994) devised a stress chart

for cows as a function of ambient temperature and relative humidity. He suggested five stress-level categories, which are functions of temperature and relative humidity. The five categories are (1) no stress, (2) mild stress, (3) distressed, (4) severe stress, and (5) fatal conditions. These stress-level ranges do not account for effects of solar radiation, physical and optical characteristics of hair coats, convective cooling due to wind, or variations in breed.

Several studies have been conducted to identify accurate predictors of bovine thermoregulatory status. These include studies of rectal (Bligh, 1957) and tympanic temperature (Hahn et al., 1992). It is often desirable to obtain continuous deep-body temperature records for longer periods of time for studies of reproductive and environmental physiology. An automated radio telemetric system for continuous monitoring of vaginal temperature has been shown to be effective for the prediction of estrus in dairy cows (Bergen and Kennedy, 2000). Kyle et al. (1998) also studied the feasibility and effectiveness of using vaginal temperature, as measured by radio telemetry, for the prediction of estrus in suckled beef cows.

There are different temperatures that may represent the internal body temperature including subdermal, tympanic membrane, rectal, and vaginal temperatures. The question is which one is a measure of or is equivalent to deep-body temperature. Hahn et al. (1990) reported that subdermal, rectal and tympanic membrane temperatures agreed closely in steers exposed to high ambient temperatures. Rajamahendran et al. (1989) obtained a correlation between rectal and vaginal temperatures ($R^2 = 0.95$) in cycling dairy cows. Similarly, Hillman et al. (2009) obtained a correlation between rectal and vaginal temperatures ($R^2 = 0.90$) from measurements made from 20 pregnant dairy cows. Bergen and Kennedy (2000) obtained a correlation between vaginal temperature and tympanic membrane temperature ($R^2 = 0.77$) of nine crossbred beef heifer calves (8 months of age and weighing 282 ± 27 kg) continuously monitored over five to six days.

Elevated body (rectal) temperature and respiration rate are physiological responses to exposure to stressful environments. Rectal temperature is a more reliable indicator of heat stress than respiration rate or skin temperature (Hillman et al., 2005). However, rectal temperature measurement using a rectal probe can disturb the behavior of a cow, and the procedure is time consuming, and more importantly, does not provide a continuous record. An alternative approach that is reliable, accurate, cost effective, easy to implant, and produces continuous measurements of vaginal temperature was reported in Hillman, et al. (2009). The vaginal temperature device was designed and fabricated by molding a special plastic anchor (similar to the original design by Redden et al., 1993) to encase a data logger.

Skin temperature is a dynamic quantity and is affected by physiological and thermal factors and physical and optical properties of hair coat. One of the physiological factors that influences skin temperature is evaporative cooling. This occurs when sensible heat on the skin surface is converted to latent heat. A higher level of evaporation, therefore, means a higher level of cooling on the skin surface.

Air Temperature and Evaporative Cooling

Livestock strive to maintain a reasonably constant internal body temperature by balancing metabolic heat production with heat exchange to the environment. Internal body temperature is maintained constant through a wide range of ambient temperatures by adjusting metabolic heat production. The range of thermoregulatory responses is quite diverse, and livestock express this diversity.

Heat loss from cows is divided into sensible and latent (evaporative). Sensible heat loss comprises heat loss by conduction, convection and radiation, whereas evaporative heat loss

involves cutaneous (water evaporation from the skin surface) and water loss through respiration. Evaporative heat loss represents a small fraction of metabolic heat production at low ambient temperature. Heat loss by cutaneous evaporation accounts for 20 to 30% of the total heat loss when air temperature is between 10 and 20°C but when air temperature is greater than 30°C, cutaneous evaporation becomes the primary venue for heat loss, accounting for approximately 85% of the total heat loss, while the rest is lost by respiratory evaporation (Maia et al., 2005). When ambient temperature equals internal body temperature, sensible heat loss is zero and evaporative heat loss via sweating and panting becomes the only available venue for heat loss. Both sweating and panting have the undesirable side effect of depleting body water reserves, especially when water is in limited supply.

When ambient temperature is high, the temperature gradient between the skin surface and air is reduced, thus lowering sensible heat loss from the skin surface. As sweating is increased at high ambient temperatures, evaporative cooling becomes the dominant mode of heat loss. Evaporative cooling is affected by wind velocity, relative humidity, and thermal and solar radiation. Other factors that affect the efficacy of evaporative cooling from the skin surface are hair coat physical and optical characteristics. Hair coat density and thickness, hair length and color, and skin color are also factors that influence evaporative cooling. For example, black, hair and skin enhance solar absorption and thus increase heat load on the skin surface. Other properties such as hair coat density obstruct evaporation of water from the skin surface by trapping a thin film of water at the skin-hair coat interface.

Wetting as Supplemental Cooling

Sweating moistens the skin surface and usually leaves the hair coat dry. Wetting the hair coat with a mist of water adds water to the hair coat and skin surface. The process of evaporative cooling is a complex interaction of humidity and temperature difference between air and skin, air velocity, and hair coat characteristics such as density and depth. Cooling by evaporative heat loss resulting from wetting the hair coat is proven to be more effective than sweating (Kimmel et al., 1991). Hillman et al. (2005) reported that heat-stressed cows actively stand under water spray to wet their bodies. The authors further reported that this cooling method lowered core body temperature. A faster drop in core body temperature was recorded when water spraying was done at short time intervals and was further enhanced with air velocity over the body (Brouk et al., 2003; Hillman et al., 2001a).

Air Velocity and Evaporative Cooling

A common method of cooling cows is to blow air over them. Wind greatly increases evaporative cooling of the skin surface. Wind penetrates the hair coat and reduces the effective thermal resistance of the hair coat (McArthur, 1987; Berman, 2004). Thermal resistance of the hair coat decreases linearly with increasing air velocity. Hillman et al. (2001b) reported that increasing air velocity over a dairy cow from about 0.2 to 0.9 m/s increased sweating rate from 75 g/m^2-h to about 350 g/m^2-h.

Impact of Solar Radiation on Sweating

Continuous recording of the sweating rate of cattle in their natural habitat is not easy. It is also difficult to compare sweating rates or moisture production data that exist in the literature

because of incompatibility in measurement methods and environmental conditions under which the data were collected. Another important factor is that moisture production data from dairy cows are primarily from studies conducted in the 1950s, 1960s, and 1970s (Ferguson and Dowling, 1955; Yeck and Stewart, 1959; McDowell et al., 1961; McLean, 1963; Schleger and Turner, 1965; Joshi et al., 1968; Allen et al., 1970), and thus do not reflect the moisture production of present-day high producing cows. Recent studies by Gebremedhin et al. (2008, 2010) provide sweating rates of different breeds of high producing dairy and feedlot heifers in their natural habitats. There is also considerable variation in sweating rates between cows of the same breed (Gebremedhin et al., 2010), perhaps due to genetic variation in thermal regulation.

When cows sweat, they sweat in a cyclic (periodic) manner (Gebremedhin et al., 2010). This suggests that there is a filling and secretory phase of the sweating process in cattle, similar to what was reported for sheep. Robertshaw (1968) reported that the pattern and control of sweating in one breed of goat and six breeds of sheep resulted in periodic discharges of moisture onto the surface of the skin. He further reported that for the same number of active sweat glands, the frequency of discharge showed considerable variation between individual animals.

Continuous recordings of sweating rates are necessary to study the cyclic pattern. Static or instantaneous spot measurements would lead to erroneous conclusions because it would not be evident where the measurement was made in the cycle. This explains the considerable variation in sweating rates, or moisture production values, seen in the literature.

There is considerable variation in sweating rates between cows of the Holstein breed (Gebremedhin et al., 2010). The variations may be attributed to genetic variation in thermal regulation. A similar variation in sweating rates was reported for the Angus breed (Gebremedhin et al., 2008). Also, a physiological upper limit of sweating rate, which is different for each cow, seems to exist. The maximum rate of sweating recorded (Gebremedhin et al., 2010) was 668 g/m^2-h and that was during a hot and dry exposure (average air temperature = 35.1°C, average relative humidity = 23.1%, average temperature-humidity index (THI) = 79.6, and solar load = 550 watts/m^2). In a different study, Gebremedhin et al. (2008) reported a maximum calculated sweating rate mean of 522 ± 127.7 g/m^2-h (the range being between 189 ± 84.6 and 522 ± 127.7 g/m^2-h), in which the absolute maximum would be about 660 g/m^2-h. The THI and wind velocity were similar in both studies. Based on these two independent studies, therefore, one can conclude that the maximum rate of sweating of dairy cows and feedlot heifers is around 660 g/m^2-h. During this exposure, core body temperature ranged between 39.3 ± 0.53°C and 41.7 ± 0.19°C when the cows were exposed to solar radiation greater than 500 W/m^2 (average 833 ± 132 W/m^2), an average THI of 82.7 ± 1.64, and air velocity between 0.2 and 1.8 m/s. The recorded core (rectal) temperature was greater than the threshold for heat stress, which was 38.8°C. Jersey cows sweat less (189 ± 84.6 g/m^2-h) than Holstein black (414 ± 158.7 g/m^2-h) or Holstein white (281 ± 119.4 g/m^2-h; Gebremedhin et al., 2008).

It has been reported (Gebremedhin et al., 2010) that sweating rates and core and skin temperatures are higher in hot and dry conditions (average air temperature = 35.1°C, average relative humidity = 23.1%, average THI = 79.6, and solar load = 550 W/m^2) than those in hot and humid conditions (average air temperature = 29.1°C, average relative humidity = 69.2%, average THI = 79.6, and solar load = 550 W/m^2). When relative humidity is higher, the moisture gradient between the skin surface and ambient air is reduced, consequently decreasing the efficacy of evaporative cooling. Therefore, in a hot and humid environment, an inverse relationship occurs between relative humidity and sweating rate. In a hot and dry environment, however, sweating rate increases because of higher moisture gradient between the skin surface and ambient air.

Sweating, and thus evaporative cooling, is primarily driven by skin temperature (Gebremedhin et al., 2010). This conclusion was verified by "turning off" solar load on dairy and beef heifers. When solar load was turned off, sweating rate, respiration rate, and skin temperature decreased almost instantaneously. However, there was a time lag before the core temperature started to come down. These responses suggest that skin temperatures are most likely the driving force for sweating.

Effect of Animal Hair-Coat Color on Evaporative Cooling

In a study of the effect of hair color on thermoregulation, Hillman et al. (2001a) reported that when Holstein cows were exposed to direct sunlight average surface temperatures increased by 4.8°C in black Holstein cows compared to 0.7°C for white cows. The difference in temperature between black and white cows is because of higher solar absorptivity by black than white. They also reported that rectal temperature increased at a rate of 0.7°C/h for black cows and 0.3°C/h for white cows, and that black cows had higher evaporative heat loss (800 W/m^2) than their white counterparts (500 W/m^2). The study concluded that providing shade is crucial to shield cows from direct solar radiation.

Da Silva et al. (2003) investigated radiative properties of skin and hair coat of various breeds of cattle with respect to shortwave radiation. The study concluded that light-hair coats exhibited much higher reflectivity than dark-hair coats for wavelengths ranging from 300 to 850 nm. Kovarik (1964) suggested that transmission of solar radiation would be stronger in light-hair coats than in dark-hair coats. The same conclusion was reached by Gebremedhin et al. (1997). At low wind speed, the effect of solar absorption exceeded the effect of penetration of solar radiation into the hair coat, which would cause a greater heat load in dark-colored hair coats (Hutchinson and Brown, 1969).

In another study, Hillman et al. (2005) reported that heifers exposed to sunlight gained more sensible heat than those under shade. The heat gain was profoundly higher for heifers with dark black (e.g., Black Angus) and dark red hair coats than those with white and tan hair coats. The authors reported an increase in sensible heat flux in the order of 26% for dark-red, 22% for black, 5% for tan, and 4% for white.

Hair Coat and Evaporative Cooling

Sweating rates from shaved and unshaved black and white hair-coat areas of cows exposed to sunlight are shown in Figure 3.1. Sweating rates from the shaved areas are higher than those from unshaved areas, regardless of hair coat color. On average, the sweating rate from black shaved areas was 1.84 times higher (655 $g/h\text{-}m^2$) than that from unshaved black hair coat areas (356 $g/h\text{-}m^2$). Similarly, the sweating rate from a white shaved area was 1.64 times higher (509 $g/h\text{-}m^2$) than that from unshaved white hair coat (310 $g/h\text{-}m^2$).

What happens when the hair coat is shaved? Conversion of sensible heat to latent heat is unobstructed because sweat (water) on the skin surface is directly exposed to ambient air and solar radiation. On the other hand, when the hair coat is not shaved, the presence of the hair coat above the sweat glands might act as a moisture trap creating locally a more humid condition. The presence of moisture in the hair coat results in a lower moisture gradient between the skin surface and the hair-coat layer above it, causing less evaporation to occur, and consequently

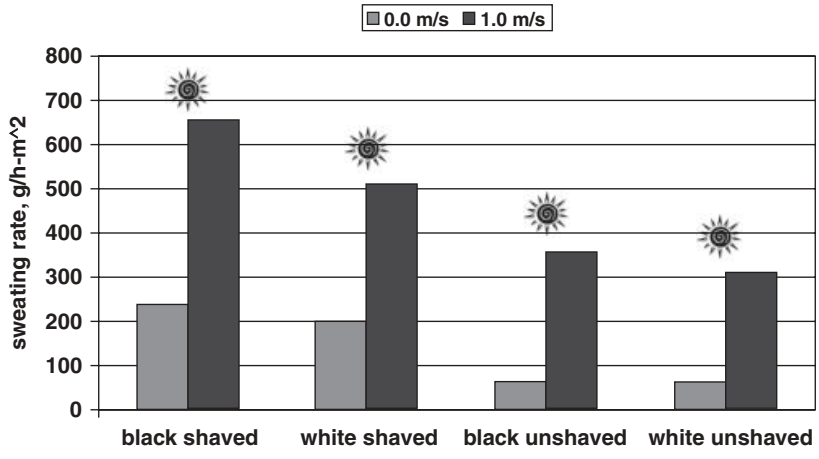

Figure 3.1. Average sweating rate of cows with black and white hair coats, shaved or unshaved, under direct sunlight for two air velocities.

depressing heat loss from the skin surface. The presence of the hair coat conserves heat by trapping air within it. The trapped air serves as insulation when the weather is cold but becomes an obstruction to the evaporation of moisture from the skin when the weather is hot. This is perhaps why cows shed some of their hair during the summer.

Shade as a Solar Shield

Shade provides an efficient means to shield an animal from direct sunlight. Trees render natural shade for cattle outdoors; however, if there are not enough trees to provide shade, man-made shade must be provided to keep cows cool. Providing artificial shade to all cattle can be cost prohibitive. Thus, a dairy farmer may selectively put cows that are vulnerable to heat stress under shade. The cows that are more likely to experience heat stress can be determined from various physical characteristics and measurable indicators.

When cows are under shade, sweating rates from black and white hair coats are not different, as evaporation from the skin surface is driven by a moisture gradient without solar input. When cows are exposed to direct sunlight (no shade), cows with black hair coat absorb more heat (sensible heat gain) than cows with white hair coat thus elevating the skin temperature. The absorbed heat evaporates the moisture (sweat) on the skin surface, but if the skin temperature becomes higher than the core temperature because of solar gain, heat flows inward thus raising the core temperature and consequently increasing the thermoregulatory effort of the animal.

Gebremedhin et al. (2007) reported that when cows were exposed to direct sunlight, the average temperature of cows with black hair coat was 42.9°C but when they were in shade it dropped to 37.6°C. This drop was due to the absence of solar load. Similarly, the average temperature of cows with white hair coat in sunlight was 39.1°C and in shade was 36.8°C. The difference in skin temperature between black and white hair coats when exposed to sunlight is due to the higher solar absorption characteristics of black surface.

Measuring Evaporative Cooling

As mentioned previously, continuous measurements of sweating rate, core body temperature, skin temperature, and respiration rate are necessary to determine thermoregulatory status of a cow. It is even more challenging to monitor these responses for cows in their natural habitats and during normal activities. This section discusses measurement systems used and procedures followed by the author and his collaborators in various research activities.

We designed and successfully fabricated a Portable Bovine Evaporation Meter that (a) allows measurements of temperature and relative humidity of air coming in and leaving out from a sample area on the body of a cow, (b) accounts for long- and short-wave radiation, and (c) allows air velocity (up to 2.0 m/s) to flow through the sample area. The system allows for continuous measurements of sweating rates for cows in their natural habitat. Further details of the system can be found in Gebremedhin et al. (2008).

Continuous measurements of internal body temperature (vaginal temperature) can be accomplished by inserting a temperature logger encased in a specially constructed soft plastic anchor into the vagina of a cow. An anchor with "fingers" would be required to hold the logger in place (inside the vagina), as it is smooth, relatively small, and cylindrical in shape. The anchors are manufactured from plastisol – a flexible translucent plastic that could be molded to a desired configuration. The material is contact compatible with dairy products but is not known if it qualifies for a long-term implant. Details of fabrication of the anchors are given in Hillman et al. (2009). For example, the temperature sensor in the Water Temp Pro is located inside at the end, next to the mounting hole, which is left uncovered by the plastisol anchor. The Water Temp Pro was selected for discussion because it is waterproof, non-toxic to animal tissues, can be used up to a temperature of 50°C, contains 6-year battery life and is replaceable, is accurate to ± 0.2°C at 0 to 50°C, and records up to 21,580 measurements, which is equivalent to 75 days of measurements at five-minute intervals.

Before insertion into the vagina, the anchors were placed in warm (39°C) sterilizing solution and the vulva was disinfected. The warmth of the solution makes the fingers more flexible, which makes insertion easier. The anchor with the logger in place is inserted at least 10 cm into the vagina with the sensor of the probe facing the anterior of the cow.

The advantage of the aforementioned system is continuous recording of vaginal temperatures. This procedure provides vaginal temperature responses of cows in their natural habitat and during normal activities. These procedures emphasize the importance of looking at heat stress on a continuous basis under normal activities of cows. The system also allows one to study behavior of cows under heat stress without intruding into their comfort zone and changing the normal behavioral responses. It allows one to determine the crucial temperature when a cow seeks relief from heat stress and monitors core body temperature changes for normal activities such as eating, lying down, standing, walking, etc. Relating these natural events to physiological responses would enable scientists and dairy producers to devise management schemes and housing facilities to improve animal well being. Continuous monitoring of vaginal temperature without affecting the normal behavior of cows is one critical component in our understanding of heat stress on dairy cows.

Skin surface temperature can be measured using a handheld infrared thermometer. Respiration rate can be obtained visually by counting chest movements of a cow. Air temperature, relative humidity, wind speed, and solar radiation can be continuously recorded with a weather station system. All measuring instruments must be calibrated against National Standards and Technology, which is traceable to give desirable accuracy within the ranges of measurements.

Measuring Hair Coat Physical and Optical Properties

The hair coat of animals plays a critical role in heat and moisture transfer from the skin surface. Endotherms interact with the thermal environment, which affects their growth, production, and reproduction potential at the skin-hair coat interface. An animal's hair coat traps air to provide insulation from cold but becomes an obstruction for evaporative cooling by reducing the velocity and moisture gradient through the hair-coat layer in hot and humid conditions.

Hair coat properties are inputs to models of bioenergetics (heat and mass balances) of animals. It is therefore imperative that physical and optical properties of the hair coat are accurately characterized for modeling heat and moisture transfer through the hair coat. In addition, hair coat properties can provide information on the breed of animals that are more likely to adapt to a particular environment. Availability of physical and optical properties of hair-coat data in the literature are sparse at best.

Da Silva et al. (2003) measured physical properties (hair-coat depth, hair length, hair-coat density, and hair diameter) and solar reflectivity of hair coat from Simmental, Canchim, Brangus, and Nelore breeds of cattle. The samples were collected from only one central area of the trunk, and no information was given with respect to the age of the cattle or the season in which data were collected. The breeds were chosen for their distinguishable hair-coat colors. The study reported that light hair coats had higher reflectance values than dark hair coats for 300 to 850 nm of wavelength.

Maia et al. (2003) studied the physical and optical properties of Holstein cow hair coats, and reported that the white hair coat was denser, longer, and made up of thinner hairs than the black hair coat, which was less dense, shorter, and made up of thicker hairs. Solar absorptivity of the hair coat was higher in the black hair coats with long and thick hairs. Similarly, Brown et al. (2006) observed cattle for heat stress signs when the cattle were exposed to direct sunlight over a two-year period. The author reported that various breeds of cattle have shown high stress in hot environments. In a hotter climate, Charolais (white colored) have shown to be the most temperament. Brown et al. reported that higher stress was linked with lower health and immunity for cattle. The study further discussed the potential for poor growth, production losses, and the rare cases of losses through death.

Solar reflectivity and transmissivity of hair coat can be measured using a fiber optic spectrometer. A light source that has a halogen bulb with resemblance to natural lighting can be used. To prepare samples for measurements, a surgical blade can be used to make an incision parallel to the skin surface, directly below the skin. The skin is cut out as close to the hair coat as possible without disturbing the hair coat. The samples need to be dried before use.

Hair density (hairs/cm^2) – the number of hairs per area – can be determined by counting images of follicles at 12x magnification using a special digital camera mounted onto a microscope. Hair diameter is measured with a digital vernier caliper. Hair-coat thickness can also be measured using the end tip of the digital vernier caliper by gently pushing it against the skin surface.

Modeling

Mathematical models have been developed for over 30 years to simulate the thermal interactions of animals and their environment. Models are useful to predict the outcome of the complex interactions of multiple environmental and physiological variables. Mechanistic models have been developed over the years to examine the complexities of sensible and latent (evaporative) heat transfer within the hair coat of cattle, the interface between the cow and the

environment (Gebremedhin, 1987; Gebremedhin et al., 1997; Gebremedhin and Wu, 2001). These models predict cutaneous evaporative heat loss. Cutaneous evaporative heat loss increased with increasing ambient temperature, solar load, wind speed and hair density but decreased with increasing relative humidity and thickness of the hair coat. Mechanistic models that predict heat loss from cows in a ventilated space where the airflow in the space is modified by the cows themselves have also been developed (Gebremedhin and Wu, 2003, 2005). A more specific model for cattle in hot conditions has been developed by McGovern and Bruce (2000) and includes a coded user-friendly software package to aid cattle farmers in managing the environment for their herds. Brown-Brandl et al. (2005) and Eigenberg et al. (2005) have developed models that provide indicators of heat stress so that livestock producers can intervene in a timely fashion by providing appropriate cooling. Additional physiological response measurements under a known set of environmental conditions are needed to further validate existing models.

Conclusions

The following conclusions can be drawn from this chapter:

1. It has been estimated that the U.S. dairy industry alone loses up to nearly 900 million dollars annually due to heat stress.
2. Living objects interact with the environment in complex ways. There exists no optimum temperature in which an animal is, on average, under the least amount of thermal stress with respect to health, growth, production performance, reproduction potential, etc. Each of these factors has optimum temperatures, which usually differ from one another.
3. Various behavioral mechanisms (seeking shade, changing orientation with respect to the sun, increasing water intake) and autonomic thermoregulatory mechanisms (sweating, panting) are utilized by cattle to relieve heat stress.
4. Rectal temperature is a more reliable indicator of heat stress than respiration rate or skin temperature. Respiration rate is the first responder to counter rising internal body temperature. Skin temperature is a dynamic quantity and is affected by physiological and thermal factors, as well as physical and optical properties of the hair coat.
5. Evaporative heat loss represents a small fraction of metabolic heat production at low ambient temperature. Heat loss by cutaneous evaporation accounts for 20 to 30% of the total heat loss when air temperature is between 10 and 20°C, but when air temperature is greater than 30°C, cutaneous evaporation becomes the primary venue for heat loss, accounting for approximately 85% of the total heat loss, while the rest is lost by respiratory evaporation.
6. Cooling by evaporative heat loss resulting from wetting the hair coat is proven to be more effective than sweating.
7. Dairy cows and feedlot heifers sweat in a cyclic manner. A continuous and prolonged exposure to a stressful thermal environment as well as continuous sweating rate measurements are necessary to establish the cyclic phenomenon of sweating. The data of moisture production available in the literature corresponds to static or instantaneous measurements and thus cannot show the cyclic nature of sweating.
8. A physiological upper limit of sweating rate, which is different for each cow, seems to exist. The maximum rate of sweating recorded was 668 g/m^2-h and that was during a hot and dry exposure.

9. Skin temperature seems to be the primary driving force for sweating/evaporative cooling. Blowing air onto the skin increases cutaneous evaporation.
10. Shade provides an efficient way of shielding an animal from direct sunlight. In direct sunlight, cows with black hair coat absorb more heat (sensible heat gain) than cows with white hair coat thus elevating the skin temperature. The absorbed heat evaporates the moisture (sweat) on the skin surface, but if the skin temperature becomes higher than the core temperature because of heat gain, heat flows inward, thus raising the core temperature and consequently increasing the thermoregulatory effort of the animal.
11. Vaginal temperature can be continuously recorded by using a data logger encased in a plastic anchor with fingers. The system is reliable, accurate, easy to implant and retrieve, and does not fall out. The data can be downloaded to a computer with ease. The system allows observation of cows in their natural habitat without any negative effects on their activities.

Future Research Directions

Several stress index equations exist in the popular literature. These equations are generally regression equations – some link a physiological response to environmental factors (Eigenberg et al., 2005; Gaughan et al. 2008) and others simply calculate temperature-humidity indices without correlating them with physiological responses (Thom, 1959; Mader et al., 2006). Farmers need user-friendly computer programs that are based on rational indices of heat stress derived from fundamental principles of heat and mass balance calculations of biological objects. These user-friendly programs can then be used to help manage herds faced with stressful environmental conditions. A program should be designed that translates indices of heat stress into providing useful herd management decision. The program should incorporate an interactive excel worksheet that is flexible to account for the necessary stress factors and that is easily and periodically updated as new information is available and models are improved.

It is also important to note that correlating a physiological response to environmental stressors alone may lead to misleading (inadequate) results. For example, a physiological response such as sweating rate, is affected by environmental stressors (e.g., solar load, air temperature, relative humidity), as well as skin temperature, a dynamic physiological response, which itself is affected by environmental stressors.

It is difficult to utilize measurements reported in the literature for validation of existing models because many fail to include important values of environmental stressors and animal responses of stress indicators for extended periods of time. Simultaneous measurements of skin temperature, air temperature, core temperature, ground and sky temperatures, wind speed, skin wetness, respiration rate, solar radiation, relative humidity, and hair coat physical and thermal properties are required to validate, for example, coupled heat and mass-balance based models.

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Chapter 4

Regulation of Acclimation to Environmental Stress

Kajal Sankar Roy and Robert J. Collier

What Is Acclimation?

A variety of environmental factors such as ambient temperature, solar radiation, relative humidity, and wind speed are known to have direct and indirect effects on domestic animals (Collier et al., 1982, 2004, 2005). The direct effects involve impacts of the environment on thermoregulation, the endocrine system, metabolism, production, and reproduction. Indirect effects include impacts of the environment on food and water availability, pest and pathogen populations, and resistance of the immune system to immunologic challenges. Animals have developed coping mechanisms to minimize the impact of these environmental stressors on their biological systems. These responses are broadly described as acclimation, acclimatization, and adaptation. Acclimation is the coordinated phenotypic response developed by the animal to a specific stressor in the environment (Fregley, 1996), while acclimatization refers to the coordinated response to several individual stressors simultaneously (e.g., temperature, humidity, and photoperiod; Bligh, 1976). In general, there is hardly ever a case in the natural environment where only one environmental variable changes. Thus, in the vast majority of cases the animal is undergoing acclimatization to the changing environment. Acclimation and acclimatization involve phenotypic and not genotypic change, and the acclimation responses will decay if the stress is removed. The overall impact of acclimation and acclimatization is to improve the fitness of the animal in the environment. In many cases the acclimation response is induced by sudden environmental change. In other examples the acclimation response is driven by changes in photoperiod or other environmental cues such as the lunar cycle, which permit the animal to "anticipate" the coming change in the environment leading to seasonal acclimation adjustments in insulation (coat thickness, fat deposition), feed intake, or reproductive activity in advance of the actual environmental change. However, in every case, the process is driven by the endocrine system and is "homeorhetic." Homeorhesis is defined as the "coordination of

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metabolism to support a specific physiologic state" (Bauman and Currie, 1984). In this case the specific physiologic state is the "acclimatized animal."

Adaptation: *Bos indicus* versus *Bos taurus*

If environmental stressors are present for prolonged periods of time (e.g., years) the metabolic and physiologic adjustment can become "fixed genetically" and we refer to this state as the "adapted" state of animal. Examples are *Bos indicus* breeds of cattle, which have evolved under conditions of high temperature and humidity and display a number of genetic differences that endow them with improved thermotolerance, compared to *Bos taurus* breeds of cattle, which evolved under temperate weather conditions.

Bos indicus cattle have greater thermoregulatory capability than *Bos taurus*. As pointed out by Hansen (2004), *Bos indicus* cattle produce less heat, have increased capacity to lose heat toward the environment, or a combination of both. This suggests that low metabolic rates resulting from reduced growth rates and milk yields of many Indicus breeds constitute a major contributing factor to thermotolerance. The basal metabolic rate of *B. indicus* is in fact lower than that for *B. taurus* (Finch, 1985). The physiological and cellular basis for this difference has not been identified. One possibility for improved heat loss in *B. indicus* is that the density of arteriovenous anastomoses is higher in *B. indicus*. Since these structures have lower resistance to flow than vascular passages involving capillary networks, they facilitate increased blood flow to the skin during heat stress (Hales et al., 1978).

The vascularity and degree of insulation of the skin and quality of the hair coat (hair and skin coat color, thickness and density of hair fibers) also contribute to the effectiveness of heat loss in cattle (Gebremedhin et al., 2008, 2010). All of these are affected by breed and contribute to well-known genotype × environment effects.

The actual rate of heat loss via sweating depends not only upon the extrusion of water at the skin surface but also upon the evaporation of that water. It has been observed that evaporative heat loss rates were less affected by humidity for Indicus cows than for Holstein and Brown Swiss cows. For example, studies showed that the sweating rate in Indicus cattle exposed to heat stress was unaffected by humidity of the surrounding air while the sweating rate of Shorthorn cattle was reduced as humidity increased (Finch, 1985). This result was interpreted as reflecting the greater trapping of humidified air in the dense hair coat of the Shorthorns. There is no evidence that respiratory capacity for heat loss is superior for Indicus cattle. The proportion of evaporative heat lost via respiration was roughly similar for Indicus, Holstein, Jersey, and Brown Swiss (Kibler and Brody, 1952). During heat stress, evaporative heat loss via respiration rate can be greater for European breeds and this occurrence also probably reflects the greater engagement of heat loss mechanisms for the less-adapted breeds.

There is a general belief that the appendages of *B. indicus* cattle contribute to their superior thermoregulatory ability, as the appendages increase the surface area per unit body weight as compared to *B. taurus*. The actual importance of these anatomical features is not likely to be crucial for thermoregulation because surgical removal of the dewlap or hump of Red Sindhi bulls did not have a measurable impact on thermoregulatory ability (McDowell et al., 1958). Additionally, differences in regulation of rectal temperature in response to heat stress were observed between Jersey and Red Sindhi × Jersey even though surface area per unit body weight or metabolic body weight was similar between the two genotypes.

Heat stress has less severe effects on semen quality of Indicus bulls than it does on bulls of European breeds, and this phenomenon reflects not only adaptations that affect whole-body

thermoregulation but also specific adaptations that enhance the local cooling of blood entering the testis. A study by Brito et al. (2004) demonstrated that the anatomical features of the testicular thermoregulatory system differed between Nelore, crossbred (5/8 or 5/16 Charolais × Zebu) and Angus bulls. For example, the ratio of testicular artery length to testicular volume was greatest for Nelore bulls, intermediate for crossbred bulls, and least for Angus bulls. In addition, the testicular artery wall thickness and the distance between arterial–venous blood in the testicular vascular cone were least in Nelore, intermediate in crossbreds, and greatest in Angus. These anatomical differences were related to differences in testicular intra-arterial temperature, which was lowest in Nelore, intermediate in crossbreds, and highest in Angus (Brito et al., 2004).

When animals are adapted the physiologic differences between them and non-adapted animals do not disappear when the environment changes. This is not the case in acclimation where differences do disappear if the stress is removed. However, it is becoming clear that the same systems that are involved in acclimatization are the systems that endow animals with thermotolerance or adaptation to heat. Therefore, obtaining a better understanding of the gene networks involved in response to environmental stress will also lead us to those pathways which offer promise to improve thermotolerance.

Acclimatization requires several days to weeks to fully develop, there is a hormonal link between the central nervous system and the effector cell types involved, and the effect of the hormonal change is to alter the responsiveness of the effector cells to environmental change (Bligh, 1976). These key features are hallmarks of a homeorhetic process in which metabolism of multiple tissues and organs is coordinated to support the new acclimatized state as contrasted to a homeostatic process (Bauman and Currie, 1984; Collier et al., 2004), and where regulation is occurring around a set point. We then need to consider the stages of acclimation, the hormones that are driving acclimation, and what changes are occurring in effector tissues to accomplish development of the acclimatized state.

What Are the Stages of Acclimation?

Acclimatization is generally considered to occur in two stages: acute or short term and chronic or long term (Johnson and Vanjonack, 1976; Horowitz, 2002; Garrett et al., 2009). The acute phase includes a shock response at the cellular level (Carper et al., 1987; Sonna, 2002) and homeostatic endocrine, physiological, and metabolic responses at the systemic level. The chronic or long-term phase results in acclimation to the stressor and involves the reprogramming of gene expression and metabolism (Horowitz, 2002; Collier et al., 2006).

In agricultural animals there is generally a loss in productivity as animals progress through the acute phase and some or even all of this productivity is restored as animals undergo acclimation to the stress.

What Is Involved in the Systemic Response?

The systemic response to environmental stress is driven by two systems: (1) the central nervous system (CNS) and (2) peripheral nervous system and endocrine components (Charmandari et al., 2005). The central component is comprised of nuclei in the hypothalamus and the brainstem, which release corticotropin-releasing hormone (CRH) and arginine vasopressin (AVP). The peripheral components of the stress system include the pituitary-adrenal axis,

the efferent sympathetic-adrenomedullary system, and components of the parasympathetic system (Habib et al., 2001). However, relative to environmental stress and acclimation, the initial phases of the response involve receptor systems at the periphery that drive autonomic and endocrine responses to the changing environment (e.g., skin thermoreceptors and photoreceptors in the retina).

Sweating and panting are two of the primary autonomic responses exhibited by animals under heat stress. Sweating results in increased evaporative heat loss from the skin surface, whereas in panting, sensible heat from the body core is used to heat the water vapor and expel heat in the form of vaporized moisture from the lungs. However, these responses are likely driven more by surface temperatures than core body temperatures. As shown in Figures 4.1 and 4.2, evaporative heat loss from skin and the respiratory tract is highly correlated with skin temperature. In fact, skin temperature is more highly correlated with these parameters than core temperature suggesting that thermal receptors in the skin initiate the autonomic systemic response to thermal stress. Another potential route of information flow from the surface to the whole system would be via secreted heat shock protein (HSP) released from skin epithelium during heat stress, which would act as an alarm system to assist in mobilizing the acute response to thermal shock. An examination of the relationship between skin temperature and expression of the gene for inducible heat shock protein 70 (see Fig. 4.3) revealed that gene expression is increased several-fold as skin temperature approaches 35°C, which is below body temperature but represents the upper limit of the thermoneutral zone of cattle. Berman (2005) estimated that the stress response system in cattle would be activated at effective temperatures at and above 35°C. Previously, it has been demonstrated that evaporative heat loss and rectal temperature rise dramatically above an effective environmental temperature of 35°C (see figs. 4.1 and 4.2; Collier et al., 2008). It is now apparent that the heat shock response in bovine skin epithelial tissue is activated at effective environmental temperature of 35°C as well. Activation of the heat shock response in cells in many cases leads to secretions of HSPs into the extracellular space and plasma (Ireland et al., 2007).

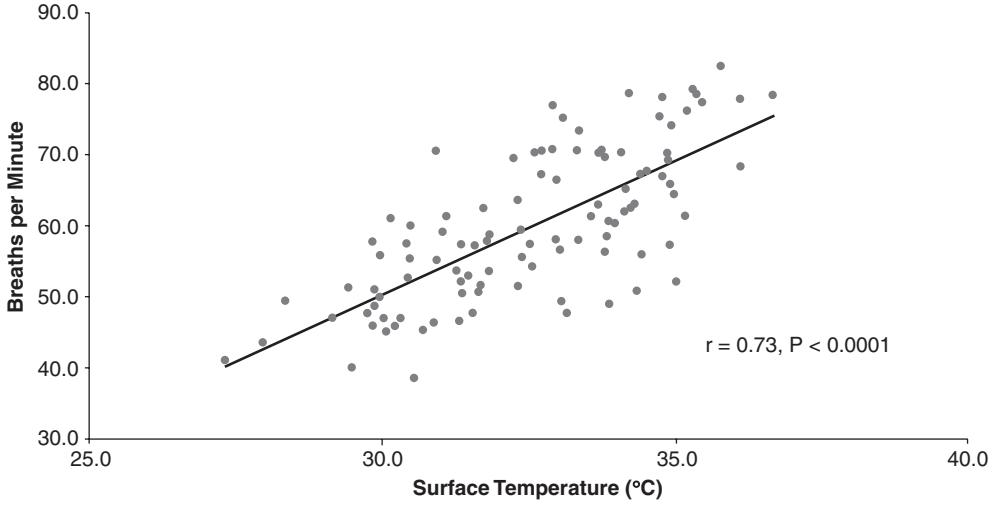

Figure 4.1. Correlation of left side surface temperature and respiration rate in Holstein cows in a semi-arid environment.

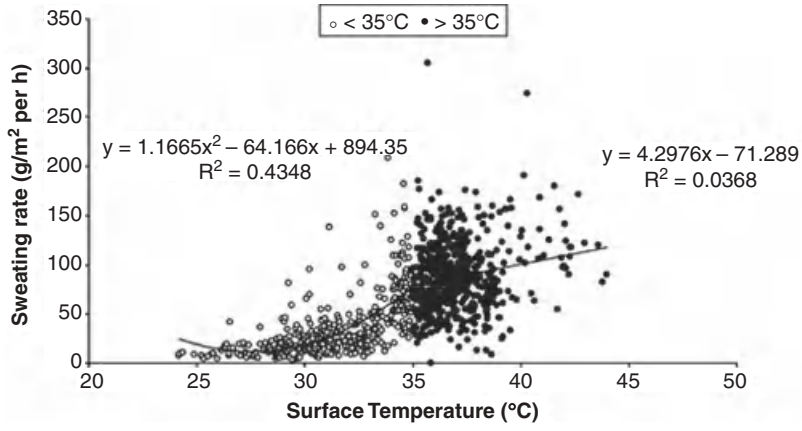

Figure 4.2. Relationship between infrared coat surface temperature and evaporative heat loss (EVHL) in Holstein dairy cows. Open circles and regression correlation ($R^2 = 0.4348$) denote EVHL below 35°C. Closed circles and regression correlation ($R^2 = 0.0358$) denote EVHL above 35°C. Slopes of two regressions differ, $P < 0.001$.

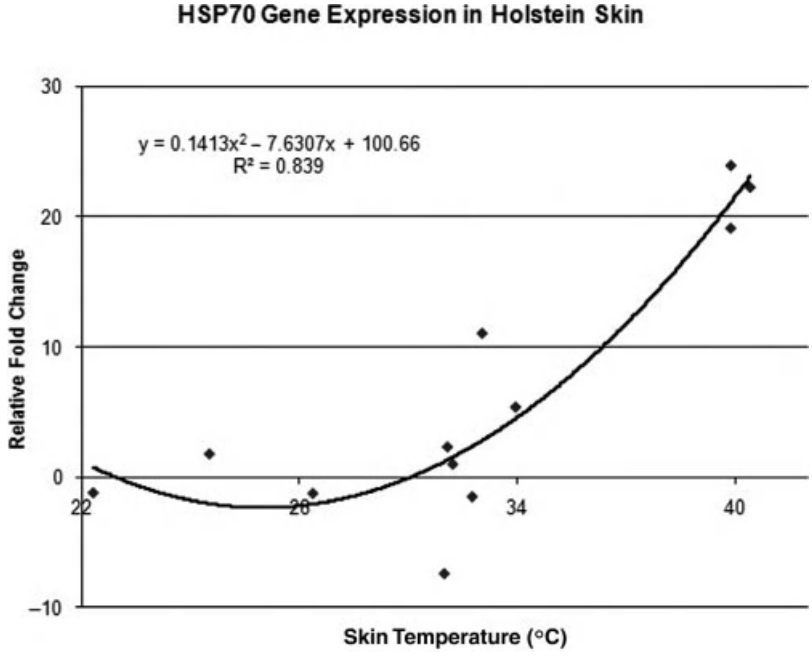

Figure 4.3. Relationship between skin temperature and fold increases in heat shock protein 70 gene expression in cattle skin.

Recently, secreted heat shock protein was identified in plasma of cattle. Kristenson and colleagues (2004) in Australia have demonstrated that secreted HSP concentrations rise in plasma when the effective environmental temperature exceeds 35°C (Gaughan and Bonner, 2009). Thus, activation of the heat shock response in cells also leads to secretion of HSPs into the extracellular space and plasma (Ireland et al., 2007). It has been hypothesized that secreted heat shock protein acts as an alarm signal for the immune system and several measures of innate immunity are increased following increases in secreted heat shock protein in blood (Fleshner and Johnson, 2005). Secreted heat shock protein has also been shown to improve survival of neural cells subjected to environmental and metabolic stressors (Tytell, 2005; Guzhova et al., 2001).

Thus, the acute response in cattle is initially driven by thermal receptors in skin that activate the CNS and subsequently, the endocrine system and the peripheral components of the autonomic system. This response is augmented by secreted HSPs that rapidly rise in plasma and are believed to provide protective effects to a variety of cell types as well as activating the innate immune system. At a skin surface temperature of 35°C the respiration rate of cattle will reach or exceed half maximal which is about 60 to 70 breaths per minute (see Fig. 4.1). At this point, the animal is entering the acute phase of the stress response.

During the acute phase there is rapid decline in productivity of domestic animals and this is especially true in high producing dairy cows. The decline in productivity begins on the day the stress is initiated but is not maximal until 48 hours following the initiation of the stress (Collier et al., 1981). This suggests there are intermediate events between the rise in body temperature and the reduction in milk yield. Rhoads et al. (2009) demonstrated that reduced feed intake only accounted for 40% of the decline in milk yield and that other factors were likely involved in the rapid decline in production to severe heat stress. They postulated that reduced glucose availability could potentially reduce lactose synthesis rates and contribute to the reduced milk volume. Silanikove et al. (2009) reported that acute heat stress reduced milk secretion in lactating cows by up-regulating the activity of a milk-borne negative feedback regulatory system, specifically an n-terminal fragment of β-casein. They also reported that this fragment has an inhibitory activity on the mammary epithelial cell potassium channel. Identification of the exact mechanisms by which milk yield is reduced in response to heat stress offers potential in improving productivity of animals in warm climates.

After five to seven days of continuous stress, animals enter the chronic "acclimation" phase of the stress response. During this phase there is a reprogramming of metabolism resulting in altered responses to homeostatic signals. The overall impact of these changes is a reduction in the impact of the stress on the animal. The transition of animals from the acute to the chronic phase of the stress response has been extensively studied in laboratory models by Horowitz and coworkers (Horowitz, 2002; Horowitz et al., 2004; Maloyan et al., 2005; Horowitz, 2007). These changes are driven by the endocrine system and result in global changes in gene expression as well as post-translational alterations in protein function. Hormones that have been identified as being homeorhetic regulators are also linked to acclimation responses to thermal stress and changes in photoperiod related to season. These hormones include somatotropin, prolactin, thyroid hormones, glucocorticoids, and mineralocorticoids. Several of these hormones are known to contribute to regulation of HSP gene expression, as noted in Table 4.1. The changes that occur at the cellular level and provide improved cytoprotection are described in the section on the cellular response to heat stress.

At the systemic level, metabolism is coordinated to support a new physiological state. Some of the changes that occur include a lowering of the threshold for vasodilation and evaporative

Table 4.1. Partial list of hormones affecting heat shock protein (HSP) gene expression or protein activity

Hormone	Effect	Reference
ACTH	Stimulates HSP production	Blake et al. 1991,1994
Insulin	Stimulates HSP gene in cardiac tissue	Li et al. 2006
IGF-1	Increased HSPs in epidermis of IGF transgenic mice	Shen et al. 2007
Prolactin	Stimulates HSP-60 in rodent luteal cells	Stocco et al. 2001
Growth Hormone	Stimulates HSP in whole blood of Sea Bream	Deane & Woo 2005
Glucocorticoids	Increases cytosol HSPs and HSP gene expression	Vijayan et al. 2003
Melatonin	Increases HSP gene expression in pancreatic AR42J cells	Bonior et al. 2005
Leptin	Down regulates HSP-70 in chicken liver and hypothalamus	Figueiredo et al. 2006
Vasopressin	Stimulates HSP in renal tubular cells	Xu et al. 1996
Catecholamines	Stimulates HSP in Brown Adipose tissue	Matz et al. 1996
Prostaglandin A	Increased expression of HSP in bovine	Collier et al. 2007
	Mammary epithelial cells & human K562	Amici et al. 1992
	Cells and human monocytes	Elia et al. 1999
Estrogensa & Androgens	Increased HSP gene expression in human neurons	Zhang et al. 2004

Adapted from Collier et al. (2008).

cooling (Roberts et al., 1977), reduced metabolic rate, increased resistance to thermal injury, and improved cardiac performance (Horowitz, 2002). Endocrine changes occurring with acclimation to heat stress in cattle include increased plasma prolactin, reduced glucocorticoid, somatotropin, and thyroxine concentrations, and in pregnant cattle endocrine changes led to increased progesterone concentrations and decreased estrone sulfate concentrations (Collier et al., 2004). Somatotropin is a homeorhetic regulator and has been shown to be beneficial in improving evaporative heat loss and thermal balance in cattle during summer heat stress (Manalu et al., 1991). Despite large reductions in feed intake and energy balance during heat stress there appears to be a tighter coupling of the somatotropin-IGF axis during summer, resulting in higher IGF concentrations during summer months compared to winter months and only slight decreases in plasma IGF to severe heat stress even when somatotropin concentrations are reduced (Collier et al., 2008; Rhoads et al., 2009). This fact reinforces the importance of somatotropin in dealing with environmental stress (Collier et al., 2005). Additionally, the somatotropin response to GRF is not affected by severe heat stress (Rhoads et al., 2009). The seasonal variation in coupling of the growth hormone-IGF axis is also associated with effects of increased photoperiod on growth rate and milk yield in cattle (Collier et al., 2006).

Cellular Heat Shock Responses

Heat tolerance at the cellular level is directly related to the ability of the cell to maintain elevated levels of heat shock proteins (HSPs). As stated by Horowitz and Assadi (2010), "A hallmark of the acclimation process is the enhancement of cytoprotective networks – that of the heat shock proteins, anti-oxidative and apoptotic – and the stabilization of the Hypoxia Inducible Factor (Iα), the master regulator of oxygen homeostasis."

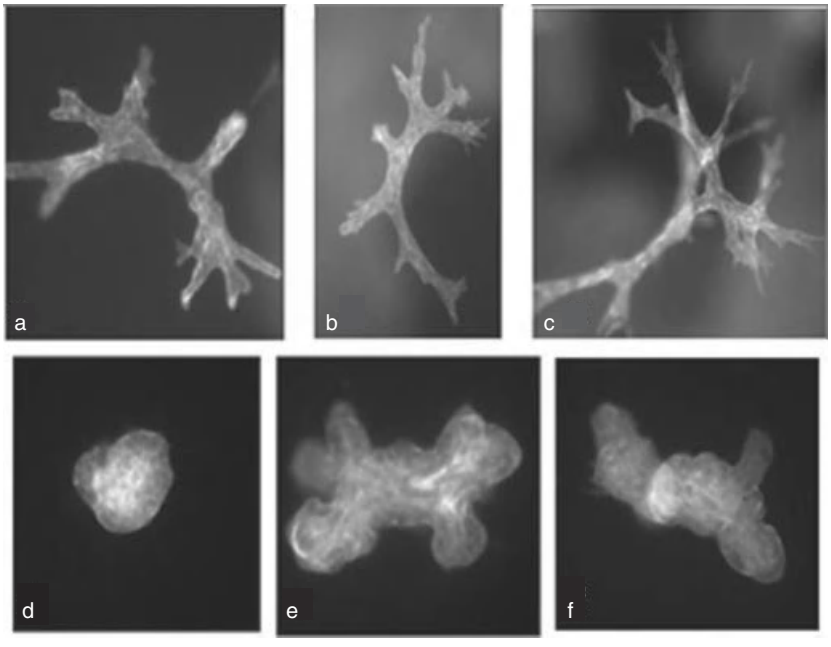

Figure 4.4. Regression of ductal structures in response to 24 hours of heat stress; samples represent three separate cultures in which control samples (a, b, c) were cultured at 37°C but were otherwise treated identical to the thermal stress (42°C) samples (d, e, f).

The heat shock response of bovine embryos and mammary epithelial cells to heat stress has been described (Edwards et al., 1997; Jousan and Hansen, 2004; Collier et al., 2006, 2008). The dramatic effect of heat shock on mammary epithelial cell growth and structure is shown in Figure 4.4. Heat shock acutely down-regulates DNA synthesis and adversely affects the ability of cells to maintain their cytoskeleton, leading to a collapse of cell structure.

The transcriptome profile of heat-shocked bovine mammary epithelial cells indicated down-regulation of genes involved in cell structure, DNA synthesis, cell division, metabolism, biosynthesis, and intracellular transport, while genes associated with cellular and protein repair and degradation were up-regulated. The up-regulation of the heat shock family of proteins during thermal stress is characterized in Figure 4.5 which displays the pattern of HSP-70 gene expression during thermal shock. Also apparent in Figure 4.5 is the drop in expression of HSP-70 message after four hours at 42°C. At the cellular level, loss of HSP expression coincides with loss of thermotolerance and initiation of apoptosis. The heat shock response is induced by accumulation of misfolded proteins in the cytoplasm and is mediated by heat shock transcription factors (HSF; Voellmy and Boellmann, 2007). There are four forms of HSF but HSF-1 is considered to be the primary transcription factor involved in the heat shock response (Akerfelt et al., 2007). Regulation of HSF-1 activity has been reported to be largely controlled post-translationally and not at the level of synthesis/degradation of the transcription factor (Voellmy and Boellmann, 2007). Once activated, the HSF-1 monomer trimerizes with other HSF-1 molecules, which is essential for DNA binding (Sarge et al.,

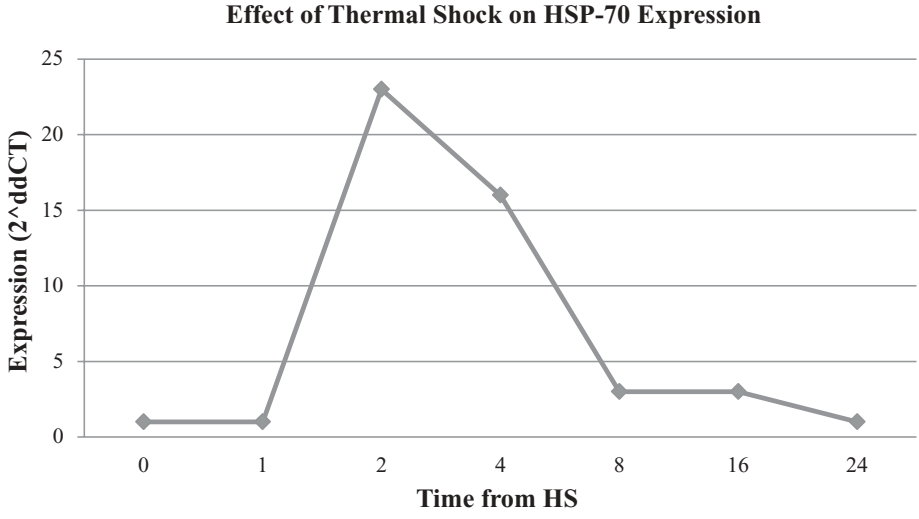

Figure 4.5. Effect of thermal stress (42°C) on Heat Shock Protein 70 gene expression in cultured bovine mammary epithelial cells.

1993). The activated complex can then enter the nucleus and initiate transcription of heat shock proteins.

Thermal acclimation and thermal adaptation are associated with increased basal levels of HSPs (Carpar et al., 1987; Kregel, 1992; Maloyan et al., 1999). Thermal acclimation and cyclopentenone prostaglandins have been shown to increase the DNA-binding activity of HSF-1 leading to increased HSP gene transcription (Amici et al., 1992; Straus and Glass, 2001; Ianaro et al., 2003; Buckley and Hofmann, 2002). Several investigators have shown that heat acclimation also provides cross-tolerance against other types of stress such as hypoxia, ischemia, acidosis, and energy depletion (Horowitz, 2002; Kregel et al., 2002), and that HSF-1 is involved in this process. Although there is little evidence for endocrine regulation of HSF-1 gene expression activity there is substantial evidence that expression of heat shock proteins and other cytoprotective proteins are modulated by the endocrine system. A partial list of hormones affecting heat shock protein gene expression is shown in Table 4.1.

The separate evolution of *Bos taurus, Bos indicus,* and *Sanga* cattle has resulted in differing genotypes of *Bos indicus* and *Sanga* cattle that confer improved thermotolerance compared to *Bos taurus* cattle in both beef and dairy populations (Paula-Lopes et al., 2003; Hansen, 2004). In addition, large genotype × environment interactions in dairy cattle for milk yield (Cerón-Muñoz et al., 2004; Ravagnolo et al., 2000; Bohmanova et al., 2006) for Holstein cattle indicate that there is considerable opportunity to improve thermal resistance and performance in dairy cattle. These differences include thermoregulatory capability, feed intake and production responses, and cellular differences in heat shock responses (Hansen, 2004; Collier et al., 2008).

There are genetic differences in cellular resistance to elevated temperature in cattle. It is possible that the same gene or genes conferring cellular thermotolerance are present in Indicus, Senepol, and Romosinuano, especially because of the contribution of *B. indicus* genotypes to these two other breeds (Magee et al., 2002). An alternative explanation is that

distinct thermotolerance genes are present in the different genotypes. Identification of the genes conferring cellular thermotolerance offers the possibility of transferring these genes to heat-sensitive breeds to improve reproduction and other physiological systems compromised by hyperthermia. Little is known regarding the molecular basis for the improved cellular resistance to elevated temperature in thermotolerant cattle. There were no detectable differences between Indicus, Senepol, and Angus in the amount of heat shock protein 70 (HSP-70) in heat-shocked lymphocytes (Kamwanja et al., 1994) although the tendency for lower cellular concentration of HSPs in Brahman and Senepol may indicate that protein denaturation in response to elevated temperature (one of the signals for HSP-70 synthesis; Shamovsky and Nudler, 2008). The capacity for transcription in response to elevated temperature seems to be important for expression of genetic differences because there were no differences between Indicus and Holstein embryos in resistance to elevated temperature at the two-cell stage, a time when the embryonic genome is largely inactive (Hansen, 2004). Also, in vitro effects of elevated temperature on spermatozoa were similar for Indicus, Indicus-influenced breeds, Angus, and Holstein (Block et al., 2002).

The cellular thermotolerance of crossbred embryos is dependent upon the genotype of the oocyte and not the spermatozoa. Embryos produced by insemination of Brahman oocytes with Angus spermatozoa were more thermotolerant than embryos produced by insemination of Holstein oocytes with Angus semen (Block et al., 2002). In contrast, there were no differences in thermotolerance between Indicus × Holstein embryos and Angus × Holstein embryos. These results indicate that either genes conferring thermotolerance are paternally imprinted (only the maternal allele is expressed) or thermotolerance in embryos depends upon some genetically controlled factor produced in the oocyte. Regulation of body temperature is the most critical factor for genetic differences in reproductive function during heat stress since the depression in fertility per unit increase in body temperature is the same for *B. indicus* × *B. taurus* crossbred cows as for Hereford × Shorthorn cows (Hansen, 2004).

New genomics tools are also beginning to provide information on specific gene networks associated with thermotolerance. Lillehammer et al. (2009) identified single nucleotide polymorphisms (SNPs) that were associated with gene × environment interactions for production traits in cattle. Hayes et al. (2009) also reported on a genome-wide association study aimed at identifying differences related to adaptation to environmental change. It is envisioned that in the not too distant future use of SNP markers will lead to greater progress in improving thermotolerance of high producing dairy breeds.

Conclusion

Acclimation is a homeorhetic process driven by the endocrine system, which enables animals to respond to a stress. The resulting cellular, metabolic and systemic changes associated with acclimation reduce the impact of the stress on the animal and allow it to function more effectively in the stressful environment. These changes are lost if the stress is removed so the process is not based on changes in the genome. However, if the stressful environment is not removed over successive generations these changes will become "genetically fixed" and are referred to as adaptations. A better understanding of genetic differences between adapted animals will contribute useful information on the genes associated with acclimation. Likewise, study of gene expression changes during acclimation will assist in identifying genes associated with improved thermotolerance.

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Chapter 5

Environment and Animal Well-Being

S. D. Eicher

Introduction to Animal Well-Being

Changing Climate

Predictions for climate change include swings in climatology, increased temperatures, duration of extremes, and changes in precipitation patterns (Helmuth et al., 2010). An international think-tank believes that by 2020, agricultural and food commodities could be 50 to 100% higher than they were at the beginning of the millennium. The impact of weather affecting physiological adaptations and behavior are on the immediate vicinity. Therefore, to an animal, the only relevant changes are local although many extreme weather events can be highly localized and unpredictable. Additionally, changing conditions may affect food availability (Smith, 2010) and in turn may increase interactions with predators as they change the scope of their territory in response to altered vegetation growth. We have already seen this happening as humans intrude on wildlife space. With greater draught or rainfall, this could become more prevalent.

The ways in which animals have traditionally been managed and handled may need to be quickly revisited when temperatures shift or when animals are transported to new environments. This was observed when water buffalos were moved after auction from their natural environment, where water is readily available, to a confined environment where they were tethered under direct sunlight for hours with little heat relief and limited watering (Alam et al., 2010). Many suffered extreme heat stress compared with the cattle. The water buffalo had higher skin and rectal temperatures and greater respiration rates. Differences in heat-stress responses were partially because of the sparse hair coat and the dark hide on the buffalo compared to cattle. Water buffalo also have fewer sweat glands and excrete higher volumes of urine. This report underscored the influence that species, breed, and genetic influences – such as hair coat type and color – have on susceptibility to heat stress.

Environmental Physiology of Livestock, First Edition. Edited by R. J. Collier and J. L Collier.

Helmuth et al. (2010) noted that recorded heat index changes do not always extrapolate into expected behavioral changes. Animals may not always select the most appropriate behaviors for climate change. For instance, unacclimated donkeys in India that were moved to a novel environment, which resulted in heat stress, huddled together in their shed leading to morbidity and mortality (Dey et al., 2010). Reports of cattle grouping together under extreme heat stress suggest that under stress, herd animals resort to "herd behavior" and move into a close group. This not only inhibits any air movement, but also increases temperature gain from other animals thereby intensifying the heat stress. Because environmental changes are not just specific to animal agriculture, or even to all agriculture; human behavioral changes and development of comprehensive, flexible, and long-lasting solutions within a society will be needed during these changing circumstances to effectively aliquot limited resources for multiple industries' needs.

Five Freedoms

The Farm Animal Welfare Council in the U.K. established Five Freedoms to define the provisions necessary to promote the welfare states of animals that might have been determined by the animals' own choices. They include both physical and mental needs (Webster, 2001).

Environmental stressors can affect nearly all Five Freedoms, dependent upon the environmental stressor and the degree and persistence of that stressor (see Table 5.1). For instance, the First Freedom – freedom from thirst, hunger, and malnutrition – can be deemed not to be met when range cattle are in the grips of a blizzard during which they become unable to get to food, which is even more critical to maintain body temperatures during extreme weather conditions. The Second Freedom – freedom from discomfort – is typically associated with environmental stressors. Animals exhibit behavioral changes and choices that are indicative of discomfort. Some changes are very obvious, while others are discreet and require careful observation or the use of new technologies to monitor (e.g., accelerometers or temperature probes). Heat-stress conditions are associated with intestinal permeability for pathogens residing in the gut or commensal bacteria, which may become opportunistic pathogens. It is also currently believed that this may be one of the mechanisms behind increased incidence of lameness during later summer months. This may lead to an infraction of the Third Freedom – freedom from pain, injury, and disease. The Fourth Freedom – freedom to express normal behaviors – may be compromised by inadequate housing; pigs that are free-range and not allowed a wallow to maintain body temperature during heat stress are not in a state of well-being. Freedom from fear and distress – the Fifth Freedom – is explained as ensuring conditions that avoid mental suffering. This freedom plays a critical role when animals are housed in more "natural," or

Table 5.1. Potential infringement of environmental stress on the Five Freedoms.[1]

Freedom	Potential Environmental Impact
1. Freedom from thirst, hunger, and malnutrition	Heat Stress/Cold Stress; Impact on feed and water availability
2. Freedom from discomfort	Heat Stress/Cold Stress
3. Freedom from pain, injury, and disease	Heat Stress/Cold Stress
4. Freedom to express normal behavior	Heat Stress creates a need for altered behavior
5. Freedom from fear and distress	Social stress with other animals and humans can elevate body temperature

[1] Adapted from Webster (2001).

free-range, environments, where exposure to predators can become a concern but there is also a potential for inappropriate handling by humans. For instance, as climate changes occur, predatory wildlife may be displaced and come into contact with extensively managed farm species, creating fear in the livestock.

In contrast, the Five Freedoms can be particularly relevant to confinement systems, since the environment is under the control of the caretakers with little expression of choice left to the animal. Most well-managed confinement systems have plans for some degree of environmental stress, and thus have some methods in place to counteract a heat or extreme cold event. However, many of the worst environment and well-being interactions occur in "natural" settings. Many well-being issues can occur in extensive housing systems, such as heat stress experienced by dairy cattle in a grazing system during a heat episode where there's little plan for relief except near the parlor. Because of the cooling mechanisms of swine the free-range systems offer challenges on pasture where wallows are necessary for swine to dissipate heat. Poultry are most likely to experience heat stress under free-range conditions, as confined birds are typically in temperature-controlled and ventilated buildings. However, free-range does not imply lack of shelter, and this form of housing offers a greater opportunity for an interaction with the environment.

In this chapter, some of the most common well-being issues that can be directly related to environmental conditions will be considered. Some issues are relevant to specific stages of life such as thermal needs at the neonatal stage, others issues are relevant to particular management practices such as animal transport, while other issues are intrinsic, such as the interaction between heat stress and genetics. Environmental variables that are particularly pertinent to well-being are thermal stressors, with the inclusion of wind speed or lack of wind, and their interaction with housing and other animals. Many of the well-being issues mentioned previously can exacerbate the effects of the environment, particularly heat stress.

Animal Well-Being and Stress

Animal well-being and animal welfare are terms that are frequently used interchangeably. However, recent suggestions are to use the term animal "welfare" to connote long-term conditions (the larger picture) and to use animal "well-being" to refer to specific instances or an animal's current condition (Gonyou, 1993). Swanson (1995) asserts that because of the societal role in these definitions, the definition of animal well-being or welfare is as dynamic and evolving as societal expectations of animal care. Animal well-being is also frequently equated with the degree of stress an animal experiences in its environment.

The definition of stress presents a conundrum (Moberg, 2000). Stress can be positive, even necessary, for environmental enrichment. Without it, animals become bored and may develop undesired behaviors. But on the dark side of stress, when it interferes with life events it may limit the well-being (welfare) of an animal. When an animal experiences a stressor, numerous physiological and psychological systems are set in motion. For the purpose of this chapter, the definition coined by Moberg will be used: Stress is "the biological response elicited when an individual perceives a threat to its homeostasis." However, proponents of recent concepts advocate using allostasis rather than homeostasis as the desired end-point in a correct definition. They suggest that allostasis is stability through change that enables an animal to cope, rather than a single setpoint, which homeostasis implies (Korte et al., 2007). For instance, an immune response after exposure to a pathogen is a good response, but a lack

of response or an over-extended response is not good for state of well-being. So, it is a range and an ability to move from one response to another that selects for good animal welfare. As will be seen, aspects of the animal environment easily fall into this model.

Stressors differ in the effects they may have on biological systems. For instance, restraint stress does not induce an Il-1 (acute phase cytokine) response, but an isolation stressor increases Il-1 concentrations. Therefore, determining what stressor will develop into a stress that alters an animal's well-being becomes a complicated task. Environmental stressors are among those with complex motifs. Animals have substantial buffer capacity against environmental changes, requiring multiple days of heat stress to become distressed. If the stressor can be adapted to, is it a well-being issue? Combining that with variation created by age, stage of life, and genetics, a single answer can be obscure.

There are many potential stressors in an animal's environment (adequate space, mixing with unfamiliar animals, handling and transport, and normal biological processes such as calving) that may interact with environmental stress.

In contrast, stressful events can elevate body temperature and alter physiological and immune responses, thus decreasing an animal's ability to respond to environmental temperature changes. A 2°C (3.6°F) increase in body temperature has been found in cattle when they are handled (Mader et al., 2009), and elevated body temperatures were shown to occur in rats that had experienced social stress (Bhatnagar et al., 2006).

Physiological changes that are typical under stress are increased secretion of cortisol (hypothalamus-pituitary-adrenal axis, HPA) and catecholamine (epinephrine and norepinephrine). Other changes that are frequently reported are changes in the circulating immune cell population that results in a greater neutrophil-to-lymphocyte ratio. Additionally, blood glucose increases with many stressors. All of these changes then impact other body systems and ultimately may reduce the well-being of an animal (see Fig. 5.1).

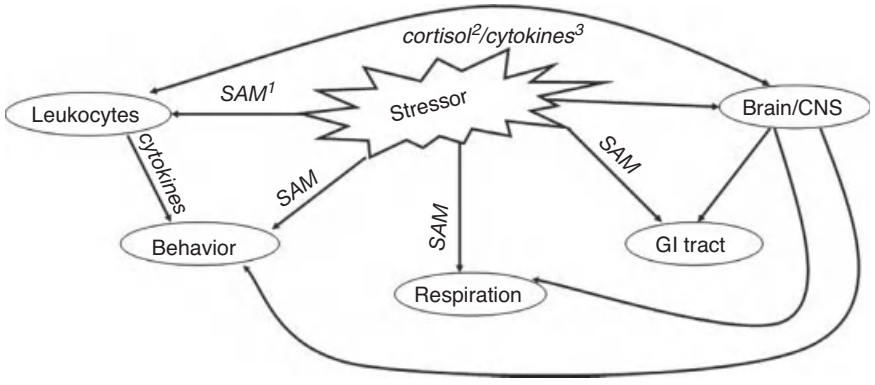

Figure 5.1. Stressors impact many biological factors and systems including immunity, respiration, gastrointestinal health, the brain, and behavior. These systems communicate by hormones and cytokines (immune communication molecules).

[1] SAM = sympatho-adrenal-medullary axis. Adrenaline and noradrenaline are among the hormones of SAM.

[2] Cortisol is the hormone of the hypothalamic-pituitary-adrenal (HPA) axis.

[3] Cytokines include tumor necrosis factor-α (TNF-α) and interleukin-1 (IL-1) that initiate elevated temperatures and sickness behavior.

Physiological Responses of Altered Body Temperature

The area of the brain that is stimulated by stress varies depending on the type of stressor (see Table 5.2). There are a number of heat shock factors and the activation of these is stress specific (Marcuccilli et al., 1996).

The interaction of cold or heat exposure with brain regions is complex and can be differentiated from responses to other stressors. Long-term isolation elevated basal plasma adrenocorticotropic hormone (ACTH) and corticosterone, but did not affect the catecholamines (noradrenaline and adrenaline). When further exposed to two hours of immobilization or cold, the catecholamines were elevated along with coricosterone. Both long-term crowding or isolation had similar, but less pronounced effects on cytosol glucocorticoid receptor and heat shock protein 70 in the hippocampus, compared to acute immobilization and cold stress, thus demonstrating the complexity of the type of stressor and possibility of additive effects when stressors are combined.

Horses exposed to thermal stressors had changes in plasma β-endorphin concentrations that may be a sensitive indicator of thermal tolerance before and after acclimation, but plasma cortisol concentrations appeared limited as a specific indicator of heat stress (Williams et al., 2002). This study suggests that thermal stress has a stimulatory effect on β-endorphin responses. Non-heat-acclimated horses also had increased plasma adrenaline and noradrenaline levels in high temperatures with humidity, which supports the theory that catecholamines play a key role in adaptation to increased cardiovascular and thermal stress during exercise. This study showed that only specific neuroendocrine responses could be attenuated by acclimation.

One of the neurotransmitters, orexin (Harris and Aston-Jones, 2006), is differentially expressed; depending on age and stressor type different areas of the brain are stimulated. Orexin has roles in both stress activation and reward-based learning and memory. Thermo-regulatory stress is known to activate the sympathetic nervous system similarly to mental stress. However, patterns of activation are different: Cold only increased blood pressure while heat stress increased heart rate and sweating. In contrast, mental stress co-activated heart rate, blood pressure, peripheral vasodilation, and sweating. Other molecules such as endothelial nitric oxide (NO) synthase regulated local skin temperature, while another form (neuronal nitric oxide synthase-NOS) mediated vasodilator response to heat stress (HS; Kellog et al., 2009).

Table 5.2. Comparison of known common responses to environmental and restraint stressors.[1]

	Cold Stress	Heat Stress	Restraint Stress
Cortisol	↑	↑	↑
Catecholamines	↑	↑	↑
Neutrophil function	↓		
Lymphocyte function	↓	↓	↑
Cytokines/chemokines		↓	
Acute Phase Proteins		↑	
Blood Glucose	↑		↑
Blood Pressure	↑		
Heart Rate		↑	
Body Temperature	↓	↑	↓

[1]Data from Pitman et al. (1988); Kainuma et al. (2009); Dronjak et al. (2004); Fechir et al. (2009).

Regulating NO synthesis and the resulting vasodilation lead to skin blood flow and sweating changes that decreased both internal and skin temperature.

Curiously, skin cooling is more effective under severe heat stress than under moderate heat stress. Additionally, the vasodilation response can be attenuated by hyperosmolality. This is a function of an altered internal temperature threshold for active vasodilation and not by enhancement of vasoconstriction activity; it is caused by inhibition of hypothalamic thermosensitive neurons by hyperosmolality. The combination of hyperosmolality and heat stress result in an inability of an animal to adequately respond to a thermal challenge (Shibasaki et al., 2009). Sows that were exposed to inescapable elevated flooring heat had elevated plasma cortisol, but oxytocin and behavior did not change (Malmkvist et al., 2009).

Heat Stress and Well-Being

Environmental temperatures are frequently depicted by zones of neutrality and effects on animal metabolism and stress as temperature extremes are approached. In a figure provided by Silanikove (2000), a zone of optimal well-being extends beyond the zone of homeothermy through a stage of both heat and cold stress. As such, feed consumption and thermogenic hormone secretion decreases to lower basal metabolism (adaptation). Based on Silanikove's diagram, it is not clear how this translates to animal responses and their well-being on the farm. Therefore, to have a well-being definition using objective (scientific) measures that are free from moral considerations is imperative; well-being can be determined by using environmental indices, animal coping responses, or signs that the coping mechanisms are failing. These objective measures may be either behavioral or physiological.

Although many variables can affect body temperatures, rectal temperature is still believed to be the best physiological parameter to objectively monitor animal welfare. For animals that are not in confinement systems (free-ranging animals) breathing rates are an accurate measure of increased stress and an inability to cope. This enables assessment without further disturbing the animals. The method used by the animal to cope with heat varies by species and by housing. For example, chickens pant to dissipate heat and they spread their wings – quite different behaviors than those demonstrated by cattle. So the observations used to determine the degree of stress need to be varied for the species and the situation.

The most extreme heat-stress event is drought, which is defined by a higher than normal temperature, lack of moisture, and persistence of the period without moisture. Consequences of drought can result in significant agricultural, economic, and social changes. Australia and New Zealand have determined codes of practice for the welfare of animals during drought (Clayton, 2007). This includes planning for periods of drought as a normal seasonal occurrence. In the United States, a model has been developed to predict an acute heat-stress event (Brown-Brandl et al., 2006). In all instances, acting early is important to keep the greatest number of choices available to ameliorate the situation. Relieving animal suffering is of paramount importance; this may include feeding, sending them to slaughter if they are able to rise and walk (although not through sale yards), or in the most desperate cases the animal may need to be humanely euthanized on the farm. Similarly, U.S. recommendations include monitoring changing conditions and weather forecasts, managing cattle based on their coat color and body condition, adjusting rations, and transporting them early in the day (prior to 6:00 a.m.). Additionally, not processing cattle past early morning is recommended, as is ensuring that the animals have access to adequate water and space for hydration and their cooling behaviors of holding their tongue and nose in the trough. Create comfort zones using sprayers or sprinklers

(keeping in mind that additional wetting is usually, but not always, beneficial, because humidity can exacerbate disease) and maximizing airflow to the most susceptible. Change feeding schedules or rations, control flies and parasites, and provide cooling for cattle in very confined areas such as pens for the sick or small groups being handled individually. Most importantly, monitor early warning signs of heat stress by monitoring the temperature-humidity index (THI) in early morning and develop strategic and emergency heat-stress plans. Panting scores and the THI table should be used to assess dangerous situations (Mader et al., 2009).

Prior to reaching that crucial point, management recommendations are to provide shade at temperatures greater than 24°C (75.2°F) and when THI is greater than 70; provide adequate water (allowing for at least two visits per day for grazing cattle, and once per day for goats and sheep); raise appropriate breeds for the climate; and limit transport based on thermal conditions (heat, cold, wind, humidity, or moisture). Additionally, factors dark-hided animals, those with a prior history of pneumonia, greater body condition scores, or excitability increased heat stress in animals. Calm cattle gain 5% more weight than excitable cattle. Dairy cows and calves both had improved mortality rates when their environmental temperature (from weather stations in each geographical area) was between 14 and 24°C (57.2 and 75.2°F; Stull et al., 2008). Additionally, the total monthly precipitation was negatively associated with milk production. However, the authors suggested that this effect could be ameliorated by providing appropriate housing.

A major well-being concern for dairy systems is lameness. It not only has the well-being impact, but also a monetary impact because of decreased production and reproduction. The impact of heat-stress on lameness in dairy cattle is multi-faceted. The amount of time spent standing increases with greater temperature and humidity. The longer a cow stands, the greater the amount of time that the hooves are subjected to weight and the time that they are relieved by lying is reduced. Lameness peaks at the end of summer (Cook, 2004), possibly due to weakened hooves caused by respiratory alkalosis from panting for heat dissipation, which results in vasoconstriction and dilation. Additionally, the wet environment that is created by mist and spray cooling results in wet environments that are known to be detrimental to hoof health. Therefore, the type of freestall flooring for the comfort and hygiene of dairy cows must depend on the microenvironment in which they will be used. For example, in conditions of heat stress, the material used for a freestall must perform important additional functions such as dissipating heat and absorbing or removing sweat, transpiration, or residual moisture from misting or spraying (de Palo et al., 2006).

Besides housing changes, some dietary methods can be used to reduce the influence of heat stress. Some methods that have shown promise include antioxidants, feeding yeast cultures and extracts, niacin (Zimbelman et al., 2010), and extracts from tamarind (Aengwanich, et al., 2010). Because stressful conditions, including heat stress, lead to the production of free radicals, antioxidant treatment improved animal coping with heat stress (Ayo et al., 2006; Megahed et al., 2008). Yeast mannan-oligosaccharide products improved broiler stress responses and some immunity during heat stress (Sohail et al., 2010); yeast β-glucan without heat stress decreased the chemokine IL-8 and iNOS expression (Cox et al., 2010). It is those cytokine and chemokine modulations that may be beneficial to the birds during heat stress. However, feeding a yeast culture to cows was not beneficial for conception rates or incidence of lameness under a THI greater than 71, but severity of lameness was reduced (Bruno et al., 2009). Niacin supplementation was beneficial in reducing rectal and vaginal temperatures. The extract of tamarind seed coat reduced heat stress and associated oxidative stress and improved growth rates of heat-stressed broilers.

Well-Being and Cold Stress

Cold stress is a concern more frequently for neonatal animals. This is particularly true for neonates in free-range environments and during transport. It has become a frequent occurrence to transport newly weaned piglets for long distances. This practice exposes them to weaning, thermal, dietary, and transport stress, all concurrently. Alleviating thermal stress can help them to cope with the other stressors. Prenatal and birth environments can affect a neonate's ability to cope with environmental stress. Calves born to dams that were fed diets with cottonseed hulls and subjected only to cold stress for a short period of time (90 min) had altered body weight, and tended to have a better vigor score and required less time to stand (Dietz et al., 2003). Ability of newborn calves to cope with cold stress is compromised by difficult births (i.e., dystocia; Bellows and Lammoglia, 2000). Body temperatures were lower, blood glucose higher, and serum cortisol was lower in calves requiring greater assistance during calving (not cesarean section).

Additionally, newly hatched chicks are extremely vulnerable to cold stress. Cold stress decreased behavioral activity of neonatal chicks and increased sleep-like behavior. These alterations of behavior can reduce heat production and can potentiate sensitivity to cold exposure (Mujahid and Furuse, 2009). Selective activation of discrete groups of neurons, within central autonomic control circuitry, coordinates stimulus-specific responses in a defined target tissue (Cano et al., 2003). This showed the complexity of distinct neuronal pathways embedded in a larger regulatory circuit, each activated under different conditions, which lead to changes in brown adipose tissue thermogenic activity to restore energy balance.

Adult animals on free-range conditions not only have metabolic shifts to maintain body temperature, but also compromised food availability, if the cold is accompanied by snow or ice. Water access that is critical for proper digestion may be frozen. So, plans to intervene must be made early to preserve the freedom from thirst, hunger, and malnutrition.

Expected cow's lying is the percentage of cows that were lying at a given observation time and the cow comfort index is a calculation of the number of cows lying divided by the number of cows that were in the lying area. Therefore, time of day that behavioral evaluations are made is critical. O'Driscoll and colleagues concluded that although a negative relationship exists between environmental temperature and the cow comfort index and the estimated cow lying index, the correlation is relatively weak. The lowest temperature was just below 2°C (35.6°F) and the greatest was below 12°C (53.6°F). Time of day, housing environment, and management routines had greater influence on the outcome of those indices. Additionally, cows were found to adjust their behavior to compensate for higher wind speeds (Morgan et al., 2009).

Environment, Immunity, and Disease Resistance

Freedom from pain, injury, disease, and ultimately death is a major concern during both heat and cold stress. Immune functions in dairy cattle are altered during heat stress. Prolactin, responsible for many cellular processes, is enhanced during heat stress, resulting in decreased cellular proliferative responses in vitro. Gene expression of several important signal transduction regulators (SOCS-1 and SOCS-3) were altered, ultimately increasing tumor necrosis factor-α and interleukin-4 cytokine concentrations (do Amaral et al., 2010). Both heat and cold stress (i.e., thermal stressors) alter natural killer (NK) cell cytotoxicity and cortisol concentrations in mice. This is important for some farm species since NK cells are important immune cells used by pigs (particularly neonatal pigs). Fish also had reduced catecholamine responses

in hypothalamus and immune organs following cold stressors, but plasma catecholamines and cortisol concentrations increased (Chen et al., 2002). Phagocytosis decreased and IgM concentrations decreased. The decrease in phagocytosis was predominantly in response to increased cortisol.

Effects of heat stress on neonate well-being begin before birth. Although heat-stressed sows only tended to have lower IgG concentrations in colostrum at parturition, their piglets had significantly lower plasma IgG, which remained lower for 20 days (Machado-Neto et al., 1987). The sows also had elevated cortisol, indicating a chronic stress during pregnancy. Dairy calves are frequently housed in hutches with a small outside exercise area. But in high heat-stress times and areas in the country, these may not be the best choices. Mortality was greatest for calves housed in hutches during the first 20 days after birth compared with calves that were housed in pens with only shade or those in those pens with cooling (Stott et al., 1975). This study showed the benefit of having air movement and the importance of heat stress on passive immunity; the calves that were in the greater heat-stress environment had lower IgG and higher mortality. Both studies demonstrate that although adequate IgG may be available in colostrum, pre- or post-natal heat stress can impact protective absorption.

Disease incidence of severe diarrhea was greater for calves born during summer than those born in winter, but incidence of respiratory disease was greater for the calves born during the winter (Svensson et al., 2003). However, Brown-Brandl et al. (2009) did not detect any greater shedding of *Escherichia coli* and *E. coli* O157:H7 in feces of cattle that were under heat or handling stress.

When heat stress, social rank, and incidence of porcine reproductive and respiratory syndrome (PRRS) virus were investigated together, heat stress did not have additional negative impact on physiological or performance traits in pigs challenged with PRRS virus (Sutherland et al., 2007). Heat stress reduced plasma cortisol and increased rectal and tympanic temperature. Lying with contact was reduced during heat stress and lying without contact increased to reduce transfer of body heat between pigs.

Further study with elevated temperatures around parturition in loose-housed sows, showed only a trend for CD4+ cells to change with floor heating. Many other variables (body temperature, water intake, cortisol, toll-like receptor 4, CD4+, and CD8+ cells) only changed with parturition. Others found increased TLR4 and a trend for greater TLR2 in acutely heat-stressed pigs within the 24 hours after exposure (Eicher et al., 2007), but the common indicator of stress, cortisol, did not differ between heat-stressed and control pigs.

Handling and Transport

A common time for animals to experience adverse effects from their environment is during transport. Although transport during extreme weather is discouraged, it is sometimes inevitable. Conditions during transport, which constitute a total complex of stressors during transport, are variable. Climatic conditions and the resulting thermoregulation vary by species, age, genetics, condition of the animal, hydration, and food deprivation. The truck design can also influence the environmental impact on animals in transport (Fiore et al., 2009). The previous housing experience of the animal (crate vs. group raised calves) alters the stress level experienced during the transport. The impact of other stressors, also affect heat production (Schrama et al., 1996). Handling of animals, in and of itself, increases body temperature. This is due to increased physical activity, social interactions (with humans and other animals), and sometimes reduced space allowance and access to water.

The Guide for the Care and Use of Agricultural Animals in Research and Teaching (Swanson and McGlone, 2010) provides recommendations regarding transport during extreme weather conditions. Additionally, specific instructions to not handle animals during periods of high temperatures are given for beef cattle (Mader et al., 2009). The Cattle Industry's Guidelines for the Care and Handling of Cattle gives specific heat-stress procedures that include providing adequate water; finish working them before a THI of 84 is reached; handle cattle that are more prone to heat stress during the least stressful time of the day; limit the time they are in handling facilities; and use shades and sprinklers if natural shade is not available. During transport, to minimize stress during sorting and loading, use properly designed facilities that are located near the holding and sorting pens.

Strangely, piglets spent less time drinking the first day after a transport in summer than they did in winter or fall (Lewis and Berry, 2006). Resting during transport was greater in fall and winter, suggesting that the early weaned pigs were cold. During longer journeys, piglets required additional coping strategies to cope with cold stress, which increased the risk of dehydration. Greater number of days of resting post-transport in summer and winter may be indicative of post-transport fatigue (suggesting requirements of greater adaptation in those seasons). Thus, it appears that for this age of piglet it is important to determine which environmental stressors are present and their duration, requiring development of strategies to alleviate the impact of these stressors during and after a transport.

Market-weight pigs had elevated body temperature caused by aggressive handling and when they were moved a greater distance (Ritter et al., 2009). This was supported by a visible skin discoloration and open-mouth breathing, which corresponded to the aversive handling and greater distance that they had been moved (25 m compared with 125 m). Using animal well-being measures, behaviors, neutrophil and lymphocyte levels, cortisol levels, and other blood variables, a space requirement of 0.06^2 m was determined as preferable for summertime transporting of pigs weaned at 18 days of age. Temperature-humidity index affected the frequency of morbidity (i.e., the number of fatigued and injured animals) and mortality after transport to a commercial abattoir (Fitzgerald et al., 2009). Curiously, pigs that were transported June through July experienced fewer losses compared with those transported in November to December. The temperature during a journey seems to be a predominant factor in pig transport, and when associating temperature during transport and risk of mortality, mortality was not affected by length of a journey (Averós et al., 2008).

Chickens respond to the stress of crating at high (34°C) temperatures with increased blood glucose and increased heterophil-to-lymphocyte ratios. Apparently 40°C at 20% humidity is not averse to broilers (Abeyesinghe et al., 2001). Birds don't seem to be too adversely affected by cold temperatures, but above 17°C, mortality increases abruptly (Warriss et al., 2005). Feed withdrawal before transport is a frequent practice that had no effect on body temperature, but crating density more than doubled the body temperature change. Corticosterone concentrations and HSP-70 mRNA expression reflected a similar pattern.

Feeding intervals for young calves is important during cold stress. Extending the time between feedings may hinder the calves' abilities to maintain lower critical temperature (LCT) during transport (Stull and Reynolds, 2008). When considering the disruption during transport, Knowles et al. (1997) suggested that completing the journey in as short a time as possible is most desirable. The decision as to whether to use lairage during a long transport must also include consideration of the lairage facility and the additional handling and exposure to pathogens. The benefit of providing lairage is that the animal is given the opportunity to rest and regenerate body stores, especially hydration (Williams et al., 2008). The relative

humidity within the truck generally increases during the transport and must be considered (Williams et al., 2008; Knowles et al., 1999). Additionally, because THI increases during vehicle stationary periods (e.g., meal breaks for drivers and at truck inspection stations or border crossings), the animals must be accommodated with some type of heat relief if the THI approaches critical ranges (Fisher et al., 2002, 2004).

During loading, transit, and unloading, calves need protection from solar load and heat by providing shade, proper ventilation, and, when required, wetting the calves. Conversely in winter, it is necessary to provide protection from wind and drafts by obstructing air flow from the sides and front of the truck; clean, dry, deep bedding with high insulation values (e.g., straw) is also necessary. Since very young calves prefer to lie during transport, the bedding consideration is more critical than for older calves that prefer to stand.

Many factors are known to affect the ability of cattle to cope with stressors associated with transport. Among the variables that impact thermal thresholds and an animal's ability to cope with transport are food and water deprivation, stocking densities, humidity and air velocity, and temperature (Schrama et al., 1996). Considering vehicle movement or stationary times, vehicle and container design in cold weather conditions during transport increase bruising, but summer transport results in reduced meat quality. Thus, seasons and various weather stressors affect product quality, but vehicle design did not change these outcomes (dalla Costa et al., 2007).

Guidelines

There are several published works that afford guidance in the area of housing heat, cooling, and ventilation. A general guide is provided in the *Guide for Care and Use of Agricultural Animals in Research and Teaching*. In this guide some specific recommendations can be found for various species. Animal well-being is a function of many variables: species, physical surroundings, nutrition, social interactions (with animals and humans), and biological states. Well-being implies that environmental conditions are such that stress, illness, morbidity and mortality, injury, or behavioral problems are minimized (*Guide for Care and Use of Agricultural Animals,* p.17). The environment can be divided into a macro-environment (housing) and microenvironments (immediate physical, biological and social environment). As indicated in various chapters of *The Guide,* particular genetics, age, and purpose contribute to the determination of what is a proper environment.

Within the physical environment, comfort may be modified by air temperature, water vapor pressure, and ventilation. Health status and genetics can alter the thermal balance (allostasis) and thereby mitigate changes in behavior, metabolism, and ultimately performance.

The well-being of free-range animals compared with confined animals is quite different when environment is considered. On one hand, free-range (or pastured) animals have a degree of freedom to seek shelter that confined animals do not. In contrast, confined animals are usually under closer scrutiny and their environments are more highly regulated with the use of ventilation and artificial heating and cooling. When unexpected weather conditions occur, animals in either macro-environment may be compromised unless managers act quickly.

Domesticated animals are diurnal in nature, being active during the day and resting at night (Silanikove, 2000). During hot weather, these behaviors shift. Grazing occurs before sunrise, at dawn, and during the night. The animals tend to lie down and decrease their locomotion during the day. Other adaptations that may occur are postural changes such that

Table 5.3. Audits contain these concerns for environments of dairy cattle.

	Calves	Cows
Housing		
Temperature	LCT[1]	UCT[2]
Ventilation	X	X
Drafts	X	
Shade	X	X
Misters or sprayers		X
Dry bedding	X	X
Transport		
Weather	X	X
Bedding material	X	X
Wind protection	X	X
Shade	X	X
Time of day	X	X
Space allowances	X	X

[1]LCT = Lower critical temperature.
[2]UCT = Upper critical temperature.

the animal's body is vertical to the sun (decreasing exposure to solar load), or the animal moistens its body with water, saliva, or nose secretions to increase heat loss by convection and conduction.

Much less has been investigated regarding the needs of swine and poultry in free-range settings. Swine need wallows to allow them to regulate their temperatures, but along with that comes changes in exposure to pathogens.

Well-Being Audits Include Measures of Environment

Auditing and certification processes are measurements used to relay to the public whether animals are living in the most appropriate environments. There are several certifications that are available, each with its own emphasis (Stull et al., 2005). An audit is performed to determine whether a farm meets the standards to achieve certification. Validus audit standards include providing comfort during heat stress and shade for calves, but there was no obvious mention for providing relief from cold stress. Humane Farm Animal Care that provides "Humane Certified" certification also provides a section on thermal environment and ventilation. In their assessments, relative humidity values are specified and shade provisions and hypothermia in calves are addressed. Hutch designs that minimize heat stress include adequate ventilation, but also provide shelter from prevailing weather and drafts.

The Dairy Quality Assurance program, which has been the gold standard and longest running program, also addressed environmental temperature, humidity, and air quality. It provided signs to watch for and some specific values that must be achieved. Other audit tools are available and are based on elements contained in these two audit tools with varying degrees and emphasis. Although in general the plans are very similar, some elements that occur in one are not included in the other, and the emphasis placed on various factors within the overall audit lead to quite a different outcome (Stull et al., 2005).

Summary of the Impact of Environmental Stress on Well-Being

Animal well-being can be defined by the Five Freedoms established by the Farm Animal Welfare Council. Environmental stressors can affect an animal's well-being during all ages and stages of production. However, environmental extremes caused by unexpected changes in weather or movement to a new region can result in poor well-being of the animal. The time of handling that leads to transport and conditions during transport present critical times during which the environment can have an impact on the animal's well-being, even for a short transport. Concerns over the well-being of animals that are used to produce our food supply have become evident. Farm audits are used to verify that the conditions that the animals are under are providing good welfare. To achieve certification from audits, environmental conditions and provisions to reduce negative impacts of the environment on that farm are evaluated.

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Chapter 6

Effects of Environment on Metabolism

Lance Baumgard and Robert P. Rhoads

Introduction

Animal productivity is maximized within narrow environmental conditions. When the temperature is either below or above the respective threshold values, efficiency is compromised because nutrients are diverted to maintain euthermia, as preserving a safe body temperature becomes the highest priority, and product synthesis (milk, meat, etc.) becomes de-emphasized. This review primarily concentrates on how heat stress affects post-absorptive metabolism and nutrient partitioning in lactating and growing farm animals.

Heat stress negatively impacts a variety of productive parameters including milk yield, growth, reproduction, and carcass traits. In addition, a heat load increases health care costs and animals can succumb to severe thermal stress (especially lactating cows and sows). Therefore environmental heat stress is a significant financial burden (losses include approximately $900 million per year for dairy and greater than $300 million per year in beef and swine in the United States alone; St. Pierre et al., 2003; Pollman, 2010). Advances in management (i.e., cooling systems, barn construction; Armstrong, 1994; Stowell et al., 2009) have alleviated some negative impacts thermal stress inflicts on animal agriculture, but production still decreases during the summer.

The detrimental effects of environmental heat stress on animal welfare and production will likely become more of an issue in the future if earth's climate continues to warm as some predict (IPCC, 2007), and models forecast extreme summer conditions in most American animal-producing areas (Luber and McGeehin, 2008). In addition, the human population continues to increase and much of this growth is expected to occur in tropical and subtropical areas of the globe (Roush, 1994). Consequently, animal agriculture in these warm areas will need to expand (Renaudeau et al., 2008) to keep pace with the global appetite for high quality protein. Furthermore, basal/metabolic heat production increases with enhanced production

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(i.e., enhanced milk yield and rapid lean tissue accretion; respectively, Spiers et al., 2004; Brown-Brandle et al., 2004). Therefore, genetic selection based upon traditional production traits may increase animals' susceptibility to thermal stress. In summary, understanding the biology and mechanisms of how heat stress jeopardizes animal performance is not only critical in developing approaches (i.e., genetic, managerial, nutritional, and pharmaceutical) to ameliorate current production issues, but it is also an obvious prerequisite for generating future mitigating strategies to improve animal well-being, performance, and agriculture economics.

Lactation

Milk synthesis appears to be extra sensitive (compared to growth models) to thermal stress and decreased yields of 35 to 40% are not unusual (West, 2003). For a detailed description of how cows accumulate and dissipate heat and how, when, and where cows become heat-stressed see Berman's articles (2003, 2004, 2005). It was traditionally thought that lactating cows became heat-stressed when conditions exceed a temperature-humidity index (THI) of 72 (Armstrong, 1994). However, recent climate-controlled experiments indicate milk yield starts to decrease at a THI of 68 (Zimbleman et al., 2009) and this is supported by field observations that evaluated the THI when cow standing time increased (a classic response to a thermal load; Cook et al., 2007). The lower THI at which cows are thought to become heat-stressed is consistent with the hypothesis that higher producing cows are more susceptible to a thermal load.

Maintenance Costs

Heat stress is thought to increase maintenance requirements in several animals including rodents (Collins et al., 1980), poultry (Yahav, 2007), sheep (Whittow and Findlay, 1968; Ames et al., 1971) and cattle (McDowell et al., 1969; Morrison, 1983; Beede and Collier, 1986; Huber, 1996). The enhanced energy expenditure during heat stress is believed to originate from panting, sweating, and because the Van't Hoff-Arrhenius equation predicts greater chemical reaction rates (Kleiber, 1961; Fuquay, 1981). Although it is difficult to quantify, in lactating dairy cattle maintenance costs are estimated to increased by as much as 25% (NRC, 1989), and some suggest cost increases may be greater than 30% (Fox and Tylutki, 1998). However, because heat-stressed animals typically have a reduction in thyroid hormones (Sano et al., 1983; Johnson et al., 1988; Prunier et al., 1997; Garriga et al., 2006), actual oxygen consumption (Hales, 1973) and energy expenditure/heat production may in fact decrease (Collin et al., 2001; Brown-Brandle et al., 2004; Huynh et al., 2005). It appears that a quadratic relationship between environment and bioenergetics exists, where maintenance costs and total body expenditure decline with mild heat stress but rapidly increase during severe heat stress (Kleiber, 1961; Yunianto et al., 1997). Adaptation also appears to influence energy expenditure during heat stress, as metabolic rate may increase during acute heat stress but decrease during chronic heat stress (Bianca, 1965).

The mechanisms involved in how environmentally induced hyperthermia reduces milk yield probably include multiple systems. An altered endocrine profile including reciprocal changes in circulating anabolic and catabolic hormones certainly contributes (Collier et al., 2005; Bernabucci et al., 2010). In addition, intracellular signaling pathways responsible for maintenance, productivity, and survival purposes are markedly impacted by heat stress (Collier et al., 2008). Recent evidence also suggests that the mammary gland utilizes a regulatory

negative feedback system to reduce milk synthesis during acute heat stress (Silanikove et al., 2009). The net result of the aforementioned changes (coupled with marked decreases in nutrient intake) is a highly coordinated event to prioritize acclimation and survivability. How much each altered system contributes to reduced milk yield is currently unknown.

Heat-stressed animals reduce feed intake and this is presumably a survival strategy as digesting (especially in ruminants) and processing nutrients generates heat (i.e., the thermic effect of feed). It has traditionally been assumed that inadequate feed intake caused by the thermal load was responsible for decreased milk production (Fuquay, 1981; Beede and Collier, 1986; Silanikove, 2000; West, 2003; DeShazer et al., 2009). However, our recent experiment demonstrated disparate slopes in feed intake and milk yield responses to a cyclical heat load pattern (Shwartz et al., 2009). This led us to hypothesize that heat stress reduces milk synthesis by both direct and indirect (via reduced feed intake) mechanisms (Baumgard and Rhoads, 2007). To examine this theory, we designed a series of pair-feeding experiments that enabled us to evaluate thermal stress while eliminating the confounding effects of dissimilar nutrient intake. Employing this type of approach is required to differentiate between direct and indirect effects of environmentally induced hyperthermia because both heat-stressed and malnourished animals share common responses (e.g., reduced milk yield, effects on growth). Our experiments demonstrated that reduced feed intake explained only approximately 35 to 50% of the decreased milk yield during environmentally induced hyperthermia (see Fig. 6.1, Rhoads et al., 2009; Wheelock et al., 2009, 2010). Our results agree with previous data (Bianca, 1965) and suggest that when overall extent and duration of heat stress exceed a given threshold (as of yet unidentified) the cumulative thermal load disrupts the nutrient intake: Milk production relationship and milk yield declines beyond expected levels. A similar experimental approach has been utilized to evaluate growth, and similar to our lactation data, reduced feed intake explained only about 50% of the reduction in chick body weight gain (Geraert et al., 1996); but nutrient intake appears to explain the majority of heat stress's effects on the body weight gain of pigs (Safranski et al., 1997) and cattle (O'Brien et al., 2010). However, heat stress growth models are limited because they generally do not take into account gain composition (Bridges and Gates, 2009). This pair-feeding design is critical in determining the extent to which an indirect effect of heat stress, such as reduced feed intake, plays a role in physiological and/or metabolic adaptations, which occur during elevated environmental temperatures.

Growth

Beef

In general, heat-stress-induced production losses for beef cattle are not as severe as those for the dairy industry. It is not entirely clear why growing cattle tolerate higher THI conditions and exhibit a greater heat strain threshold than lactating dairy cows, but likely possibilities are 1) increased surface-area-to-mass ratio, 2) reduced rumen heat production (because of their mostly grain diet), and 3) reduced overall metabolic heat production (on a body weight basis). In addition, beef cattle will often experience compensatory gain after mild or short periods of heat stress (Mitlöhner et al., 2001). The combination of these factors translate into heat-related reduced gain that is typically less than 10 kg, which amounts to approximately seven extra days on feed (St. Pierre et al., 2003). Furthermore, the impact of heat stress on reproductive indices is typically not as severe in beef cattle due to the seasonal nature of breeding programs (often occurring during the spring in the United States).

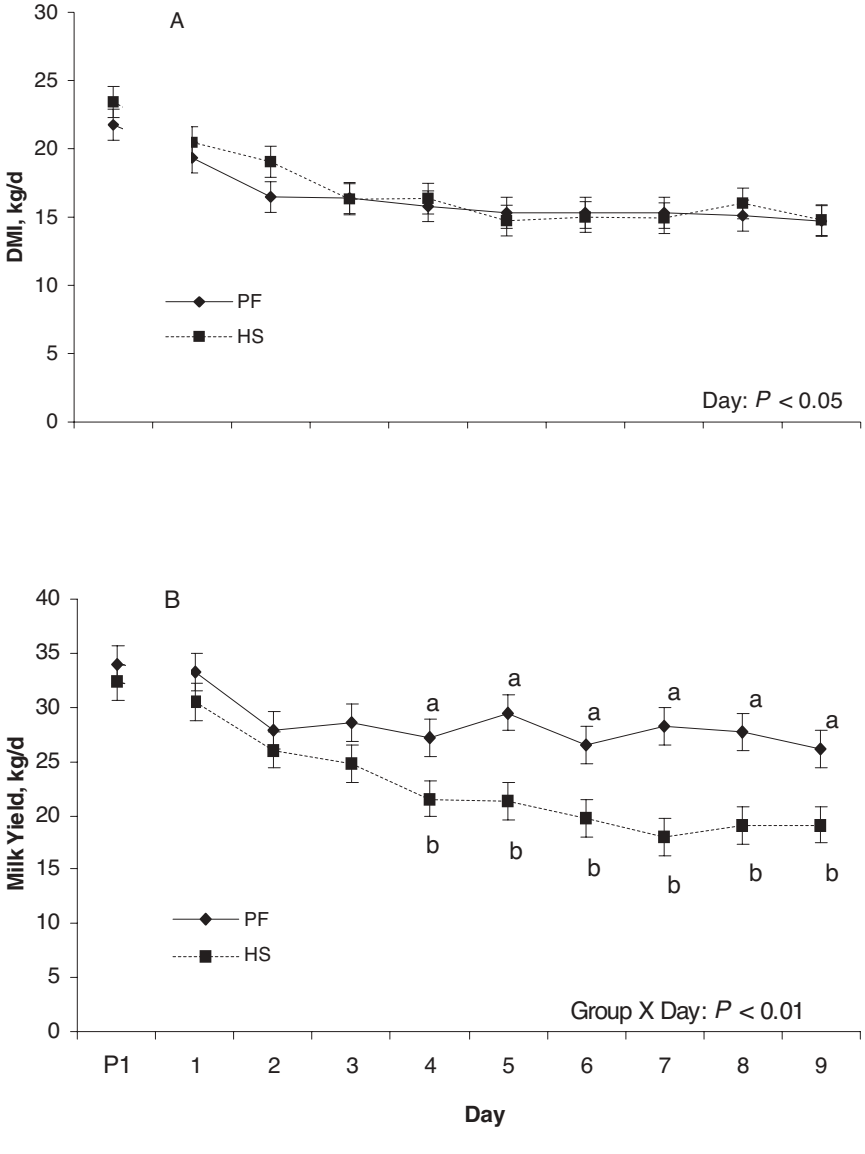

Figure 6.1. Effects of heat stress (HS) or pair-feeding (PF) on A) dry matter intake and B) milk yield in lactating Holstein cows. The mean value of the thermal neutral ad libitum period (P1) from day 1 to 9 was used as a covariate. The d 1 to 9 results are from period 2 when cows were exposed to HS or thermal neutral conditions and PF with HS. Adapted from Rhoads et al. (2009).

Swine

Accurately determining the heat-induced economic loss is difficult, but a recent estimate suggests poor sow performance alone (not including reduced growth, carcass quality, etc.) costs the U.S. swine industry $330 million annually (Pollman, 2010). Even if optimal

heat-stress abatement strategies were implemented by all pig producers at all stages of production, heat stress would still be estimated to cost the American pig industry $300 million annually (St. Pierre et al., 2003). The economic losses caused by a sustained thermal load include reduced growth and efficiency, increased health care costs, decreased carcass value (increased lipid and decreased protein) and increased mortality (especially sows and market hogs). Interestingly, the fact that pigs reared in heat-stress conditions have reduced muscle mass and increased adipose tissue has been documented frequently over the past 40 years (Close et al., 1971; Verstegen et al., 1978; Stahly et al., 1979; Heath et al., 1983, 1989; Bridges et al., 1998; Collin et al., 2001). This phenomenon is not unique to pigs, as heat stress also alters carcass composition similarly in rodents (Schmidt and Widdowson, 1967; Katsumata et al., 1990) and growing poultry (Baziz et al., 1996; Geraert et al., 1996; Yunianto et al., 1997; Lu et al., 2007).

A dramatic reduction in feed intake (up to 50%) is an obvious sign of heat stress and is thought to be primarily responsible for the negative effects heat stress has on pig performance (Collin et al., 2001). It is counter-intuitive that heat stress stimulates a decrease in nutrient intake and depresses growth, yet increases carcass lipid accretion and decreases carcass nitrogen content. In thermal neutral conditions, pigs consuming a restricted diet will deposit protein at the expense of lipid accretion (i.e., the carcass-lipid-to-protein ratio decreases, meaning the carcass becomes leaner) and the quantity of lipid deposited per unit of energy consumed decreases (Le Dividich et al., 1980; Van Milgen and Noblet, 2003; Oresanya et al., 2008). As stated above, a hallmark of heat stress is increased lipid deposition at the expense of protein. Hence, the reduced feed intake to body composition relationship is exactly opposite in pigs reared in heat-stress conditions and is independent of plane of nutrition. Surprisingly, despite its enormous economic impact, little is known about how heat stress directly (not mediated by reduced nutrient intake) and indirectly alters metabolism and nutrient partitioning in pigs.

Metabolic Adaptations to Reduced Feed Intake

A prerequisite for understanding metabolic adaptations that occur with heat stress is an appreciation for the physiological and metabolic adjustments lactating and growing animals initiate during malnutrition. These changes in post-absorptive nutrient partitioning occur to support a dominant physiological state (i.e., milk and skeletal muscle synthesis; Bauman and Currie, 1980), and one well-described homeorhetic strategy is the "glucose sparing" effect that both lactating and growing animals utilize when on a lowered-plane of nutrition.

Lactation

Early lactation dairy cattle enter a unique physiological state during which they are unable to consume enough nutrients to meet maintenance and milk production costs and animals typically enter into negative energy balance (NEBAL; Drackley, 1999). Negative energy balance is associated with a variety of metabolic changes that are implemented to support the dominant physiological condition of lactation (Bauman and Currie, 1980). Marked alterations in both carbohydrate and lipid metabolism ensure partitioning of dietary and tissue-derived nutrients toward the mammary gland, and not surprisingly many of these changes are mediated by endogenous somatotropin, which naturally increases during periods of NEBAL (Bauman

and Currie, 1980). During NEBAL, somatotropin promotes non-esterified fatty acids (NEFA) export from adipose tissue by accentuating the lipolytic response to β-adrenergic signals and by inhibiting insulin-mediated lipogenesis and glucose utilization (Bauman and Vernon, 1993). This reduction in systemic insulin sensitivity is coupled with a decrease in circulating blood insulin levels (Rhoads et al., 2004). The reduction in insulin action allows for adipose lipolysis and NEFA mobilization (Bauman and Currie, 1980). Increased circulating NEFA are typical in "transitioning" and malnourished cows and represent (along with NEFA derived ketones) a significant source of energy (and precursors for milk fat synthesis) for cows in NEBAL. The severity of calculated NEBAL is positively associated with circulating NEFA levels (Bauman et al., 1988; Dunshea et al., 1990) and it is generally thought that there is a linear relationship (concentration-dependent process) between NEFA delivery, tissue NEFA uptake, and NEFA oxidation (Armstrong et al., 1961). The magnitude of NEBAL and thus lipid mobilization, in large part explains why cows lose considerable amounts (>50 kg) of body weight during early lactation.

Post-absorptive carbohydrate metabolism is also markedly altered by NEBAL and this is also in large part, mediated by reduced insulin action. During either early lactation or inadequate nutrient intake, glucose is partitioned toward the mammary gland and glucose's contribution as a fuel source to extra-mammary tissues is decreased (Bell, 1995). The early lactation or NEBAL-induced hypoglycemia accentuates catecholamine's adipose lipolytic effectiveness (Clutter et al., 1980). This is a key "glucose sparing" mechanism because elevated NEFA levels decrease skeletal muscle glucose uptake and oxidation – this is referred to as the "Randle Effect" (Randle, 1998). The fact that insulin simultaneously orchestrates both carbohydrate and lipid metabolism explains why there is a reciprocal relationship between glucose and NEFA oxidation. Ultimately, these are homeorhetic adaptations to maximize milk synthesis at the expense of tissue accretion (Bauman and Curie, 1980). A thermal neutral cow in NEBAL could be considered "metabolically flexible" because she can depend upon alternative fuels (NEFA and ketones) to spare glucose, which can be utilized by the mammary gland to copiously produce milk.

Growth

Inadequate nutrient consumption during thermal neutral conditions is associated with a variety of metabolic changes implemented to support the synthesis of high priority tissues like skeletal muscle (Van Milgen and Noblet, 2003). Marked alterations in both carbohydrate and lipid metabolism ensure partitioning of dietary derived and tissue originating nutrients toward muscle, and many of these changes are mediated by altered concentrations of anabolic and catabolic signals. One characteristic response is a reduction in circulating insulin coupled with a decrease in adipose insulin sensitivity. Compared to a well-fed pig, the reduction in insulin action allows for adipose lipolysis and NEFA mobilization (Mersmann, 1987). Increased circulating NEFA are typical in restricted-fed animals and represent a significant source of energy. The enhanced fatty acid oxidation during nutrient restriction is a classic strategy to "spare" glucose. Post-absorptive carbohydrate metabolism is also altered by reduced insulin action during feed restriction resulting in reduced glucose uptake by adipose tissue. In adipose tissue, the reduced nutrient uptake coupled with the prolonged net release of NEFA is a key homeorhetic mechanism implemented by malnourished pigs in order to prioritize protein synthesis (Vernon, 1992).

Post-Absorptive Changes during Heat Stress

Lipids

Some production data suggest heat stress alters metabolism differently than would be expected based upon calculated whole body energy balance. For example, heat-stressed sows (Prunier et al., 1997) and heifers (Ronchi et al., 1999) do not lose as much body weight and body condition, respectively, as do their pair-fed thermal neutral counterparts. In addition, carcass data indicates that rodents, chickens, and pigs have increased lipid retention when reared in heat-stress conditions. We and others have demonstrated that basal plasma NEFA levels (a product of adipose lipolysis and mobilization) are typically reduced in heat-stressed rodents, pigs (our unpublished results) sheep, and cattle, despite marked reductions in feed intake (Sano et al., 1983; Ronchi et al., 1999; Shwartz et al., 2009), and especially when compared to pair-fed thermal neutral controls (see Fig. 6.2; Rhoads et al., 2009; Wheelock et al., 2010). Furthermore, we have recently demonstrated that heat-stressed cows have a blunted NEFA response to an epinephrine challenge compared to pair-fed thermal neutral controls (Wheelock et al., 2009). These observations agree with rodent results indicating heat stress reduces in vivo lipolytic rates and in vitro lipolytic enzyme activity (Torlinska et al., 1987). Moreover, heat stress increases adipose tissue lipoprotein lipase (Christon, 1988), suggesting hyperthermic animals have an increased capacity to uptake and store intestinal and hepatic-derived triglycerides. The changes in carcass composition, blood lipid profiles, and lipolytic capacity are surprising as heat stress causes a well-described increase in stress and catabolic hormones (e.g., epinephrine, cortisol, and glucagon; see reviews by Bianca, 1965; Beede and Collier, 1986). Additionally, the blunted lipolytic capacity of adipose tissue is especially unusual as heat-stressed cows are severely nutrient-restricted (30–40%), are in a calculated NEBAL (~ -5 Mcal; Moore et al., 2005; Shwartz et al., 2009; Wheelock et al., 2010) and lose considerable amounts of body weight (>40 kg; Rhoads et al., 2009; Wheelock et al., 2010); and these parameters are typically associated with elevated circulating NEFA levels (Bauman et al., 1988; Dunshea et al., 1990).

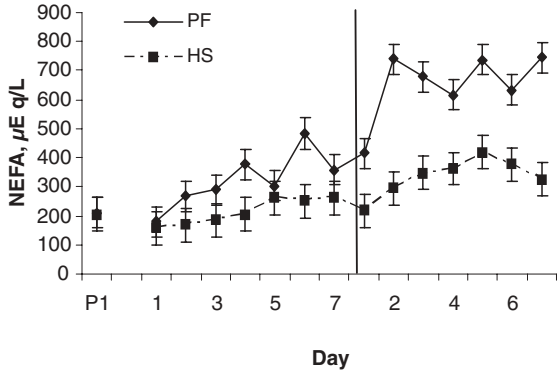

Figure 6.2. The effects of heat stress (HS) or pair-feeding (PF) and rbST on NEFA levels. The mean values of the final two days of the thermal neutral ad libitum intake period (P1) are represented on the x-axis. The vertical line separates period 2 (P2) from period 3 (P3). On day 1 of P3, all cows were administered rbST. Adapted from Wheelock et al. (2010).

Carbohydrates

Evidence from many species suggests that carbohydrate metabolism is altered during heat stress. For example, acute heat stress was first reported to cause hypoglycemia in cats, which was originally thought to be the reason for reduced worker/laborer productivity during warm summer months (Lee and Scott, 1916). In addition, human athletes consistently have increased hepatic glucose production and whole-body enhanced carbohydrate oxidation at the expense of lipids (Fink et al., 1975; Febbraio, 2001; Jentjens et al., 2002). Furthermore, hepatic glucose production typically decreases after ingesting carbohydrates; however exogenous sugars are unable to blunt heat-stress induced liver glucose output (Angus et al., 2001). The increased hepatic glucose output originates from increased glycogenolysis (Febbraio, 2001) and increased gluconeogenesis (Collins et al., 1980). Hepatic pyruvate carboxylase gene expression (a rate-limiting enzyme controlling lactate and alanine entry into the gluconeogenic pathway) is increased during heat stress in multiple animal models (Wheelock et al., 2008; O'Brien et al., 2008; White et al., 2009) and hyperthermic rodents' lactose contribution to gluconeogenesis increases (Collins et al., 1980; Hall et al., 1980). Interestingly, numerous studies indicate plasma lactate concentrations rise during heat-induced hyperthermia including exercising humans (Rowell et al., 1968; Fink et al., 1975; Angus et al., 2001), porcine malignant hyperthermia (Hall et al., 1980), heat-stressed growing steers (O'Brien et al., 2010), and heated melanoma cells (Streffer, 1988) and this presumably stems from skeletal muscle efflux. Surprisingly, the increased muscle lactate production and efflux is not the result of reduced muscle blood or oxygen flow (Yaspelkis et al., 1993). Collectively, these studies appear to indicate that peripheral tissues increase anaerobic glycolysis and the Cori cycle may be an important mechanism to maintain glucose and energy homeostasis.

Our recent environmental physiology experiments in lactating dairy cows indicate that heat-stressed animals are secreting approximately 200 to 400 grams less milk lactose per day compared to pair-fed thermal neutral controls (Rhoads et al., 2009; Wheelock et al., 2009, 2010). The quantity of secreted lactose is generally equivalent to a similar amount (on a molar basis) of secreted glucose, but it is unclear whether the liver produces less glucose or if extra-mammary tissues utilize glucose at an increased rate. We have generated two lines of evidence suggesting the latter. First, heat-stressed cows dispose of exogenous glucose quicker following a glucose tolerance test (Wheelock et al., 2010). Second, despite reports suggesting the liver becomes partially dysfunctional during heat stress (Ronchi et al., 1999; Willis et al., 2000; Ramnath et al., 2008), we have shown (using stable isotopes) that whole-body (presumably primarily from hepatic tissue) glucose production does not differ between heat-stressed and pair-fed thermal neutral controls (Wheelock et al., 2009). As a consequence, it appears glucose is preferentially being utilized for processes other than milk synthesis (ostensibly via insulin-responsive tissues) during heat stress.

Protein

Heat stress also affects post-absorptive protein metabolism and this is grossly illustrated by changes in the quantity of carcass lean tissue in a variety of species (Schmidt and Widdowson, 1967; Close et al., 1971; Lu et al., 2007). Muscle protein synthesizing machinery, and RNA and DNA synthesis capacity is reduced by environmental hyperthermia (Streffer et al., 1982) and it appears that similar effects occur with regards to mammary α and β casein synthesis (Bernabucci et al., 2002). It also appears that skeletal muscle catabolism

is increased in a variety of species during heat stress, indicated by increased plasma markers of muscle breakdown (Bianca, 1965; Hall, 1980; Marder et al., 1990; Yunianto et al., 1997; Wheelock et al., 2010).

Effects of Heat Stress on Aspects of the Endocrine System

Somatotropin Axis

Somatotropin and insulin-like growth factor I (IGF-1) are two of the most potent and well-characterized lactogenic hormones (Bauman and Vernon, 1993). Normally, somatotropin partitions nutrients toward the mammary gland by decreasing nutrient uptake by extra-mammary tissues and by stimulating hepatic IGF-1 synthesis and secretion. During NEBAL (i.e., early lactation), the somatotropic axis uncouples and hepatic IGF-1 production decreases despite increased circulating somatotropin concentrations (McGuire et al., 1992). We originally hypothesized that NEBAL caused by heat stress and early lactation differentially affects the somatotropic axis. For example, although acute heat stress increases somatotropin levels in steers (Mitra and Johnson, 1972), chronically heat-stressed cows (which are presumably in NEBAL) had or tended to have reduced somatotropin levels (Mohammed and Johnson, 1985; Igono et al., 1988; McGuire et al., 1991). To evaluate this further, we analyzed basal somatotropin pulsatility characteristics and the pituitary's responsiveness to a somatotropin secretagogue and reported no differences in either parameter in heat stress versus pair-fed thermal neutral controls (Rhoads et al., 2009). However, we did measure a modest reduction in circulating IGF-1, which may indicate the metabolic milieu favors uncoupling of the somatotropic axis during heat stress (Rhoads et al., 2009). We investigated whether hepatic growth hormone (GH)-responsiveness was altered during heat stress by measuring GH receptor abundance and signal transducer and activator of transcription 5 (STAT-5) phosphorylation (Rhoads et al., 2010). Heat stress, independent of reduced feed intake, decreased hepatic GH receptor abundance although both heat stress and malnutrition were sufficient to decrease STAT-5 phosphorylation. Consistent with reduced GH signaling through STAT-5, hepatic IGF-1 mRNA abundance was lower in heat-stressed animals. Thus, the reduced hepatic GH responsiveness observed during heat stress appears to involve mechanisms independent of reduced feed intake. The physiological significance of reduced hepatic GH receptor abundance during heat stress is unclear at this time but may serve to alter other GH-dependent hepatic processes such as gluconeogenesis regulation. Moreover, we hypothesize that reduced IGF-1 may be one mechanism by which the liver and mammary tissues coordinate the reduction in milk synthesis so nutrients (e.g., glucose) can be utilized to maintain homeothermia.

Insulin

Despite hallmarks traditionally associated with hypoinsulinemia such as 1) marked reductions in feed intake, 2) calculated NEBAL, and 3) rapid body weight loss (>40 kg) we have demonstrated that basal insulin values gradually increase in lactating heat-stressed cows (Wheelock et al., 2010) and we have confirmed this in growing heat-stressed calves (Fig. 6.3; O'Brien et al., 2010) and pigs (unpublished data). Increased plasma insulin concentrations in our experiments are in line with data from another heat-stressed ruminant report (Itoh et al., 1998), a malignant

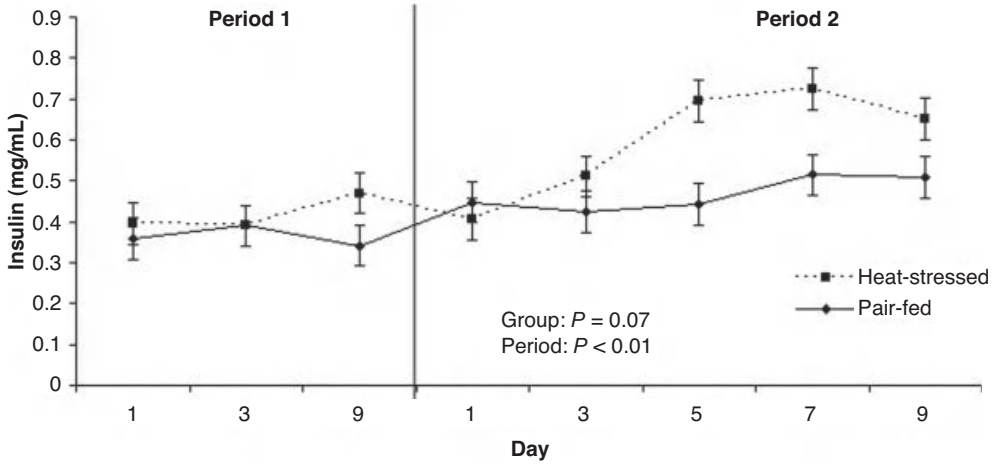

Figure 6.3. Effects of heat stress and pair-feeding on basal insulin concentrations in growing Holstein bull calves. The vertical line separates period 1 (thermoneutral conditions and ad libitum feed intake) from period 2 (either heat stress conditions and ad libitum feed intake or thermoneutral conditions and pair-fed). Adapted from O'Brien et al. (2010).

hyperthermic pig model (Hall et al., 1980), and a heat-stressed rodent report (Torlinska et al., 1987). In addition, we have shown that heat-stressed cows and calves have increased insulin response to a glucose tolerance test (Fig. 6.4; O'Brien et al., 2010; Wheelock et al., 2010) and this also supports other reports utilizing different insulin secreteagogues (Achmadi et al., 1993; Itoh et al., 1998). Reasons for insulin increases during heat stress are not clearly understood, but they likely include insulin's key role in activating and up-regulating heat shock proteins (Li et al., 2006). The lack of a NEFA response during heat stress may allow for the

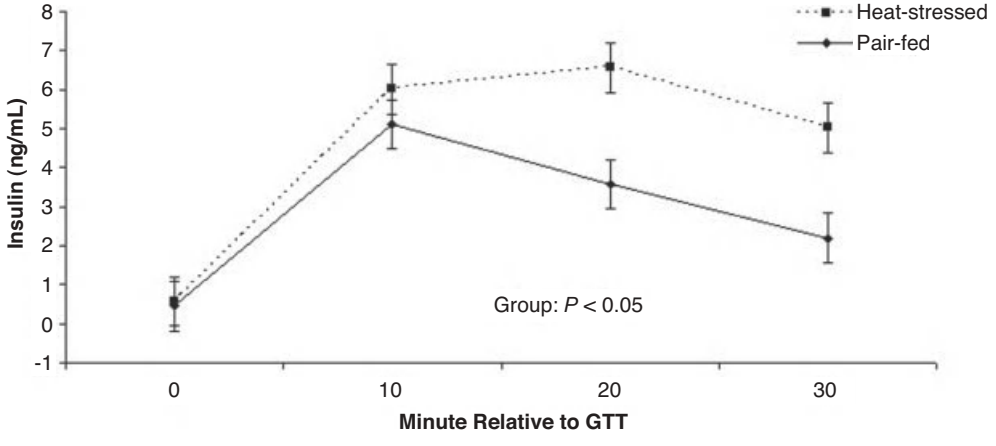

Figure 6.4. Effects of heat stress (ad libitum feed intake) and pair-feeding (thermoneutral conditions) on insulin response to a glucose tolerance test (GTT) in growing Holstein bull calves during period 2. Adapted from O'Brien et al. (2010).

increase in circulating insulin as excessive NEFA cause pancreas β-cell apoptosis (Nielson et al., 2001). Regardless of the reason, heat stress is one of the very few non-diabetic models we are aware of where nutrient intake is markedly reduced but basal and stimulated insulin levels are increased.

The increased insulin may be an essential part of the heat-stress adaptation mechanism. For example, diabetic humans are more susceptible to heat related illness and death (Shuman, 1972; Semenza et al., 1999; Kovats and Hajat, 2008). Similarly, diabetic rats have an increased mortality rate when exposed to severe heat, and exogenous insulin increases their survival time (Niu et al., 2003). Furthermore, non-lethal heat stress ameliorates proxies of insulin insensitivity in diabetic rodents (Kokura et al., 2007, 2010) or rodents fed high-fat diets (Gupte et al., 2009). This is similar to reports that indicate thermal therapy (saunas and hot baths) improves insulin sensitivity in humans (McCarty et al., 2009). Consequently, it appears that insulin and/or maintenance of insulin action plays a critical role in the ability to respond and ultimately survive a heat load.

Ghrelin

A potentially novel participant in heat-related metabolic changes may be ghrelin, a peptide produced primarily by the gastrointestinal tract. Originally discovered as a potent GH releasing factor (Kojima et al., 1999); this effect has been documented in a number of species including humans, rodents, and ruminants (van der Lely et al., 2004; Hashizume et al., 2005; Itoh et al., 2005; ThidarMyint et al., 2006, 2008; Wertz-Lutz et al., 2006). In experiments designed to examine its GH-releasing properties, ghrelin was also shown to acutely regulate appetite, as a single ghrelin injection caused a temporary increase in feed intake (Wren et al., 2000; Asakawa et al., 2001; Nakazato et al., 2001). On a chronic basis, ghrelin administration leads to persistent hyperphagia and weight gain in rodents. During periods of food deprivation, circulating ghrelin levels increase in cattle, mice, rats, and humans (van der Lely et al., 2004; Wertz-Lutz et al., 2006, 2008). In rodents, ghrelin promotes lipogenesis and decreases lipolysis (Choi et al., 2003; Thompson et al., 2004) despite its potent stimulation of GH (which can accentuate lipolysis depending upon the animal's energetic state, Bauman et al., 1988). The in vitro treatment of rat preadipocytes with ghrelin stimulated glycerol-3-phosphate dehydrogenase activity and increased peroxisome proliferator-activated receptor γ2 (PPAR-γ2) mRNA, which are both indicators of preadipocyte differentiation (Choi et al., 2003). Ghrelin infusion into rats also increased lipogenesis in vivo but appears to be mediated by a receptor other than the GHSR-1a (Thompson et al., 2004). Furthermore, ghrelin inhibited isoproterenol-induced lipolysis in rat adipocytes (Choi et al., 2003; Muccioli et al., 2004). Ghrelin treatment also increased the overall triglyceride content of most rodent tissues and decreased the abundance of phosphorylated adenosine monophosphate-activated protein kinase (AMPK), which stimulates fatty acid oxidation (Barazzoni et al., 2005; van Thuijl et al., 2008). The effects on AMPK are of particular interest because decreased AMPK phosphorylation (as seen during ghrelin treatment) is associated with higher levels of intramuscular fat in beef animals (Underwood et al., 2007). In support of a possible role for ghrelin during heat stress, we recently demonstrated that the diurnal pattern of circulating ghrelin differs between heat stress and pair-fed lactating cows. Moreover, chronically elevated plasma insulin (via the hyperinsulinemic-euglycemic clamp technique) suppressed plasma ghrelin in pair-fed but not heat-stressed cows (Cossel et al., 2010). Taken together, the information above indicates changes in ghrelin that may support alterations in lipid metabolism observed during periods of heat stress.

Coordinated Metabolic Consequences of Heat Stress

Insulin is a potent regulator of both carbohydrate and lipid metabolism and may play an important role in mediating how heat stress regulates post-absorptive nutrient partitioning. Insulin stimulates glucose uptake via GLUT-4 in responsive tissues (i.e., muscle and adipose tissue) and is likely responsible for the heat-induced hypoglycemia frequently reported in multiple models (e.g., rodents, Mitev et al., 2005; poultry, Rahimi, 2005; cats, Lee and Scott, 1916; dogs, Kanter, 1954; sheep, Achamadi et al., 1993; heifers, Itoh et al., 1998; bulls, O'Brien et al., 2010; and cows, Settivari et al., 2007; Wheelock et al., 2010). This occurs despite an increase in intestinal glucose absorptive capacity (Garriga et al., 2006), and enhanced renal glucose re-absorptive ability (Ikari et al., 2005).

Insulin is also a potent antilipolytic hormone (Vernon, 1992) and may explain why heat-stressed animals do not mobilize adipose tissue triglycerides. Limiting adipose tissue mobilization is the key step by which heat-stressed animals are prevented from employing glucose sparing mechanisms normally enlisted to maintain milk or skeletal muscle synthesis during periods of temporary malnutrition. The lack of available NEFA to systemic tissues for oxidative purposes is coupled with reduced volatile fatty acid (primarily acetate because of decreased feed intake in ruminants) availability and thus both glucose and amino acid oxidation may increase. The efficiency of capturing ATP from amino acid oxidation is low (meaning metabolic heat production is high; Berg et al., 2007) so it is an unlikely fuel choice during hyperthermia. Therefore, it appears glucose becomes a favored fuel for heat-stressed animals (Streffer, 1988), which is supported by the increase in respiratory quotient (RQ) in hyperthermic humans (Febbraio, 2001).

The increase in skeletal muscle protein catabolism (mentioned above) is peculiar given insulin's role in stimulating protein synthesis and preventing proteolysis (Allen, 1988). Heat stress is thought to increase membrane permeability allowing for cytostolic Ca^{+} leakage which may increase protein sensitivity to heat stress (Roti, 2008). We believe it is likely that breaking down skeletal muscle is a strategy to supply precursors for gluconeogenesis and acute phase proteins rather than for supplying oxidative substrates (because of the inefficiency in capturing ATP).

Potential Reasons for Heat-Induced Metabolic Shifts

Reasons for the changes in heat-stress induced post-absorptive metabolism are not clear, but are presumably adaptive mechanisms employed in an attempt to maintain a safe body temperature. The increased basal and stimulated insulin response likely prevents fatty acid mobilization while simultaneously ensuring glucose uptake – we hypothesize this is one strategy to minimize metabolic heat production (O'Brien et al., 2010). Utilizing glucose as a fuel is most efficient (Baldwin et al., 1980), as in vivo glucose oxidation yields 38 ATP or 472.3 kcal of energy (assuming -12.3 kcal/mole as the ΔG for ATP hydrolysis under cellular conditions; Berg et al., 2007) compared to the 637.1 kcal of energy released from glucose oxidation in vitro (74.1% efficiency). In contrast, in vivo fatty acid (i.e., stearic acid) oxidation yields 146 ATP or 1,814 kcal of energy compared to 2697 kcal from complete oxidation in vitro (67.3% efficiency). This hypothetical decrease in heat production (a consequence of the 10% improvement in capturing energy) may be one strategy why heat-stressed animals initiate the aforementioned metabolic adaptations.

Summary and Conclusion

Clearly, the heat-stressed animal initiates a variety of post-absorptive metabolic changes that are in large part independent of reduced feed intake and whole-animal energy balance. Seemingly these changes in nutrient partitioning are adaptive mechanisms employed to prioritize the maintenance of euthermia. The primary difference between a thermal neutral and a heat-stressed animal in a similar energetic state is the inability of the hyperthermic beast to employ "glucose sparing" mechanisms to homeorhetically prioritize product (milk and meat) synthesis. From an animal agriculture standpoint, these survival strategies reduce productivity and seriously jeopardize farm economics.

Although science has identified some changes that heat stress induces in post-absorptive metabolism, there are a plethora of unknowns. For example, how heat stress signals for an increase in circulating insulin is not clear. We presume insulin prevents adipose tissue mobilization but the mechanism is currently unknown, especially during periods of enhanced catabolic signals and hypoglycemia. Defining the biology and mechanisms of how heat stress jeopardizes animal health and performance is critical in developing approaches to ameliorate current production issues and is a prerequisite for generating future mitigating strategies to improve animal well-being, performance (lactation, growth, and reproduction), and agriculture economics.

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Chapter 7

Impact of Hot Environment on Nutrient Requirements

Umberto Bernabucci

Introduction

High environmental temperature, relative humidity, and radiant energy adversely affect productivity and reproduction efficiency of animals in temperate, tropical, and subtropical regions (Hancock, 1954; Bianca, 1965; Johnson, 1987b; Nardone et al., 2010). Johnson (1987a) has effectively described the thermal comfort (TC) and high ambient temperature (HAT) conditions for farm animals. The estimation of how "comfortable" or "stressful" environmental conditions are is complicated. This is mainly due to the various combinations of factors such as temperature, humidity, wind, and direct and indirect radiation. A plethora of biometeorological indices have been developed and these empirical formulas would ideally predict the weather conditions under which ruminants start to experience heat stress (Bohmanova et al., 2007) and become susceptible to heat-induced death (Vitali et al., 2009). The temperature humidity index (THI) is generally used to characterize these conditions (Armstrong, 1994). Most temperature-humidity indices (THI) are a combination of only ambient temperature (often referred to as dry bulb temperature) and relative humidity (Hahn et al., 2003). Although solar radiation can be a strong contributor to heat load, it is often not easily measurable and its effect is partially dependent upon animal coat characteristics. Therefore, THI equations that do not incorporate a wet bulb variable (a measure of temperature, humidity, wind, and solar radiation) have limitations for pasture and feedlot based systems. The primary difference among most THI equations is how much weight is given to relative humidity, and thus different equations will be better suited for different geographic locations (Bohmanova et al., 2007).

The THI values for cattle can be calculated according to Kibler's (Kibler, 1964; cited by Johnson, 1987b) or Kelly and Bond's (Kelly and Bond, 1971) formulas.

Environmental Physiology of Livestock, First Edition. Edited by R. J. Collier and J. L Collier.

Kibler's formula:

$$THI = T_{db} + 0.36T_{dp} + 41.2°C \quad (7.1)$$

Where:

T_{db} = Dry bulb temperature (°C)
T_{dp} = Dew-point temperature (°C)

Kelly and Bond's formula:

$$THI = (1.8 \times T_{db} + 32) - [(0.55 - 0.55 \times UR/100) \times (1.8 \times T_{db} + 32) - 58)] \quad (7.2)$$

Where:

T_{db} = Dry bulb temperature (°C)
UR = Relative humidity in %.

Farm animal performance is affected by HAT (Gaughan et al., 2009; Bernabucci et al., 2010), as these environmental factors combined with metabolic heat production and the difficulty in losing heat (Morrison, 1983) create difficulties in maintaining thermal balance (Yousef and Johnson, 1966) leading to an increase in body temperature. To maintain body temperature within the normal range, animals need to increase heat loss and reduce the endogenous heat production to re-establish homeothermy and homeostasis. To reduce heat gain, the sudden responses of animals to heat include increased heat dissipation (primarily through evaporative heat loss), reduced feed intake and milk yield, increased water intake (Gaughan et al., 2009), and the subsequent reduction of metabolic rate (Bernabucci et al., 2010). These acclimation responses are essential for survival of animals but may lead to alteration of normal physiological balance (energy, minerals, and water balance) and endocrine equilibrium (Johnson, 1987a; El-Shafie, 1991; Webster, 1991). Then, health, fertility, and productivity are negatively affected (Nardone et al., 2006).

In terms of adaptation measures, it is generally faster to improve welfare, production, and reproduction performances by altering the environment (West, 2003; Mader et al., 2006) and improving genetic heat-tolerance and nutritional management practice (West, 1999; Mader and Davis, 2004, Spencer et al., 2005).

Feeding and nutritional adjustments to balance the effects of heat stress, other than the reduction of feed and nutrient intake, should consider the modification of metabolic responses and the alteration of rumen and intestine health of animals when exposed to heat stress. It is now clear that it is not sufficient to simply replace the nutrients for improving the efficiency of animals exposed to hot conditions. The acclimation to heat stress is responsible for strong changes in glucose and lipid metabolism and nutrient partitioning (Shwartz et al., 2009; Bernabucci et al., 2010; O'Brien et al., 2010) and in alteration of rumen function (Bernabucci et al., 2009) as well as intestine function and epithelial integrity (Karol et al., 2005; Lambert, 2009), which all are responsible for changes and reduction of feed efficiency.

The aim of this chapter is to review the literature on the impact of environment (specifically, hot weather) on changes in nutrient requirements and feeding practices, with particular attention to domestic dairy ruminants. However, the references cited in this paper represent only a portion of the voluminous literature available on this subject.

Effects of Hot Environment on Feed Intake and the Efficiency of Nutrient Utilization

Feed Intake

Environmental conditions affect dry matter intake (DMI) in all species (National Research Council, 1981). Exposure to heat reduces the voluntary feed intake and this is related to the length and the severity of heat stress, to the species and breed, to the physiological phase, and to the level of production (especially milk production).

For both dairy and meat cattle the effect of environmental temperature on changes of DMI have been reported (National Research Council, 1981, 1989; Mader, 2003). In lactating dairy and feed lot cattle, dry matter intake begins to decline at mean daily environmental temperatures of 25 to 27°C. The National Research Council (1989) reported that feed intake in lactating cows begins to decline at ambient temperatures of 25 to 26°C, drops more rapidly above 30°C, and at 40°C, dietary intake may decline by as much as 40 to 60%. The Scientific Committee on Animal Health and Animal Welfare (SCAHAW, 2001) suggested that the threshold temperature at which adverse effects on DMI, growth, and feed efficiency are readily apparent in beef cattle is 30°C with relative humidity below 80% and 27°C with relative humidity above 80%.

Johnson et al. (1963) reported that DMI significantly declines when maximum THI reached 77 in Holstein cattle. Igono et al. (1992) found that the critical values for minimum, mean, and maximum THI were 64, 72, and 76, respectively. West et al. (2003) reported that the mean THI two days earlier had the greatest effect on milk yield, while DMI was most sensitive to the mean air temperature two days earlier. Those authors reported that DMI declined 0.85 kg for each degree (°C) increase in the mean air temperature. In contrast, other studies established that there was a significant negative correlation between THI and DMI for cows (Johnson, 1987b, Holter et al., 1996, 1997). In heavy (70 to 120 kg) swine feed consumption began to decline at about 20 to 22°C, whereas the decline started 3 to 7°C higher in lighter weight pigs (40 to 70 kg; National Research Council, 1981).

The effect of THI is probably mediated through the effects of increasing body temperature on cow performance (Nardone et al., 1992; Spiers et al., 2004). Nardone et al. (1992) found a negative relationship between rectal temperature and dry matter intake in dairy cows maintained under hot conditions (see Fig. 7.1), indicating that feed intake was related to the individual responses to heat stress conditions. Spiers et al. (2004) measured the relationship between thermal status (rectal temperature) of cows and DMI. The authors reported a negative relationship between rectal temperature and DMI and concluded that ambient temperature produced a change in rectal temperature that was related to changes in feed intake. A direct negative effect of elevated temperatures on the appetite center of the hypothalamus may exist (Baile and Forbes, 1974). Moreover, an associated effect is reduced gut motility and rumination, which, along with increased water intake, lead to gut-fill.

The resulting reduction of feed intake in heat-stressed cattle is also accompanied by change in feeding pattern. Schneider et al. (1988) and Nardone et al. (1992) found that heat-stressed cows changed their feeding behavior. In particular, heat-stressed cows ate 12% more during the nighttime, when temperatures were cooler, compared with daytime (see Fig. 7.2). Under heat stress conditions cattle reduce roughage intake (Collier et al., 1982; Coppock et al., 1986; Bernabucci et al., 1999). This leads to changes in the forage-to-concentrate ratio of the diet ingested (Bernabucci et al., 1999). This behavior is considered an adaptive response to reduce heat production from rumen fermentation (Beede and Shearer, 1991). The decreased

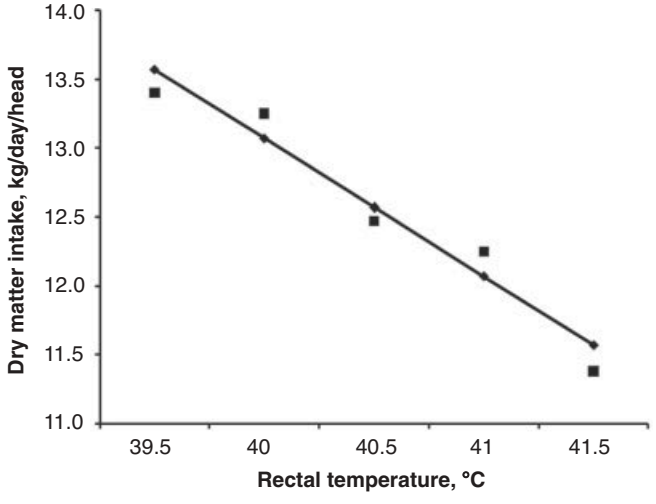

Figure 7.1. Change in dry matter intake as a function of rectal temperature for animals housed in a climatic chamber and maintained under hot conditions (Nardone et al., 1992).
$y = 53.07 - (1.00 \pm 0.34) * x$; $r = -0.48$; $P < 0.05$.

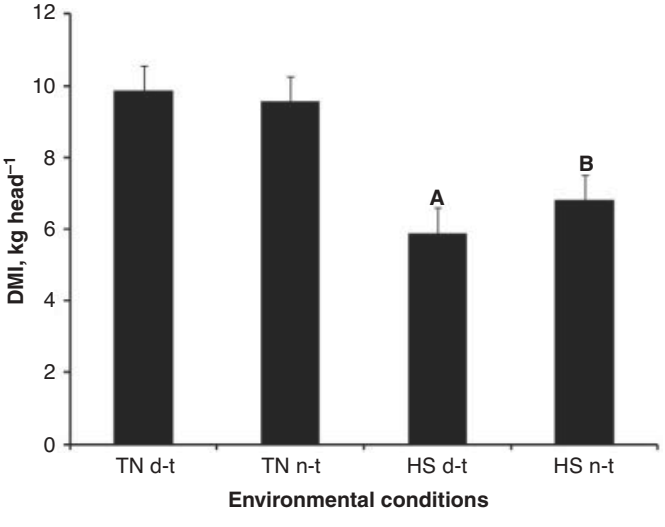

Figure 7.2. Dry matter intake (DMI) in dairy cows housed in climatic chambers maintained under thermoneutral (TN) and heat stress (HS) conditions. Feed intake was measured during the daytime (d-t: from 10:00 to 20:00 h) and nighttime (n-t: from 22:00 to 8:00 h).
[A,B]Means within HS differ ($P < 0.01$).

roughage intake and changes in forage-to-concentrate ratio of ingested diet may contribute to decreased VFA production and may lead to alterations in the ratio of acetate and propionate and to a decrease of rumen pH during heat stress (Collier et al., 1982; Bernabucci et al., 2009).

Digestion

Rumen Health

High environmental temperature adversely affects rumen health (Mishra et al., 1970) due to a variety of biological and management reasons (Bernabucci et al., 1999, 2009; Kadzere et al., 2002). Heat-stressed cows consume less feed and consequently ruminate less (Aganga et al., 1990) and this results in decreased buffering agents (ruminating is the primary stimulant of saliva production) entering the rumen. In addition, because of the redistribution of blood flow to the periphery (in an attempt to enhance heat dissipation) and subsequent reduction in blood delivery to the gastrointestinal track, digestion end products (i.e., volatile fatty acids, VFA) are absorbed less efficiently and thus the total rumen VFA content increases (and pH decreases). Furthermore, increased respiration rates also contribute to rumen acidosis because panting causes enhanced CO_2 to be exhaled. In order to be an effective blood–pH buffering system, the body needs to maintain a 20:1 HCO_3^- (bicarbonate) to CO_2 ratio. Because of the hyperventilation-induced decrease in blood CO_2, the kidney secretes HCO_3^- to maintain this ratio. This reduces the amount of HCO_3^- that can be used (via saliva) to buffer and maintain a healthy rumen pH. In addition, panting cows often drool, reducing the quantity of saliva available for the rumen. The reduction in saliva HCO_3^- content and the decreased amount of saliva entering the rumen make the heat-stressed cow much more susceptible to subclinical and acute rumen acidosis (Kadzere et al., 2002).

Changes in cow eating behavior probably also contribute to rumen acidosis. Cows in thermal neutral conditions typically consume 12 to 15 meals per day but decrease eating frequency to 3 to 5 meals per day during heat stress. The decreased frequency is accompanied by larger meals and thus more acid production post-eating. Furthermore, cows will typically gorge (over-eat) the day following a heat wave and this gluttonous behavior is well known to cause rumen acidosis.

To compensate for the reduced nutrient and energy intake caused by heat stress and the metabolic heat load associated with fermenting forages, nutritionists typically tend to increase the energy density of the ration using extra grains/concentrates. However, this practice should be conducted with care as this type of diet can be associated with a lower rumen pH. The combination of a "hotter" ration and the cow's reduced ability to neutralize the rumen directly increases the risk of rumen acidosis and indirectly enhances the risk of developing negative side effects of an unhealthy rumen environment (i.e., laminitis, milk fat depression, etc.).

In summary, in periods of heat stress factors that can contribute to rumen acidosis problems are: decreased DM intake with lower proportion of forage and higher levels of fermentable carbohydrates; decreased rumination; and decreased saliva to the gut, a source of bicarbonate, with a reduction in its buffering power due to increased CO_2 being expelled (via panting). Additionally, the decreased rumen pH impairs fiber digestion efficiency: rumen fibrolytic bacteria are the most affected when rumen pH drops (below 6.0). All of these factors may contribute to decreasing feed efficacy and acidosis is proven to affect the animals overall health status, fertility, and longevity.

Intestine Health

Intact intestinal epithelial tight junctions (TJ) are crucial barriers against paracellular penetration of pathogenic bacteria and toxic luminal antigens including endotoxins (Dokladny et al., 2006). The disruption of intestinal TJ barrier may result in a leaky TJ barrier favoring the permeation of toxic luminal substances. Various types of stresses, including heat stress, can cause increase of intestinal permeability to luminal endotoxins and lead to bacterial translocation (Lambert, 2009). The gut-derived endotoxins and pathogenic bacteria have been proposed to be responsible for the increased incidence of health problems such as heat stroke, sepsis, burn injury, and ischemia-reperfusion injury.

The effect of heat stress on intestinal permeability has been studied in rat models. Hall et al. (2001) observed a significant increase in portal lipopolysaccharide concentration in rats heated to core temperatures of 41.5°C. Lambert et al. (2002) reported significant increases in intestinal permeability at core temperatures of 42.5°C in rats and at 41.5 to 42°C in everted rat intestinal sacs. Dokladny et al. (2006) showed Caco-2 cell monolayers maintained at 41°C over 24 h have significantly increased paracellular permeability and reduced epithelial resistance. The mechanisms underlying the effects of heat stress on intestinal barrier function is reported in a recent review paper by Lambert (2009). This author highlights that the combination of reduced intestinal blood flow and hyperthermia can cause loss of tight junction integrity and likely enterocyte membrane damage. Reduced intestinal blood flow occurs with acclimation to heat stress as blood is diverted away from the splanchnic region to provide adequate perfusion of the skin (vasodilatation) for heat dissipation (Engelhardt and Hales, 1977; Thatcher and Collier, 1982; Hales et al., 1984; Lough et al., 1990). This can lead to intestinal hypoxia (Hall et al., 1999), which likely results in reduced cellular viability and increased paracellular permeability.

Reduced blood flow can also result in oxidative and nitrosative stress (Hall et al., 2001), which can damage cell membranes and open TJ (Hall et al. 1994). Furthermore, hyperthermia alone produces reactive oxygen and nitrogen species (Bernabucci et al., 2002; Hall et al., 2002) leading to damaged cell membranes and TJ opening. Taken together, the dual effect of reduced intestinal blood flow and tissue hyperthermia during heat stress likely promotes significant intestinal mucosal damage (Lambert et al., 2002) leading to the passage of substances such as lipopolysaccharide into the internal environment.

Hyperthermia alone is responsible for enterocyte membrane damage. Intestinal barrier dysfunction with consequent increased permeability facilitates the penetration of endotoxins with consequent inflammatory response (Lambert, 2009). As reported previosuly, exposure to hot conditions is responsible for alteration of rumen functionality and changes in ingested diet with the increase in grain intake. Those factors are recognized to be responsible in a markedly greater concentration of rumen (Zebeli and Ametaj, 2009) and serum (Emmanuel et al., 2008) lipopolysaccharide.

The alteration of gastrointestinal health together with changes in rumen functionality and increased risk of rumen acidosis make subjects exposed to heat stress conditions more susceptible to inflammation and oxidative stress and requires us to consider feeding adjustments to reduce the risk of serious problems these effects can produce.

Passage Rate and Digestibility

Heat stress affects the nutrition of animals by altering the dynamic characteristics of the digestion processes (Beede and Collier, 1986). After feed intake, the second function in acquisition of nutrients is digestion. In a review, Kadzere et al. (2002) concluded that exposure

to a hot environment is responsible for an increase of digestibility that may be explained by the reduction of DMI and prolonged retention of feed in the gastrointestinal tract. Nevertheless, results available in literature on the effects of hot exposure on diet digestibility are often conflicting. Some authors reported an increase in diet digestibility in cattle exposed to hot environments (Lippke, 1975; National Research Council, 1981; Christopherson, 1985; Miaron and Christopherson, 1992; Weniger and Stein 1992; Bernabucci et al., 1999). In contrast, negative or no relationships between high ambient temperatures and diet digestibility have been reported in dairy cattle (McDowell et al., 1969; Mathers et al., 1989; National Research Council, 1981) and small ruminants (Silanikove, 1985, 1992; Bernabucci et al., 2009). Some differences in responsiveness of sheep and cattle to thermal stress have been reported. Lippke (1975) found significant increases in digestibility of dry matter and fiber components of alfalfa pellets fed to steers housed at 32°C compared with 21°C, but no environmental temperature effects were found on digestibility in wethers. Goats adapted to a harsh environment (e.g., desert Bedouin goats) have higher digestion capacity for a high-fiber diet than non-desert goats (e.g., Saanen goats).

The increase in diet digestibility in heat-stressed ruminants was explained by increased mean retention time in the whole gastrointestinal tract (Coppock and West, 1986; Miaron and Christopherson, 1992). Indeed, slower passage rate and longer mean retention time of digesta have been described in ruminants maintained under hot environments (Warren et al., 1974; Faichney and Barry, 1986; Silanikove, 1992; Bernabucci et al., 2009).

Reduction in DMI is generally associated with a decrease of rumen passage rate and an increase of diet digestibility in ruminants maintained in thermoneutrality (Mulligan et al., 2001; Warren et al., 1974). Conversely, several authors have reported that under hot conditions, diet digestibility and rumen passage rates were not affected by the changes of DMI (Attebery and Johnson, 1969; Miaron and Christopherson, 1992; Silanikove et al., 1993; Bernabucci et al., 1999; Bernabucci et al., 2009). In a previous study carried out in Holstein heifers (Bernabucci et al., 1999) rumen passage rate was not a determinant factor influencing digestibility after prolonged exposure to hot conditions. A recent study, carried out on dairy sheep exposed to different periods in a hot environment (Bernabucci et al., 2009), clearly demonstrated that diet digestibility of ewes chronically exposed to heat stress is not related to changes in DMI or rate of passage of digesta into the gastrointestinal tract (see Table 7.1). Our studies (Bernabucci et al., 1999, 2009) clearly excluded digesta outflow rate and feed intake as determinant factors influencing digestibility of diet, in particular when animals are chronically exposed to heat stress. Factors other than DMI or gut retention time may affect diet digestibility of heat-stressed ruminants. As reported previously, heat stress is recognized to adversely affect rumen and intestine functionality. During heat stress, blood flow to rumen and intestine epithelium is reduced and the acid-base balance is altered. Heat stress induces a reduction in the amount of saliva produced and salivary HCO_3^- content, which may impair rumen functionality (Kadzere et al., 2002). Also, dilution of rumen content due to higher water intake, reduction in rumen bacteria activity, and decline in rumen motility may be responsible for digestibility changes when animals are chronically exposed to hot environments. The negative effect of a depression of rumen bacteria activity on diet digestibility might overcome the positive effects caused by the decline in DMI and digesta outflow rate, resulting in a net reduction of diet digestibility in chronically heat-stressed subjects. Other than alteration of bacterial activity, the reduction in digestibility might be related to the changes of ruminal and intestinal absorption of nutrients that might be dependent on an adaptive redistribution of cardiac output from the digestive system to peripheral tissues and respiration system to increase heat loss (Thatcher and Collier, 1982; Christopherson, 1985) as an acclimatization

Table 7.1. Least square means of dry matter intake, digestibility coefficients and passage rates of digesta in the gastrointestinal tract of ewes exposed for different periods to heat stress conditions (Bernabucci et al., 2009).

	TC[1]	ETHI[1]			TC[1]	
Item	Trial 1[§]	Trial 2[§]	Trial 3[§]	Trial 4[§]	Trial 5[§]	SEM*
Dry matter intake, g d^{-1}	874^{Bcd}	938^{Bd}	847^{Bcd}	737^{A}	846^{Bc}	14.5
Digestibility coefficient, %						
Dry matter	70.8^{B}	68.4^{B}	62.2^{A}	62.0^{A}	69.4^{B}	0.83
Organic matter	83.1^{Cd}	79.8^{Ce}	74.0^{B}	71.1^{A}	75.3^{B}	0.95
Crude proteins	64.7^{a}	67.4^{a}	65.2^{a}	64.0^{a}	70.8^{b}	0.55
Neutral detergent fiber	70.7^{B}	70.6^{B}	62.4^{A}	64.4^{A}	60.0^{A}	0.97
Acid detergent fiber	58.4^{B}	61.2^{B}	47.9^{Aa}	48.9^{Aa}	55.2^{Ab}	1.16
Non-fiber carbohydrates	79.8^{Bc}	70.3^{A}	71.5^{A}	71.1^{A}	75.5^{Bd}	0.80
Digesta passage rates						
RRPR[¥], % h^{-1}	4.9^{b}	4.3^{a}	4.0^{a}	3.7^{a}	4.0^{a}	0.09
CCPR[¥], % h^{-1}	16.4^{b}	16.6^{b}	15.1^{b}	10.7^{a}	11.6^{a}	0.55
MRT[¥], h	47.6^{a}	48.2^{a}	55.9^{b}	63.9^{c}	63.3^{c}	1.57
LPR[¥], % h^{-1}	7.6^{a}	9.7^{b}	7.6^{a}	7.7^{a}	10.0^{b}	0.24

^{a,b,c,d,e}Means within row with different superscripts differ ($P < 0.05$).
^{A,B,C}Means within row with different superscripts differ ($P < 0.01$).
[1]Environmental conditions: TC = thermal comfort (65 temperature-humidity index), ETHI = elevated temperature-humidity index (82 temperature-humidity index).
[§]Trial 1 conducted under thermal comfort condition (65 temperature-humidity index), trial 2 carried out 10 d after ewes were placed under hot environment (82 temperature-humidity index), trial 3 carried out after ewes were under hot environment for 25 d and trial 4 carried out after ewes were under hot environment for 40 d, trial 5 carried out with animals replaced under thermal comfort conditions.
[¥] RRPR = solid reticulum-rumen passage rate; CCPR = solid caecum proximal colon passage rate; MRT = solid mean retention time; LPR = liquid passage rate.
*Standard error of the mean.

response to hot environments (McGuire et al., 1989). A direct effect of heat stress on changes in blood flow that may alter the supply of nutrients may be involved (Beede and Collier, 1986; West, 1999).

Nutrient Requirements and Feeding Strategies in Hot Environments

Several extensive reviews of nutritional management for ruminants – dairy cows in particular – in hot climates are available (Fuquay, 1981; Collier et al., 1982; National Research Council, 1984; Beede and Collier, 1986; Fox et al., 1988; Huber et al., 1994; Sanchez et al., 1994; West, 1994, 1999, 2003; Kadzere et al., 2002).

Attempts to maintain thermoneutrality and homeostasis during thermal stress may alter requirements for some nutrients and energy compared with normothermic animals. Therefore, nutrient requirements should be modified during hot weather and there are several key areas of nutritional and feeding managements that should be considered. Because there is a reduction in voluntary feed intake these areas include reformulation to account for reduced DMI, greater nutrient requirements during hot weather, heat increment of feeding, and avoidance of nutrient excesses. Different recommendations are needed to define feeding guidelines for heat-stressed animals. Here, carbohydrates, fats, proteins, minerals, vitamins, and water will be considered.

Carbohydrates

Efficiency of utilization of energy is reduced in heat-stressed subjects. This is due to higher maintenance requirements of thermal stressed animals resulting from elevated body metabolism and activity to alleviate excess heat load (National Research Council, 1981).

Heat production from cows producing 18.5 and 31.6 kg milk/day was 27.3 and 48.5% higher than non-lactating cows (Purwanto et al., 1990). Moreover, a cow weighing 700 kg and yielding 60 kg milk/day produces about 44,171 kcal of heat/day; the same cow produces 25,782 kcal of heat/day at the end of lactation (milk yield of 20 kg/day; Nardone et al., 2006). Moreover, heat production for a 600 kg cow yielding 40 kg of 4% fat milk amounted to 31.1% of consumed energy, which was second to fecal energy losses of 35.3% (Coppock, 1985).

Heat increment for fermentation is higher for fiber than concentrates (Webster, 1983) and heat production is more associated with metabolism of acetate than with propionate. Reynolds et al. (1991) reported an increase of heat production and less retained energy in cattle that were fed pellet diets of 75% alfalfa and 25% concentrate, compared with cattle that were fed diets containing 25% alfalfa and 75% concentrate. Therefore, the reduction of fiber intake by animals when exposed to hot weather is logical and rational. However, the heat increment is not only linked with fiber content of diet but also to the total intake (West et al., 1999) or type of fiber fed. In sheep, heat production in the gut was not greatly affected by diet composition but increased exponentially with increasing metabolizable energy intake (Webster et al., 1975). The authors concluded that 25 to 30% of the total heat increment resulted from intake and digestion. Reynolds et al. (1991) found heat production for low and high intake heifers (4.2 and 7.1 kg/day DMI) was 38.2 and 56.1 MJ/day, respectively. Adin et al. (2008) studied the effect of two diets differing in their roughage content. Control diet contained 18% roughage neutral detergent fiber (NDF; 30.8% total NDF content of the diet) while experimental diet contained 12% roughage NDF and used soy hulls as a partial wheat silage replacer (36.0% total NDF content of the diet). Although total NDF was higher in the experimental diet, heat production was not different and animals fed with the experimental diet had lower respiratory rates. Kurihara (1996) fed diets of Italian ryegrass or corn silage plus soybean meal to cows exposed to temperature conditions of 18, 26, or 32°C. Kurihara reported that ryegrass resulted in a greater heat increment and lower energy retention at higher temperatures. Therefore, both the amount of intake and characteristics of fiber must be considered in designing an effective nutritional and environmental management program. Due to the reduction in feed intake, energy intake is a limiting factor in hot weather, and usually a common approach is increasing energy density, reducing forage, and increasing concentrate content of the ration. The logic is that less fiber (and less forage) will encourage intake, while more concentrates increase the energy density of the diet. Moreover, low fiber and high fermentable carbohydrate diets may lower dietary heat increments compared with higher fiber diets.

Generally, cattle under warm environments selectively decrease the quantity of forage consumed relative to concentrates (McDowell, 1972; Bernabucci et al., 1999). The increase of concentrates in a hot diet is a common practice. Coppock (1985) reported that maximal benefit from concentrates appears to be approximately 60 to 65% of the diet and an excessive concentrate feeding may lead to acidosis and the associated production, health, and metabolic difficulties.

The greater high fiber diets may affect the performances of animals exposed to hot conditions. In a review paper, West (1999, 2003) reported that cows fed low fiber diets during hot weather had greater daily milk yield, lower body temperatures, and slower respiratory rates compared with those fed high fiber diets. Stahly and Cromwell (1986) studied the responses

of growing pigs to dietary fiber addition in a cold, warm, or hot thermal environment. These authors reported negative effects of dietary addition of alfalfa meal on gain-to-feed ratios, percent of carcass – lean-cut and belly – in pigs exposed to warm (22°C) or hot (35°C) environments. The conclusion was that the nutritional value of a low lignin, fibrous feedstuff (15% total dietary NDF or less) for growing pigs allowed to consume feed ad libitum was greater in animals housed in a moderately cold thermal environment than in a warm or hot environment.

The addition of fermentable carbohydrates has positive effects on DMI and milk energy produced per unit of feed energy. Probably, additional fermentable carbohydrates contribute to greater efficiency of energy use (West, 1999). In an early study, Tyrrell et al. (1979) found an increase of the infused acetic acid in nonlactating cows fed with diets containing 30% alfalfa plus concentrates compared with cows fed 100% alfalfa hay. Usually diets fed to ruminants in intensive livestock production systems contain forages and the carbohydrate furnished in mixed diets, such as those in practical total mixed rations, may improve the efficiency of energy use.

Data from the literature indicate that feeding diets with lower fiber and higher grain content are capable of reducing metabolic heat production and may contribute to lower heat load in the animal. Moreover, the low fiber, high grain diets seem to improve the efficiency of nutrient use, which may contribute to lower dietary heat increment. However, considering the effects of heat exposure on rumen and intestine health, low fiber, high grain diets must be carefully balanced with the need for adequate fiber to promote chewing and rumination to maintain ruminal pH and cow health. Some indication of the possible use of different quality of fiber (quality of forages, beet pulp, soy hulls, etc.) are reported but more research is needed to evaluate the effects on energy and heat increment using fiber (quantity and quality) versus high concentrate diets for hot weather.

Fats

One goal in formulating diets for animals exposed to hot environments is to increase nutrients (energy in this specific case) and to reduce heat generated by alimentary tract fermentation and tissue metabolism, thus reducing total body heat load. As previously discussed, this can be achieved partially by decreasing forage-to-concentrate ratios of diets and increasing grains.

The addition of fat to the diet of lactating dairy cows is a common practice. Under thermoneutral conditions, diets for cows supplemented with protected tallow showed 8 to 13.6% higher efficiency for use of metabolizable energy for lactation than those not receiving supplemental tallow (Kronfeld et al., 1980). The conversion of dietary fat to body fat is highly efficient when compared with the conversion of acetate to fatty acids (Baldwin et al., 1980). Moreover, feeding fat is associated with reduced metabolic heat production per unit of energy fed (Baldwin, et al., 1980) and compared to starch and fiber, fat has a much lower heat increment in the rumen (Van Soest, 1982). As such, it can provide energy without a negative thermal side effect. Therefore, feeding fat may improve efficiency and reduce heat increment and therefore may be beneficial during hot weather.

Results on the effects of fat supplementation under hot conditions are conflicting. Literature reports that feeding fat may be beneficial (O'Kelly, 1987; Skaar et al., 1989), ineffective (Bunting et al., 1992, 1996; Knapp and Grummer, 1991; White et al., 1992), or detrimental (Huber et al., 1994; Gaughan and Mader, 2009) for heat-stressed ruminants.

O'Kelly (1987) fed diets containing 9.2% fat during hot weather to both Brahman cross and British crossbred steers and reported lower body temperatures (0.3 to 0.4°C lower) compared

with steers fed diets containing 2.5% fat, which suggests less heat production in those steers. Other studies carried out on thermal-stressed laying hens (Reid, 1979), broilers (Dale and Fuller, 1980), and ruminants (Moody et al., 1967, 1971; Saunders et al., 1990) reported inconsistent results. Gaughan and Mader (2009) reported an increase of body temperature and respiration rate in finishing steers fed high-fat diets exposed to hot conditions.

Differences between studies carried out on ruminants are probably due to the fact that excess ruminally active fat in the diet may impair ruminal fermentation (Van Nevel and Demeyer, 1988). Only diets with 3 to 5% added fat have no toxic negative effects on ruminal microflora (Palmquist and Jenkins, 1980). However, ruminally protected fats allow the inclusion of a substantial quantity of fat in the diet, which could lower the heat increment significantly. Milk production and efficiency have been enhanced by feeding protected lipids (Kronfeld et al., 1980). Skaar et al. (1989) fed cows high levels of prilled fatty acids (5% of diet DM) and reported improvement of milk yield only for the warm season. In a study carried out in Georgia, cows that calved in fall or summer and were fed diets with or without added tallow to supply 1 kg/d fat had improved net-energy intake with added fat. Milk yield was unchanged and efficiency of net energy for lactation utilization was reduced by added fat (Nianogo et al., 1991). Knapp and Grummer (1991) offered diets containing 5% added fat (60% prilled fatty acids, 40% tallow) to cows held at thermoneutral (20.5°C, 38% relative humidity) or hot environmental conditions (31.8°C, 56% relative humidity) and reported a non-significant increase in milk yield (1.1 and 0.3 kg in the cool and hot environments, respectively), although fat-corrected milk increased by 2.7 and 1.8 kg/d. No diet × environment interaction occurred. Feeding diets containing 4.6% or 7.4% fat (from 3% added prilled fatty acids) and housing in shade or shade plus an evaporatively cooled environment did not improve milk or fat-corrected milk yields and had no effects on rectal temperatures (Chan et al., 1997), again indicating no apparent benefits from lower heat increment associated with fat feeding.

The literature for fat supplementation is inconclusive relative to the benefits of added fat during hot weather; however some considerations on fat can be made. Animal and vegetable fats, oils, and greases may reduce the palatability of the ration and/or interfere with microbial growth in the rumen. Therefore, fats should be used with extreme caution in rations for heat-stressed cows. The best option is feeding dietary fat (rumen inert/rumen bypass) that has been treated to allow the fat to escape the rumen intact, thereby not affecting rumen microbial growth to be digested in the small intestine.

Practical applications are to add fat, not exceeding 5 to 7% total fat in the diet. Fat levels beyond these should be supplied using a rumen inert fat. As a general guideline, no more than 30 to 40% of total dietary fat should come from whole oil seeds (a source of unsaturated oils), 40 to 45% from other basal ingredients, and 15 to 30% from ruminally inert fats. Another commonly used guideline is that 1/3 of dietary fat comes from fats contained in the feedstuffs, from oilseeds, and from ruminally inert fats. Additional research is needed to compare several levels and sources of added fat imposed over an extended period of time, implemented before the exposure to temperatures above the upper critical level. An example about the new approach to study the effects of fat supplementation in heat-stressed ruminants is the study from Moore et al. (2005). This study evaluated whether conjugated linoleic acid (CLA) induced milk fat depression (MFD) during heat stress would allow for increased milk and milk component synthesis. Dietary supplementation of conjugated linoleic acid (CLA) improved the calculated energy balance during heat stress, but this did not result in increased milk yield or other milk components. Inhibition of milk fat synthesis (e.g., extent, day of nadir, milk fat composition) by CLA was similar in Brown Swiss and Holstein cows. Brown Swiss cows converted feed to milk less efficiently and had higher milk fat cis-9, trans-11, and total CLA

content than Holstein cows, independent of treatment. The use of CLA may be beneficial in reducing negative energy balance of heat-stressed cows and improving nutritional value of milk.

Proteins

Studies on metabolism have clearly indicated that heat-stressed cattle were in negative nitrogen balance (Kamal and Johnson, 1970), basically due to the reduction of feed intake, which is usually observed under hot conditions (Ronchi et al., 1999; Shwartz et al., 2009; O'Brien et al., 2010). Thus, increasing protein content of the hot diets above requirements seems advantageous but some metabolic and nutritional views should be taken in consideration.

Considering the reduction of energy intake and increased energy maintenance requirements during heat stress, supplemental natural protein may be utilized as fuel to meet energy requirements of the animal. Increasing nitrogen intake in a situation in which energy is a limiting factor may lead to energy/protein imbalance, excess of non-protein nitrogen, and reduced efficiency and impairment of animal health. Finally, it should be considered that feeding excess protein is associated with an increase in energy cost. Tyrrell et al. (1970) reported that dietary nitrogen (N) above requirement reduces metabolizable energy by 7.2 kcal/g of N.

Danfaer et al. (1980) found a reduction in milk yield by over 1.4 kg when animals were fed 23% crude protein (CP) diets compared to diets containing 19% CP. The energy cost associated with synthesizing and excreting urea accounted for the reduced milk yield (Oldham, 1984). This is corroborated by the fact that the energy necessary to form urea from excess protein appears as heat production and decreases the proportion of net energy for lactation in metabolizable energy, and the energy lost in excreted urinary N from excess protein decreases the proportion of metabolizable energy in digestible energy (National Research Council, 1989). In this regard, Hassan and Roussel (1975) found a positive correlation between blood non-protein nitrogen levels and rectal temperature, suggesting reduced energy efficiency and greater heat production with excessive dietary N.

In an early study, Ames and Brink (1977) reported that rations properly matched to existing environments by reducing protein above that for maintenance in proportion to reduced rate of growth resulted in more constant values of protein efficiency ratio during thermal stress. Practically, the removal of supplemental protein on a daily or at least a seasonal basis should reduce its use as an energy source during thermal stress. Those authors concluded that "it seems logical that altering protein to match thermal environments would improve protein efficiency ratio of growing animals." Also, studies carried out in swine (Spencer et al., 2005; Silva et al., 2009) clearly indicate that under hot environments decreased CP content improves finishing pig average daily gain. Those authors concluded that negative effects of heat stress may be mitigated in finishing pigs by decreasing the crude protein level of the diets.

Other than the amount of proteins fed, quality of protein sources (solubility and/or degradability, and biological value) should be taken into account especially under heat-stress conditions. Studies investigating dietary protein content as well as composition suggest an interaction between protein availability and environment and indicate that dietary protein degradability may be particularly critical under heat-stress conditions.

Zook (1982) studied the effects of two different levels of protein solubility (40 and 20%) during thermoneutral and heat-stress conditions. Cows fed a less soluble protein diet had improved N balance and showed higher feed intake and milk yield than those that were fed

a highly soluble protein diet. White et al. (1992) reported positive effects of feeding fish meal on the daily gain of finishing steers and suggested its use to increase the proportion of high-quality ruminal escape proteins in the diet of heat-stressed finishing cattle. Lopez et al. (1994) improved feed efficiency and carcass leanness in gilts exposed to hot conditions increasing lysine content of diets. Also, dairy cows fed diets richer in lysine (241 g/d, 1% of DM) increased milk yield by 3 kg compared to those fed diets containing 137 g/d lysine (0.6% of DM; Huber et al., 1994). Diets with low (31.2% of CP) and high (39.2% of CP) ruminally undegradable protein fed during hot weather had no effect on DMI; however, milk yield increased by 2.4 kg/d and blood urea declined from 17.5 to 13.3 mg/100 mL for the diet containing higher undegradable protein (Belibasakis et al., 1995). Chen et al. (1993) reported that cows fed high-quality ruminal undegradable proteins (blood, fish, and soybean meals) yielded 3.8 and 2.4 kg more milk than those fed low-quality proteins (corn gluten meal). These authors suggest that the greater response to high-quality protein for cows in the cooled environment was because the amount of protein metabolized for energy was reduced and less energy was used in converting NH_3 to urea. Higginbotham et al. (1989) compared the effects of diets with high (18.4%) and low (16.1%) CP and high (57 to 60%) and medium (40%) protein degradability during hot weather. Milk yield and persistency was lowest for cows offered the high protein, high solubility diet, whereas blood urea N was highest for this group. Huber et al. (1994) suggested that when cows are subject to hot weather conditions ruminal degradable proteins should not exceed 61% of dietary CP, and total protein should not exceed recommendations by greater than 100 g N/d. One hundred grams N is equivalent to about 3.1% CP in the diet, assuming 20 kg DMI/d (West, 1999).

In summary, as DMI is progressively depressed due to heat stress, it is necessary to increase the protein level of the ration. However, this increase must be provided as rumen undegradable proteins or improving protein quality and essential amino acids (lysine in particular). Oversupply of rumen degraded intake protein leads to its inefficient use in the rumen, which, in turn, will require the animal to expend energy to convert this wasted protein (as nitrogen) to urea which is largely excreted in the urine and milk. Thus, in heat-stressed cows it is particularly important to not only meet the cows' requirements for protein but not to exceed them. There is still much to be learned about protein nutrition for heat-stressed cows. Additional evaluations of the efficiency of dietary protein utilization in meeting maintenance and production requirements are needed.

Minerals and Acid-Base Balance

The imbalance of minerals in animals exposed to hot conditions is expected, due to the decline in DMI. Other factors related to acclimation responses in animals regarding hot conditions (and not to the reduction of feed intake) are responsible for the alteration of mineral metabolism (Ronchi et al., 1999). Also, associated nutritional-physiological ramifications may affect macromineral needs (Beede et al., 1983; Schneider et al., 1986).

Electrolyte status is altered by the exposure of animals to hot weather (Collier et al., 1982; Shalit et al., 1991; Schneider et al., 1988). Shalit et al. (1991) found that water turnover and the output of Na, K, and Cl in milk and sweat increase markedly under hot conditions. Potassium (K) is the main cation in bovine sweat, and under hot exposure secretion of K through sweat increases (Mallonee et al., 1985). Increased sweating during hyperthermia is responsible for the increased loss of K (Johnson, 1970; Beede et al., 1983). Jenkinson and Mabon (1973) noted marked increases in the rates of loss of Na, Mg, Ca, and Cl, but not P, and the authors found

significant correlations between losses and sweating rates. Kume et al. (1987, 1989) reported a decline in the absorption of macrominerals, including Ca, P, and K, during hot temperatures and also reported that trace element requirements may increase with elevated environmental temperatures. Ronchi et al. (1995, 1997) found a reduction of calcemia and phosphoremia and acid/base imbalance in cattle exposed to hot conditions. A high ambient temperature has been shown to increase mineral excretion (Smith and Teeter, 1987) and decrease concentrations of iron, zinc, and chromium in serum and liver (Sahin et al., 2001) in broilers. Similarly, El-Husseiny and Creger (1981) reported that high environmental temperatures (32°C) had decreased rates of Ca, Fe, K, Mg, Na, and Zn retention in broilers. El-Nouty et al. (1980) reported relationships among thermal stress, plasma aldosterone concentrations and urine electrolyte excretion. With prolonged exposure to 35°C in climate-controlled rooms, plasma aldosterone concentrations of non-lactating Holstein cows were 40% lower than at 20°C. Heat stress caused the reduction of serum and urinary K concentrations. It was suggested that the fall in serum K may have been related to depressed aldosterone secretion, possibly reducing urinary K losses. As reported before, the reductions in serum and urine K concentrations may be related to increased losses of K during sweating.

Urinary Na excretion also increased under hot conditions. Therefore, under heat stress, cattle increase Na excretion while reducing K losses and the result is that Na and K may be limiting factors for performance under hot conditions.

Potassium, Na, and Cl are the cations and anions involved in the maintenance of acid-base chemistry. Decreases in K and Na and increases in Cl are observed in blood of animals exposed to hot conditions (Ronchi et al., 1995, 1997, 1999). Therefore, animals subjected to hot climatic conditions may experience acid-base disturbances resulting from respiratory alkalosis (due to panting; Schneider et al., 1984), with subsequent renal compensation by increasing urinary excretion of bicarbonate and Na, renal conservation of K (Collier et al., 1982), and increase of Cl retention (Escobosa et al., 1984; West et al., 1991; Ronchi et al., 1995). These responses are responsible for changes in the blood cation-anion balance (CAB = Na + K – Cl as described by West et al., 1992). Higher values of CAB means higher levels of Na and K and/or lower levels of Cl; therefore, CAB is reduced by hot exposure (Ronchi et al., 1995, 1997). Although respiratory alkalosis, which was indicated by elevated blood pH, suggested an excess of bicarbonate (HCO_3^-), the elevated pH actually was a result of a carbonic acid deficit created by CO_2 expiration via hyperventilation (Benjamin, 1981), and the increase of Cl is a response to counteract the decrease of HCO_3^- (Block, 1984; Schneider et al., 1988) in maintaining the acid/base balance.

Since electrolytes are a key element in acid-base chemistry their supplementation may be critical to homeostatic mechanisms during heat stress. In this regard, studies carried out on heat-stressed lactating cows (Mallonee et al., 1985; Schneider et al., 1984; West et al., 1987) reported positive effects of K supplementation above minimum recommendations (NRC, 1989) on milk yield. Moreover, Schneider et al. (1986) supplemented cows with 0.55% Na during hot climatic conditions and found greater feed intake and milk yield compared with cows that received 0.18% Na. Silanikove et al. (1998) found higher DMI, milk, protein, fat, and lactose yields in cows receiving a ration with increased amounts of Na, K, and Cl, compared with cows that consumed the same ration with a lower concentration of these ions. Escobosa et al. (1984) found that providing diets that were high in Na and K and normal in Cl resulted in greater DMI and milk yield, compared with diets high in Cl and normal in Na and K. Others have reported similar results, with greater DMI and milk yield from higher cation-anion balance (alkaline) diets (West et al., 1991).

Increasing K and Na intake is useful in maintaining higher levels of K and Na in the blood. This condition may increase the values of CAB due to the reduction of blood Cl. The levels of Cl in the blood were found to be negatively related with DMI ($r = -0.36$; $P < 0.05$) in lactating dairy cows exposed to hot conditions (Ronchi et al., 1997). In a study carried out on Holstein heifers (Ronchi et al., 1995), the levels of CAB were negatively related to rectal temperature ($r = -0.40$ / -0.52; $P < 0.01$) and positively with DMI ($r = 0.33$; $P < 0.05$) in subjects exposed to hot conditions.

Some authors (Beighle et al., 1988; Freeden et al., 1988) associated changes in electrolytes balance to some alteration of calcium and phosphorous metabolism. Positive relationships between CAB and Ca and CAB and inorganic P ($r = 0.44$; $P < 0.01$ and $r = 0.49$; $P < 0.01$, respectively) have been reported in subjects exposed to hot conditions (Ronchi et al. 1995), confirming that alteration of CAB may be linked to changes in Ca and P under hot conditions.

West et al. (1992) in a study designed to compare efficacy of increasing cation-anion difference using either K or Na to increase cation content of the diet, reported a linear increase of DMI with increasing cation content. During heat stress conditions DMI was improved as dietary cation-anion difference (DCAD) was increased from 120 to 464 mEq Na + K − Cl/100 g feed DM (West et al., 1992). West et al. reported that the improved intake or milk yield were observed when more alkaline diets were fed to lactating cows, and this may result from improved blood buffering or correction of mineral deficiencies. Perhaps acid-base chemistry for the cow is optimized by providing the correct balance or ratio of electrolytes. Sanchez et al. (1994) studied the cation-anion difference approach to electrolyte formulation through empirical modeling of numerous macromineral research studies from several locations. Dietary K and Na at levels above recommendations correlated with an increase of DMI, whereas increasing dietary Cl depressed DMI, especially during hot weather. West et al. (1991) found that feed intake was improved by 5.5 and 5.2 kg/d in cool and hot weather when the cation-anion difference was increased in the range of −79 to 324 mEq/kg of feed DM.

The need for alkaline diets is consistent with addition of buffers to the diet, since the ideal means to increase DCAB for lactating cows is with Na or K in association with a metabolizable ion such as bicarbonate. The diet cannot be made more alkaline by the use of sodium (NaCl) or potassium (KCl) chloride. Use of dietary buffers is a common practice, especially during hot weather, and DCAB may provide further justification for the use of buffers during hot weather. Work with potassium carbonate as a source of supplemental K and dietary buffering showed positive results during heat stress (West et al., 1987).

Additional research is needed to more closely define the desired DCAD and resolve the issue of K versus Na supplementation. Nutritional modifications accounting for changing nutrient requirements are necessary to adjust for the impact of heat stress due to reduced DMI and altered nutrient requirements. The use of buffer and Na and K sources are also beneficial in helping rumen to lowering pH.

Vitamins

Stress (including heat stress) increases vitamin mobilization from tissues and their excretion (Siegel 1995), and thus may exacerbate a marginal vitamin deficiency or an increased vitamin requirement. The topic of heat stress and vitamin requirements has been addressed briefly in regards to niacin use (NRC, 1989), and regarding vitamin A for poultry (NRC, 1981).

Considering studies in poultry, it has been reported that some vitamins such as vitamin E (Vit-E; Sahin et al., 2001; Bollengier-Lee et al., 1999), vitamin C (Vit-C; Sahin and Kucuk. 2001; Farooqi et al., 2005), and a combination of Vit-E and vitamin A (Vit-A; Sahin et al., 2002) can be supplemented to reduce the negative effects of hot environments. Heat stress generally increases the production of free radicals, leading to oxidative stress (Bernabucci et al., 2002; Pamok et al., 2009; Azad et al., 2010). Vit-E and Vit-C supplementation may mitigate the negative effects of heat stress by reducing oxidative stress.

Aréchiga et al. (1998) reported that timed artificial insemination in combination with β-carotene supplementation improved pregnancy rates during periods of heat stress in dairy cows. Supplementation with selenium and Vit-E was found by Aréchiga et al. (1998) to have a beneficial effect on fertility in cows in hot environments. In contrast, Ealy et al. (1994) reported that cooling improved pregnancy rates slightly in heat-stressed cows, but supplementation with Vit-E had no evident positive effect on pregnancy rates.

Cattle supplemented with niacin (6 g/d) during summer months increased milk yield by 0.9 kg/d compared with controls (Muller et al., 1986). Those authors speculated that niacin improved milk yield by affecting lipid and energy metabolism, by stimulating protein synthesis by ruminal microorganisms, or by causing other effects on ruminal microorganisms. Di Costanzo et al. (1997) reported that supplementation with niacin (12, 24, or 36 g/cow·d^{-1}) resulted in a reduction of skin temperatures of about 0.3°C, but rectal temperature and milk yield were unchanged.

In practical terms, it appears that adjustments in vitamin content to account for reduced DMI are justified. Further research for improving knowledge concerning the effects of high ambient temperature, and subsequent heat stress, on the requirement and metabolism of specific vitamins is needed.

Water Use and Metabolism

Water is undoubtedly the most important nutrient for animals subjected to heat stress. Increased water loss via skin and respiratory evaporation (sweating and panting, respectively) in an attempt to dissipate heat can disturb body water levels, particularly within vascular and extracellular compartments. The altered-heat induced changes in circulating water interfere with the animal's ability to maintain proper osmotic balance and blood pressure. In fact, Silanikove (1994) reported that increased body fluid loss due to sweating and panting in heat-stressed ruminants can increase the risk of cardiovascular dysfunction and inability to maintain euthermia.

Heat-stressed, high-producing dairy cows may have problems maintaining a steady plasma volume. However, in a controlled environment study, Nardone et al. (1992) reported a positive correlation ($r = 0.62$; $P < 0.01$) between water intake and rectal temperature in heat-stressed lactating cows. In addition, Silanikove (1992) reported that heat stress influences water metabolism by increasing plasma and extracellular fluid volume in proportion to the thermoregulatory requirement of the cow. Kadzere et al. (2002) suggested that either the increased efficiency of water transfer through the biological membranes (by about 50%) and/or increased plasma volume provides a thermoregulatory advantage. Detailed discussion on water metabolism and heat stress has been reviewed (Silanikove, 1989, 1994).

Increased water consumption is a sudden and major response to thermal stress. Consumed water exerts effects on animal comfort by directly cooling the reticulo-rumen (Bianca, 1964)

and by serving as the primary vehicle for heat transfer and dissipation through sweating and panting (Beede and Collier, 1986).

In dairy cows, there are two types of sweating that occur: Both are appreciably involved in heat dissipation (Beede and Collier, 1986). The first type is insensible sweating or perspiration that leaves the body at all times, unless the relative humidity is 100%. Another type, thermal sweating, occurs as the principle evaporative cooling mechanism of the cow when ambient temperatures rise. The heat required to convert water into vapor is referred to as the latent heat of vaporization. The vaporization of 1 ml of water requires 2.43 Joules and this is the amount of heat lost when 1 ml of sweat evaporates from the skin. Berman et al. (1985) reported that the maximal rate of water evaporation in lactating cows was 1.5 kg/h, which translates to 4.3 kJ/day. This rate of heat loss is close to the heat production of a dry, non-pregnant 600-kg cow but only about half that produced by a cow producing 30 kg of milk a day.

Numerous factors, such as levels of feed intake and physical form of diet, physiological state, species and breed of animal, and quality, accessibility, and temperature of water, may influence intake during thermal stress (National Research Council, 1981). Under field conditions, water intake seems to increase rather rapidly above 27°C ambient temperature (National Research Council, 1981).

Water requirements have not been extensively investigated probably because water is usually supplied in abundance. Water requirements of livestock are supplied from 1) metabolic water, derived from tissue oxidation of organic substrates; 2) water contained in ingested feeds; and 3) drinking water (Beede and Collier, 1986). The latter is most significant quantitatively in meeting needs of thermal-stressed animals. Water in feed is highly variable depending upon season, rainfall, and feeding management system.

As is well known, water intake is closely related to DMI and milk yield (West, 2003), but minimum temperature is the second variable to enter a stepwise regression equation (after DMI), indicating the influence that ambient temperature has on water consumption (Murphy et al., 1983). Water consumption increased from 35.6 L/d at 24 days prepartum to 65.2 L/day at 42 days postpartum as DMI increased from 9.6 to 16.2 kg/day and milk production increased to 25.7 kg/day (Woodford et al., 1984).

Many studies show significant positive correlations between water intake and ambient temperature (National Research Council, 1989). Water intake increased by 1.2 kg/°C in minimum ambient temperature, but regardless of rate of increase it is obvious that abundant water must be available at all times under hot conditions. In climate-controlled chambers water intake of lactating cows increased 29% at the warmer temperature, fecal water loss declined 33%, but loss of water via urine, skin surface, and respiratory evaporation increased 15, 59, and 50%, respectively (McDowell, 1972). Holstein heifers exposed to hot environment increased intake of drinking water by 60% (Ronchi et al., 1995). Cows acclimated to 21.1°C and then exposed to 32.2°C for 2 weeks increased water consumption by 110% and water losses from the respiratory tract and from the skin surface increased by 55% and 177% at the higher temperature (McDowell and Weldy, 1960). Such changes increase the volume of water needed. The rate of water use by heat-stressed Holstein heifers was 2.84-fold higher (0.56 vs. 0.20 l/kg$^{0.75}$ body weight) than heat-stressed Sardinian female lambs (Bernabucci et al., 1999, 2009). This indicates higher susceptibility of cattle to heat stress compared with other ruminants.

Quality and temperature of water may affect consumption. Water added with a complex salt mixture (4,100 mg/L of total dissolved salts) increased water consumption compared with fresh water (450 mg/L total dissolved salts), but persistency of milk yield was reduced by 25 and 27% in winter and summer, respectively, by the high salt water intake (Wegner and Schuh, 1988). In Kuwait, brackish well water, which contained 3,574 mg/L of total dissolved

solids, had little effect on water consumption when fed under hot arid conditions and resulted in a slower rate of decline in milk yield during the course of the experiment when compared with fresh water (Bahman et al., 1993). Greater water content in the rumen tends to accelerate ruminal turnover (Silanikove, 1992), which may be beneficial to cows during hot weather because the rate of passage of digesta is slower and may contribute to gut fill.

As reported before, consumed water has a direct cooling effect via the reticulo-rumen (Bianca, 1964). Cows offered drinking water at 10°C or 28 to 30.2°C consumed more DM (Baker et al., 1988; Milam et al., 1986) and yielded more milk in the cool water treatment (Milam et al., 1986). Anderson (1985) observed the highest water intake and milk production from dairy cows when 17°C water was offered. Ittner et al. (1951) in the Imperial Valley of California reported that beef cattle increased weight gain when given 18.3°C drinking water compared with 31.2°C water in summer. Cows offered chilled drinking water generally consumed less of the chilled water, but the amount of heat absorbed by the chilled water was still significantly greater than for the warm water treatment. This is confirmed by Lanham et al. (1986) who reported reduced respiratory rate in cows drinking chilled water. Economic benefit for the practice must be considered, but the benefits of the consumption of large quantities of cool water on the comfort of the cow and ultimately DMI and milk yield is apparent and should be considered when devising a water supply system for the dairy herd. A key husbandry practice in warm climates is to provide an abundant clean source of drinking water in reasonable proximity to the feeding area and shade.

Summary and Conclusion

Hot temperatures are a fact of life for livestock. If extreme temperatures overwhelm the ability to prevent heat stress, then the ration can be reformulated to help the cows maintain performance in spite of reduced DMI. However, reformulation requirements to deal with depressions in DMI of 10% or more are extreme, and may introduce other problems unless overall dairy management is high. Concomitantly with reduced DMI, increased maintenance costs during hot weather are responsible for decreasing energy balance and increasing energy deficit in the heat-stressed animals. The reduced DMI and increased maintenance costs are due to elevated body temperatures. Therefore, protection from the ambient environment is the first step toward maintaining DMI and performance during hot weather. Heat stress is responsible, directly and indirectly, for the impairment of rumen and intestine health and functionality, which contribute to the reduction of feed efficiency utilization.

The goal is to adjust rations to increase energy, protein, and nutrient intake while contemporarily maintaining animal health (rumen in particular) when animals are exposed to heat-stress conditions. The usual temptation is to increase the quantity of grain fed and decrease the quantity of forage in the ration because the efficiency of use for metabolizable energy is higher and endogenous heat production is lower when high fermentable carbohydrate diets are given during hot weather. This shift will frequently induce rumen acidosis and impair cow health. Metabolic heat increments may be reduced by adding fat, but results from research on fat-feeding during hot conditions are variable, mainly due to different amounts and types of fats fed. Rumen protected/inert fats may allow an increased addition of relatively high levels of fat in the diet. Interactive effects of dietary LCFA with nutrients other than fiber have received little attention; experiments to elucidate the effects of feeding these diets during hot weather should be conducted.

Some nutrients are required at higher levels during heat stress (K and Na, vitamins A, E, and C, and microelements such as Se and Zn). Although, supplementation of Na and K is fully studied and results in improved production and health, the research investigating the effects and requirements of vitamins and microelements during hot weather is scarce.

Of course, water quality, temperature, and availability are a must for animals when exposed to hot conditions. Water should be available in holding pens, travel alleys, and near feed bunks, and it has to be clean.

Some ration adjustments should be considered. Fiber is important for rumen health. Use of high quality forages (high digestible fiber) and some non-fiber byproduct feeds (soy hulls, beet pulp, or citrus pulp) may guarantee adequate content of digestible fiber, improve content of fermentable sugars, improve salivation (higher rumen pH), and enhance production of rumen VFA. Consider adding some additional fat to the ration. Total ration fat levels should not exceed 5.5% of total ration dry matter, and rumen protected/inert fats should be used while balancing ration protein levels to minimize high levels of soluble and rumen degradable protein. The animal must expend energy to excrete excess protein from the body. Increase protein content when feeding ruminally undegradable protein and rumen protected essential amino acids. Consider adding buffers (sodium bicarbonate, magnesium oxide, and sodium sesquicarbonate) to help in maintaining a normal rumen environment and increase Na supplementation. Increase potassium levels in the diet to counteract the higher potassium losses in heat-stressed cows. Ration magnesium levels may also need to be increased.

Feeding management practices also offer opportunities in trying to minimize the effects of heat stress. For example, high-quality, fresh, and palatable feed should be in the feed bunk at all times to provide maximum opportunity for feed consumption. Fresh feeds stimulate frequent feeding. Making the feeding area as comfortable as possible through shading and (or) cooling should enhance feeding frequency and total intake. It may be useful to shift feeding times to match cow behavior. Cows tend to change meal patterns and eat more feed during the cooler times during the day. To maximize water intake, water must be clean and fresh; there should be at least 5 to 7 cm of water space per cow and water has to be available, since water intake increases by 20 to 50% during heat-stress conditions.

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Chapter 8

Effects of Environment on Animal Health: Mechanisms and Regulatory Inputs

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Introduction

In our present society, there are not many words with more context-dependent frames of reference than environment and health. In this regard, without some form of a structured framework, the answer to the question of how the environment might impact animal health rapidly could become so diffuse that it would be more confusing to the topic than explanatory. How cells respond to stress is like the classic children's stick puzzle – move one piece and all the other sticks in the entire stack change position to accommodate the new relationship among the pieces. Some sticks move more than others. Some simple reconfigurations are readily evident and others are more obtuse. Remove a critical stick or add one in the wrong place and the symmetry and integrity of the stack disintegrates.

As with the sticks, the cause and effect relationships through which the environment interacts and shapes aspects of animal health are not necessarily straightforward. First, the intracellular matrix, that is everything from ionic composition to ATP abundance, changes during the response to a given stress. Like the stick puzzle, each cellular change impacts the function of another process. Where the new formation commands a use of cellular resources of processes for an unscheduled use, again the intracellular processes are restructured. This gets complicated for the cell when stress conditions prevent the generation of ATP, causing the cell to perform its functions with limited resources. Second, additional complexity in both the understanding as well as in the testing of how environment and health interact resides mainly in the basic patterns of responses common across many forms of so-called stress. For example, a two-stage response is a common theme for both environmental as well as immune stress – an initial assessment/survival response followed by an adaptation response. Perhaps more importantly though, when response pathway elements common to each stress pathway exist (e.g., NF-κB, BCL-2, heat shock proteins, oxidation-reduction potential, nitric oxide and superoxide

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anion generation, protease activity, apoptosis), the impact of one stress on a given pathway element can serve as a conditioning factor (termed preconditioning) for the response to another stress. Examples of experimental cross-stress preconditioning include: (a) mild hyperthermic preconditioning protection against subsequent hypoxia/reperfusion injury to the heart (Yamashita et al., 1998); (b) subacute endotoxemia protection against free radical damage in the pancreas prior to hypoxia/reperfusion injury (Obermaier et al., 2005); (c) mild preconditioning heat-stress protection against proinflammatory peroxynitrite reactions in macrophages (Szabo et al., 1996); and (d) heat preconditioning stabilized enterocyte mitochondria in animals that had undergone surgical manipulation of the intestine (Thomas et al., 2002).

In reviewing the available literature, it becomes evident that numerous authors have addressed the impact of the environment on animal health with the majority of these associated with very specific environmental factors acting on particular aspects of health. This database is so extensive that a discussion of this, topic by topic, would warrant an entire book, let alone a single chapter. However, one sizable gap in the information stream exists in the assessment of how environmental impact on animal health is sensed or detected at the cellular level. This information can serve to define critical control points in pathways that might be exploited toward the development of intervention and management strategies to improve animal health.

With regard to this review of environment × health interaction, three areas of primary focus will be addressed. First, it is necessary to remove the constraints of compartmentalism, where the mechanisms through which individual stresses affect animal health are looked at as individual entities. Where environment is concerned, we will use examples from commonly encountered factors like heat, cold, anoxia, or toxicants and demonstrate that what is called the cell stress response (Vigh et al., 2007) to these factors which occurs biochemically through a set of pathway response mediators shared across all of these environmental stress factors. As such, the multiplicity of signals that impact NF-κB/Iκ-B (Yamamoto and Takeda, 2008; Nizet and Johnson, 2009; Marcu et al., 2010) will be a recurring theme here. Therefore, if a mechanistic pathway process is presented for a heat stress, it most likely shares response pathways elicited from hypoxia/reoxygenation with the two differing only in sensitivity and magnitude and targeted location of sensing (like the plasma membrane, endoplasmic reticulum (ER), or mitochondria). Second, relevant information will be presented for the environment × health interactions that affect the neonate, given that the initial time after birth is so homeostatically confused, and collectively, so many environmental factors impact this critical time. Just from the processes of parturition and birth, even slight environmental perturbations open the door to increased morbidity and mortality, as this is a delicate time (Elsasser, et al., 2006). Finally, this concept of proinflammatory response as a measure of health status will be expanded to apply not only to overt pathological situations, but also to many physiological processes otherwise thought of as normal (like birth and parturition), along with being actually definable as a proinflammatory state based on the generation of proinflammatory mediators (immune cytokines, prostaglandins, prostacyclines, thromboxanes, oxygen and nitrogen free radicals, and reactants).

Understanding the Temporal Determinates of Stress Responses

Critical control points that regulate physiological processes also become the targets for the myriad factors that mediate environmental and proinflammatory stress. Within proscribed

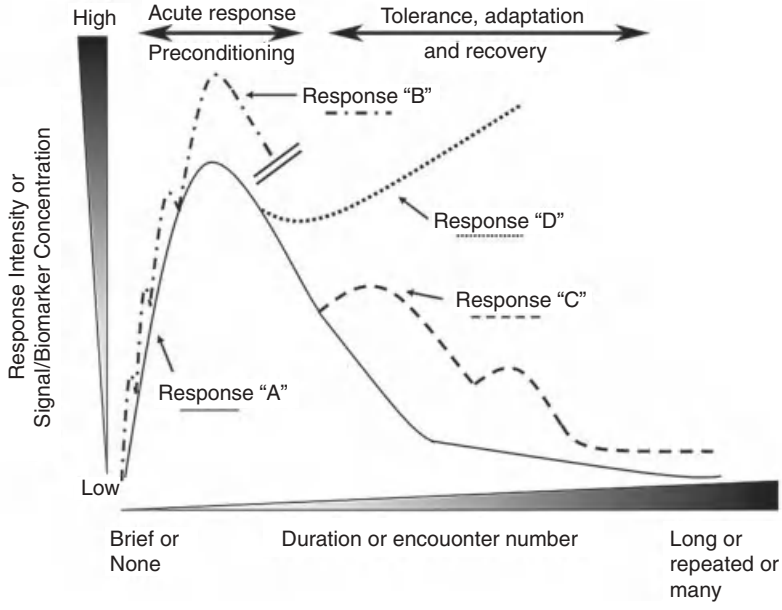

Figure 8.1. The line between physiological and pathological response is determined by the magnitude of one or more perturbations converging on critical control points in the proinflammatory cascade shared across diverse causes. The duration of the environmental or immune challenge further shapes the normal pattern of response and recovery by directing an acute response through a programmed series of biochemical accommodations leading to adaptation and tolerance. Each point labeled "A," "B," "C," or "D" represent a distinct aspect of the biphasic pattern of response, detailed in the body of the text, with response "D" constituting the most severe breakpoint in the stress response, unrecoverable cell damage and cell death.

timelines and levels of severity, environmental influences can further modulate pathophysiological responses to create situations that constitute disease for the affected animal when the physiological boundary between appropriate and aberrant is breached.

A generalized theme for cell response to single or multiple stressors is depicted in Figure 8.1. The vertical axis represents the intensity of a cell's response to particular stressor stimuli. Experimentally, we might quantify this in terms of an increased concentration of some chosen biomarkers relevant to the nature of the perturbation. Examples of this might be concentrations of superoxide anion, inflammatory cytokines and acute phase/heat shock proteins, or membrane resistance/ conductance, protein phosphorylation, DNA fragmentation, and so on. The horizontal axis represents the duration of a stress encounter, or the number of repeated encounters of the same stress or the number of combined stresses in a matrix of time and number. Examples of this might be a focused single experimental challenge with the Gram-negative bacterial membrane endotoxin (LPS), or repeated challenges with LPS, or a heat stress accompanying an LPS challenge. Across the top one sees that the 2-component response can be divided into an acute response that can also serve as a conditioning phase for shaping the character of the continued response and a secondary phase most typically, though not always, observed as a recovery phase. The response curve designated as "A" represents

a typical biomarker response to a single time-stress challenge – an acute increase followed by a decrease in the change in biomarker response. The decrease can occur as a result of the termination of the stimulus or the elimination of the stimulus via metabolism of the stressor or its mediators. However, sometimes the decrease in the response occurs as a result of a programmed down-regulation of response in spite of the stimulus still being present. These responses are termed tolerance responses or down-regulated responses and are typical of many stressor encounters. They have evolved to insure that cells don't harm themselves in the process of generating their highly chemically active reactants like tumor necrosis factor (TNF)-α, nitric oxide (NO), superoxide anion ($O_2^{-}\bullet$), or hydrogen peroxide (H_2O_2) and other lipid peroxides. Endotoxin generates this tolerance response wherein with even a continuous infusion of LPS, the initiating cytokine responses (TNF-α and interleukins −1 and −2) peak between two and four hours after the initiation of the infusion and subside over the course of the next four to five hours (Foley et al., 1993; Gerros et al., 1995). Importantly, tolerance to one mediator can also carryover between other mediators even when the stresses seem unrelated, a state termed cross-tolerance. This is evidenced when LPS challenge facilitates not only tolerance to additional exposure to LPS but also to further challenge with TNF-α; challenge with TNF-α confers tolerance against LPS (Ferlito et al., 2001; Fitting et al., 2004). In fact, additional data have broadened some aspects of this cross tolerance phenomenon to suggest that the tolerance, as defined by the relative decrease in functionality associated with a challenge subsequent to an initiating challenge, can develop at different points in the critical control pathway (Fitting et al., 2001). More recently, properties of cross tolerance have also been demonstrated between endotoxin and multiple toll-like receptors, the cellular determinants of pathogen challenge and responsiveness (deVos, et al., 2009). Multiple layers of interacting tolerance is nature's way of establishing a system of checks and balances to limit collateral damage to cells that are impacted by multiple acute stimuli that would otherwise be additive during the acute response period. As will be demonstrated later in this chapter, environmental challenges such as heat stress and anoxia also have cross-tolerance impacts on the innate immune proinflammatory response cascade and vice versa (Sanlorenzo et al., 2004).

The section of the curve labeled as "B" is typical of how cells respond to more than one challenge stimulus, wherein some elements common to each stimulus pathway are jointly activated in a similar time frame. A simple example of this augmentation of proinflammatory response is observed where co-treatment with myramyldipeptide, a mediator of Gram-positive toll-like receptor (TLR)-2 action, increases the proinflammatory cytokine response to endotoxin, the active proinflammatory constituent of Gram-negative-TLR-4 pathogen response (Takada et al., 2002). Thus under the proscribed time frame, the capacity for a stress, environmental or immune, to activate a particular arm or element of a signal transduction pathway (elements like NF-κB, JAK-2, STAT5, AKT, and MAP-kinase) can result in concentration changes or activity states (for example phosphorylation or dephosphorylation) that become additive, exceeding the generation capacity of either stimulus alone and increasing the magnitude (and in many cases the severity) of the adverse cellular response (Poderoso, 2009). It is this capacity, which shares common activation elements in the cell response to stress, that dissolves the differences between the various stimuli and links and defines their interactions. Interestingly, the cellular expression of these links is highly conserved across evolutionary channels present in bacteria, eukaryotic cells, and to some extent also plant cells (Kirkwood et al., 2000; Ottavaini and Franceschi, 1998; Sharma et al., 2009).

The biochemical events occurring during the timeframe reflecting curves "A" and "B" for the most part suspend otherwise normal metabolic processes of the affected cells (protein synthesis, cell division, etc.). The degree to which the impact manifests itself is proportional

to the sensed perturbation (Elsasser et al., 2000, 2008). The cell's normal response is to initiate a complex sequence of protection mechanisms wherein new patterns of protein synthesis (acute phase proteins, heat shock proteins) and enzymatic capacity (lipid desaturases, kinases, phosphatases) are called upon to stabilize the internal environment of the cell (Elsasser et al., 2000). Remembering the earlier point made regarding the two stages of response to a stress, especially in terms of infection on top of environmental stress, evolutionarily conserved innate immune responses are geared toward the elimination of the threat, as in the case of infection with a bacteria or virus, etc. Eliminating the agent often calls for the generation of an intracellular environment potentially deleterious to both the invading organism and the host, at least for a short duration. This is typically what is observed in monocytes activated by pathogens to generate the superoxide and NO burst (Xia and Zweier,1997; Vazquez-Torres et al., 2000). Toxicity is moderated and attenuated by the rapidity of NO diffusion, its brief reactive half-life, and short physical distance of diffusion before degradation (Thomas et al., 2001).

It appears that when the stimuli of multiple stresses converge on a signaling element common to the response pathway of each factor, the summated responses generate reactive compounds that can be interpreted as a pathological response within the affected cell. In essence this occurs because a localized concentration or spatial proximity of intracellular reactants [for example $O_2^{-}\bullet$, H_2O_2, or the highly reactive nitrating compound peroxynitrite ($ONOO^-$) generated by each stimulus exceeds the capacity of the cell to eliminate the impending insult. Why this occurs in cells at all is a topic well beyond the scope of this review. However, the process is effective though sometimes costly to the host. The essence of the conflict is elegantly reflected in a quote from Lewis Thomas, M.D., noted pathologist and scientific philosopher (Thomas, 1971):

> The microorganisms that seem to have it in for us in the worst way – the ones that really appear to wish us ill – turn out on close examination to be rather more like bystanders, strays, strangers in from the cold. They will invade and replicate if given the chance, and some of them will get into our deepest tissues and set forth in the blood, but it is our response to their presence that makes the disease. Our arsenals for fighting off bacteria are so powerful, and involve so many different defense mechanisms, that we are in more danger from them than from the invaders. We live in the midst of explosive devices; we are mined.

The section labeled "C" is typical of the patterned host response where the major insult has been dealt with and the process of recovery and adaptation takes place. This is the temporal location where issues of cross tolerance and the impact of preconditioning are evident.

Section "D" of the cell response represents the summation of events that culminate in catastrophic failure to compensate for and eliminate the impinging stress threat. In this instance, the cell is basically overwhelmed by a matrix of reactive molecules that largely short-circuit the needed intracellular membrane compartmentalization of function with irreversible impacts on membrane potential, ATP generation, ionic balance, and red-ox processes. A further specialized case exists where some animals have also lost the capacity to generate the second phase of the response (tolerance and adaptation, where the continued acute response further overwhelms the cell's capacity to eliminate self-generated cytotoxic reactants; Elsasser et al., 2005). In this scenario, Angus × Hereford steers received two separate challenges with a low dose of *E. coli* (055:B5 LPS four days apart). Retrospective evaluation of the TNF-α response indicated that the responses could be stratified into two phenotypes: one that exhibited lower TNF-α concentrations following the second challenge (tolerance) and another wherein the

TNF-α response to the second challenge was higher than the response to the first (hyper-responder). Six months later, these challenges were repeated at a higher LPS dose. The same TNF-α profiles (along with higher concentrations of TNF-α) were evident in the same animals with the added observations that time to recover was longer in the hyper-responder steers, and feed intake and weight loss were significantly different in the hyper-responders compared to the tolerant animals (Elsasser et al., 2005). More recently, this hyper-responder phenotype was correlated with SNPs in the promoter region of the TNF-α gene with the G-C-rich regions of the SNP correlated to NF-κB/Crel DNA regulatory regions (Kahl et al., 2009). A critical feature of this NF-κB association resides in the fact that this regulatory region of the TNF-α promoter is known to modulate the tolerance response to repeated exposure to Gram-negative bacterial toxins (Nagar et al., 2010).

The rest of this chapter will outline salient aspects of a landscape of factors that influence animal health in a manner wherein evolutionarily conserved mechanisms of survival function (or sometimes compete!) in concert with newly evolved mechanisms of response. Specifically, this chapter will focus on the cellular response to the environmental challenges of temperature, oxygen content, and red-ox characteristics as they influence cellular well-being in conjunction with how these factors shape cell responses to the activation of the proinflammatory axis.

A Proposed Model of Environment-Health Interactions

Three general principles can be defined that establish a model that organizes the impacts of the environment on the animal proinflammatory axis (see Fig. 8.2). As will become evident, the activation of the proinflammatory axis is not simply the innate immune response to pathogen invasion, but rather it is the coordinated and highly evolutionarily conserved processes that activate what is called the "cell stress response."

Within this model, it is important to recognize that, where animal cells exist today, their integrated response to all of the signals that impinge on them at a given time is the culmination of evolved specialization that often conflicts with conserved and preserved evolutionarily ancient mechanisms of sensing the environment (Lindahl, 2009). Responses range from physical change in membranes to the generation and release of highly reactive compounds like free radicals, compounds that both communicate information at the most basic level and serve as noxious deterrents to competing organisms (Blackstone, 2000; Shpakov and Pertseva, 2008). The best example of this is derived from the mitochondria. Mitochondria appear to be evolved from ancient microorganisms that took up a symbiotic residence inside other cells providing an energy source for the cell, which in turn gave the mitochondria a protected environment (Davidov and Jurkevitch, 2009). Under homeostatic balance, mitochondrial generation, and release of NO, H_2O_2, $O_2^{-}\bullet$ (1 to 2% of mitochondrial electrons do not transfer down the electron transport chain to ATP resulting in the generation of $O_2^{-}\bullet$; Nijtmans et al., 2004), serve to communicate regulatory information back to the cell largely for protection against further damage (Costa et al., 2008). The downside of the relationship is that when cells are affected by stress (heat stress, pathogen challenge, etc.), the mitochondria feel the heat and respond with additional levels of aberrant electron transport chain dysfunction and increased generation of NO, $O_2^{-}\bullet$, H_2O_2 and a calcium/proton flux that triggers myriad adverse impacts on the cell, ranging from post-translational modification of proteins to DNA fragmentation and apoptosis (Kadenbach et al., 2004).

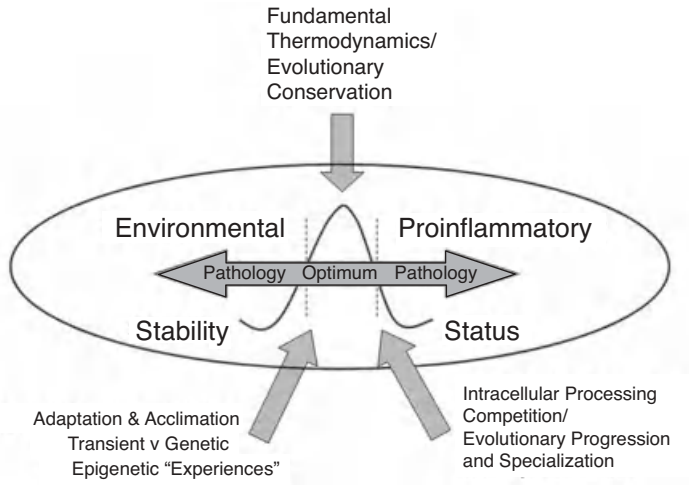

Figure 8.2. Biochemical reactions that define cellular wellbeing and overall good animal health have evolved to function within limits of optimum conditions as defined by, but not limited to, temperature, pH, osmolarity, redox state, and energy status. These generally are typified by biphasic activity or response curves with the "normal" state, for the most part, constituting the optimum and pathology creeping in at the extremes. Cellular "health" is maintained through the interaction of coupled stimulus – response processes based on the thermodynamics of the interacting factors, the acquired adaptation to prolonged stimuli, and the capacity of resources to be partitioned to survival mechanisms in preference to otherwise genetic propensities (to grow, to divide, to synthesize, etc.). The "bell shaped" nature of responses also carries with it an age component where the mechanisms that confer homeostatic balance to sound health are immature and compromised in the young neonate, mature to top functionality across the ages associated with reproductive capacity and nurturing, and fall off again in the ageing animal. For this reason the very young and the very old suffer the consequences of the aggregate of stresses.

Some Aspects of Thermodynamics and the Biology of Adaptation

The thermodynamic underpinnings of all physiological processes have evolved to function biochemically within a relatively narrow ideal range of conditions. From the standpoint of receptor-ligand interactions (described with the same mathematics as used for enzyme kinetics), substrate and cofactor concentrations, or membrane-based compartmentalization, these conditions dictate the three-dimensional spatial orientation of proteins and lipids and therefore their interactions. Biochemically speaking, the rate at which biological processes proceed is regulated by the capacity for subcomponents to interact within a membrane structure. Furthermore, entropy effects associated with mobility and orientation govern these interactions (Vats et al., 2010). These are physically defined by such factors as temperature, pH, and ionic character interacting with the physical characteristics of amino acids (linear sequence and their inherent secondary structural characteristics) in concert with the hydrophobic-hydrophilic properties of long chain fatty acids constituting the lipid bilayer.

The operating conditions of most life-chemistry processes reflect the bell-shaped nature of the activity curves. Optimum activity occurs within an ideal range of conditions and then rapidly declines as the difference from the ideal condition increases. The lipid bilayer

organization of membranes facilitates the sequestering of key interacting and signal transduction elements into what are termed microdomains (Vereb et al., 2003). Microdomains, caveolae (caveolin-caged protein-lipid structures that serve as biochemical workbenches to coordinate signal transduction processes), and lipid rafts (cholesterol/sphingomyelin-enhanced membrane areas) exist in plasma membranes as well as in mitochondrial compartments and in the endoplasmic reticulum. The influences of the microdomain-associated conditions mostly impact interactions across nanometer-scale distances affecting discrete hydrogen bonding and charge character of critical amino acids that, in return, change a protein's three-dimensional structure (de Bakker et al., 2008; Giocondi et al., 2010). This altered spatial configuration is in part the result of the protein-lipid microdomain interactions that dictate the function or activity state of several membrane kinases and receptors critical to the detection of conditions that constitute stress for a cell. At some point in the life of that protein it will be associated with some manifestation of a lipid matrix, perhaps during its synthesis and intracellular transport or when anchored in a substructural organelle. In terms of thermodynamic impacts, the changes in body temperature associated with hyperthermia as well as hypothermia are sufficient to locally alter membrane fluidity (Song et al., 1999; Park et al., 2005) and therefore protein environment and structure. Similar processes occur in response to anoxia/reoxygenation and imbalances in red-ox pairs, where the result is the generation of a local instability in bilayer-protein fluidity and thermodynamic order that releases (de-inhibits) select proteins to become active regulators of gene transcription and phosphorylation activation (Vereb, et al., 2003). These discrete fluctuations in the relative balance between fluidity and rigidity, superlattice formation, and order-disorder phase transitions are locally affected within the membrane by cholesterol and sphingomyelin content, along with the interaction of these with secondary (especially α-helical) structure of proteins. The dynamic character of these membrane areas is reflected in the rapid assembly and disassembly of temporally (on the order of microseconds to milliseconds) and spatially (10 to 50 nm) discrete signal transduction areas termed "clusters," in a process termed "clustering." Caveolae represent a specialized, longer-term clustered area due to the presence of anchoring proteins, but short-term clustered areas develop as a result of lateral trafficking of proteins as affected by changing membrane fluidity (Vereb, et al., 2003). Additionally, lipid rafts also may serve as reservoirs from which functional proteins such as $\alpha 2\beta 2$-integrin, can rapidly translocate into caveolae as conditions dictate (Upla, et al., 2004). Furthermore, lateral trafficking of interacting proteins as affected by changing membrane fluidity coordinates many aspects of T-cell response to molecular antigens and, therefore, influences the timing of immune response to pathogen challenge (Pecht et al., 2005) as well as the response to bacterial products such as endotoxin and peptidoglycan (Triantafilou et al., 2004).

A case can be made for environmental impacts that reorder plasma, endoplasmic and mitochondrial membrane fluidity, and dynamic membrane trafficking as significant determinants of the responsiveness of both the innate and adaptive immune system to immune challenges (Bogdan et al., 2000; Bishop and Brandhorst, 2003). This was recently shown to be the case with regard to how membrane order influences the assembly of plasma membrane receptors for various classes of immune system ligands. Where previous theories suggested that receptor subunit associations were dependent on the binding ligand forming and stabilizing the link between the subunits (for example the growth hormone receptor; Wells et al., 1993), new data suggest that many plasma membrane receptors are distributed across several pools within the membrane with different relative states of activating capacity (as reviewed by Groves and Kuriyan, 2010). The data have been interpreted to suggest that preassembly of receptor subunits can be ordered through membrane clustering; with the introduction of ligand there

Table 8.1. Examples of immune system-associated receptors demonstrated to have subunit assembly and packaging in association with other signal transduction elements regulated through membrane clusters and membrane microdomain substructure.

	Receptor	Reference
Innate Immune System	• Interleukin-2 (IL-2)	Damjanovich et al., 1997 Matko et al., 2002 de Bakker et al., 2008
	• Tumor Necrosis factor-α (TNF-α)	Chan et al., 2000
	• Toll-like Receptor (TLR-)-4	Triantafilou et al., 2004
	• Interleukin-15 (IL-15)	Waldman, 2003 de Bakker et al., 2008
	• Lymphotoxin	Lorenz et al., 2003
Adaptive Immune System	• T-cell Antigen Receptor-coupled tyrosine kinase	Bunnell et al., 2002
	• CD-8	Pecht and Gakamsky, 2005
	• CD-4	Chuck et al., 1990
	• MHC Class 1 and 2	Jenei et al., 1997 Vogt et al., 2002
	• Integrin-coupled protein kinase-C	Upla et al., 2004

occurs a rapid initiation of catalytic and signal transducing capacity, which is accelerated and fine-tuned through shuttling of receptor components into or out of the domain. A summary of these cluster effects on immune-related receptors is summarized in Table 8.1.

The implication from these data is that factors capable of changing the fundamental properties of membranes in microdomains impact how immune cells respond to challenge stimuli and how nonimmune cells respond to the elicited immune signals. In essence, shifts in membrane stability due to heat, intracellular proinflammatory mediators, or membrane potential (Fromherz, 1988) promote the loss of steric compliance. Stresses are imparted on the system when the lowest energetic structure is not maintained, forcing conformational shifts in proteins and the overall topography of the membranes (Vereb et al., 1995; Giocondi et al., 2010). This process constitutes a physical compression (or decompression) of proteins with a reciprocal deformation of the lipid bilayer thereby opening or closing access to reactive epitopes on stress sensing microdomains (Brannigan and Brown, 2006).

Intracellular Competition and Physiological Optima

The second principle of the model is that warm-blooded animals have the capacity to regulate their internal environment in a manner that maintains the biochemical activity in a narrow optimal range, in spite of huge differences in the external environment. As discussed by the originator of the concept of adaptation to stress (Selye, 1976), the body has the capacity to sense and monitor its own state of wellness and maintains its healthful balance through a series of interconnected feedback and response loops. However, the ability to maintain the balance of the internal environment comes at the expense of active energy expenditure in which the more extreme the environment, the greater the energetic demand to stabilize the internal environment. In the situation where a young animal is experiencing the stress challenge of infection, the energetic cost of the febrile response is a significant drain of the body's tissue resources. The cellular energy needed to generate fever has been estimated to require a 10 to

30% increase in metabolic rate for every 1°C rise in core temperature (Reviewed by Baracos et al., 1987; Kluger**,** 1991). This is often accompanied with a reduction in voluntary intake with the deficit made up for by catabolic tissue processes (Elsasser et al., 2000, 2008). In fact, the concomitant use of growth promoters, such as growth hormone, to try and offset the growth deficits at this time has been shown to worsen some aspects of the catabolic effects of infection through increased lipolysis and muscle degradation (Elsasser et al., 1998). The simple fact is that biological processes can be thought of as competing for attention and in this case the attention sought is observed as a conflict between the programmed need to grow or maintain a certain metabolic capacity or function versus the need to combat the invading organism. The young animal is genetically engineered to grow with the goal of attaining reproductive maturity. This drive is relatively strong, but not as strong as the drive to survive. Where animals are challenged with immunological threats to their well-being, the response to that threat will be proportional to the severity of that threat and correspondingly command more energy resources (Elsasser et al., 2008). The result is that an animal may need to suspend its growth to spare energy resources for the biologically higher priority of surviving the threat. The animal's body is now challenged to prioritize how it will partition energy across processes in the face of a decrease in energy availability.

Response Magnitude: The Difference between Coordination, Communication, and Stress

A third principle describing how the environment impacts animal health is associated with the need to recognize that the interaction is a process that functions according to what one could call the rule of magnitude. Historically, we have defined most pathophysiological processes in reference to some rather overt, and detrimental, response on or to a cell. For the most part this usually has been ascribed to too much of some mediator being present, i.e., too much NO, too much lipid peroxidation, too much protein nitration, too much H_2O_2, etc. However, overtime and largely with increases in the sensitivity of detection, many of these same molecules and compounds, to which were attributed disease-causing character, have taken on new functions under normal states of physiology as signal transduction and cellular communicating factors but at much lower content or for briefer periods of time that those associated with tissue harm. This is true for the proinflammatory cytokines TNF-α and IL-1 that participates in normal remodeling of reproductive tissues as well as bone and adipose tissue at very low expression levels (Bowen et al., 2002; Hauguel-de Mouzon and Guerre-Millo, 2006; David and Schett, 2010; Suganami and Ogawa, 2010). It is also true for several of the mediators of the environmental and immune stress signals including nitric oxide (Rada, et al., 2008; Napoli and Ignarro, 2009) and superoxide anion (Brüne, 2005). One can consider the level of cellular response at which the concentration or duration of an effector compound changes its role from normal function to abnormal function to be a breakpoint. In reference to proinflammatory processes, these effector molecules that possess these function-breakpoint characteristics are generated at one or more critical control points (CCPs) in a biochemical pathway. Examples of CCPs's relevance have been reviewed previously (Elsasser et al., 2008) illustrating the progression of signaling intermediated from sensing of endotoxin to binding of TNF-α to its receptor to the nutritional and metabolic inputs that modulate NO generation from arginine to the production of cell-damaging $ONOO^-$. Highly reactive products

such as $ONOO^-$ directly impact the mechanisms through which normal endocrine signal processing becomes disrupted during proinflammatory stresses (Elsasser et al., 2007a, 2007b) and are consistent with observations suggesting that many environmental factors and toxicants also function through these relevant CCP pathways (Filipov et al., 1999a; Monroe and Halvorsen, 2009).

This breakpoint can be modulated by some rather basic influences (for example, plane of nutrition, heat stress, periparturient syndrome). However, the breakpoint response can be thought of with more specificity if viewed as a component of a larger matrix more appropriately defined by animal-dependent factors (species and breed, age, genomic-phenotypic diversity) and environmental factors. Collectively, this also embraces the issue of what can be termed collateral environmental factors. Collateral factors can be separated into two broad areas. The first considers how long the animal has been in that particular set of prevailing environmental conditions. Is the environmental factor in a state that will force a homeostatic response to rebalance the body's internal environment back toward optimum, and has it persisted sufficiently long so as to prompt accommodation and adaptation on the part of the animal? Second, climatic conditions also determine prevalence of other species of animals, plants, insects, fungi, parasites, and bacteria that can challenge aspects of animal physiology ranging from nutrient availability, plane of nutrition, and energy partitioning to another somewhat context-dependent process we term immuno-competence.

How Does the Cell Sense Its State of Wellness? (And Other Challenges!)

On the whole organism/animal level, the cumulative sensing of being out of one's comfort zone is sensed in some brain functions that indicate that the climate is too hot, too cold, the animal is in ionic imbalance (thirsty), it's infected (fever, lethargy, malaise), and so on. The information for the appropriate behavioral response to attend to the insult is derived from various sensors that detect disturbances – pain receptors, pathogen recognition receptors (toll-like receptors, etc.), numerous nervous system-connected temperature and pressure sensors, as well as the general functioning of the neuroendocrine system. Since many of these whole animal aspects of stress control are well-characterized and summarized elsewhere (Epel, 2009; Denver, 2009; Caspi et al., 2010), this review will focus on cellular responses to stressors that form a powerful link between the environment and animal health.

So how does a cell know that it is being challenged and stressed and furthermore needs to alter its biochemical routine to survive? Why is the cellular response to several different stress challenges apparently handled through just a few mechanistic processes common across these different challenges? At the cellular and subcellular level, this sensing is elegant in its simplicity and for the most part quite traceable evolutionarily to some of the most basic unicellular organisms. This sensing is so ancient that one can make a case for its origin being the separation of an internal environment from the external environment via a membrane (Monnard and Deamer, 2002) as a fundamental constituent of the definition of a living organism.

Figure 8.3 is a composite of the major ways through which a cell can sense that its surrounding environment or the signals that impinge on it are innocuous or harmful. While complicated at first sight, the organization of the diagram is easily understood when the critical control points (numbered 1 through 7) are individually evaluated.

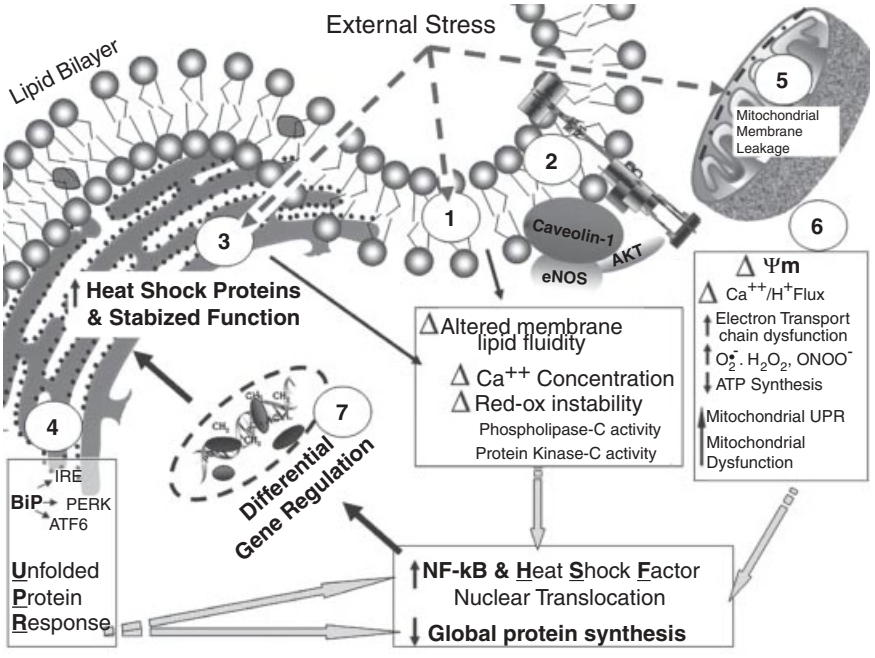

Figure 8.3. Several factors common to many response pathways are critical control points (CCPs) in the cellular scheme of integrating environmental and immune stresses. CCPs 1 (plasma membrane), 3 (endoplasmic reticulum), and 5 (mitochondria) share the common feature of being membranes or membrane-bound structures and physical deformations of the lipid bilayer and associated proteins serve as evolutionarily conserved sensors of heat, red-ox state, pH, osmolarity, swelling, shear stress, etc. These deformations and physical protein activations set into motion cascades of processes, some common and some unique to the respective structure. Plasma membranes cluster interacting proteins (including cytokine and toll-like receptors, and an assortment of signal transduction proteins like JAK-2, AKT and MAP kinases) in caveolae (CCP 2) and with significant processing through NF–κB to the nucleus. In the ER, membrane sensing launches the unfolded protein response (UPR) initiated by release of nuclear transcription factors from BiP (CCP 4) to signal nuclear events through heat shock factor-1 and NF–κB. In the mitochondria, stress responses initiate Ca^{++} fluxes and perturbations in the electron transport chain that further initiate kinase signaling to effect selective migration of transcription factors to the nucleus including NF–κB.

Critical Control Points 1 and 2: Compartmentalization and the Fundamental Gel State of Membrane Lipids

Membrane lipid asymmetry – where the distribution of lipid components across the bilayer is ordered and specialized among and between cell types – underlies the capability of different membranes having different physiological functions and being affected by different physical stresses (Critical Control Point 1; Lenoir et al., 2007). It is not surprising therefore that if a membrane's constituents evolved to confer some aspect of biofunctionality onto a cell, perhaps it is the actual physical attributes of those constituents that play a role in sensing perturbations impinging on that cell. The theory is that the perturbation-induced changes in membrane

fluidity (too fluid or too rigid) transiently (on the order of minutes to a few hours) alter the thermodynamic entropy to reorder and destabilize hydrogen bonding, and van Der Waals forces within the membrane lead to the generation of signals that ultimately induce the heat-stress cascade and heat shock protein generation (Vigh et al., 1998; Park et al., 2005). The basis for this theory in mammalian tissues was derived largely from work done on unicellular membrane models. For example, researchers demonstrated that by acutely increasing membrane fluidity in *Saccharomyces cerevisiae* (Vigh et al., 1998) or cyanobacteria (Horvath et al., 1998) using heat or chemical induction, or mutations in a lipid desaturase gene, the heat shock response pathway appeared to be triggered in coordination with apparent activation of membrane-embedded regulatory enzymes like PK-C1 (Kamada et al., 1995) or ion transporting processes involving H^+-ATPase (Oosawa et al., 1997) or even Ca^{++}, Na^+, and K^+ fluxes in mammalian cells, all of which are highly affected by temperature (Park et al., 2005).

For the most part, warm-blooded animal cell membranes are composed of interacting lipid matrices delicately balanced between a fluid and a semi-rigid state at temperatures between approximately 33 and 42°C (Brannigan and Brown, 2006), with more rigidity at the low temperature and more fluidity at the high temperature. Membranes are not static, but rather flux or flex with lateral cis-movements dominating over the energy-requiring trans-movement. Consequently, as proteins are anchored into these bilayers, speculation has emerged to suggest that changes in membrane fluidity can actually alter protein conformation in a compression-relaxation manner (Vigh et al., 1998; Park et al., 2005; Balogh et al., 2005). This has important implications for the three-dimensional form of a protein, given that a relaxation of conformational stress might lower the activation energy to facilitate an increased efficiency of signal transduction or electron transfer. This would apply also to mitochondrial membranes and the function of its membrane-embedded proteins. An important criteria for efficient signal transduction to proceed within a cell is the strategic close proximity of interacting signal transduction elements that put reactive intermediates in the needed spatial and temporal proximity to interact (Elsasser et al., 2007a, 2007b). Membrane specialization, plasma membrane microdomain caveolae in particular, serve this spatial/temporal organizing function (Critical Control Point 2; Hong et al., 2008; Fielding, 2001). Caveolae not only have novel arrangements of lipids in the amphipathic membrane (patterns that suggest these regions are highly sensitive to reorganization as affected by subtle changes in heat and cold, pressure, and red-ox potential) but they also have juxtaposed accumulations of signal transduction elements.

Recent data indicate that for bilayer membranes to serve as stress-sensing/signal transducing entities, a physical process needs to occur wherein selective compression/decompression-associated conformational changes in a few select kinases and ion/proton ATP-coupled transporters trigger the response pathway. Addressing this point, Vigh et al. (1998) reviewed and summarized relevant experiments that collectively pointed toward protein kinase-C (PKC) isoforms as enzymes particularly well suited to function as membrane perturbation sensors. In particular, the altered entropy of the membrane lipid rearrangements favored the generation of signals necessary to launch the heat-stress cascade. A unique hypothesis applicable to mitochondrial membrane signaling during bouts of stress was developed by the Russian membrane biologist Dmitriev (2001), suggesting that signaling across mitochondrial membranes to other parts of the cell might be generated when free radical oxidation of membrane fatty acids transfers NADPH-dependent energy to results in what are termed lipid pulsations (essentially a looser association of hydrophobic moieties that permits more lateral motion), which causes the activation of several membrane enzymes. Speculating, one might consider the existence of multiple mechanisms through which physical deformation of membrane components to initiate protein signal transduction cascades to be one of the ways that environmental issues interact

with and reshape or modify more traditional immunological responses to disease threats and influence the overall health status of animals.

The final point to be made regarding membrane fluidity and its capacity to sense environmental perturbations surrounds the growing body of evidence suggesting intervention therapies can be developed to remediate the fluidity heat shock response. Coined membrane-lipid therapy (Vigh et al., 2007), the principle is based on the administration of compounds such as hydroxylamine that intercalate within the membrane lipid causing re-stabilization of the membranes, down-regulation of HSPs, and the return of biomarkers of disease stress to relatively normal levels. The potential for this to aid in prophylactic intervention of increased morbidity in the neonate has been explored in recent studies (Uauy et al., 2000; Rooke et al., 2002; Edwards, 2002). Feeding gestation diets supplemented with long chain fatty acids (22:6 n-3) to sows prior to farrowing was associated with increased neonatal vigor and decreased overall mortality, an effect the researchers attributed to improved neural development. Reviewing the relevant literature on the topic, Edwards (2002) suggested that perinatal intervention strategies to improve neonatal survival in the fact of all the potential environmental and physiological insults might best be supplied to the neonate via the mother prior to birth. Similarly, Lammoglia et al. (1999) demonstrated that supplemental fat feeding to cows during gestation improved survival of calves born in cold climates. These researchers attributed the effect to improved glucose metabolism in the calves, giving them a survival advantage through their greater capacity to generate heat from the energy resources.

Critical Control Points 3 and 4: Endoplasmic Reticulum and the Unfolded Protein Response

For the most part, all nucleated cells in the body possess the necessary machinery to synthesize protein. In the cell's efficiency, the functional synthesis of protein occurs in the matrix called the endoplasmic reticulum (ER). In this location, messenger RNA, amino-acid-laden transfer RNAs, ribosomes, initiation, elongation, and termination factors converge with the result being energy-driven formation of peptide bonds and a complex molecule. This resulting molecule is further processed through the addition of sugars that are folded, stabilized, and, most importantly, monitored for correctness. Proteins are folded and refolded in an iterative process involving the binding of calnexin (CX) and calreticulin (CRN) to the post-translationally added sugars where the CRN and CX recognize a $\alpha(1,3)$-glucose mannose bond at select asparagine residues, resulting in proper assembly of disulfide bonds (High et al., 2000). Compared to other parts of the cell, the ER compartment is highly oxidizing. Due to the oxidizing environment, in conjunction with CX/CRN-mediated instructions and the protein disulfide isomerase ERp57, only properly folded and configured proteins are exported to the Golgi (Ellgaard and Helenius, 2003). As vital to the activity of a cell as a properly functioning protein is, the converse is equally true. Misfolded and inappropriate proteins will not be processed further and their accumulation in the ER causes endoplasmic reticular proteotoxic stress. In that the ER is laden with CA^{++}, the ER stress perturbations cause the release of this stored CA^{++} (Critical Control Point 3), and this serves as an intracellular messenger to turn on several important stress signal transduction pathways, leading to the heat shock response in the larger ER response process termed "the unfolded protein response" (UPR; Shen et al., 2004; Kohno, 2010). The UPR is a critical self-assessment process on the part of the cell in which several actions occur rather simultaneously to (a) stop whatever is metabolically occurring in the

cell and (b) launch a cascade to re-establish intracellular equilibrium to include red-ox and membrane potentials, ionic balance, regeneration of injured subcellular components, or at the extreme, eliminate the faulty cell (DuRose et al., 2006).The UPR has the following characteristics: (a) up-regulation and synthesis of heat shock proteins (HSP) to aid in stabilizing proteins inside cells (survival factors) and as a intercellular communicator when released into the circulation; (b) termination of bulk protein syntheses (reduce the burden on misfolded proteins); (c) cell cycle arrest through blockade of cyclin D1; and (d) altered apoptosis signaling (Davenport et al., 2008). Under some stress circumstances in which glucose deficiency associates from nutritional (nutrient availability including poor maternal nurturing) or pathophysiological response (like sepsis-induced hypoglycemia), the fate of affected cells can be determined by the state of balance in the ER stress responses, where eIF2α kinases function as a proapoptotic mediator while PERK functions as a cell survival factor (Muaddi et al., 2010). As these responses ultimately initiate the production of heat shock proteins, they also serve to initiate immune responses through a collateral activity termed chaperokine activity, where several factors critical to the detection and processing of proinflammatory challenges (including Toll-like receptors 2 and 4 – pathogen sensors for Gram negative and Gram positive pathogens and toxins, respectively – and CD-14, a scavenger receptor superfamily consisting of CD-36, CD-40, CD-91) serve as receptors for these HSP-70 class molecules (Asea, 2005). Environmental factors that up-regulate HSPs also stand to change the sensitivity of these proinflammatory mediators to their natural immune stimulants. According to when this occurs in the temporal pattern of the acute response/preconditioning versus the recovery/adaptation phase (see Fig. 8.1), the interaction of the environmental challenge on top of the immune challenge can be either intensified or attenuated.

Recent data from Catalani et al.(2010) indicate that in the periparturient dairy cow, the variability in immune and metabolic parameters was positively correlated with the expression of HSP-72. These parameters included the peripheral blood mononuclear cell content of CD-14, TLR-2, and TLR-4. The data also underscore that by definition of increased elaboration of the HSPs, the periparturient period is a proinflammatory period subject to conflicts in homeostatic balance associated with rapid changes in the interplay between stresses. The relevance of these observations are consistent with the data of Shinohara et al. (2004) that suggested estrogen administration down-regulated HSP-72 induction, as well as several cardioprotective effects downstream of the HSP-72 associated with ischemia/reprofusion injury in the heart. As reviewed and summarized by Shen et al. (2004) and DuRose et al. (2006), data support the concept that two factors place the ER uniquely in position to serve as a stress-monitoring and response-initiating organelle in the cell. The first, already mentioned, is what occurs in the ER membranes. Where the ER membrane is the first to experience protein insertion or protein interaction following peptide synthesis and processing, factors, including thermal stress (heat as well as cold), oxidative stress (unbalanced red-ox pairs, free radicals, reactive oxygen, and nitrogen intermediates) uncouple the efficiency of protein folding (especially where disulfide formation is perturbed), unleashing the ionic stimulus throughout the cell. Secondly, however, normal proteins intrinsic to the ER are affected by these stresses and initiate a cascade of signal transduction mediators leading to direct activation of heat shock genes as a part of this UPR.

Membrane-bound BiP (IgH-chain Binding protein) is one of many molecular chaperone proteins associated with the management and folding of proteins in the ER. In addition to this chaperone function, BiP also binds to several ER stress response activating proteins (Critical Control Point 4, Davenport et al., 2008) with that binding constituting a cessation of transcription activating function of those elements (Nakayama et al., 2010). The first of

these is PERK or PKR-transmembrane endoplasmic reticulum kinase. PERK is kinase that traverses the ER membrane and has attached to it on the inner surface of the ER a regulator and mediator of mRNA translation, eukaryotic initiation factor-2α (eIF2α). The phosphorylation of eIF2α on SER-51 by PERK leads to the pan-cessation of the initiation of translation by blocking the capacity of the S-methionine-tRNA initiator to establish a union with the ribosome (Scheuner et al., 2001; Muaddi et al., 2010). BiP also regulates the activity of ATF6 (activating transcription factor-6). Phosphorylation activation and BiP release of ATF6 leads to further processing of a 90 kD ATF6 to a 50 kD truncated protein through the Golgi network to release to the nucleus a transcription initiating factor that specifically binds to genes containing the promoter regulatory sequences for endoplasmic reticulum response elements (ERSEs). The binding of ERSEs to specific regulatory regions of the gene promoters increase survival factors such as GRP78, GRP94, CHOP, XBBP1, CRN, and protein disulfide isomerases (Yoshida et al., 1998; Luo et al., 2003).

Critical Control Points 5 and 6: A Gradient of Mitochondrial Signals Covering Energy Production through Apoptosis

In 1953, Lundegardh described a process through which cytochrome pigments in plants facilitated a transmembrane flow of protons in a series of oxidation-reduction reactions wherein oxygen was reduced on one side of the membrane and substrates were oxidized on the other side of the membrane. With this in mind, Mitchell (1972) elaborated a mechanism (i.e., chemiosmotic coupling hypothesis) present in mitochondrial membranes through which the generation of ATP from ADP could be coupled to electron transfers through a chain of red-ox reactions perpetuated via a proton gradient. The proposed model contained three elements that were then critical to not only energy generation in cells, but also as a component of the mechanism of cellular sensing and reaction to stress. These elements were (a) membranes form a barrier through which the flux of protons facilitated a flow of electrons across a series of linked proteins towards the conditions needed to phosphorylate ADP; (b) ATP synthases are located in the same membranes in a spatial orientation that facilitated the use of the proton gradient to form ATP; and (c) the membrane needed to be contiguous and intact so as to maintain the differential separation of protons, ions, and metabolites on the inside of the mitochondria from the outside. A critical feature of this whole process is that oxygen is the final sink for these electron fluxes and when the flow is interrupted, the result is an increase in oxygen free radical ($O_2^{-}\bullet$) production (Raha and Robinson, 2001). The magnitude of this is realized when one considers that the (a) daily turnover of ATP in a 65 kg man requires that 3×10^{21} protons be pumped per second with a corresponding consumption of 380 liters of O_2 (Rich, 2003); (b) under normal circumstances 1 to 2% of the electrons escape the electron transport chain and form free radicals (Nijtmans et al., 2004); and (c) even a 0.1% further decrease in the efficiency of electron passage down the chain results in a daily gain of 2.59×10^{24} protons per day that are potentially available for participation in free radical production.

Mitochondria (Critical Control Point 5) hold an interesting place in the detection of and progression through proinflammatory signaling. As with the ER, a combination of membrane fluidity changes and aberrant red-ox reactions create instabilities in integrity of mitochondrial membranes (Critical Control Point 6) permitting inappropriate ion fluxes, Ca^{++} and H^{+} in particular, and loss of needed membrane potential ($\Delta\Psi m$). Balogh et al. (2005) studied fluidity perturbations in mitochondrial membranes as generated by mild heat stress as well

as chemical fluidizers and suggested that the hyperpolarization of membranes and increased flux of Ca^{++} from 2º to 3°C increases in ambient heat were sufficient to liberate inositol-1, 4, 5-triphosphate that in turn activated phospholipase-C, Phospholipase-A_2, and protein kinase-C, which initiated cytoplasmic translocation of nuclear transcription protein heat shock factor-1 (HSF-1), culminating in the launch of heat shock protein synthesis. Qian et al. (2004) established several criteria that define mitochondrial stress, which include opening of membrane transition pores, uncoupling of electron transport chain electrons, and mitochondrial swelling. Whereas the ER targets its responses to stress largely at the point of protein syntheses, the first impacts of stress on mitochondria progressively perturb energy generation, followed by the elaboration of compounds that promote nitrooxidative stress (like ONOO- and $O_2^{-}\bullet$), and at the highest levels, cessation of protein synthesis and cell death (Balogh et al., 2005). In addition to responding to physical stress stimuli like heat, the mitochondria also are affected in a similar destabilizing manner in response to immune proinflammatory signals initiated through the binding of cytokines like TNF-α to the Type-1 receptor and triggering the mitochondrial cascade away from the prosurvival NF-κB processes toward the cell death/apoptotic response (Garcia-Ruiz and Fernández-Checa, 2007). The complexity of this process is further illustrated by the initiation of the nitric oxide cascade within the mitochondria. In this process, both signal transduction and electron transition processes are modulated in large part through NO binding to its two mitochondrial targets, cytochrome C oxidase and guanylate cyclase (Clementi and Nisoli, 2005). This results in perturbations to the oxidative phosphorylation system (termed "Complex I," NADH-ubiquinone oxidoreductase) and the associated accessory proteins. The damaging effects of cytokine driven proinflammatory stress are presumed to be largely initiated and channeled through a cascade of events starting with the elaboration of the proinflammatory-initiating cytokine TNF-α, which further triggers increased cellular NO.

With mitochondria organized in a complex arrangement of interacting inner and outer membranes of bilayer and imbedded protein configurations, it is not surprising that the mitochondrial membranes are capable of generating their own version of the unfolded protein response. In fact, it is possible that mitochondria may exhibit more plasticity and adaptability across the spectrum of stress mediators. First, mitochondria have retained a significant genome of their own, independent of the cellular genome and code for the five major electron transport chain multicomplexes including the Complex V / F_1F_0-ATP synthase (Schon and Gilkerson, 2010). Second, the processes of mitochondrial atresia and biogenesis are quite active during the stress response, the theory being that by the cell regulating the numbers and activity of mitochondria, they can partially regulate the excessive flow of electrons to damaging nitrooxidative stress molecules (Protti and Singer, 2007). Third, if the bacterial or prokaryotic evolutionary entry of mitochondria into more complex cells (endosymbiosis, approximately 1.7 billion years ago) is assumed (Emelyanov, 2003), and if the premise that bacteria grown, for example, in stresses of heat or cold, adapt over a relatively short time by changing the lipid properties of their membranes to re-establish proper fluidity (Weber et al., 2001; Moorman et al., 2008), then one might expect that mitochondria may have retained some self-determination as it regards lipid incorporation into membranes in response to stress. It is surprising that there is not more research published on this topic, but typical of the seven papers that exist at this time, the data of Thomas et al. (2002) point to auto-regulation of mitochondrial lipid content and its favorable rearrangement during thermal preconditioning as a potential critical control point capable of being exploited in securing increased animal well-being in the face of anticipated environmental threats.

Our laboratories recently investigated this interplay between heat stress and the proinflammatory response to LPS in a model where Holstein steers were placed in environmental

chambers, challenged acutely with a cyclic pattern of heat stress, and co-challenged with two injections of LPS four days apart to further evaluate LPS tolerance (Elsasser et al., 2009; see Fig. 8.4). Heat stress caused an overall increase in rectal temperature ($P < 0.05$). Additional stress of the LPS challenge further increased rectal temperature an average of 1.4°C in heat-stressed steers compared to the 0.8°C increase observed in thermoneutral steers. Respiratory rates of heat-stressed steers were almost double those of thermoneutral steers with a significantly greater increase in rate in heat-stressed animals after LPS. Because the TNF-α response to LPS is considered a major initiator of the proinflammatory cascade (Elsasser et al., 2008), we expected that the acute heat stress might have provoked a more robust increase in TNF-α after the LPS challenges, the timing of the LPS challenges relative to the introduction of the steers to the heat being rather short. Instead, we found no difference in the incremental change in TNF-α response, but did find a significantly augmented response in nitric oxide after the LPS; where this aspect of the response had accommodated in thermoneutral steers

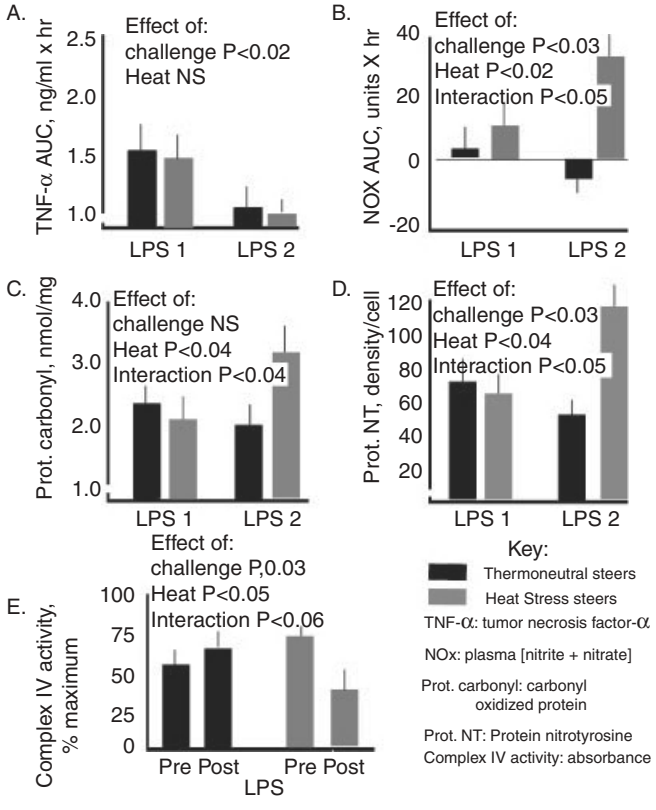

Figure 8.4. The complex nature of heat stress modulation of proinflammatory responses is observed where Holstein steers maintained at thermo neutral and heat stress conditions in environmental chambers and further challenges with low levels of bacterial endotoxin (Elsasser et al., 2009). Data are presented on the changes in select biomarkers of the proinflammatory response including TNF-α (Panel A), nitric oxide (panel B), carbonyl proteins (panel C), nitrated proteins (panel D), and mitochondrial cytochrome-C oxidase enzyme activity (panel E).

after LPS, nitric oxide production was significantly greater after the second LPS challenge in heat-stressed steers.

Mitochondrial involvement was suspected based on greater perturbations in the plasma concentration of lactate-to-pyruvate ratio. Liver tissue contents of carbonyl proteins (biomarker of protein oxidation) as well as tyrosine nitrated proteins (biomarker of peroxynitrate-mediated nitrooxidative stress) were greater after LPS in tissues for heat-stressed steers than from thermoneutral steers with no change in xanthine oxidase activity (indicative of superoxide anion generation stemming from mitochondrial sources); correspondingly, homogenized preparations of liver tissue mitochondria from heat-stressed animals had significantly lower cytochrome-C oxidase enzyme activity than similar preparations from thermoneutral animals. More recent data collected using mass spectrometry suggest that much of this mitochondrial electron transport chain disruption may also arise as a consequence of tyrosine nitration of key chain elements, including the F_1F_0-Complex V ATPase, which contains in its linear amino acid sequence several epitopes consistent with previously deduced nitration motifs (Souza et al., 1999; Lanone et al., 2002). Collectively, these data point to the compromised mitochondrial function associated with heat stress being a critical target upon which multiple stresses can converge. This concept is consistent with experimentally observed impaired energy production in septic patients and with the rationale for targeting mitochondrial therapy as a potential intervention strategy to improve clinical outcomes and survival (Dare et al., 2009).

The important point to remember here is that the timing and degree of heat challenge dictates how pathways interact. The issue of cross-tolerance between heat shock and proinflammatory immune responses is tremendously complex and can potentially also lead to deleterious modulation (attenuation, in this case) of the proinflammatory component. In a study by Sanlorenzo et al. (2004), severe heat shock induced with rapid temperature increases up to 43°C followed shortly afterward with an endotoxin challenge resulted in the inhibition in TNF-α response in vitro as well as in vivo. The effect was tracked back to an increase in the activity and nuclear localization of phosphatase (MKP-1) that in turn shortened the activity cycle of ERK-1/2 and p38 kinase, signal transduction elements necessary for the induction of TNF-α. This may explain why animals experiencing stressful levels of temperature may be more prone to infections where the initiating response to the infecting agent is blocked. Conversely, heat stress of monocytes at only 1º to 2°C lower was demonstrated to increase cellular presentation on toll-like receptors-2 and -4, possible to the benefit of the host where increased sensitivity to Gram-negative and Gram-positive bacteria may call for the proinflammatory response earlier in the bacterial propagation cycle with greater antibacterial activity.

Critical Control Point 7: Stress, DNA, and Epigenetics: Gene Expression and Genes That Learn from Stress Responses

With the emergence of domestic animal genome maps and sequences, the challenge is unfolding as to how the observed sequence changes between animal populations translate into a phenotype. Epigenomics is an emerging subfield of applied genomics aimed at identifying protein-DNA interactions, as well as chemical modifications to DNA, that give functional meaning to observable changes in the gene expression and phenotypic expression that do not arise purely because of polymorphisms or other linear differences in genes sequences. From a collection of diverse phenomena, epigenetics has evolved to a defined and far-reaching field of study (Goldberg et al., 2007). Fundamental epigenetic analysis is based on how the regulation

of expression of genes is capable of being activated or repressed as a function of specific changes in DNA associated with histone proteins, modification of histones via acetylation and methylation and chromatin remodeling – the selective condensation or compaction and relaxation of the chromatin coils. While the data amassed from gene array experiments are clear that environment × health interactions create a spectrum of differential gene expression responses, new data generated from epigenetic histone marker evaluation and mapping clearly show that a host of genomic interrelationships exist with the external environment and show further that gene responses to stress do not need to be a constant. Rather, expression profiles can be modified by experiences in a manner where new expression profiles for a gene can develop after new histone patterns are impacted on the DNA. More interestingly, these changes can be passed from one generation to the next with significant implications for the development of increased risk of disease (Nadeau, 2009). Thus, the function of DNA is not as fixed as previously thought. The interaction between genes and the environment plays a crucial role in determining human and animal resistance to stress.

The Expression of Genes in Response to Environmental Stress

Cells exposed to different kinds of environmental stress rapidly alter gene transcription, resulting in the immediate down-regulation of housekeeping genes, while crucial stress-responsive transcription is drastically increased (Uffenbeck and Krebs, 2006). Those changes are often referred to as a cell stress-response (Jaattela, 1999; Lindquist, 1986). Since a majority of the world's human and domestic animal populations are in regions where seasonal stressors adversely influence productivity and result in economic losses, there is renewed interest in identifying specific genes that could improve resistance to stressors without adversely affecting productivity (Collier et al., 2006a, 2006b). Certainly, these cell stress-responses are also of great interest to basic biology and to biomedicine. It has been known for a long time that thermal stresses (from both cold and heat) trigger a complex program of gene expression and biochemical adaptive responses (Fujita, 1999; Lindquist, 1986; Sonna et al., 2002). Many of such responses that result in global transcriptional changes are highly conserved from bacteria to humans. Most stress responses follow a similar two-pronged approach: a specific and immediate response, which allows the cell to survive immediate damage while concurrently preparing itself for more severe or long-term stress. The heat shock response, characterized by increased expression of heat shock proteins (HSPs), is induced by exposure of cells and tissues to extreme conditions that cause acute or chronic stress. HSPs function as molecular chaperones in regulating cellular homeostasis and promoting survival. If the stress is too severe, a signal that leads to programmed cell death, apoptosis, is activated, thereby providing a finely tuned balance between survival and death. In addition to extracellular stimuli, several nonstressful conditions induce HSPs during normal cellular growth and development (Pirkkala et al., 2001). Heat shock transcription factors (HSFs) are transcription factors that regulate HSPs expression through interaction with a specific DNA sequence in the promoter, the heat shock element (Sonna et al., 2002). The importance of HSFs as regulators of the heat shock response is reflected by their high cross-species conservation in evolution (Pirkkala et al., 2001). The secondary stress response results in transcriptional changes that enable the cell to adapt to environmental stress and possibly enable the normal cell cycle to continue (Uffenbeck and Krebs, 2006). In a domestic animal model, a recent study, which utilized microarrays to evaluate environmental stress tolerance at the cellular level in cattle (Collier et al., 2006b),

revealed that thermal stress triggers a dramatic and complex program of altered gene expression in bovine mammary epithelial cells (BMEC). The patterns of altered gene expression are similar to patterns reported in other cell types exposed to heat stress (Sonna et al., 2002). The gene transcription profiles indicated that genes involved in cell structure, metabolism, biosynthesis, and intracellular transport are generally down-regulated; while the majority of genes up-regulated are those involved in cellular repair, protein repair and degradation, and apoptosis after loss of thermo-tolerance when heat-shock protein (HSP)-70 gene is expressed (Collier et al., 2006b).

Diverse Regulatory Epigenetic Modifiers

Stress-induced transcription is very complex and involves diverse regulation mechanisms. It is becoming increasingly apparent that genetic information and environmental influences are not independent of each other and that information acquired from the environment provides instructions on how the genetic material is used (Allis, 2006). The rapid activation of gene expression in response to stress develops in large part through the regulation of RNA polymerase II dependent transcription. In order to allow large amounts of genetic material to fit into the relative small nucleus, chromatin is organized into various levels of compaction. The first level of compaction is a histone octamer with two copies each of the core histones H2A, H2B, H3, and H4 wrapped around the DNA to form nucleosomes. Every core histone has an amino-terminal tail and histone H2A also has a significant carboxy-terminal. The core histone tails play a significant function in the further compaction of chromatin, while the core histone tail domains are key regulators of eukaryotic chromatin structure and function (Zheng and Hayes, 2003a, 2003b). Covalent and non-covalent modifications of histone proteins and DNA, as well as the mechanisms of such modification changing overall chromatin structure have been researched intensively in recent years as major epigenetic mechanisms that regulate gene expression (Bernstein et al., 2007; Mikkelsen et al., 2007).

Thermosensitive neurons were first discovered in the preoptic anterior hypothalamus (PO/AH; Nakayama, 1985; Boulant, 1974). The thermal control setpoint is regulated by thermosensitive neurons of the PO/AH and this thermoregulatory site completes its development during an early postnatal critical sensory period soon after birth. Until recently, however, it was not recognized that external stimuli, like an increase in environmental temperature, influenced the neuronal protein repertoire and, ultimately, cell properties via activation or silencing of gene transcription. Both activation and silencing of gene transcription are regulated by chromatin remodeling or histone modification. Chromatin remodeling is a dynamic means of altering chromatin structure so that transcription machinery can access previously condensed DNA. Much of chromatin remodeling occurs through interactions between chromatin remodeling/modifying complexes and histones.

Histone modification is another mechanism used by cells to control access to regulatory DNA regions in chromatin. Histone-modifying complexes alter the state of chromatin through covalent modification of histones (Kouzarides, 2007). Few, if any, examples of regulation at this level have been documented in mammalian farm animals, and the best such examples in a relevant domestic animal are found in research on the chick. It has been demonstrated that an increase in global histone H3 lysine 9 (H3K9) acetylation as well as H3K9 dimethylation occurs in neurons in the chick PO/AH during heat conditioning at the critical period of sensory development. Acetylation and dimethylation patterns of H3K9 in the gene promoter region

of the catalytic subunit of eukaryotic translation initiation factor 2B (Eif2b5) were opposite to each other. During heat conditioning, there was an increase in H3K9 acetylation at the Eif2b5 promoter, simultaneously with decrease in H3K9 dimethylation. These alterations coincided with Eif2b5 mRNA induction. Exposure to excessive heat during the critical period resulted in long-term effects on both H3K9 tagging at the Eif2b5 promoter and Eif2b5 mRNA expression (Kisliouk et al., 2010). Those data are the clearest indication that dynamic H3K9 post-translational modifications regulate the gene expression at translational level during the thermal control establishment. Findings of induction of global histone H3 lysine 27 (H3K27) dimethylation, with no changes in its trimethylation levels, in the frontal hypothalamus, as well as at the promoter of the brain-derived neurotrophic factor (BDNF) gene during thermal-control establishment also highlight the specific epigenetic role of chromatin modifications in thermal-control establishment (Kisliouk and Meiri, 2009).

Epigenetic and Transcription Factors: Targeting Gene Responses before and after Stress

Heat-shock transcription factor 1 (HSF1) also has a major regulatory function in a large-scale remodeling of the cell epigenome. In addition to its well-known transcriptional activities, HSF1 mediates a genome-wide and massive histone deacetylation (Fritah et al., 2009), which specifically associates with and uses HDAC1 and HDAC2. This heat-shock response indicates a potent and unique model to understand the link between gene activity and chromatin remodeling (Fritah et al., 2009).

Increasing evidence suggests that HSP-90 has a role in modifying the chromatin conformation of many genes (Ruden et al., 2005). The data from Drosophila studies revealed that HSP-90 affecting chromatin remodeling might be the mechanism underlying transgenerational inheritance of epigenetic information acquired from environmental stimuli (Ruden and Lu, 2008). HSP-90 is required for optimal activity of the histone H3 lysine-4 methyltransferase SMYD3 in mammals. HSP-90 has been shown to increase the activity of the histone H3 lysine-4methyltransferase SMYD3, which activates the chromatin of target genes (Sims and Reinberg, 2004; Rakyan et al., 2002). Further evidence for chromatin-remodeling functions is that HSP-90 acts as a capacitor for morphological evolution by masking epigenetic variation. Release of the capacitor function of HSP-90, such as by environmental stress or by drugs that inhibit the ATP-binding activity of HSP-90, exposes previously hidden morphological phenotypes in the next generation and for several generations thereafter (Rutherford and Lindquist, 1998; Sollars et al., 2003).

Steroid hormones also participate in stress response. Epigenetic regulation of expression of genes involved in steroid hormones provide an additional layer of gene regulation, even though epigenetic regulation of key steroidogenic enzymes does not look like a predominant regulatory pathway (Martinez-Arguelles and Papadopoulos, 2010). Steroid hormones wield their action in target cells through nuclear receptors belonging to the NR3A and NR3C families. Those nuclear receptors include estrogen receptor, androgen receptor, glucocorticoid receptor, and mineralocorticoid receptor. DNA methylation and other epigenetic modifications play important roles in regulating and directing the expression of the nuclear factors, which, in the return, have secondary impacts on the expression of steroidogenic enzymes (Martinez-Arguelles and Papadopoulos, 2010). Epigenetic modifications to either steroid hormone biosynthesis or steroid receptor functions are likely to modify their associated signaling.

The multiple layers of regulatory control of gene expression provides to cells options in the pathway(s) used to control their responses to external stimuli. An explosion of research efforts in recent years has begun to uncover common molecular mechanisms underlying epigenetic phenomena. It is worthwhile mentioning that the study of epigenetics in farm animals is still in its infant stage. The rapid development of understanding of epigenetic regulation in laboratory animals and the vast potential that exists to manipulate the principle to improve animal health is just starting to attract strong interest in animal agriculture. We should expect to see a clear epigenetic landscape unfold in the near future in the field of animal science.

Integrated Examples of How Environment Impacts Animal Health

From the Beginning: A Right of Initiation

For the most part, the time elapsing between conception and birth may constitute the most secure and stress-free stage of existence a warm-blooded animal may ever experience. From the moment of birth, with the first full breath taken, the impact of environment and the challenge for that animal to cope with the environment never stops until death. This occurs, for the most part, because the fetus is buffered from the wide range of environmental conditions present in the world outside the uterus compared to those within the uterus. So within this process of birth we see the first example and principle of how the environment interacts with physiology to impact animal health. Based on the measured increase in proinflammatory cytokines in conjunction with the depression in anti-inflammatory cytokines, plus the large releases of prostaglandin and nitric oxide, the very process of parturition and birth are, in fact, examples of a proinflammatory process. These response markers include prokineticins (Catalano et al., 2010; Jabbour, 2010), toll-like receptors (Patni et al., 2007), up-regulation of proinflammatory and down-regulation of anti-inflammatory cytokines (Norman et al., 2007), vasoactive factors (Lévy et al., 2005), and patterns of NO and S-nitrosothiols (Christen et al., 2007; Elsasser et al., 2008).

For the neonate that crosses into this new environment, it is not so much the prevailing environment that impacts animal health as much as it is the change between the environments, how severe the change is, over what period of time the change is encountered, and whether the needed physiological feedback and regulatory systems have matured sufficiently to permit the animal to cope with and finally adapt to the change. This last point is quite significant. Let's consider the transition from umbilical oxygen delivery to pulmonary free breathing. Anatomically, the process involves severing the maternal blood supply, the neonate making its way down the birth canal, clearing the lungs of embryonic fluid, expanding the alveolar air spaces, and then changing the entire dynamic of how metabolic acid-base balance is accomplished with the onset of a pulmonary compensatory mechanism (Armstrong and Stenson, 2007). At best, the transition process is somewhat complicated for the neonate, in that transient hypoxic conditions can develop during uterine contractions and this can progress further to a repeated pattern of hypoxia/normoxia, to a rather prolonged axoxia as often times is observed in bovine dystocia (Mee, 2008). These more severe birthing perturbations associated with breech birth, chord stricture, and cardiovascular compression and restriction present to the neonate its first challenges that are only further complicated if the ex utero environment is severe (for example, severe cold or heat is present; Laptook and Corbett, 2002). For the neonate the complicating issue is not necessarily the hypoxia but (a) the paradoxical insults of reoxygenation (Painter, 1995); (b) the repetitive cycling of this occurring with difficult births; and (c) differential

blood shunting between organ beds. This insult – reoxygenation after hypoxia – is a major cause of oxygen free radical production and a major cause of pulmonary, renal, and central nervous system injury (Greene and Paller, 1991; Michelakis et al., 2004). Reiterating the role of mitochondrial membranes and transmembrane ion trafficking, oxygen sensing is largely associated with the ability of mitochondria membranes to deform in response to changes in red-ox pair status as affected by the prevailing partial pressure of oxygen in blood (Michelakis et al., 2004).

At birth, for many physiological systems, the basic feedback regulatory processes operational in young animals are neither fully functioning nor organized yet, with regard to a physiological setpoint, factors particularly important to the endocrine system and its role in metabolism and stress (Gluckman et al., 1999). Examples of this are apparent in the stability of the vascular system in the neonate where the regulation of blood pressure (and therefore distribution of blood and oxygen to different organ beds) is relatively unbalanced (Black et al., 1998; Lévy et al., 2005). If decompensating factors associated with heat stress, cold stress, dehydration, and acid-base imbalance are added to these basic birth-associated dilemmas, the cell responses to the additive stresses can easily overwhelm the fragile resources available to the neonate to cope with the collective stress and the animal could ultimately succumb.

Certainly neonatal stress constitutes a major cause of the incidence of morbidity and mortality in young animals. As exemplified in the 2007 National Animal Health Monitoring System report on calf health (http://NAHMS.aphis.usda.gov) calving difficulty imposes all of the potential risks associated with the documented increases in neonatal morbidity. While calf size and cow parity are the major sources of dystocia (calving difficulty) environmental contribution to the issue is significant with cold shock and hypothermia increasing chances of mortality via a number of factors (Assam et al., 1993; Mee, 2008). The interesting issue of cold stress is that, like heat stress, the impacts are felt through membrane sensing where fluidity of the bilayer decreases with the concomitant launching of a cold-shock cascade (Al-Fageeh and Smales, 2006). Confounding this overall effect on cold shock protein gene expression, as the mildly lowered temperatures decreased membrane fluidity, normal patterns of signal transduction and ion gating slow down and the availability of oxygen to cells is further decreased because of lower oxygen solubility in colder fluids coupled with poor trans-alveolar permeation of oxygen into red blood cells due to epithelial edema thickening and bronchiolar constriction. Finally, the confounding nature of this interaction is exacerbated because the cold shock and hypoxic stress share common stress pathway elements (Gon et al., 1998) and therefore constitute for the neonate a period of additive stresses and therefore increased risk of more severe pathophysiological response. The capacity for the neonate to overrespond (essentially the observed increases in morbidity and mortality) to the impinging multiplicity of stress factors can be linked to the concept that too many stimuli activating common pathways sum to a breakpoint. At this time the mechanisms needed to rebalance the responses are immature and unregulated (Elsasser et al., 2008) and thus progress towards pathology.

More recently, the main driving regulator of hypoxic stress, hypoxia inhibitory factor (HIF-1, Nizet and Johnson, 2009), was shown also to be a major link between cellular response to low oxygen level and co-activation of the innate immune system via NFκ-B signaling pathways (Frede et al., 2006). HIF-1 transactivation is further associated with concomitant activation of toll-like receptor signaling (TLR-2, TLR-6; Kuhlicke et al., 2006; TLR-4, Peyssonnaux et al., 2007) increased proinflammatory cytokine production by CD4+ and CD8+ cells (Nizet and Johnson, 2009), and modification of target cell response to proinflammatory cytokines. Interestingly, however, and quite relevant to the stress-compromised neonate, Peyssonnaux et al. (2007) further demonstrated that the experimental deletion of HIF-1 in mice decreased

the lethality of LPS challenge. This occurred concomitant with decreased maximal responses in TNF-α and proinflammatory interleukins and further in conjunction with improved clinical signs of LPS distress. Affected in the positive were core temperature change and amelioration of hypotension. The authors concluded that the targeting of HIF-1 as a novel intervention strategy to modulate septic shock might prove to be clinically valuable. As always, some other factors add into the picture to cause more problems for the neonate. Difficult birth associates with poor maternal nurturing right after birth and abnormal patterns of suckling by the neonate. Collectively, the absence of the needed maternal stimuli for the neonate coupled with the inadequate intake to colostrum leave the door open to opportunistic infection and increased mortality (Edwards, 2002).

Interaction between Collateral Environmental Factors and Animal-Dependent Factors

Numerous innovative management strategies are effective in offsetting many of the adverse environmental factors that impact upon animal health (reviewed in other chapters of this book). However, by the very nature of geographic and regional animal production and the breeds used in these environments, certain adverse conflicts between animal factors and collateral environmental factors are sure to arise. Many of these conflicts are common across species with some breeds within species more accommodating to the environment than others, and some environmental conditions universally facilitating the emergence of factors detrimental to animal health. This can be examined in some detail using the example of how cattle and sheep are affected by a hot and humid climate: how the climate impacts the development of ingestible toxicants and how differences in cattle and sheep increase or decrease the sensitivity to these environmental issues. Varieties of grasses and grains are developed to provide animal feeds that provide cost-effective nutrition. In the eastern United States fescue and rye grasses are popular feedstuffs for cattle and sheep because of hardiness, insect resistance, and efficient growth. While hot and humid climatic conditions favor good fescue and rye cover, they also facilitate the growth of the fescue fungus (*Acremonium coenophialum*) leading to the ergot and loline alkyloid-derived fescue syndrome/toxicosis and a related fungus (*A. lolii*) in rye, the toxicants of which cause the neurodegenerative disorder called ryegrass staggers. Similarly, harvested grains or matured grain-bearing plants awaiting harvest can become molded with heat and humidity generating numerous toxicants like aflotoxin and mycotoxin with significant impact on animal performance and reproduction (Cheeke, 1995). The issue of animal × environment interaction becomes relevant to this discussion in the following scenario. Animals can adapt to hot environmental conditions over time where a temperature range that initially might have induced heat stress becomes tolerable with behavioral and physiologic adjustments. However, one of the problems associated with the added presence or emergence of these feed-related toxins is that they often possess a neurochemical mimetic activity that alters the thermoregulatory set point in the hypothalamus and the effector mechanisms that regulate blood flow to the surface and heat loss, many regulated through serotonin and dopamine pathways (Rusyniak and Sprague, 2005). In fact, fescue toxins selectively interact with both the dopamine and serotonergic neurotransmitter systems in a manner analogous to bromocriptine and lergotrile (Silbergeld and Hruska, 1979) in the brain peripherally and underlie the physical manifestations of fescue syndrome ranging from hypoprolactinemia to peripheral vascularopathy to behavioral changes. Additional complications in the fescue × heat interaction were observed by Settivari et al. (2009), in which liver gene transcription activity assessments

revealed that gluconeogenesis and apoptosis were up-regulated while significant decreases in oxidative phosphorylation, antioxidative mechanisms, immune function, cellular proliferation, and chaperone activity were observed with the combined effects of heat and fescue. Burke et al. (2007) observed similar exacerbated effects of heat and fescue in heifers. The heating capacity of sunlight alone was demonstrated to cause hyperthermia (Bourke, 2003) in cattle ingesting ergot of rye (*Claviceps purpurea*) when air temperature and humidity were relatively mild. Further complicating the issue, breeds traditionally associated with northern or subtropical environments appear to respond differently to these combination stresses. For example, Browning and Leite-Browning (1997) demonstrated that heat stress in combination with the fescue-associated toxicants led to greater thermoregulatory and cardiovascular perturbations in cattle, and later, these effects were found to be more severe in Hereford as compared with Senepol breeds (Browning, 2004). Finally, even the intensity of the proinflammatory response is amplified to deleterious levels in cattle consuming toxic fescue and experiencing challenges with bacterial endotoxin, where both proinflammatory cytokines and nitric oxide are over produced (Filipov et al., 1999a, 1999b).

Concluding Thoughts

The critical feature of the model presented here is the understanding of how environmental factors affect animal health. This needs to be defined with regard to magnitude, timing, and duration. As an example, where general comparisons of the differences in cellular responses to mild or severe heat stress are summarized in Table 8.2, we need to remember that activation of many of these same cell pathways occur in response to many different sources of stress.

Several small perturbations can become a severe collective stress, if the timing is right! While cellular responses to both mild and severe heat stress share some common ground, given the capacity of physiological processes to adapt, mild heat stress basically reprograms cells and organ processes toward a beneficial adaptation over time, whereas the impact of severe heat stress is so immediate that compensatory responses simply cannot be activated in time or to a sufficient level to minimize cellular damage.

With the present discussion focused on the biochemical mechanisms through which cellular responses to a variety of environmental and health challenges converge, a few areas stand out as needing additional input to guide future research to the next level of understanding and implementation. Ultimately, this should translate into the development of new and novel management and intervention/stabilization strategies that can be affected in anticipation of environmental impacts on animal health and well-being. With the recent sequencing of several domestic animal genomes, we are closer to gaining understanding of how genotype correlates with phenotype. However, with the expression of genes being the critical element in phenotype, this emerging area of epigenetic modulation stands out as having great potential. Not only do we stand a chance of understanding more about how genes react to the environment, but because of the potential to condition animals with induced changes in histone regulation, we may also be able to exploit epigenetic modulation in a manner favorable to improved animal health, perhaps while in utero. Second, the area of membrane therapy may hold promise as a strategy to modulate animal responses to environmental challenge. While not an easy task to impart changes in basic lipid components of bilayers, some select short-term applications of intercalating agents such as tocopherol isomers or even novel fatty acids may serve to stabilize cell membranes against anticipated changes in environmental exposure or at any rate

Table 8.2. Differences in cell responses to mild versus severe heat stress (adapted in part from Park et al., 2005).

	Mild Heat Stress	Severe Heat Stress
Biological significance: Cell, organ, whole body	Beneficial to slightly deleterious	Detrimental and destructive
Induction of Unfolded Protein Response (UPR)	+/− Severity/duration dependent	++
Denaturation of:		
Nascent peptides	+	+
Pre-existing peptides	−	−
Increased Membrane Fluidity	+/−	+
Heat Shock Factor-1	+	++
Activation	Rac 1-dependent	Rac 1-independent
Heat Shock Protein	+	++
Synthesis	Rac 1-dependent	Rac 1-independent
Cell Cycle Arrest	−	G1/S and G2/M arrest
Cell Cycle Proliferation	+/− cell type dependent	−
Cyclin D1	+	↓
Cyclin A	+	−
Differentiation	+/− cell type dependent	−
Apoptosis	−	+
Development of Thermotolerance	+	(+/−) Cell death may precede tolerance
Signal Transduction Pathways:		
Ras/Rac-1	+	−
PI3 Kinase/AKT	+	−
ERK 1 / 2	+	+
SAPK/JNK	+	+
P38 MAP kinase	+	+
Adaptation of growth conditions	Depressed function → rebound: Adaptation Timing dependent Collateral stresses	Cell death/↑morbidity
Crosstalk with additional stress pathways	+ Additive/preconditioning →Tolerance	++ Additive → Breakpoint

provide nutritional resources that are beneficial toward maintaining sufficient energy to drive homeostatic compensation.

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Chapter 9

Effect of Environment on Immune Functions

Nicola Lacetera

Introduction

In 1965, Brambell suggested that a satisfactory environment is one that satisfies "the health and behavioral needs of the animals." Approximately 20 years later (1983), Webster proposed that a satisfactory environment may be defined according to criteria that include physical and thermal comfort, disease control, and behavioral satisfaction. Furthermore, describing what should be intended regarding disease control, Webster specified that "the environment should be such as to minimize disease, either by restricting the spread of infection or by avoiding stresses liable to decrease resistance to infections, or both."

This chapter will identify advances in the understanding of the influence that selected environmental factors may have on the immune system. Emphasis will be given to findings regarding food-producing animals and to some of the unfavorable environmental conditions that these animals are likely to be exposed to under intensive production systems.

The driving idea is that if we develop an understanding of which and how environmental factors affect immune processes, we may be able to prevent, predict, or counteract these changes and avoid or attenuate deleterious events, which may be consequent to alteration of the immune functions.

Immune Functions

Although several researchers indicated that the immune cells may respond to a variety of external or internal stimuli and regulate non-defensive functions (Haddad 2008; Hattori 2009), the immune system has evolved as a complex of mechanisms to protect the host from invasion

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by pathogenic organisms. The analysis of the non-defensive role of the immune system is beyond the scope of this chapter, which will thus deal only with the immune system's protective role against infectious agents.

Before the development of an acquired immune response to a pathogen, there are innate immune mechanisms, which provide some degree of protection from disease. The innate immune mechanisms are non-specific, in that they are effective against a variety of pathogens, they do not require prior exposure for their induction, and they include mechanical barriers, secreted products, inflammatory cells, and physiologic functions (Gershwin et al., 1995). The major functions of the innate immune system include recruitment of immune cells to infection sites throughout the production of chemical factors, which include specialized chemical mediators called cytokines; activation of the complement cascade; identification and removal of foreign substances by specialized white blood cells (phagocytes); and activation of the acquired immune system throughout a process known as antigen presentation.

The ability of the immune system to respond specifically to a foreign substance, commonly named an antigen, forms the basis for the acquired (specific) immunity. The initial exposure to an antigen (virus, bacteria, parasites, etc.) elicits a primary immune response, which serves to prime the immune system and to create a system of immunologic memory, such that subsequent exposure to the same antigen will elicit a faster, greater, and longer-lasting immune response than the initial exposure. The adaptive immune response may be considered as divided in three major phases: the antigen recognition and presentation phase, the phase of lymphocyte activation, and the effector phase (Tizard, 1992). The latter phase may be distinguished in humoral immunity, which deals with infectious agents present in the blood and body tissues and cell-mediated immunity, which deals with body cells that have been infected. In general terms, the humoral system is managed by B-lymphocytes (with help from specific subsets of T-lymphocytes), and the cell-mediated system is managed by T-lymphocytes. Both systems exhibit fascinating complexity and interrelationships that allow them to fine-tune the immune reactions to almost any antigen.

Environmental Parameters and Their Fffects on Immune Functions

The fundamental role of the immune system in a living organism is thus the defense against invading pathogens, and a large body of literature demonstrated that environment may impact efficiency in responding to challenges.

The following subchapters will take into consideration how selected environmental features may impact immune functions. Environmental parameters considered will be some of those that farm animals are more likely to be exposed to, especially under intensive production systems, and will be categorized as physical (space, temperature, and light), chemical (diet/metabolism and toxic substances), and social.

If housing certainly protects animals from adverse weather events and provides structured management (feeding, drinking, health check, etc.) under controlled conditions, housing and management must guarantee sufficient spaces, and proper conditions in terms of temperature, humidity, ventilation, gases, light, hygiene, and so on. This will avoid induction of repeated state of stress that may alter behavior, performance and health of food-producing animals (Ingvartsen and Andersen, 1993; Fisher et al., 1997a, 1997b).

Physical Environment

A general definition of the physical environment may be that it refers to the external, tangible surroundings in which an organism exists and which can influence its behavior, development, and health.

Space

Housing animals under restricted floor spacing has been and still is a frequent trend in many livestock production systems; the objective is to maximize pen efficiency and reduce facility cost per unit of production (Kornegay et al., 1993). However, it must be underlined that in several countries, the legislation in force on farm animal welfare gives emphasis to space allowances, and even if limited to some species, provides precise indications on minimum space to be guaranteed at farm level. Furthermore, for all species of food-producing animals, the same legislation also indicates the minimum space allowances to be ensured during transport. Also to be noticed is the fact that, when provided, precise prescriptions of minimum space were mainly based on results of literature data referred to physiological and/or behavioral measures of stress (i.e., hormones of the hypothalamic-pituitary-adrenal axis, aggressive behavior, etc.).

The following paragraphs will be aimed at reviewing literature data relative to the relationships between space allowances and immune functions in the principal farm animal species, and to understand whether results from different studies may permit us to draw conclusions on the optimal space to be guaranteed for optimal immune responses.

In a recent dairy ewes study, Caroprese et al. (2009) observed that increased space allowance positively affected milk yield and composition, mammary gland health (lower content of milk somatic cell counts), and humoral immunity, and that regardless of density, the availability of an outdoor area had a positive effect on cell-mediated immune response. Interestingly, this latter finding would testify the role of the "quality" of the space available.

Gupta et al. (2007) reported that housing finishing bulls at a reduced space allowance (1.2 vs. 2.7 and 4.2 m^2) did not alter average daily feed intake but reduced average daily gain without causing substantial alterations of immune parameters. Analogously, in two distinct studies carried out in finishing beef heifers, Fisher and colleagues (1997a, 1997b) observed that overcrowding (1.5m^2 average individual space allowance) had a detrimental effect on daily live weight-gain and no effects on anti-keyhole limpet haemocyanin (KLH) antibody responses. They indicated that 2.0 m^2 would be adequate for cattle of 450 to 500 kg initial body weight for a housing duration typical of a winter finishing period. Conversely, Hickey et al. (2003) reported that a space allowance of $<$2.0 m^2 per steer was responsible for an attenuation of the immune response, and Grasso et al. (1999) reported that a higher spatial density was associated with reduced cellular immunity, as measured by evaluating the hypersensitivity to an intradermal injection of phytohemagglutinin and lower antibody titres against KLH in buffalo calves.

Kornegay et al. (1993) reported that restriction of the floor space allowance in weanling pigs (0.14 vs.0.28 m^2/pig) decreased daily gain and daily feed intake, whereas gain/feed and humoral immune response, as measured by the level of antibodies produced after two injections of ovalbumin, were not affected. Conversely, in another pig study, Turner et al. (2000) observed that even if no benefit in performance was derived from offering growing pigs a large space allowance (32 kg/m^2), there was evidence for greater aggression and depressed immune response to inactivated Newcastle disease virus when housed at 50 kg/m^2; these results encourage the use of a larger space allowance. Furthermore, in a pig study

designed to determine a first estimate of space requirements for weaned pigs during summer transport, Sutherland et al. (2009) concluded that even if different space allowances during transport did not influence immune or physiological measures considered in the study, the greater neutrophil-to-lymphocyte ratio and increased standing behavior in pigs transported at 0.05 m^2/pig suggest that space allowances of 0.06 and 0.07 m^2/pig are preferable when transporting pigs during periods of hot weather. Finally, in a chicken study, Dafwang et al. (1987) observed that increasing stocking density improved the efficiency of food utilization and that high density regimen resulted in decreased weights of the bursa and thymus relative to body weight with no concurrent reductions in antibody response, spleen weight, or mortality in broiler chicks.

In synthesis, results from these studies discourage setting the minimum space allowances considering only reduction of the facility cost per unit of production and do not permit us to draw conclusions about the optimal space allowance for an optimal immune response. Furthermore, they highlight a certain degree of discrepancy that will also characterize the following section of this chapter.

Thermal Environment

For each species, strain, and individuals within species there is a range of environmental temperatures, defined as a thermoneutral zone (TZ), within which the metabolic heat production is unaffected by temperature change and homeothermic animals can maintain a fairly constant body temperature (heat loss is equal to heat gain) and an efficient level of growth, reproduction, and lactation. The TZ is bounded at its lower and upper ends by the lower critical temperature and upper critical temperature, respectively. Below the lower critical temperature and above the upper critical temperature, homeothermic animals must defend themselves against hypothermia (heat loss > heat gain) and hyperthermia (heat loss < heat gain), respectively. The constancy of body temperature outside the TZ is achieved by behavioral and physiological changes.

Several studies reported that exposure to temperature below the lower critical temperature (cold stress) or above the upper critical temperature (heat stress) may affect immuno responsiveness of food-producing animals (see Table 9.1).

Table 9.1. Effects of heat and cold stress on immune functions.

Species and Categories	Type of Stress	Effects	References
Dairy cows	Heat	Enhancement	Soper et al. 1978; Lacetera et al. 2005a
Chickens	Heat	Enhancement	Beard and Mitchell 1987
Chickens	Heat	Impairment	Regnier and Kelley 1981
Dairy cows	Heat	Impairment	Nardone et al. 1997; Lacetera et al. 2005a, 2006a
Weanling pigs	Heat	No effects	Bonnette et al. 1990
Chickens	Heat	No effects	Donker et al. 1990
Dairy cows	Heat	No effects	Lacetera et al. 2002a
Weaned pigs	Cold	Enhancement/ No effects	Jones et al. 2001
Fishes	Cold	Impairment	Engelsma et al. 2003
Chickens	Cold	Enhancement	Hangalapura et al. 2006

First of all, it should be noted that heat stress received greater attention than cold stress in the past. Furthermore, ongoing global warming, predicted highest frequencies of extreme climate events (e.g., heat waves), and general climatic scenarios relative to the next several decades encourage continuation of the studies in this area in attempts to identify adaptation measures, which may help food-producing animals keep efficient and healthy under conditions of climatic constraints (Segnalini et al., 2011).

A series of studies indicated that exposure to high ambient temperatures was associated with an enhancement of the immune response. Soper and colleagues (1978) described a summer increase in proliferation of mitogen-stimulated lymphocytes of Holstein dairy cows. Beard and Mitchell (1987) reported that geometric mean serologic hemagglutination-inhibition responses of chickens housed at extremely high temperatures for four days before being injected with an inactivated vaccine against Newcastle disease virus were significantly greater than those held at moderate temperatures. Accordingly, Lacetera et al. (2005a) demonstrated that severe heat stress was associated with enhancement of humoral immune response as measured by the in vitro immunoglobulin (Ig) M secretion from lymphocytes isolated from heat-stressed cows and stimulated with pokeweed mitogen.

Conversely, other authors reported an impairment of the immune response in heat-stressed animals: Regnier and Kelley (1981) reported that chronic exposure to heat-stress conditions impaired expression of contact sensitivity in vivo and proliferation of T-lymphocytes in vitro in the avian species; Nardone et al. (1997) indicated that conditions of severe heat stress during the dry period significantly reduced the concentration of colostral IgG and IgA in Holstein cows; Lacetera et al. (2005a) described a dramatic depression of the ability of lymphocytes isolated from severely heat-stressed peri-parturient dairy to proliferate in response to mitogens. Furthermore, Lacetera et al. (2006a) also reported that susceptibility to in vitro heat shock differed when comparing peripheral blood mononuclear cells isolated from Holstein or Brown Swiss cows, and that the ability of these cells to proliferate in response to mitogens is inversely related to gene expression of heat shock protein 72 kDa molecular weight.

Interestingly, in the 2005 ex vivo study carried out by Lacetera et al. in severely heat-stressed dairy cows, conditions of extreme heat were associated with the enhancement of humoral and impairment of cellular immunity. In the attempt to explain such apparent conflict, the authors suggested that the increase of plasma cortisol, and/or the body hyperthermia occurring in the heat-stressed cows, may have been responsible for a shift from a T-helper 1to a T-helper-2 pattern of immunity, with a consequent boost and suppression of humoral and cell-mediated immunity, respectively.

Finally, others reported that high environmental temperatures were not associated with changes in immune responses. Bonnette et al. (1990) observed that mitogen stimulation index of white blood cells and antibody titers against sheep red blood cells did not differ between weanling pigs housed at 19 or 30°C. Donker et al. (1990) reported that heat stress was found to have little or no effect on antibody production in two chicken lines selected for high and low immune responsiveness, and Lacetera et al. (2002a) described no effects of moderate heat stress on colostral immunoglobulins and cellular immunity in transition Holstein cows and on passive immunization of the offspring.

As already explained above, the effects of cold stress on immune parameters did not receive the same attention that was given to heat stress. In addition, it has to be noticed that most of the studies carried out in this field involved species (chickens and pigs) and/or age categories (young animals) known as having limited ability to avoid hypothermia under low environmental temperatures. Finally, in the context of the ongoing and predicted climate changes, it may be

supposed that the increase of temperatures during the winter season is likely to reduce the risk of exposure of intensively managed farm animals to cold challenges.

However, also in this case, the literature review reveals a large variety of results and experimental conditions. Jones et al. (2001) documented that a short-term cold stressor (12°C for 48 hours) in three-and-a-half week old piglets that had been given an oral dose of enterotoxigenic *E. coli* and a novel harmless antigen (ovalbumin) caused an increase of the IgG response to F4 (K88) fimbrial antigen and had no effects on antibody responses to ovalbumin or on lymphocyte proliferation assays.

In a fish study, Engelsma et al. (2003) observed that a relative mild and acute stress model for carp (a 3 h drop in ambient water temperature of 9°C) differentially altered the distribution of B-lymphocytes and granulocytes in blood, increased the percentage of apoptotic blood lymphocytes, and was associated with lower antibody titers to a T-lymphocyte-independent antigen.

Finally, in a chicken study carried out in 20-day old hens, Hangalapura et al. (2006) observed that cold stress (10 ± 0.4°C), irrespective of duration, enhanced expression of mRNA for pro-inflammatory (interleukin-1b, 6, and 12b), and the T-helper-2 (interleukin-4) cytokine genes.

The analytical evaluation of studies aimed at evaluating the effects of temperatures on immune response indicates that the type of effect that thermal stress may exert on immune functions (enhancement, suppression, or no effect) depend on several factors, which include: species, breed, genotype, age, social status, acclimation level, intensity and duration of the exposure to the unfavorable conditions, recovery opportunities, the immune parameter taken into account, the experimental models adopted (in vivo, ex vivo, and in vitro), and their interactions. It is likely that all these aspects provide a contribution in explaining the discrepancy among results from different studies and ultimately make difficult to design the optimal thermal environment for the immune functions.

Photoperiod

In addition to the well-known influence on reproduction and lactation (Dahl and Peticlerc, 2003), there is growing evidence that the wavelength, timing, and intensity of light contribute to immunomodulation in several species (Nelson et al., 1995; Haldar and Ahmad, 2010).

Ionizing and nonionizing ultraviolet radiation (below 400 nm) has been found to suppress immune function by a skin-mediated response. Instead, on the basis of literature data relative to visible light and referred to a variety of animal species, immune cell function is generally enhanced by exposure to short days. Visible radiation may affect the immune system through both skin and eye-brain mediated mechanisms. Therefore, specific areas of the brain such as the pituitary, hypothalamus, and pineal glands may receive stimuli to produce hormones that could affect immune functions (Haldar and Ahmad, 2010).

A series of studies performed on dairy cows revealed that short day photoperiods exert a positive impact on the immune status, and therefore photoperiod treatment may have potential immune benefits especially if realized during periods characterized by a tendency of cows to develop immuno suppression. First of all, Auchtung et al. (2003) reported that short day photoperiod was associated with greater lymphocyte proliferation in vitro, and that this was reversed with reversal of photo period treatment in Holstein steers. Thereafter, the same research group demonstrated that, relative to long days, short day length during the dry period increased neutrophil chemotaxis and lymphocyte proliferation in Holstein cows during both

the dry and postparturient periods (Auchtung et al., 2004). With regard to food-producing animals, further studies are necessary to establish whether both light wavelength and intensity may have a role in immunomodulation.

Chemical Environment

The chemical environment may be defined as that part of the animals' environment that is composed of chemicals (e.g., those contained in feed) and which can affect their metabolism, development, and health by influencing their bodies' internal environments. In the following sections, the effects of nutrients (direct and indirect effects) and of some toxic substances animals can consume through feeds will be considered.

Nutrients

Several studies documented that the nutritional status of a number of nutrients may influence the ability of human beings and domestic animals to mount an immune response (Kidd 2004; Fernandes 2008; Spears and Weiss 2008). In general terms, deficiency of nutrients interfering with the immune system functions is associated with immune suppression, whereas their excess may either enhance or depress immune functions.

In the wide context of nutritional immunology, particular attention was given to the immunomodulating action of vitamins. The immuno enhancing effects of vitamin E provided at concentrations higher than those normally considered sufficient has been pointed out in pigs (De la Fuente et al., 2000), trout (Puangkaew et al., 2004), cows (Spears and Weiss 2008), and chicks (Zhang et al., 2009). However, a study carried out measuring immune parameters in two genetic lines of White Leghorn chickens injected with sheep red blood cells and *E. coli* pointed out that genetic selection might have changed immune competence in relation to responses to high concentrations of dietary vitamin E, and the optimum dietary concentration of vitamin E depends on genotype, among other factors (Yang et al., 2000).

Vitamin A has also been shown to affect immuno responsiveness, even if, in this case, both deficiency and excess may cause immuno suppression and increased morbidity and mortality in chickens injected with pathogenic *E. coli* (Friedman et al., 1991). Furthermore, a study from Ametaj et al. (2000) also suggested that dietary excess of vitamins A and D inhibits interferon-gamma secretion in the naturally immuno suppressed post-parturient dairy cow. Furthermore, studies on human beings or laboratory animals also testified that availability of one nutrient may impair or enhance the action of another's effect on the immune system, as reported for vitamin E and selenium, vitamin E and vitamin A, zinc and copper, and fatty acids and vitamin A (Kubena and McMurray, 1996).

Finally it has also to be noticed that nutrient availability can modify the effects of unfavorable environmental factors on the immune system. In this context, Niu et al. (2009) reported that dietary selenium supplementation may counteract the alteration of both humoral and cellular immune response observed in heat-stressed broilers.

Although nutritionists have long been concerned with minimum nutrient requirements for maintenance, maximal growth rate, milk yield, or egg production, in the last few decades investigators began to look at the nutritional requirements that provide optimal immune responses, and started to make differentiation between requirements and recommendation. In other words, in line with what was already suggested by others for fat-soluble vitamins in dairy cows (Weiss, 1998), a requirement may be defined as: the amount of a nutrient needed

to maintain the animal's health, to guarantee successful reproduction, and an optimal level of growth, and milk or egg production under optimal environmental conditions. Whereas a recommendation would be: the amount of a nutrient that may also be beneficial to physiological functions (i.e., immune response) with the potential to affect health, reproduction and productive efficiency by indirect mechanisms.

Metabolic Status

The availability of nutrients may also affect the immune system by causing alterations of the metabolic status and changes of metabolite concentration. In this regard, several studies have been performed in peri-parturient dairy ruminants. In early lactating dairy cows and late pregnant sheep and goats, energy intake is usually lower than energy required for maintenance, milk production, or pregnancy, which results in negative energy balance (NEB) and mobilization of body reserves. Different studies also demonstrated that dairy cows, sheep, and goats are likely to suffer from immunodepression around parturition (Kehrli et al., 1998; Lacetera et al., 2004a, 2006b), and hypothesized that this may explain the higher incidence of infections in this period.

Several studies have thus been performed in the attempt to establish possible cause-and-effect relationships between NEB and impairment of the immune response in peri-parturient dairy ruminants. The first studies in this area were based on the observation that also ketotic ruminants are immune suppressed (Andersson, 1993; Suriyasathaporn et al., 1999), and were aimed at verifying the hypothesis that immune suppression under conditions of NEB might be due to increased concentration of ketone bodies (Targowski and Klucinski 1983; Franklin et al., 1991; Suriyasathaporn et al., 1999). However, results of those studies were conflicting and did not support this hypothesis. More recently, other authors (Lacetera et al., 2001) reported negative relationships between immune functions and plasma concentration of nonesterified fatty acids (NEFA), which also increase sharply in ketotic ruminants, and indicated plasma concentrations of these metabolites as possible diagnostic markers of impaired immunity around parturition. Following these observations, several studies have thus been performed to verify more accurately whether increased plasma NEFA may have a role in the immune suppression taking place around parturition. In vitro studies demonstrated that a mixture fatty acids reflecting the composition of ruminants' plasma NEFA at concentrations mimicking intense lipomobilization altered the ability of PBMC to proliferate or secrete IgM and interferon-γ in response to polyclonal stimuli (Lacetera et al., 2002b, 2004b) or viability and oxidative burst of polymorphonuclear cells (Scalia et al., 2006). Therefore, an ex vivo study revealed that the larger extent of lipomobilization taking place in over-conditioned cows compared to normal or thin cows was associated with a more pronounced immune depression around calving (Lacetera et al., 2005b).

Findings from these trials spurred several epidemiological studies aimed at establishing whether the amount of body fat and/or the intensity of lipomobilization around calving were associated with the susceptibility to infections in the same period. Hammon et al. (2006) reported that an intense lipomobilization around calving was associated with high incidence of metritis, and Rezamand et al. (2007) observed that cows identified with a new subclinical intrammammary infection had greater pre-partum body condition score, body weight, and greater body weight loss compared with cows that did not develop a new intrammammary infection. Finally, Moyes et al. (2010) reported that substances in blood, especially NEFA, may be potential markers for the risk of mastitis in early lactating dairy cows, and Ospina et al.

(2010) indicated that postpartum serum NEFA concentration was associated with the risk of developing metritis during the first 30 days in milk.

Studies focused on laboratory animals and humans indicated that cellular effects of fatty acids are attributable to partition of these highly hydrophobic molecules into cellular membranes with subsequent perturbation of their biophysical and functional properties (Anel et al., 1993). Incorporation of fatty acids into the cellular membranes of lymphocytes can negatively influence the fluidity of the lipid bilayer and render the cell membrane more rigid, consequently resulting in possible alterations involving transportation of ions or substrates into the cells, activity of membrane-associated enzymes and receptors, and activity of lymphocyte-signaling pathways (Richieri and Kleinfeld, 1989; Breittmayer et al., 1993; Calder and Newsholme, 1993). Analysis of results from another study (de Pablo and de Cienfuegos, 2000) suggests that the NEFA-related reduction of lymphocyte functions may also depend on suppression of cytokine synthesis. The mechanism involved in modification of cytokine synthesis attributable to fatty acids remains unclear, but a possible explanation could be found in regulation at the transcriptional level because fatty acids may inhibit cytokine mRNA production (Robinson et al., 1996). Additional mechanisms have been proposed to explain modulation of the immune system attributable to the effects of fatty acids. Among these are formation of lipid peroxides and eicosanoids, gene regulation, and apoptosis (de Pablo et al., 1999; Stulnig et al., 2000).

Toxic Substances

Farm animals are susceptible to a wide range of toxins, which may be naturally occurring in the environment (e.g., plants, microorganisms, etc.) or the product of chemical synthesis. A recent European study indicated that several plants and mycotoxins, a few pesticides and metals, together with contaminants of industrial origin, such as dioxins, are responsible for most of the recorded cases of poisoning, and that cattle are the species most frequently reported as affected (Guitart et al., 2010). Even if the effects of toxins (sublethal or lethal) depend on the doses, exposure types (acute, subacute, chronic and subchronic), and routes (oral, dermal, inhalation and injection), and on the animal species, several studies reported that numerous toxins may exert immunotoxic effects (Pistl et al., 2003; Salazar et al., 2008).

In farm animals, great attention has been given to the effects of mycotoxins that are a family of secondary metabolites of fungi that grow on a variety of feed consumed by animals, and that in their complex, may cause immuno-suppression by depressing T- or B-lymphocyte activity, suppressing antibody production, and impairing macrophage/neutrophil-effector functions (Oswald et al., 2005). Among fungal toxins, aflatoxin B1 (AFB1) and fumonisin B1 (FB1) are a matter of particular concern due to their worldwide diffusion, mainly as contaminants of cereals.

Social Environment

The social environment refers to interactions going on in groups of which an individual is a member and is under the influence of physical surroundings (e.g., space allowance) and community resources (e.g., availability of feed). Social confrontation with aggressive conspecifics may represent a meaningful source of daily stress, and a number of studies carried out in laboratory animals testified that even in a stable, social hierarchical rank, submissive animals may be subjected to higher levels of stress, with putative biological relevance to host susceptibility to disease.

In a recent review paper, Costa-Pinto et al. (2009) reported that submissive mice have a consistent reduction in oxidative burst and cytotoxicity of natural killer cells isolated from the spleen or blood targeting a tumor cell line and also a number of metastasis per animal 50% higher than in their dominant cage mates.

Furthermore, a series of studies also carried out in farm animals (mainly in pigs) provided support that social status may have an important role in mediating the effects of some environmental features on immune function (Salak-Johnson and McGlone 2007). Pyter et al. (2005) reported that social cues may interact with photoperiod to regulate seasonal adaptations of immunity in photoperiod-responsive rodents. Specifically, results from this study documented that photoperiod-induced regulation of immune function differed among individuals in heterosexual pairs, same-sex pairs, or isolation. In a pig study aimed at assessing interactions between heat stress and social status, Morrow-Tesch et al. (1994) reported that socially dominant or submissive pigs showed alterations in immune function (elevated numbers of neutrophils, decreased antibodyproduction) compared with socially intermediate pigs, and that thus, dominance, like submission, seems to have a cost in terms of immune efficiency. Finally, in another pig study, Sutherland et al. (2006) reported that pigs identified as submissive showed, under condition of crowding and heat stress, a stronger depression of the immune system than did their dominant counterparts.

Mechanism of Interactions between Environmental Features and Immune Functions

Understanding the mechanisms by which environmental features interact with the immune system may be of help in managing the environment for the best immune system performance, or at least in avoiding immune suppression states. However, the analysis of the environmental features considered in this chapter, outlines that different environmental factors interact with the immune system by different mechanisms.

Space allowance and social status are likely to interact with the immunological functions throughout the induction of a stress condition, which implies higher secretion of immunologically active hormones (e.g., glucocorticoids, endorphins, epinephrine and norepinephrine, etc.), which may substantially cause immunosuppression. Thermal environment may affect the immune system by complex mechanisms, which include body temperature changes, variations in feed intake and distribution of nutrients, behavioral and hormonal adaptation, circulatory adjustments, alteration of the acid-base and/or cation-anion balances, oxidative stress, an so on. As reported previously, light may interact with immune functions by skin- or brain-mediated mechanisms. In the latter case, the influence is mediated by the effects of light on melatonin and prolactin secretion, which can both have an immunomodulatory action. Finally, environmental features categorized as chemical (nutrients, metabolites, and toxic substances) exert their immunomodulatory effects by direct multiple and differentiated actions on cells of the immune system.

Concluding Remarks

As stated at the beginning of this chapter, understanding which and how environmental factors affect immune processes would provide instruments to avoid or attenuate deleterious events that may be consequent to their alteration. Impaired immune responsiveness in farm animals

may be responsible for significant economic losses, which may derive from higher susceptibility to infectious diseases, increased risk for reactivation of chronic infections, reduced efficacy of vaccinations and diagnostic testing (i.e., tuberculin skin testing), and lower drug efficacy. Conversely, the optimal functioning of the immune system has the potential to increase profitability of the livestock industry by reverse mechanisms. However, on this latter regard, it should also be taken into account that attempts to realize environmental conditions capable to ensure normal or enhanced immune response have to be compatible with other aspects, which also contribute to determine profitability (e.g., facility cost per unit of production, energy costs of cooling or warming, feed costs, etc.). Additionally, still in terms of profitability, different studies documented that immunity is a nutritionally costly process inducing a diversion of nutrients (e.g., glucose, amino acids, etc.) from productive to immunological tissues (Greer 2008), and that, therefore, interventions aimed at boosting the immune responses have the potential to exert deleterious effects on reproductive and productive efficiency.

However, as documented in this chapter, the number of environmental factors with the potential to affect immune responses, their variable degree in intensity and/or duration, the characteristics of the animals taken into consideration in terms of species, breed, social status, etc., and possible interactions among different environmental features are responsible for a frequent conflict among findings from different studies. This situation, in line with what has been already stated by others relative to stress conditions (Salak-Johnson and McGlone, 2007), thus make it difficult to reconcile the effects of the environment on the immune system into a cohesive and comprehensible set of universally applicable theories, which would allow us to design the environment for an optimal immune response compatible with farm profitability.

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Chapter 10

Strategies for Improvement of Thermal and Reproductive Responses under Heat Stress

David Wolfenson and William W. Thatcher

Introduction

Summer heat stress depresses both the milk production and reproductive performance of dairy cows. The use of efficient cooling systems is required because high milk-producing cows are not capable of maintaining normothermia in the summer. Cooling, if efficient enough, is capable of narrowing the gap between winter and summer milk production; however, its positive effect on fertility is limited. This is because the problem of low summer fertility is multifactorial in nature due to the fact that various tissues are being affected, and their function is disrupted under heat-stress conditions. Therefore, various hormonal approaches have been examined in the past to improve summer fertility. The objective of this chapter is to present central topics of heat-stress effects on reproduction and fertility in dairy cows. Among topics presented and examined are cooling approaches to ameliorate heat stress, heat-stress effects on ovarian follicular and corpus luteum responses, and strategies to improve ovarian function during summer. Programmed reproductive management approaches aimed to improve herd fertility on a seasonal basis are presented, and assessment of heat-stress effects during the periparturient period is characterized.

Severity of Heat Stress and Cooling Approaches

The disruptive level of thermal stress on fertility depends, first and foremost, on the severity of the heat stress. The best indication of strain is body temperature elevation above normothermia. However, a single daily measurement of body temperature, as provided in several studies and scientific reports, is not sufficient for estimating the severity of the thermal stress because severity depends on both the intensity and duration of the heat stress. In addition, the rise in

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body temperature strongly depends on the time at which it is recorded, as it is higher before or lower after a cooling period.

One of the most commonly used cooling systems in hot countries is based on spraying water to wet the skin, then facilitating its evaporation by air blown from fans that are positioned either at the parlor before milking (holding area) or along the feeding line (Flamenbaum et al., 1986; Bucklin et al., 1991; Berman and Wolfenson, 1992). Water sprinklers along the feeding line, which in the past were activated continuously during the daylight hours, are now only operational during specific time windows, when most cows in the barn are approaching the feeding line. This practice saves on energy and water usage and minimizes environmental pollution.

Efficient cooling requires several cooling windows consisting of cycles of water sprinkling (or spraying) and ventilation lasting at least 30 minutes. Figure 10.1 demonstrates the importance of efficient cooling. It shows the body temperature profiles of high-milk-yielding cows on three farms located in high-humidity regions in Israel (mean minimal and maximal air temperatures and relative humidities of 23.4 and 31.7°C, and 55 and 82%, respectively) that were cooled every two to four hours.

Typical fluctuations in body temperature over time, due to the activation of cooling sessions, are evident. Cows on farm A, subjected to five cooling periods per day in the holding area exhibit pronounced hyperthermia, with body temperatures above 39.5°C before noon and

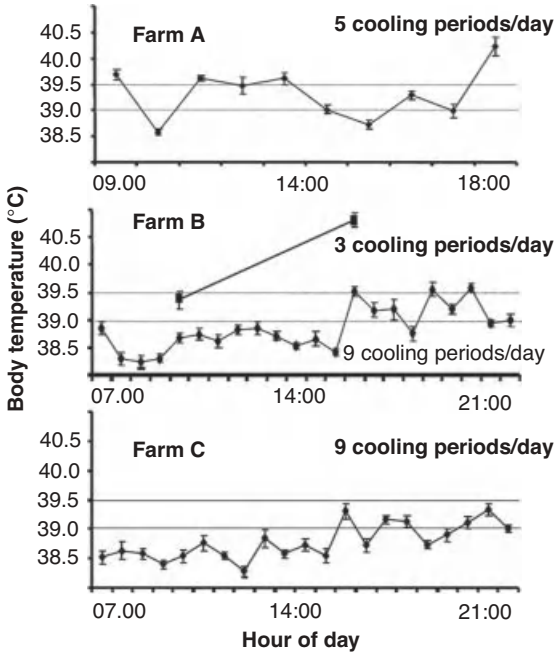

Figure 10.1. Body temperatures (means and SE) of cows exposed to heat stress during the summer in a high-humidity region in Israel. Cows were exposed to three, five, or nine cooling periods per day that comprised 30- to 60-minute cycles of sprinkling and ventilation. Each point represents measurements taken from 10 to 15 cows. Horizontal lines represent zones of normothermia (39°C) and mild hyperthermia (39.5°C).

above 40°C in the afternoon/evening hours. Cows on farms B and C, which were cooled in both the holding area and along the feeding line nine times per day, maintained a normothermic body temperature before noon and slight hyperthermia (39.0 to 39.5°C) in the afternoon hours. For comparison, a group of cows that were cooled only three times per day before milking on farm B exhibited severe hyperthermia in the afternoon hours, demonstrating the dependence of high-producing cows on efficient cooling for maintenance of normothermia.

Total cooling with an air-conditioned barn, either 24 hours a day or during only the daylight hours, resulted in normal pregnancy rates during the summer months in a sub-tropical environment with lactating dairy cows producing ~14 kg of milk daily in 1971 (Thatcher et al., 1974). However, the lactating dairy cows of today, producing 38 kg of milk daily, will have an estimated increase in energy expenditure of 21.55 Mcal/day (Net Energy for Lactation + Net Energy for Maintenance + Heat Increment). Consequently, a tremendous increase in heat exchange needs to be accommodated within a controlled environment of elevated summer temperatures to maintain a normal body temperature without decreasing dry matter intake, milk production, and pregnancy rate. This is a management challenge, and it is not surprising that heat abatement systems may not totally sustain normal pregnancy rates in the summer period. Pregnancy rate is particularly vulnerable because of the sensitivity of the oocyte and sperm at the time of insemination as well as the early developing embryo to an elevation in body temperature even for a short period of time. When uterine temperature the day after insemination is elevated 0.5°C above the mean of 38.3°C, conception rate is reduced 6.9% (Gwazdauskas et al., 1973). Thus a 38.8°C uterine temperature was associated with a decrease in conception rate. It is important to realize that mean uterine temperature was 0.2°C higher than rectal temperature. This uterine temperature relationship with conception rate is most likely similar among all cattle (e.g., *Bos taurus* and *Bos indicus,* lactating or non-lactating), but the environmental temperature to induce the detrimental threshold uterine temperature will depend upon the state of the animal (e.g., lactation or dry; cow's physiological heat dissipation capabilities; exposure to heat abatement facilities, etc.).

Temperature-Humidity Index (THI) has been used to integrate environmental temperature and relative humidity, and lactating cows are thought to experience no stress when THI is less than 72 and severe stress when THI exceeds 88. These classical guidelines may shift somewhat depending on amount of milk produced, degree of air movement, and direct solar radiation. For example, Zimbelman et al. (2009) reported that dairy cows producing more than 35 kg/day need additional cooling when average THI is 68 for more than 17 hours per day. However, the higher milk production and feed intake of cows today likely lowers the environmental conditions (e.g., THI) at which the cow begins to elevate her rectal and/or uterine temperature. Conversely, more intensive heat abatement systems are necessary to attenuate a diurnal rise in rectal or uterine temperature. As evident in Figure 10.1, intensive evaporative cooling with frequent intermittent use of fans and sprinklers resulted in body temperatures above 38.5°C in the afternoon hours that would be detrimental to conception rates.

Alternatively, more intensive and expensive cooling systems such as low profile cross ventilated (LPCV) free-stall buildings are an option for dairy cattle housing (Smith et al., 2008; Smith and Harner, 2012). These facilities allow producers to have control over a cow's environment during all seasons of the year. As a result, an environment similar to the thermoneutral zone of a dairy cow is more closely obtained in the summer, resulting in more stable core body temperatures. For example, a heat-stress audit evaluated the impact of a changing environment on the core body temperature of cows (Smith et al., 2008). Vaginal temperatures were collected from eight cows located in a LPCV facility with evaporation pads and fans and eight cows located in a naturally ventilated free-stall facility with soakers and fans. Vaginal

temperature was recorded every five minutes for 72 hours using data loggers (HOBO® U12) attached to a blank intravaginal CIDR device. Vaginal temperatures of cows housed in the LPCV facility were more consistent and did not reach the 38.9°C temperature recorded in the cows of the naturally ventilated facility with fans and soakers. However, even though cows in the LPCV facility have an attenuated fluctuation in vaginal temperature their temperatures did reach 38.8°C intermittently in the evening hours. Thus one would anticipate that there will be some reduction in pregnancy rate but not to the extent expected in the naturally ventilated free-stall facility with soakers and fans. Clearly, environmental modification with intensive whole animal cooling provides a means to enhance both milk production and reproductive efficiencies during the summer months, but with the high producing cows of the twenty-first century a full restoration of pregnancy rates to those seen in the cool season would be difficult.

Within the Holstein breed in the United States, the Predicted Transmitting Ability (PTA) for milk yield and heat tolerance was determined (Bohmanova et al., 2005; Misztal and Lovendahl, 2012). Heat tolerance PTAs of sires ranged from −0.48 to 0.38 kg milk per THI unit above 72 per day; milk yield PTAs for sires were between −8.9 and 7.9 kg per day. Based on estimated heat tolerance PTAs, the 100 most and 100 least heat tolerant sires were examined. Bulls that transmitted a high tolerance to heat stress had daughters with higher pregnancy rates, a longer productive life, but lower milk yields (Bohmanova et al., 2005). Continued selection for milk yield without consideration of heat tolerance will likely result in greater susceptibility to heat stress. Conversely, selection of bulls for heat tolerance will likely result in a decrease in milk yield. This is to be expected because as average production per cow increases the metabolic heat output increases, making cows more susceptible to heat stress. Nevertheless, when trying to match the dairy production system most practical with the local environment, use of bulls with a high PTA for heat tolerance that may also improve daughter pregnancy rate is an option for consideration.

Summary

During the summer, the high-milk-producing cow requires daily cooling to maintain body temperature within the range of normothermia to slight hyperthermia. Body temperature fluctuations during the day and particularly in the afternoon to evening hours, are practically unavoidable under open shed housing equipped with a common sprinkling and ventilation system. Maintenance of consistent normothermia during the summer under practical commercial farming conditions would require either use of total cooling systems (e.g., LPCV) or intensive and frequent cooling regimes that will vary with specific environmental conditions and level of milk production. Efficient cooling is a prerequisite for the improvement of summer fertility via other strategies such as hormonal manipulation and assisted reproductive technology. Both in-vivo and in-vitro studies (Putney et al., 1988, Rivera and Hansen, 2001) indicate that the level of hyperthermia correlates with the degree of embryo growth disruption in early pregnancy.

Ovarian Follicular Responses in the Summer and the Fall

In hot countries worldwide, fertility data show that the depressive effect of summer heat stress extends to the autumn months – October and November in the northern hemisphere. For instance, winter conception rates (pregnancies/AI) of 39% in high-milk-producing multiparous

cows in Israel drop to less than 20% in the summer, and to about 28% in the cooler autumn (Zeron et al., 2001). Pregnancies/AI on five large farms in California for 27,218 inseminations were 36.2%, 26.5%, and 31.8% for December-June, July-August, and September-November, respectively (Santos and Thatcher, unpublished observations). This indicates a carryover effect of summer heat stress on fertility in the cool autumn. It also shows that this deleterious carryover effect is transient in nature, because conception rate resumes normal values in early winter. Obvious targets, for the delayed disruptive effects of heat stress, are the ovarian follicles. This is because follicular growth is a long process, lasting on the order of months, and thus a small antral follicle exposed to thermal stress during the summer may carry the damage to later stages in the fall. Furthermore, the follicle is multi-compartmental relative to biosynthesis of steroids and intrafollicular communications between oocyte and follicular tissue.

In a seasonal study in Florida, the long-term disruptive effect of heat stress was reflected in a significantly higher concentration of circulating estradiol in early summer (July) than in late summer (September; Badinga et al., 1993). In another seasonal study it was shown that the first-wave dominant follicle on day 7 had 2.7 times higher concentrations of estradiol in the follicular fluid in the winter than in the fall (Wolfenson et al., 1997). In the same study, the theca cells were found to be more susceptible to thermal stress than the granulosa cells. Androstenedione production was lower in both summer and fall than in winter (see Fig. 10.2). These findings indicated that low concentrations of follicular estradiol during the autumn result primarily from low substrate production (androgen) for aromatization. Seasonal differences in follicular steroidogenic capacity may stem from a number of causes. First, a

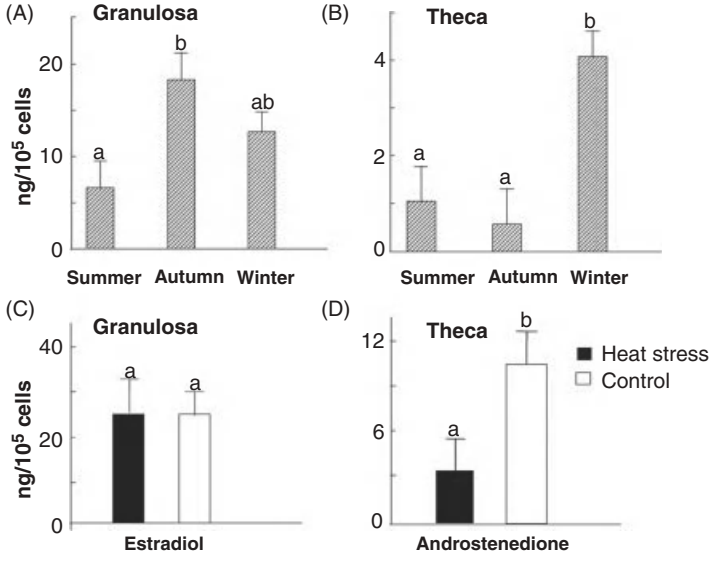

Figure 10.2. Upper panels A and B: Steroid production by granulosa cells and theca cells derived from dominant follicles on day 7 of the estrous cycle in cows during the summer, autumn, and winter following 18-h incubation. Lower panels C and D: Delayed effect of five-day heat exposure during days 2 thorugh 6 of the cycle on steroid production of granulosa and theca cells obtained, in the subsequent cycle, from preovulatory follicles 26 days later. Different letters indicate significant differences at $P < 0.05$.

heat-stress-induced decrease in feed intake, which has been documented in several studies (Flamenbaum et al., 1995; Rhoads et al., 2009) and is commonly regarded as an "indirect effect" of heat stress, may alter steroid production. Second, heat stress may alter gonadotropin secretion, which in turn, may affect follicular function (Gilad et al., 1993). Third, summer heat stress induces changes in follicular development that may not necessarily be related to alterations in gonadotropic secretion (Badinga et al., 1993; Wolfenson et al., 1995, Trout et al., 1998).

In a more controlled study, the possible delayed (carryover) effect of heat stress on follicular steroid production was examined about three weeks after a five-day period of heat exposure in an environmental chamber (Roth et al., 2001b; see Fig. 10.2). While both estradiol and androstenedione production by granulosa and theca cells were decreased by the heat stress in medium-size follicles, only the production of androgen was lower in the preovulatory follicles. Again, a clear delayed effect was evident. Similar to the seasonal study, the theca cells appeared to be more susceptible to heat stress than the granulosa cells. Although the reason for this is unknown, it might be related to later acquisition of steroidogenic capacity by granulosa cells versus theca cells during the process of follicular growth.

The above findings led to the assumption that the pool of antral follicles is damaged during the summer and that as long as those follicles are sustained in the ovaries, fertility will remain low, e.g. during the cooler autumn. A study was performed in which all small and medium-sized follicles (3 to 7 mm) were aspirated during the fall and early winter, in four consecutive estrous cycles, on days 4, 7, 11 and 15 of each cycle (Roth et al., 2001a; see Fig. 10.3). This actually enhanced the removal of follicles from the ovaries. Similar to the steroidogenic capacity of the follicles, results showed a clear delayed effect of summer heat stress on oocyte quality in the fall. Enhanced follicular removal led to earlier emergence of healthy follicles and high-quality oocytes during the fall.

A different approach used a hormonal (FSH) rather than mechanical treatment to stimulate turnover of follicles. Doses of FSH increased the number of medium-sized follicles in follicular waves following heat stress and induced an earlier emergence of high-quality oocytes (Roth et al., 2002; Friedman et al., 2010). Collectively, the above led to a series of studies that were aimed at improving follicle quality under heat stress. In one, the induction of several follicular cycles by repeated injections of GnRH and $PGF_{2\alpha}$ eliminated the disruptive effect of heat stress on follicular function (Guzeloglu et al., 2001). In another, stimulation of gonadotropins with GnRH improved follicular function, as frequent follicular waves induced by GnRH and $PGF_{2\alpha}$ during the fall increased follicular estradiol content in preovulatory follicles aspirated from previously heat-stressed cows (Roth et al., 2004).

It was thus hypothesized that induction of consecutive follicular waves by administration of GnRH + $PGF_{2\alpha}$ would improve fertility (Friedman et al., 2011). Three consecutive follicular waves induced by GnRH + $PGF_{2\alpha}$ during the summer and fall significantly improved conception rate in primiparous cows by 16%, and in cows with high body condition score postpartum by about 15%, compared to their untreated counterparts. A positive hormonal effect on conception was evident in efficiently cooled cows exhibiting a mild rise in body temperature, mainly in the afternoon hours. It is not clear why this treatment was effective in some cows but not in others, and this point warrants further investigation. It is possible, however, that a beneficial effect in primiparous cows is related to lower milk production, inducing lower endogenous heat production than in multiparous cows. It is interesting to note that Double Ovsynch (Souza et al., 2008) and Doublesynch (Ozturk et al., 2010) protocols, using other versions of the GnRH + $PGF_{2\alpha}$ combination in a season without heat stress, also had a beneficial effect on the fertility of primiparous cows but not in multiparous cows with higher milk production. This is a similar analogy to our finding under heat-stress conditions.

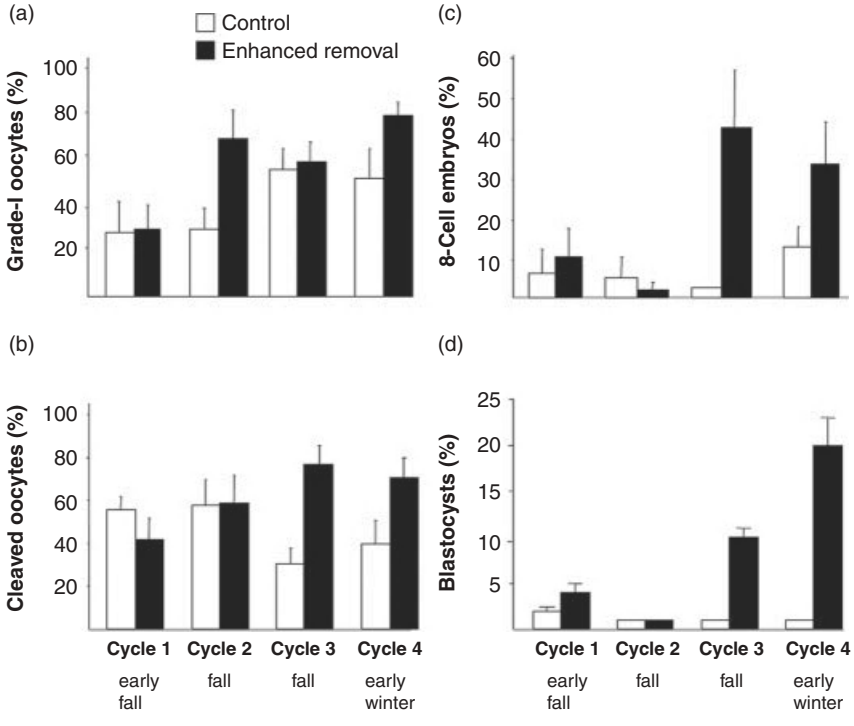

Figure 10.3. Percentages of (a) Grade-I oocytes, (b) cleaved oocytes, (c) 8-cell embryos, and (d) blastocysts, calculated from recovered oocytes, in control (n = 7 – 8, □) and treated (n = 7 – 8, ■) cows. Follicular aspiration was performed on day 4 of the oestrous cycle in the control cows and on days 4, 7, 11, and 15 in the treated cows, and $PGF_{2\alpha}$ and GnRH were injected on days 19 and 21, respectively, in both groups. Oocytes were recovered on day 4 of four consecutive oestrous cycles in late summer/early autumn (cycle 1), during the autumn (cycles 2–3) and early winter (cycle 4), following exposure to summer heat stress. For Grade-I oocytes, a treatment by cycle interaction was detected ($P < 0.05$); cleavage rate differs between treatments in cycles 3 and 4 ($P < 0.05$); For 8-cell embryos, a treatment main effect and a treatment by cycle interaction were detected ($P < 0.05$); for blastocysts, a treatment main effect was detected ($P < 0.05$). Values are means $\pm$ SEM.

Studies in Spain (López-Gatius, 2003) indicated that pregnancy per AI (P/AI) was lower in the warm season (27.4% <44.4%). During the warm season, P/AI decreased 6% for every 1,000 kg increase in annual milk production, whereas P/AI did not appear to be affected by increases in annual milk production during the cool season. Furthermore, the incidence of inactive ovaries (i.e., detection of no CL or presence of ovarian cyst) was higher in the warm season (i.e., warm versus cool season, 12.9 > 1.2% and 12.3 > 2.4%, respectively; Lopez-Gatius et al., 2001). These findings substantiate that aberrant follicle development occurs during the warm season. Reductions in plasma inhibin concentrations were detected in heat-stressed lactating dairy cows (Wolfenson et al., 1995; Roth et al., 2000). A depression of follicular dominance during periods of heat stress appears to be associated with a decrease in inhibin secretion by granulosa cells and subsequent alterations in FSH that leads to an increase in development of large follicles (e.g., non-ovulatory follicles and cysts). This may account

for the increase in twinning rate between May and July, following insemination of cows during the previous late summer and fall (Ryan and Boland, 1991). An increase in numbers of large follicles and double ovulations may occur in summer due to attenuated follicle dominance; however, due to elevated body temperature early embryo losses occur and pregnancies are not sustained. When body temperatures decline with lower ambient temperatures in early fall, cows undergo a transitional delay in recovery of follicle dominance, such that there is a temporal continuation of double ovulations with an influx of twin pregnancies. The marked detrimental elevations of elevated body temperatures causing embryo death cease. Gradually, ovarian follicle dominance is restored and the incidence of double ovulations and therefore twin pregnancies returns to normal. This temporal increase in twin pregnancies in early fall results in a subsequent summertime increase in twin births.

High environmental temperatures also increase late embryonic-fetal losses. The likelihood of pregnancy loss (i.e., from first diagnosis of pregnancy at 35 to 45 days to a second diagnosis at day 90) increased by a factor of 1.05 for each unit increase in mean maximum THI calculated from Days 21 to 30 of gestation. Pregnancy losses with maximum THI's of 55, 55–59, 60–64, 65–69, >69 were 0, 1, 2, 8, and 12%, respectively (Garcia-Ispierto et al., 2006).

Progesterone and Fertility in Heat-Stressed Cows

Following recruitment of a healthy preovulatory follicle, which results in a successful postovulatory fertilization are the processes associated with development of a corpus luteum (CL) and maintenance of pregnancy. Under normothermia, luteal insufficiency has long been linked to low fertility in cows. A major reason for this linkage is the fact that embryo mortality, from early stages after fertilization to detection of pregnancy on around days 40 through 45, is the major cause of low conception, and embryonic survival in the early stages of development is related to normal luteal progesterone secretion (Robinson et al., 2008). An association between normally high progesterone concentrations and more advanced embryo development has been shown as early as day 5 of pregnancy (Green et al., 2005). Progesterone is associated with oviductal and glandular endometrial secretions, acting through endometrial progesterone receptors. Nevertheless, progesterone supplementation during early pregnancy has proven beneficial to reproduction in some, but not all studies. A summary of several experiments performed under non-heat-stress conditions showed a significant, but not a pronounced rise (+5%) in pregnancy rate (Mann and Lamming, 1999). Interestingly, additional analysis indicated that if progesterone treatment was started after day 6 post-AI, improvement was minimal, whereas treatment begun before day 6 improved pregnancy rate by about 10%. Furthermore, a significant improvement (+19.3%) was noted when the initial fertility was low, while a small non-significant rise was noted when initial fertility was high.

Supplementation of exogenous progesterone under conditions of summer heat stress has the potential to improve fertility, provided that (a) the endogenous level of progesterone secretion is compromised, and (b) the thermal stress is at a level that permits embryo survival (e.g., mild hyperthermic conditions). This once again emphasizes the importance of implementing efficient heat abatement systems if further improvements in fertility are to be achieved. The wide variation in endogenous progesterone concentrations under thermal stress can be associated with several variables, such as adrenal release of progesterone, metabolism in the liver, hemodilution, the degree of hyperthermia, the age of the cow, its stage of lactation and milk yield, and the type of feeding (Jonsson et al., 1997; Trout et al., 1998). Nevertheless, the

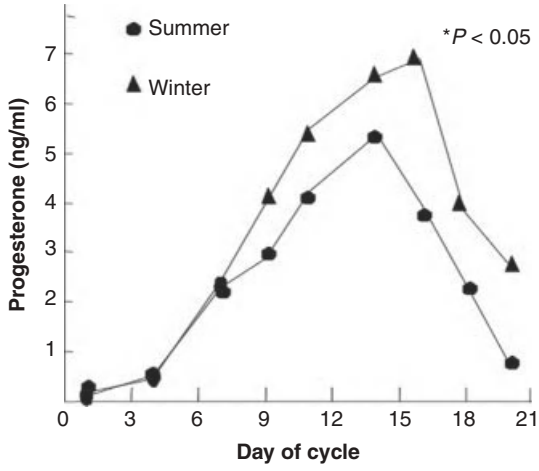

Figure 10.4. Plasma progesterone concentrations during the estrous cycle of cows in winter were significantly higher ($P < 0.05$) than those in the summer.

long-lived controversy, regarding the effect of heat stress on progesterone, most likely stems from differences in the types of thermal stress. The discrepancies among studies are probably attributable to the fact that most short-term, acute heat-stress experiments do not show the reduction in progesterone concentration that is obtained in most long-term, chronic, seasonal studies. In most studies with chronically heat-stressed cows in summer, concentrations of progesterone were lower (or tended to be lower) than those in cows cooled in the summer, or in cows in the spring or winter (Howell et al., 1994; Wolfenson et al., 1988a, 2002; Wise et al., 1988). Figure 10.4 shows a 25% decrease in plasma progesterone concentration in the summer compared to their winter counterparts (Wolfenson et al., 2002).

In contrast, in most studies in which cows were subjected to acute exposure for a few weeks to direct solar radiation or to high temperatures in environmental chambers, progesterone concentrations were either elevated or unaltered. Typical examples of this are the studies by Roman-Ponce et al. (1981), Gwazdauskas et al. (1981), Trout et al. (1998), and Wilson et al. (1998) in which cows were heat-stressed during the second half of the cycle, or in cows exposed to direct solar radiation during the entire estrous cycle (Roth et al., 2000). The higher concentration of progesterone found in acute-type studies has been hypothesized to be due to elevated adrenal secretion of progesterone or to the severity of the thermal stress (Bridges et al., 2005).

Decreased progesterone production under chronic, long-term, seasonal hyperthermic conditions could have several causes by: (a) disruption of luteinization of the CL; this was shown in rabbits exposed to heat during luteinization that exhibited depressed progesterone concentrations, unlike their counterparts exposed to heat stress after termination of luteinization (Wolfenson and Bloom, 1988); (b) depressed synthesis of progesterone, which is manifested in decreased in-vitro production of progesterone by luteal cells incubated at high temperatures (40°C vs. 38°C; Wolfenson et al., 1993); (c) the prominent difference between acute and chronic studies lies in the detrimental carryover effect of impaired preovulatory follicles exposed to long-term heat stress during the summer on the subsequently formed suboptimal corpus luteum (CL), which secretes lower amounts of progesterone. This was clearly

presented in a study in which heat-induced impairment of follicular function was carried over to the subsequently formed CL (Wolfenson et al., 2002). First-wave dominant follicles obtained from Holstein cows in the summer and winter were dissected on day 6 of the cycle, and the granulosa and theca cells were separated, dispersed, and cultured for 9 days to induce cell luteinization. Although follicle characteristics were similar in the two seasons, granulosa-derived large luteinized cells secreted lower progesterone in culture, and this was even more evident in theca-derived small luteinized cells (324 versus 100 ng progesterone/10^5 cells) obtained during the summer. Such a carryover effect is not seen when acute, short-term heat stress is imposed.

A possible approach to increase plasma progesterone post insemination is to induce ovulation of the first-wave dominant follicle with GnRH agonist or with hCG. Administration of hCG on day 5 or 6 post-AI to lactating cows in summer did not improve pregnancy rate (Schmitt et al., 1996). The authors speculated that the increase in plasma progesterone induced by hCG might have occurred at a time when survival of the embryo already was compromised by the stress of heat. Accordingly, in a similar study performed in Brazil on a limited number of cows (Beltran et al., 2008), a similar approach using hCG or GnRH on day 5 post-AI, improved conception rate in the summer, in cows that developed moderate (but not severe) hyperthermia.

Another approach to increase progesterone concentrations in inseminated cows in the summer is to insert an intravaginal device containing progesterone (CIDR) post AI. A recent study (Wolfenson et al., 2009) examined the effect of supplementing exogenous progesterone post-AI during the summer and autumn on fertility. The cows (n = 377) were efficiently cooled during the hot season in the feeding line and holding area (see Fig. 1, farms B and C). The study was conducted in Israel, with high milk-producing cows yielding, on average, 41.3 kg milk/day. Cows were inseminated following detection of estrus (day 0) during the summer and fall. Treated cows received a CIDR insert on day 5 ± 1 after AI for 13 days. Of importance was the observation that day of CIDR insertion tended to affect conception rate (43, 39 and 34% for insertion days 4, 5, and 6, respectively). Insertion earlier than day 4 will suppress conception rate in dairy heifers (Van Cleeff et al., 1991) possibly due to inducing an asynchrony in embryo development (i.e., stimulation in embryo development with advancement in uterine development) as well as a possible reduction in luteotrophic support of the developing CL due to a decrease in basal LH secretion. Overall, CIDR treatment numerically increased conception rate 6% but not significantly. However, the CIDR treatment increased conception rate by 22.5% ($P < 0.05$) in cows with low body condition score at peak lactation. Furthermore, cows that exhibited uterine disorders at parturition had an increase in conception rate from 25.6% to 47.8% ($P < 0.05$) with insertion of the CIDR device.

Summary

Chronic exposure to summer heat stress suppresses progesterone production from the CL components of the ovary. This was documented in an in-vitro study in which progesterone production by luteal cells obtained from cows in summer was lower than that by cells obtained in winter. Improving conception by exogenous progesterone supplementation under thermal stress requires that the level of hyperthermia be as mild as possible and that its daily duration be relatively short. A prerequisite for a beneficial effect is efficient cooling, otherwise embryos will not survive. Only specific physiological subgroups at high risk of suboptimal progesterone secretion (i.e., low body condition and uterine disorders at parturition) gain significant benefit from exogenous progesterone. The progesterone treatment has to be started early during embryo development (i.e., day 4 after AI).

Programmed Reproductive Management to Improve Herd Fertility Associated with Seasonal Heat Stress

Several reproductive management strategies have been implemented to improve P/AI during seasonal periods of heat stress. Increasing the submission rate of lactating cows to be artificially inseminated prior to the beginning of the heat stress summer season is a logical strategy. Current timed AI programs, in which all cows treated are also inseminated, can achieve pregnancy per AI rates of 40 to 45% (Santos et al., 2010). Such programs have optimized follicle dominance of the recruited follicle destined to be the ovulatory follicle following insemination, insured that progesterone and presence of a CL are present throughout the phase of follicular recruitment, and optimized the timing of insemination relative to the temporal events of induced CL regression and induction of ovulation. Such programs require a high degree of compliance in implementing the protocols.

Dairy Cows in Confinement

Within a confinement system involving free stall barns with heat abatement (i.e., fans and sprinklers), implementation of a timed AI program to compensate for attenuated expression of estrus and reduced heat detection rates in summer is an alternative. During the summer months, a standard Timed Artificial Insemination (TAI) program (i.e., Ovsynch) increased pregnancy rate at 120 d postpartum (27% vs. 16.5%, respectively), decreased days open, and reduced both the interval from calving to first breeding and services per conception compared to lactating dairy cows inseminated at estrus (De la Sota et al., 1998).

Injection of lactating dairy cows with GnRH at detected estrus during summer in Mississippi (Ullah et al., 1996) and within two hours from onset of standing estrus during summer and autumn in Israel (Kaim et al., 2003) increased conception rates from 18 to 29% and 41 to 56%, respectively. These findings are encouraging; however, if implemented it is vital that lactating dairy cows be managed under an efficient heat abatement system of intensive cooling. Otherwise, the reproductive manipulation has a low chance of success.

Grazing Dairy Cows

Seasonal breeding is a strategy to program insemination periods to non-heat stressed climatic conditions and at a time of available forage of adequate quality on grazing dairies. Cows must become pregnant in a short and programmed period of time prior to the heat-stressful period to maximize overall efficiency of production. Such a program on a grazing dairy in the subtropical environment of Florida was examined (Ribeiro et al., 2011). Lactating cows ($n = 1264$) were randomly assigned, between January to April, to treatments of a 2×2 factorial experiment: 1) Presynch 1: two injections of $PGF_{2\alpha}$ given 14 d apart and starting the TAI protocol 11 d later; 2) Presynch 2: one injection of $PGF_{2\alpha}$ followed 3 d later by injection of GnRH and starting the TAI protocol with GnRH 6 d later (G6G). The TAI protocol for first insemination consisted of GnRH on day 0, $PGF_{2\alpha}$ on d 5 and d 6, and GnRH + TAI on d 8. On d 12 after the TAI, half of the cows in each pre-synchronization treatment received one of two re-synchronizations: 1) re-synchronization control (RCON) cows were observed daily for estrus and inseminated starting on d 19 after TAI; 2) re-synchronization CIDR

(RCIDR) cows received a CIDR from d 12 to 19 after the first TAI and were observed for estrus and inseminated between d 19 and 35. At d 35, cows were exposed to bulls for a 65-d period so that the entire controlled breeding period was 100 d. Pregnancy diagnoses by ultrasound were done at 30 and 60 d after first TAI, 30 and 65 d after the re-synchronized AI, and at 30 d intervals following introduction of bulls. The P/AI rate following the first TAI (P/TAI; 44.3%), to re-synchronized detected estruses (P/Re-synchronized AI; 16.8%), and to the bulls (P to Bulls; 21.4%) did not differ between the four treatment groups. The overall pregnancy rate for the 100-d breeding season was 82.5%. Clearly a targeted seasonal sequential breeding program of a presynchronization/synchronized TAI followed by insemination at detected estrus and use of clean up bulls was an effective strategy to obtain a large number of pregnant cows early in the seasonal breeding season to avoid the impending summer period of heat stress.

Seasonal Evaluation of Heat Abatement

Over the last decade, Flamenbaum and co-workers conducted extensive surveys of the dairy farms in cooperation with the Israel Cattle Breeders Association (ICBA). The aim of these studies was to evaluate the effect of cooling systems, installed on commercial farms, on the response of productive and reproductive traits of high-yielding Holstein lactating cows. Specifically, ratios between summer and winter daily production of economical corrected milk (ECM) and conception rates were examined. A complete summary of the various surveys was described (Flamenbaum, 2010). Summer to winter (S:W) ECM ratios for each herd served as the response indicator by which the 24 top farms for economical corrected milk (ECM) ratio were compared to the 24 farms with the lowest ECM ratios. It was assumed that the difference between the productive ratios of these two groups represented the combined effect of cooling and better summer management on annual milk yield and reproduction traits. The average herd size of farms in the study was 400 cows, so the comparison includes nearly 10,000 cows in each group. Initial averages for productive and reproductive traits for the “high” and “low” ratio groups are presented in Table 10.1. The fact that the average winter milk production was similar in both groups supported the supposition that most of the differences in the S:W ratio among farms in the two groups can be related to better management in the summer for the high ratio group. Indeed summer conception rates in either grouping were not equivalent to the winter period. However, the mean decrease in conception rate of the high S:W ratio group was less, such that this grouping achieved 68% of the winter conception rate (i.e., 27/40∗100). In contrast, farms in the low S:W ratio group for ECM had a lower summer conception rate achieving 53% of their winter conception rate. Alternatively, summer period conception rates were 8% greater in the herds with a high S:W ratio for economical corrected milk.

Collectively, this type of record analysis of S:W ratios identifies farms that can improve their intensive cooling systems, with perhaps closer attention to proper maintenance of the systems to get maximal cooling and management of the cows during the heat stressful period. Basically the results indicate that cows in either grouping did not differ in either milk production or conception rate in the winter months. Results further demonstrate that in high producing cows an improved summer management program makes it possible to maintain milk production very close (98%) to that of winter; whereas, it is difficult to get sufficient heat stress abatement in summer to sustain reproductive function at the level obtained during the winter. Once again, it demonstrates the susceptibility of the reproductive system to thermal stress.

Table 10.1. Summer and winter averages of economical corrected milk (ECM) and conception rate CR for first three inseminations and their ratios in high and low ratio herds.

Group		
High S:W ratio	Low S:W ratio	Parameter
24	24	No. Herds
39.7	39.5	Winter Milk Production (kg/d)
38.9	34.4	Summer Milk Production (kg/d)
0.98	**0.87**	S:W ECM ratio
40	36	Winter Conception Rate (%)
27	19	Summer Conception Rate (%)
0.68	0.53	S:W Conception Rate ratio

Additional strategies involving assisted reproductive technology such as timed embryo transfer using sexed embryos to bypass the early periods of embryo sensitivity to heat stress are covered extensively by Hansen (2012).

Heat-Stress Effects during the Periparturient Period

When dairy cattle are heat stressed during the last two to three months of pregnancy, there are clear reductions in placental function (e.g., reduced concentrations of estrone sulfate), calf birth weight, and subsequent milk production during the ensuing lactation (Collier et al., 1982; Moore et al., 1992; Wolfenson et al., 1988b). Indeed, cooling of dry cows during the latter stages of pregnancy is an efficient means to improve animal productivity; this is a physiologically sensitive period that often is ignored by producers. Maintenance of fetal growth and maternal mammary gland function after parturition likely would enhance neonatal survival and production of milk.

Estimates for degree of heat stress in late pregnancy, as measured by Maximum Prepartum Degree-Days (MPDD) above 32.2°C computed as a summation of values during the last 60 days prepartum for each animal, was quantified on subsequent reproductive responses and body condition score postpartum (Avendano-Reyes et al., 2010). The period of parturitions encompassed the months of July through October in Mississippi in the United States. There were no detected gradient effects of accumulated heat stress prepartum on reproductive events such as days open or services per conception. Nevertheless, cows undergoing parturition in July and August had increased number of services per pregnancy relative to cows calving in October. Primiparous and multiparous cows that lost body condition score (BCS) from calving to 60 d postpartum experienced more days open than cows that gained BCS. Multiparous cows with higher BCS at calving were more prone to experience dystocia. Thus parturition during the hot months did influence subsequent reproduction but was not related to gradient differences in heat stress. Perhaps there is a threshold temperature stress response above which long-term herd reproductive responses were attenuated.

Lactating cows lose body condition during the postpartum period for 50 to 100 d due to homeorhetic changes that occur in the somatotropic axis, sensitivity of peripheral tissues to insulin, and upregulation of lipolytic pathways in adipose tissue (Roche, 2009). Indeed the inherent drive to nurture the calf from tissue stores results in both lipolysis and muscle catabolism and is also associated with concurrent changes in massive involution of uterine

tissue. Normally it is difficult to alter the loss in body condition during the first 4 weeks following parturition. However, management and nutrition can influence the recoupling of the somatotropic axis and restoration of tissue sensitivity of peripheral tissues to insulin. What is not presently understood is the response of homeorhetic and homeostatic mechanisms during this early postpartum transitional period to heat stress. The findings of Rhoads and colleagues (Rhoads et al., 2009, 2010) clearly indicate that decreases in milk production in response to heat stress are far greater than can be explained by declines in feed intake. The increase in energy for maintenance increases when lactating dairy cows are heat stressed, and to meet the energy needs glucose utilization by peripheral tissues is enhanced and lipolysis is reduced (Wheelock et al., 2010). As a consequence, glucose availability for the mammary gland is reduced. How these coordinated changes in nutrient utilization influence ovarian follicular recrudescence, uterine function, and embryo development are not as yet documented. Consequently, targeted strategies to optimize reproductive performance during periods of heat stress are presently limited to efficient systems of heat abatement and dietary manipulations both to maximize availability of propionate and reduce heat increment of diets.

Heat-stress abatement in the dry period improves subsequent lactation, possibly via suppression of the plasma prolactin surge around calving (Amaral et al., 2009) and alterations in peripheral lymphocyte function (Amaral et al., 2010).

Synopsis

Summer heat stress is probably the most effective stress lowering fertility of dairy cows worldwide. A prerequisite to any hormonal, nutritional or assisted reproductive technology to improve summer fertility is an efficient alleviation of the stress of heat. The best indicator for this is maintenance of normothermic, or close to normothermic, body temperatures throughout the 24-hour cycle. Summer heat stress affects the functions of ovarian follicles and their enclosed oocytes, as well as the subsequently formed corpora lutea. Potential hormonal strategies to improve summer fertility include: first, induction of consecutive follicular waves by GnRH + $PGF_{2\alpha}$, which was found to be effective for primiparous cows and cows with high body condition; second, supplementation of progesterone after insemination with an intravaginal CIDR device improved P/AI of cows with low body condition and those that experienced postpartum uterine diseases. Another option in hot climates is to consider use of AI bulls with high Predicted Transmitting Ability for heat tolerance in order to obtain a higher daughter pregnancy rate, although milk yield likely will be reduced. Programmed reproductive management tools such as timed AI programs, in which all cows treated also are inseminated, can increase pregnancy rates in summer. Seasonal controlled breeding during non-heat stressed climatic conditions could be beneficial particularly to grazing dairies. Milk production and reproduction record analyses involving calculations of summer-to-winter ratios will identify farms that can further improve their cooling systems to ultimately improve reproductive performance during the heat stressful period. Heat stress abatement during the dry period improves calf birth weight and subsequent milk production of the cow. Body condition changes postpartum influence, subsequent reproductive performance, and reflects net effects of homeorhetic and homeostatic regulations of metabolism to support milk production. Heat stress alters these regulatory systems in a manner to maintain a normothermic status. The impact of these regulatory changes and their management (e.g., nutritional and heat abatement) to optimize both efficiencies of reproduction and milk production are under intensive investigation.

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Chapter 11

Prospects for Improving Fertility during Heat Stress by Increasing Embryonic Resistance to Elevated Temperature

Peter J. Hansen

Introduction

Exploiting Embryo Plasticity to Improve Fertility during Heat Stress

The large decline in fertility in lactating dairy cows caused by heat stress is the result of a variety of adverse changes in the function of the follicle, corpus luteum, oocyte, and embryo (Wolfenson et al., 2000; Hansen, 2007a, 2007b). Many attempts at manipulating the heat-stressed cow physiologically to reduce these changes or to overcome their consequences for fertility have not been successful. Among the failed approaches for enhancing fertility in the summer are administration of human chorionic gonadotropin at day 5 after estrus to improve luteal function (Schmitt et al., 1996; Santos et al., 2001) and administration of gonadotropin releasing hormone (GnRH) at day 14 after breeding to delay luteolysis (Franco et al., 2006). There is one report that administration of GnRH at insemination or 12 days later can improve fertility of lactating cows during heat stress (López-Gatius et al., 2006). Timed artificial insemination programs can overcome effects of heat stress on estrus detection because the need for estrus detection is eliminated, but pregnancy rates remain low (Aréchiga et al., 1998a; de la Sota et al., 1998; Cartmill et al., 2001).

Fertility of the heat-stressed cow is already compromised at the moment of insemination because the oocyte is damaged by heat stress during follicular growth and oocyte maturation (Hansen, 2007b). Following fertilization, the embryo itself is susceptible to further disruption by maternal hyperthermia (Hansen, 2007a, 2007b). Thus, successful pregnancy during heat stress requires that the oocyte not be so damaged by heat stress as to prevent fertilization and formation of an embryo and that the embryo escapes the block to development caused by exposure to elevated temperature.

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Despite these formidable obstacles on the pathway to a successful pregnancy, there are opportunities to manipulate embryonic resistance to elevated temperature and so improve fertility during heat stress. One of these opportunities, represented by the use of embryo transfer, has been realized so that pregnancy rates in hot weather similar to those achieved in cool weather can be obtained using this assisted reproduction technology. Other opportunities, involving physiological, nutritional, and genetic regulation of embryonic susceptibility to maternal hyperthermia, have not yielded similar successes. The purpose of this paper is to identify determinants of embryonic resistance to elevated temperatures in the reproductive tract and describe how manipulation of these determinants might be used to improve pregnancy rates in the summer.

Circumvention of Embryo Susceptibility to Elevated Temperature: Using Embryo Transfer

As the bovine embryo advances in development, it becomes more resistant to disruption by elevated temperature in vitro or in vivo (Hansen et al., 2007a). Thus, exposure to heat stress on day 1 after breeding caused a reduction in the number of embryos becoming blastocysts while heat stress at days 3, 5, or 7 had no effect (Ealy et al., 1993). Not surprisingly, then, embryo transfer can improve pregnancy rate in the summer because it involves placement of an embryo into the reproductive tract at day 7 of gestation when the embryo has already passed the most thermosensitive period. A summary of studies demonstrating this benefit of embryo transfer is shown in Table 11.1.

Embryo transfer can improve pregnancy rate in the summer when embryos are produced by superovulation (Putney et al., 1989; Drost et al., 1999; Rodriques et al., 2004) or in vitro

Table 11.1. Improvement in fertility during heat stress by use of embryo transfer.

Location	Treatment[a]	Time of Pregnancy Diagnosis	Pregnancy Rate (%)[b]	Reference
Florida	AI	45–60	14	Putney et al., 1989
	MOET-Fresh		29	
Florida	AI	42	21	Drost et al., 1999
	MOET-Cryo		35	
	ET-IVP-Cryo		19	
Florida	TAI	45–52	5	Ambrose et al., 1999
	TET-IVP-Fresh		14	
	TET-IVP-Cryo		5	
Florida	TAI	45	6	Al-Katanani et al., 2002
	TET-IVP-Fresh		19	
	TET-IVP-Cryo		7	
Texas	TAI	97	17	Stewart et al., 2010
	TET-IVP-Fresh		36	
	TRT-IVP-Cryo		26	

[a]Abbreviations are as follows: AI, artificial insemination; Cryo, cryopreserved; ET, embryo transfer; IVP, in vitro produced embryo; MOET, multiple ovulation embryo transfer; TAI, timed artificial insemination; TET, timed embryo transfer. Embryos were either transferred fresh or after cryopreservation.
[b]Percent of cows that were inseminated or received an embryo that were diagnosed pregnant.

Table 11.2. Seasonal variation in pregnancy rates in lactating cows used as embryo transfer recipients in hot climates.

Location	Embryo Type[a]	Time of Pregnancy Diagnosis	Time of Year	Pregnancy or Calving Rate (%)[b]	Reference
Southwestern United States	MOET-Fresh	40–60	Average dry bulb temperature	51	Putney et al., 1988
			<27°C		
			27–32	57	
			32–40	62	
			>40	73	
Florida	ET-IVP-Fresh	Calving	Winter	23	Block and Hansen, 2007
			Summer	13	
Florida	ET-IVP-Fresh	Calving	Winter	23	Loureiro et al., 2009
			Summer	27	

[a]Abbreviations are as follows: ET-IVF-Fresh, embryo transfer with a fresh in vitro produced embryo; MOET, multiple ovulation embryo transfer.
[b]Percent of cows that received an embryo that were diagnosed pregnant or calved.

fertilization (Ambrose et al., 1999; Al-Katanani et al., 2002; Stewart et al., 2010). In general, embryos produced by superovulation have higher competence for establishment of pregnancy after transfer than embryos produced in vitro and are more likely to survive cryopreservation (Hansen and Block, 2004). Indeed, the improvement in pregnancy rates in the summer caused by transfer of an in vitro produced embryo has only been observed when fresh embryos were transferred (Ambrose et al., 1999; Al-Katanani et al., 2002). The use of new culture media to produce an embryo more resistant to cryopreservation has resulted in higher pregnancy rates after transfer of a cryopreserved embryo than was achieved earlier (Stewart et al., 2010). Nonetheless, pregnancy rates remain lower than after transfer of a fresh embryo and are not substantially different from pregnancy rates after artificial insemination (Stewart et al., 2010).

One would expect little seasonal variation in pregnancy rate in embryo transfer recipients. Some results on seasonal variation in fertility of embryo transfer recipients are summarized in Table 11.2. Indeed, there was no difference in pregnancy rate between lactating recipients in cool versus hot weather in several studies (Putney et al., 1988; Drost et al., 1999; Rodriques et al., 2004; Loureiro et al., 2009). In others, however, pregnancy rates were lower for recipients in summer (Block and Hansen, 2007) or were inversely related to rectal temperatures of the recipients at the time of transfer (Vasconcelos et al., 2006). There are reports that late embryonic and fetal losses were greater for cows that became pregnant in the summer (Garcia-Ispíerto et al., 2006; Santolaria et al., 2010). It is possible, therefore, that seasonal variation in pregnancy rates in embryo transfer recipients, when occurring, could reflect, at least in part, effects of heat stress later in pregnancy. Little is known about the causes of late embryonic mortality associated with heat stress.

De Vries (personal communication) has estimated that, assuming a $60 cost and a pregnancy rate that is 150% of AI, transfer of sexed embryos can increase profitability by about $24 per cow. In many cases, the cost of an embryo produced by superovulation or by in vitro fertilization of oocytes harvested by transvaginal ultrasound guided aspiration would exceed the $60 cost. Rather, an embryo produced in vitro using an oocyte collected from abattoir ovaries is the most profitable when considerations of genetic selection are not tantamount. The actual profitability

of embryo transfer is also likely to depend on seasonal variation in milk price, the value of maintaining constant numbers of lactating cows each month, and other factors.

Prospects for Using Thermoprotective Molecules to Improve Fertility during Heat Stress: The IGF-1 Example

Cells possess a variety of biochemical mechanisms to survive exposure to elevated temperature, with the most well understood mechanisms involving production of heat shock proteins to stabilize protein structure and block apoptosis (Kregel et al., 2002). Cellular thermotolerance is not a fixed property of cells but rather can be modified by physiological, nutritional, and genetic inputs. Among the physiological signals that can increase cellular resistance to elevated temperature is insulin-like growth factor-1 (IGF1). Exposure of cultured bovine embryos to 100 ng/ml IGF1 at day 5 after insemination reduced effects of elevated temperature on subsequent development and the percent of blastomeres undergoing apoptosis (Jousan and Hansen, 2004, 2007). Insulin-like growth factor-1 also protects embryos from the pro-oxidant menadione (Moss and Hansen, 2009).

As shown in Table 11.3, culture of embryos with IGF1 resulted in greater pregnancy rates after transfer into heat-stressed recipients as compared to results for control embryos. This beneficial effect is not simply the result of thermotolerance because the pregnancy rate achieved after transfer of IGF1-treated embryos in the summer exceeded the pregnancy rate after transfer of control embryos in the winter. These results are interpreted as indicating that one or more beneficial effects of IGF1 on competence of the embryo for post-transfer survival can only be expressed during the summer. Perhaps, a change in the oocyte or recipient alters responsiveness to IGF1.

Two experiments have been conducted to test whether treatment with bovine somatotropin (BST) increases pregnancy rate in the summer (Table 11.4). The rationale was that BST would increase IGF1 secretion and the elevation in IGF1 would protect the oocyte and embryo from damage caused by heat shock. In the first experiment (Jousan et al., 2007), cows subjected to a modified Ovsynch protocol were given BST at 2 weeks intervals beginning 1 week before the initiation of the protocol. There was no significant effect of BST treatment on first service pregnancy rate. Moreover, BST increased rectal temperature. A second experiment was designed to avoid any potential negative effects of increased body temperature caused by BST. In this experiment, a single injection of BST was administered 3 days before insemination

Table 11.3. Interactions between season of embryo transfer and culture with insulin-like growth factor 1 (IGF1) on calving rate of lactating cows in Florida.

Season	Treatment	Calving Rate (% of Cows Receiving an Embryo)	Reference
Winter	Control	23	Block et al., 2007
Winter	IGF1	18	
Summer	Control	13	
Summer	IGF1	33	
Winter	Control	23	Loureiro et al., 2009
Winter	IGF1	25	
Summer	Control	27	
Summer	IGF1	40	

Table 11.4. Effect of administration of bovine somatotropin (BST) on first service pregnancy rate (percent that were diagnosed pregnant) for lactating cows in the summer (Florida).

Treatment	Timing of BST	Pregnancy Rate (%)	Reference
Control	One week before a modified Ovsynch and two weeks thereafter	15	Jousan et al., 2007
BST		17	
Control	Single injection three days before insemination	18	Bell et al., 2008
BST		24	

(Bell et al., 2008). There was no significant effect of BST on pregnancy rate but, numerically, values were higher for BST-treated cows (24% vs. 18%). Further research is required to determine whether there is benefit in administering BST to improve fertility in the summer.

Effects of BST on fertility, if occurring, may represent actions other than those mediated through the thermoprotective actions of IGF1. Indeed, the two-cell embryo, which is more susceptible to heat shock than day 5 embryos (Hansen, 2007b), is refractory to thermoprotective actions of IGF1 (Bonilla, et al. 2011). In the experiment by Bell et al. (2008), BST tended to increase the percent of cows that ovulated (81% vs. 73%, $P = 0.10$). Therefore, some of the beneficial effect of BST on fertility, if real, represents increased ovulation response to synchronization rather than increased fertility.

Antioxidants

Lactating cows exposed to heat stress have been reported to experience an increase in production of reactive oxygen species (Bernabucci et al., 2002). In addition, bovine embryos exposed to 41°C in vitro had greater reactive oxygen species (ROS) production at day 0 and 2 after fertilization than control embryos but not at day 4 or 6 (Sakatani et al., 2004). Intracellular concentrations of glutathione, the major cytosolic antioxidant in cells, were lowest at the two-cell stage (Lim et al., 1996). Therefore, free radical production is greatest, and antioxidant defenses are lowest, at the early stages of embryonic development most sensitive to elevated temperature (Hansen, 2007b). Further evidence that ROS are involved in embryonic death caused by heat stress is the observation that administration of melatonin, an indoleamine with antioxidant properties, reduced effects of heat stress on embryonic survival in mice (Matsuzuka et al., 2004).

In lactating dairy cows, Aréchiga et al. (1998a) found that feeding a diet formulated to contain an additional 400 mg/d β-carotene for at least 90 days beginning at approximately 15 days postpartum increased the proportion of cows pregnant at 120 days postpartum during heat stress but not in the absence of heat stress. In contrast, short-term administration of vitamin E (Ealy et al., 1994) or β-carotene (Aréchiga et al., 1998b) had no effect on fertility during heat stress. Similarly, multiple injections of vitamin E and selenium before and after calving did not improve fertility (Paula-Lopes et al., 2003). The failure of short-term or intermittent treatment with antioxidants to improve fertility could mean that concentrations of antioxidants are not maintained at adequate concentrations in the reproductive tract to provide optimal protection to the oocyte and embryo. Additional experimentation involving long-term feeding of antioxidants to improve fertility during heat stress is warranted.

There are many molecules with antioxidant properties that could be evaluated as a feed additive for improving fertility. Among these are the polyamine resveratrol found in grape skin, which increased sperm output in rats (Juan et al., 2005), anthocyanins found in purple sweet potato, which reduced effects of elevated temperature on survival of cultured bovine embryos (Sakatani et al., 2007), and epigallocatechin gallate, a flavonoid in green tea that protected oocytes from heat stress in vivo in mice (Roth et al., 2008). All of these antioxidants are natural products found in plants. It may be that feedstuffs for dairy cattle can be identified that contain antioxidants with the potential for counteracting effects of ROS on reproductive function. Alternatively, transgenic technology could be used to introduce molecules with antioxidant properties into commonly-used feedstuffs.

Genetics

The most sustainable way to reduce the impact of heat stress on dairy cattle reproduction is to produce a cow that is genetically resistant to heat stress. There is genetic variation in resistance to heat stress among the Holstein population (Aguilar et al., 2009) and quantitative trait loci for thermotolerance have been identified (Hayes et al., 2009). Recently, an allelic variant of the Na/K ATPase gene that controls body temperature during heat stress has been described (Wang et al., 2010). Moreover, the slick gene that causes production of a short hair coat and increased thermoregulatory ability has been introduced into Holstein from the original Senepol population in which it was discovered (Dikmen et al., 2008). It is likely, therefore, that progress can be made in selecting cattle for the ability to regulate body temperature during heat stress through use of conventional as well as molecular-assisted selection and by incorporating genes that confer thermotolerance into improved dairy cattle breeds.

Genes exist not only for regulation of body temperature during heat stress but also for cellular responses to elevated temperatures. A series of experiments have demonstrated that *Bos indicus* embryos are more resistant to elevated temperature than *Bos taurus* embryos (see Hansen, 2004, also a more recent paper by Eberhardt et al., 2009). Identification of the specific genes responsible for cellular resistance has remained elusive but could result in introgression of the genes from *B. indicus* into dairy breeds.

Some evidence for an effect of genotype on embryonic resistance to heat stress comes from a study in which lactating Holstein cows were inseminated with either Holstein bulls or Gyr bulls (Pegorer et al., 2007). As shown in Figure 11.1, pregnancy rate per insemination was greater for cows bred with Gyr bulls. There are three possible explanations for the breed difference: inherent differences in fertility between bulls, heterosis expressed by the developing embryo, or increased thermotolerance of Gyr × Holstein embryos. In any case, fertility was low for both sire breeds, at least in part because effects of heat stress on the oocyte could not be reversed by choice of sire.

Summary

If projections are correct, global climate change will mean that heat stress will be of greater magnitude and occur over a wider portion of the globe than is the case now (Battisti and Naylor, 2009). Meeting the challenge that this scenario poses for animal agriculture (Thornton et al., 2007) will require new technological approaches that allow adequate production during periods of heat stress. With the exception of embryo transfer, the techniques and approaches

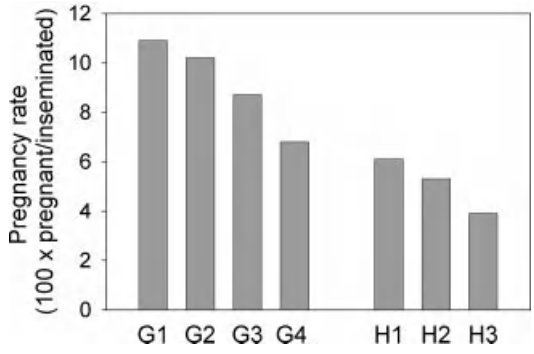

Figure 11.1. Effect of sire and sire breed on pregnancy rates per insemination in Holstein cows during heat stress. Each bar represents the pregnancy rate for an individual Gyr (G) or Holstein (H) bull (n = 132–177 inseminations per sire). Data are from Pegorer et al. (2007) and the figure is reproduced with permission from Hansen (2007b).

described here to reduce effects of heat stress on dairy cattle reproduction have not been reduced to practice. However, the underlying strategy of manipulating physiological and cellular determinants of thermotolerance to improve animal performance is attractive because it does not require the large energy utilization that characterizes some of the new housing systems designed for hot climates. A combination of physiological manipulation, genetic selection, and changes in housing may prove to be the best strategy for reducing heat stress, with the relative importance of each approach depending upon the particular circumstances in which dairy cattle are raised.

Conflict of interest: Dr. Hansen is co-owner of Cooley Biotech LLC, which makes media for production of embryos in vitro.

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Chapter 12

Environmental Heat Stress Impairs Placental Function, Fetal Growth and Development, and Postnatal Performance in Livestock

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Introduction

Environmental stressors such as heat, cold, humidity, and high altitude diminish revenue for livestock producers by negatively impacting nutrient utilization, growth, and reproductive performance. Consequences of environmental stress on early embryonic survival have been well documented, both scientifically and economically (Dutt, 1964). However, financial losses from harsh environmental conditions are not limited to embryonic wastage. During gestation, chronic exposure to heat stress can lead to lighter birth weights, increased morbidity before weaning, lower survival rates, and less desirable carcass traits. As we will explain, these complications are products of developmental adaptations to fetal malnutrition caused by placental insufficiency that results in intrauterine growth restriction. Slowed conceptus growth is considered beneficial for the dam, as a smaller conceptus yields less metabolically active tissue, greater maternal surface-area-to-mass ratio, and less nutrient strain on the mother (Wells, 2002). Although advantageous for the dam, developmental alterations to the fetus impair postnatal health and growth. Because heat-stressed offspring are smaller at term, we begin with a closer look at postnatal outcomes associated with low birth weight, irrespective of the stressor causing fetal growth restriction.

Postnatal Outcomes in Low Birth-Weight Offspring

Postnatal inadequacies caused by heat-stress induced placental insufficiency may share similarities with other types of fetal growth restriction because the end result is smaller birth weights due to intrauterine nutrient deficiencies. Reduction of birth weight is a prominent feature after prenatal heat stress and has been demonstrated in numerous species including

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mice (Ashoub, 1958), rats (Benson and Morris, 1971), guinea pigs (Jonson et al., 1976), and rabbits (Leduc, 1972). In domestic livestock, dairy cows exposed to heat stress during late gestation give birth to calves that are approximately 8% lighter than non-stressed contemporaries (Collier et al., 1982), but calves may be as much as 17% smaller when born to older heat-stressed cows (Wolfenson et al., 1988). In goats, birth weight of heat-stressed twins declines by 24% (Holmes et al., 1986), while in sheep, the reduction may reach 50% (Alexander and Williams, 1971).

In general production situations, smaller offspring exhibit greater mortality rates and are more prone to illness prior to weaning (Linden et al., 2009). In piglets that weigh less than 1 kg at birth, 11% are stillborn, and 17% die within 24 hours, and the rates increase to 24% and 33%, respectively, when birth weight is less than 0.6 kg (Quiniou et al., 2002). Small piglets lack the vigor necessary to compete with larger litter mates and, therefore, do not have the strength and stamina to maintain adequate health and growth. This contributes greatly to an inverse relationship between birth weight and mortality in swine (Milligan et al., 2002). A similar situation occurs in range cattle, where offspring that are born more than one standard deviation below average birth weight exhibit a drastically increased mortality rate in the first week of life (Azzam et al., 1993).

Smaller birth weights generally result in lower weaning and slaughter weights. Low birth weight offspring may have growth capacity near or even equal to those with normal birth weight after a few weeks due in large part to reduced energy requirements for maintenance (Greenwood et al., 1998; Milligan et al., 2002), but the deficit that occurs from restricted growth before and directly after birth is usually not overcome at weaning or slaughter. Piglets with birth weights below 1 kg grow more slowly and less efficiently (Powell and Aberle, 1980), and each additional 100 grams of weight at birth results in approximately 400 more grams at weaning (Quiniou et al., 2002). Slower growing pigs must be maintained and fed 12 to 23 days longer before reaching adequate slaughter weight (Gondret et al., 2005; Hegarty and Allen, 1978). In sheep, fetal growth restriction reduces daily gain throughout the pre-weaning period in both sexes, but males appear to be affected more profoundly (Chen et al., 2010; Da Silva et al., 2001). Reduced postnatal skeletal growth has also been observed in pigs (Hegarty and Allen, 1978) and horses (Rossdale and Ousey, 2002) of low birth weight.

Low birth-weight lambs tend to exhibit a growth pattern that yields increased fat-to-lean mass and lowers efficiency of energy utilization for growth (Chen et al., 2010; Greenwood et al., 1998). Pigs also have less lean muscle and more adipose tissue, and average daily gain suffers as well (De Blasio et al., 2007a; Wu et al., 2006). In addition to 29% more subcutaneous fat, feed conversion efficiency in low birth weight pigs falls by 10% (Gondret et al., 2005). Preliminary findings indicate that heat-stress induced intrauterine growth restricted lambs exhibit greater peripheral insulin sensitivity, along with increased insulin secretion in response to glucose at two weeks postpartum (Limesand et al., unpublished data), indicating that the postnatal catch-up growth associated with low birth weight is due, at least initially, to greater insulin sensitivity. Furthermore, fasting insulin disposition indices (insulin responsiveness x insulin sensitivity index) for glucose and free fatty acids are increased in lambs after fetal growth restriction and are, in fact, negatively correlated with birth weight (De Blasio et al., 2007b). This means that energy substrates are used more sparingly in low birth-weight offspring. More efficient use of glucose, coupled with normal or even increased dry matter intake, may explain the accelerated growth rate in low birth-weight lambs, as glucose in excess of that needed for maintenance and growth is stored as fat (Dulloo, 2008), increasing visceral adiposity in these lambs (De Blasio et al., 2007b).

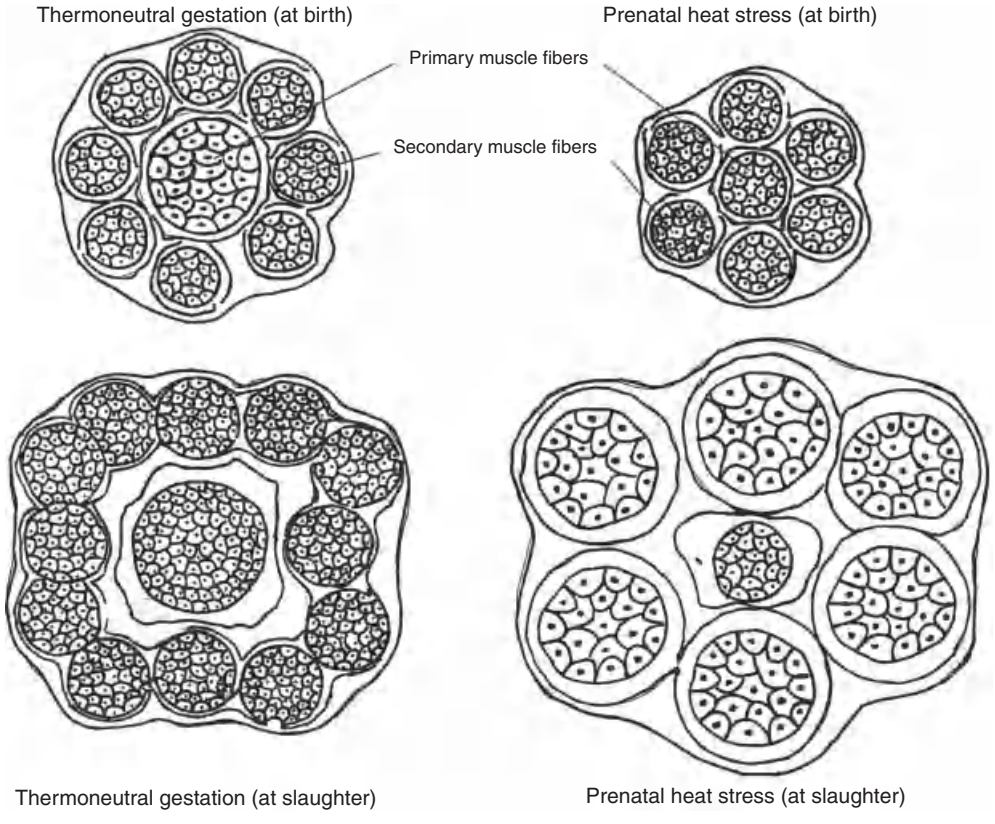

Figure 12.1. Schematic representation for the expected alteration in size and arrangement of primary and secondary muscle fibers in offspring exposed to prenatal heat stress.

The fat-to-lean mass ratio is further affected by limitation of muscle growth, as myonuclei proliferation is slower in lambs born small (Greenwood et al., 2000). In low birth weight pigs, loin area is reduced compared to large litter mates (Powell and Aberle, 1980), and muscle fibers in these pigs are 19% fewer in number and 14% larger at slaughter (Gondret et al., 2005). At birth, however, muscle size is reduced and fiber size is comparable (Hegarty and Allen, 1978), indicating compensatory hypertrophy of fibers between birth and slaughter age (see Fig. 12.1) – a phenomenon that diminishes meat tenderness (Gondret et al., 2005). Fast-twitch muscle fibers are also reduced (Wigmore and Stickland, 1983), which can greatly impact the animal's athletic performance. Together, these data indicate that reduced birth weight negatively impacts phenotype in livestock, irrespective of the cause of fetal growth restriction.

Other consequences of fetal growth restriction extend into adulthood. Alexander and Williams (1971) found that sheep exposed to prenatal heat stress exhibited a reduced ratio of secondary to primary wool follicles and were thus more likely to produce a lower quality fleece. Additionally, reproductive performance suffers in both males and females after intrauterine growth restriction (Wu et al., 2006). In young male sheep, puberty is delayed by as much as five weeks, postpubertal testosterone concentration and testicular size are reduced,

and the seasonal increase in testosterone is delayed and peaks at a lower concentration (Da Silva et al., 2001), while in females, fetal growth restriction reduces the number of follicles in the resting pool of the ovary and causes aberrant gonadotropin expression in the pituitary (Da Silva et al., 2002). Not only are these animals less fertile, but physiological alterations can also affect primordial germ cells through epigenetic modifications (Fowden et al., 2006), which can be passed on to the next generation. In equine fetuses, development of thermogenic mechanisms may be impaired, leaving the foal less prepared to handle cold stress after birth (Wu et al., 2006). Growth restricted foals also exhibit heightened sensitivity to blood pressure regulators that can result in hypertension in adulthood (Giussani et al., 2003). Additional observations include intestinal and respiratory dysfunction, as well as depressed immune activity. Piglets with low birth weights exhibited a high incidence of mucosal and submucosal necrosis in the distal ileum of the small intestine (Thornbury et al., 1993). Growth restriction in sheep fetuses can affect the length, diameter, and functionality of both the small and large intestine (Trahair et al., 1997), which may contribute to reduced neonatal feed efficiency. Pulmonary failure and aberrant respiratory patterns are often observed in growth-restricted foals in the first few days after parturition and can result from poor bronchiolar and alveolar development or from underdevelopment of laryngeal muscles (Rossdale and Ousey, 2002).

Fetal adaptations to nutrient deficiencies that result in lower birth weights represent deviations in the normal developmental progression of many tissues and organs, and complications appear to persist in offspring after parturition. Evidence suggests that many determinants of livestock value are adversely impacted in animals that are small at birth. To understand the cause-and-effect relationship between environmental heat stress and fetal adaptations that result in light birth weight, we will consider the uteroplacental unit and fetus as distinct entities.

Placental Function

The placenta serves as a selective barrier that transports oxygen and nutrients to the fetus, dispels heat and waste, and serves as an endocrine organ to support fetal development and growth (Schroder and Power, 1997). Placental formation begins when the chorion of the conceptus attaches to the uterus. At specific, preexisting sites (uterine caruncles), placentomes are formed and serve as the primary maternal-fetal interface for exchange (see Fig. 12.2). Each placentome consists of fetal cotyledon and maternal caruncle tissues that provide a highly vascularized unit for exchange between each independent circulatory system. The number and size of placentomes that develop represents the initial determinant for placental function, due to the importance of surface area available for maternal-fetal exchange. In sheep, surgical reduction of caruncular number decreases placentome number and placental transport capacity, resulting in lighter lambs at term (Alexander, 1964). Consequently, fetal growth is closely linked to placental size and functional capacity, and birth weight is strongly and positively correlated ($r = 0.74$) with placental weight (van Rens et al., 2005).

The networks of branched blood vessels and villi that develop in between cotyledonary and caruncular tissues (Steven, 1975) provide opportunities for substrate exchange by diffusion or by active transport (Fig. 12.3). Placental vascular development is governed by several angiogenic growth factors that promote vessel growth and expansion during villous formation (Anthony et al., 2001). In normal development, these signaling proteins prompt a 3.5-fold increase in placental blood vessel branching, a 10-fold increase in capillary area density, and a 14-fold increase in total villous surface area from early to late gestation (Reynolds et al.,

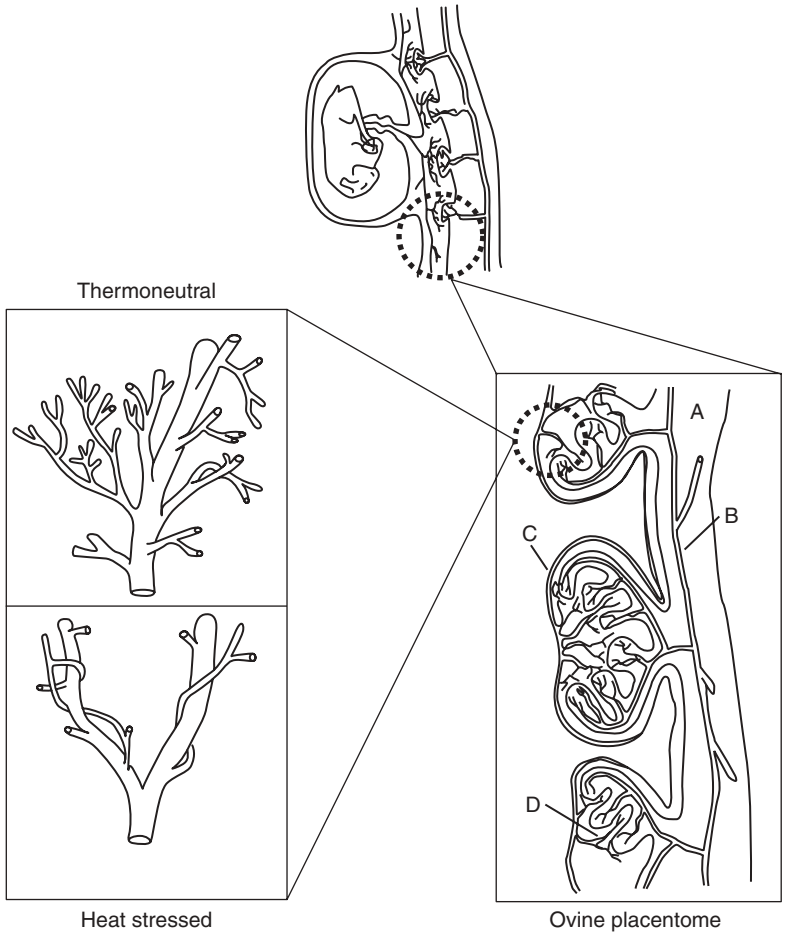

Figure 12.2. Maternal (caruncle) and fetal (cotyledon) tissues form the placentome. Cotyledonary blood vessels in heat stressed fetuses are less efficient due to reduced branching and increased coiling. A. uterine tissues, B. uterine arteriole, C. placentome, D. cotyledonary capillaries.

2005). Many placental growth factors, such as vascular endothelial growth factor (VEGF), are governed at least in part by other factors such as local oxygen content (Kingdom and Kaufmann, 1997). During early gestation, when maternal-fetal exchange is poor, the natural lack of oxygen prompts placental macrophages to release VEGF as a means of encouraging angiogenesis and improving the maternal-fetal exchange system (Regnault et al., 2002a). Thus, angiogenesis and subsequent development of placental villi are inversely related to the oxygen content in the placenta.

The initial attachment phase is followed by rapid placental growth. In sheep, the greatest rate of placental growth takes place from 40 days of gestational age to 80 days (term is ~147 days), with maximal tissue accretion rate occurring at around 55 days (Ehrhardt and Bell, 1995). After approximately 80 days, placental growth slows and dry matter content of the placenta remains constant thereafter, but the microstructure of the placenta continues to evolve

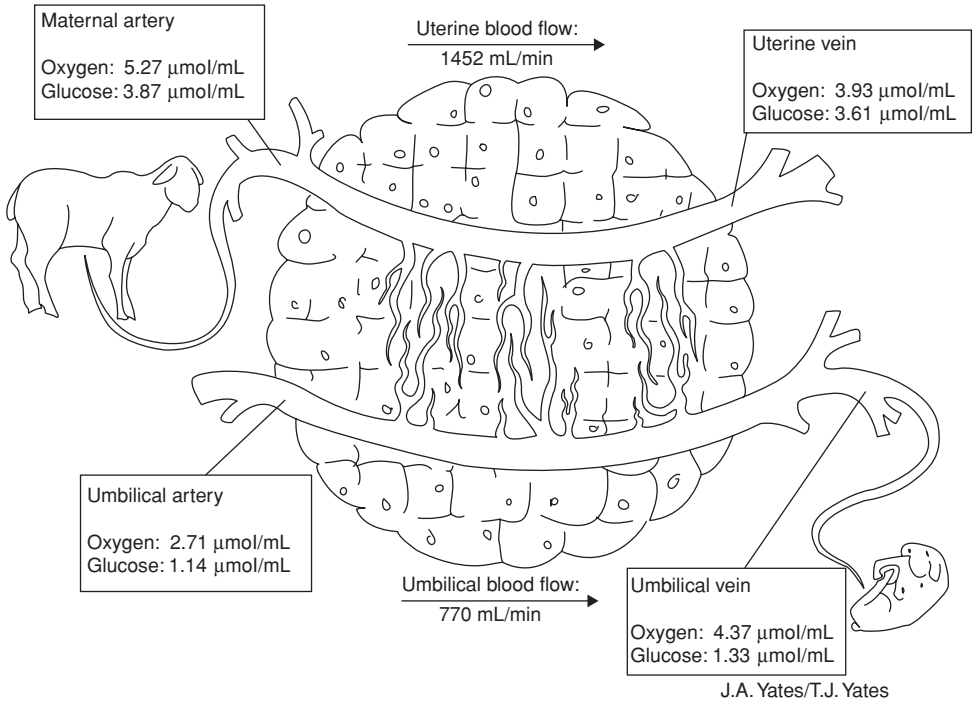

Figure 12.3. Glucose and oxygen concentrations are illustrated for uterine and placental vessels, which provide the diffusion gradient to allow placental uptake. Values are from Regnault et al. (2007). Picture by J. A. Yates/T. J. Yates.

until term in order to increase nutrient transport capacity and fulfill increasing fetal demands (Wooding et al., 1986). In this final phase of tissue reorganization, the maternal-placental interface becomes even more villous (Baur, 1977), which increases surface area for exchange, the placental wall thins (Battaglia and Meschia, 1986) and diffusion capacity increases. Additionally, blood vessels continue to develop as VEGF-driven vascular branching is replaced by non-branching and straight-line vessel growth stimulated by increased placental growth factor (PlGF; Arroyo and Winn, 2008). This increases nutrient transfer capacity (Barcroft and Barron, 1946). Improved placental transfer efficiency through increased permeability and diffusion capacity during the last half of gestation allows the placenta to keep up with fetal requirements even though tissue accretion in the placenta itself has ceased.

Effects of Heat Stress on Placental Development

Elevated ambient temperature reduces an animal's ability to dissipate body heat to its environment through convection and results in increased core body temperature (Fuquay, 1981). Although the reported 0.8° to 1.5°C increase in body temperature (Collier et al., 1982; de Vrijer et al., 2004; Regnault et al., 2005) may seem small relative to acute increases observed with fever, this chronic rise is accompanied by redistribution of maternal blood flow to peripheral tissues and a decrease in blood volume flowing to the cotyledons (Alexander

et al., 1987). Placental adaptations begin to appear in concert with chronically or repeatedly elevated core body temperatures in the mother (Alexander et al., 1987; Bell et al., 1989; Wallace et al., 2005). Dreiling et al. (1991) reported that a 1°C climb in maternal core body temperature caused a 20 to 30% drop in blood flow to the gravid uterus in sheep, and the extent of placental insult is directly related to the extent and duration of the temperature elevation (Galan et al., 1999).

Heat stress affects placental mass relatively early. Reductions can be observed in sheep as early as 75 days of gestational age (dGA; Galan et al., 1999), but are more profound in later gestation and may be reduced by as much as 66% at term (Alexander and Williams, 1971), even when heat stress is alleviated before maximal placental growth. Decreased placental weight appears to occur via reduced placentome size rather than number (Alexander and Williams, 1971; Galan et al., 1999; Thureen et al., 1992), which fits with the notion of aberrant development. Vatnick et al. (1991) and Regnault et al. (2002b) have shown that reduced placental weight precedes decreased fetal weight in sheep and that these early reductions are due to fewer rather than smaller cells, as DNA content, protein content, and protein/DNA ratios are not different between cotyledons collected from heat-stressed animals or thermoneutral controls. Heat stress imposed after the apex of placental growth at 64 days of gestation also results in smaller placental and fetal weights, indicating that exposure to environmental hyperthermia even in late gestation influences placental remodeling (Bell et al., 1989). Together, these data show that heat stress negatively influences placental formation and function, which leads to fetal intrauterine growth restriction during the final trimester of gestation.

During normal placental development, VEGF is released in response to the early local hypoxemia and promotes branching angiogenesis and oxygen extraction. As branching angiogenesis slows, it is replaced by non-branching vessel elongation that occurs with villous maturation. In heat-stressed animals, however, diminished blood flow (Dreiling et al., 1991) and reduced uterine vascular density (Regnault et al., 2002a) cause a greater degree of hypoxemia in immature placental tissue, as evidenced by increased expression of VEGF in cotyledons at the end of the first trimester in sheep (Regnault et al., 2002a). As depicted in Figure 12.4, elevated VEGF hastens branching angiogenesis, abolishes placental hypoxemia at an earlier stage of development, and may even lead to local hyperoxia (Kingdom et al., 2000; Kingdom and Kaufmann, 1997; Regnault et al., 2002a). Ironically,

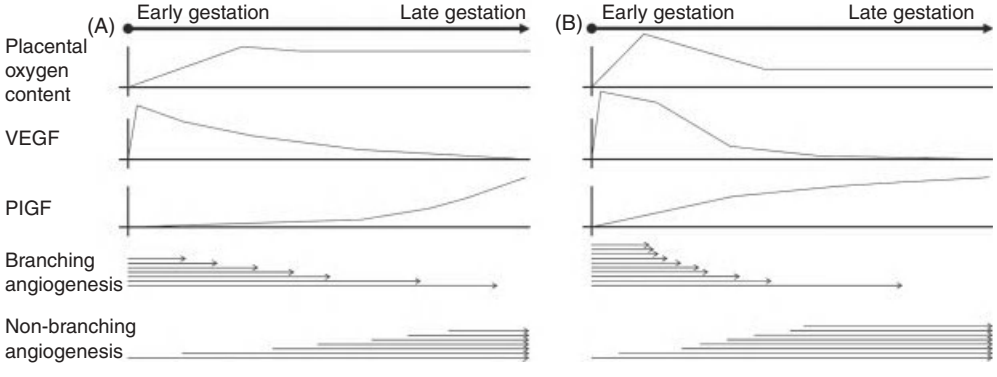

Figure 12.4. Patterns of local oxygen content, angiogenic growth factors, and angiogenesis in the placenta during thermoneutral gestation (A) or prenatal heat stress (B).

early correction of placental hypoxemia reduces the initiative to form normal villi and vasculature (Lyall et al., 1997) and results in villi that are malformed and less effective (Kingdom and Kaufmann, 1997).

In instances of placental insufficiency, placental arteries are reduced in number, lumen size, and surface area (Anthony et al., 2001). Placental vessels are often abnormally oriented, with coiling replacing the more efficient branching patterns (Regnault et al., 2002b) – possibly due aberrant expression patterns of VEGF and PlGF (see Fig. 12.4). Alterations in the structure of the placental vascular system can cause an almost four-fold increase in blood flow resistance (Galan et al., 2005; Regnault et al., 2007), which slows movement of blood through the cotyledon. Structural abnormalities in the placental villi and vascular bed do not become important until later stages of pregnancy, when the fetus begins its exponential growth. At this time, the placenta may attempt to alleviate insufficiencies by decreasing expression of VEGF receptor-1, thus directing VEGF binding toward the more active VEGF receptor-2, and by increasing expression of PlGF on the maternal side of the placentome (Regnault et al., 2002a), but this does not fully compensate for poor placental formation.

Heat stress also affects endocrine function of the placenta. Progesterone concentration in the pregnant ewe declines sharply around the time the placenta takes over production from the ovary (Bell et al., 1989; Regnault et al., 1999). Conversely, progesterone in cattle, which is produced almost exclusively by the ovary throughout gestation, may actually increase with heat stress (Collier et al., 1982). Maternal concentrations of placental-derived estrone sulfate and placental lactogen are also reduced (Bell et al., 1989; Collier et al., 1982; Regnault et al., 1999), the latter of which may affect glucose partitioning in the dam.

Heat-Stress Reduced Placental Transport Efficiency

Components of placental functional capacity must increase with fetal demands to maintain appropriate growth rates. Oxygen and nutrients are transported from maternal to fetal circulation through the placenta by passive diffusion, facilitated diffusion, or active transport (Battaglia and Meschia, 1978). Substrate exchange across the placenta is diminished by heat stress due to smaller placental mass and decreased permeability for substrates (Bell et al., 1987; Limesand et al., 2004, 2007; Regnault et al., 2002a; Thureen et al., 1992; Wallace et al., 2005). Fetal outcomes of placental insufficiency are hypoxemia and hypoglycemia, which can act to promote maternal-fetal diffusion capacity by increasing the gradient across the placenta.

Compared to unstressed control-sheep fetuses, late-term sheep fetuses exposed to heat stress through mid-gestation had lower umbilical blood oxygen content (>50%), oxygen saturation (>25%), and oxygen partial pressure (>30%). This occurs despite numerous reports (Limesand et al., 2004; Regnault et al., 2007) showing similar rates of umbilical (fetal) uptake of oxygen per placental mass (Limesand et al., 2007; Thureen et al., 1992; Wallace et al., 2005).

Umbilical (fetal) uptake rate of glucose, the primary oxidative energy substrate for the fetus, declines by as much as 50% (Thureen et al., 1992; Wallace et al., 2005). In addition to less placental mass and surface area, the increased diffusion gradient is also due to a reduction in facilitated glucose transporters (GLUT), which form pores in the membrane to allow glucose to move down its concentration gradient. Three glucose transporters, GLUT-1, GLUT-3, and GLUT-8, are present in the sheep placenta, and mRNA levels for all three are lower than normal following heat stress (Limesand et al., 2004; Wallace et al., 2005). Similar to findings in fetal oxygen uptake, umbilical uptake rates of glucose per kg fetus may (Limesand et al., 2004,

2007) or may not (Anderson et al., 1997; Ross et al., 1996) differ between hyperthermic and thermoneutral fetuses. It is unclear, however, whether this phenomenon exists because fetal compensatory mechanisms restore uptake to levels that adequately provide for the smaller fetus or if fetal mass (i.e., growth rate) is simply depressed to a degree that is proportional to the rate of placental nutrient and oxygen uptake.

In the hyperthermic placenta, improved transport capacity can be initiated by two physiological conditions that develop within the fetus as a result of placental insufficiency. First, fetal hypoxemia and hypoglycemia coupled with normal maternal oxygen and glucose levels increase concentration gradients across the placenta. These greater gradients for oxygen and glucose increase the "pull" of nutrients across the placenta to the fetus, thus helping to compensate for placental deficiencies. Figure 12.5 demonstrates this shift in maternal-to-fetal gradient to maintain adequate placental uptake for both oxygen and glucose. A second compensatory mechanism by the fetus is slower umbilical blood flow (see Fig. 12.6), which results from greater vascular resistance (Galan et al., 2005) and increases the uterine to umbilical blood-flow ratio. This promotes placental uptake in a manner that is positive for fetal energy expenditure. Surprisingly, ethanol clearance is normal in heat-stressed placentae, which demonstrates that increased uterine-to-umbilical blood-flow ratios improve clearance and that uterine blood flow is not disturbed by uneven perfusion or abnormal shunting that bypasses the placenta. Rather, placental permeability to oxygen and glucose is compromised because

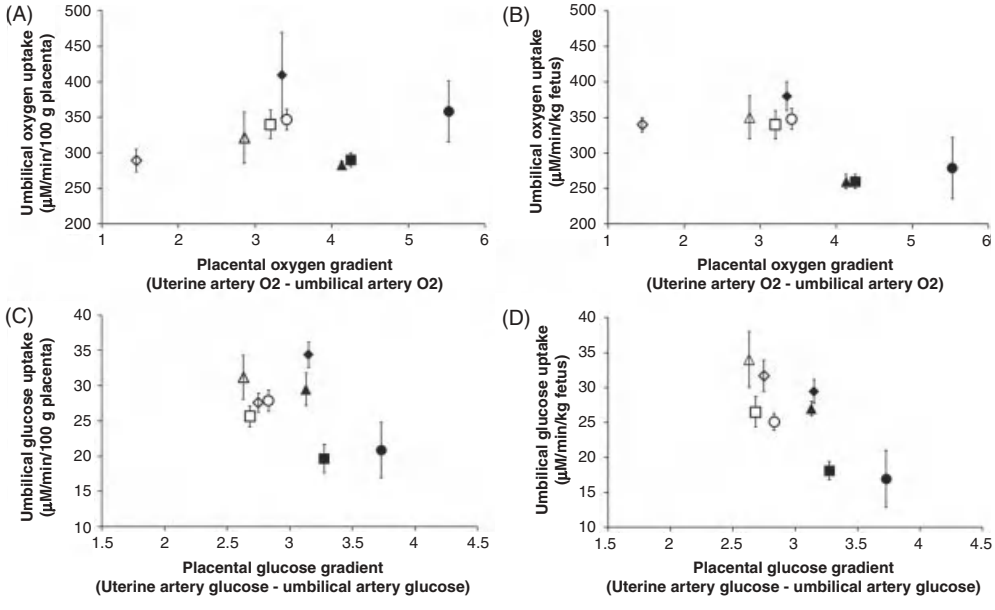

Figure 12.5. Umbilical oxygen (A, B) and glucose (C, D) uptakes per 100 g placenta or kg fetal weight (y-axis) are plotted against the difference between the uterine and umbilical artery (x-axis; mmol/L). The graphs show that increases in placental oxygen and glucose gradients exist and help maintain umbilical oxygen and glucose uptakes in prenatal heat stress (black symbols) fetuses compared to thermoneutral fetuses (white symbols). Data are from Thureen et al. (1992; diamonds), Regnault et al. (2007; squares, A and B), Limesand et al. (2004; squares, C and D), de Vrijer et al. (2004; triangles), and Limesand et al. (2007; circles).

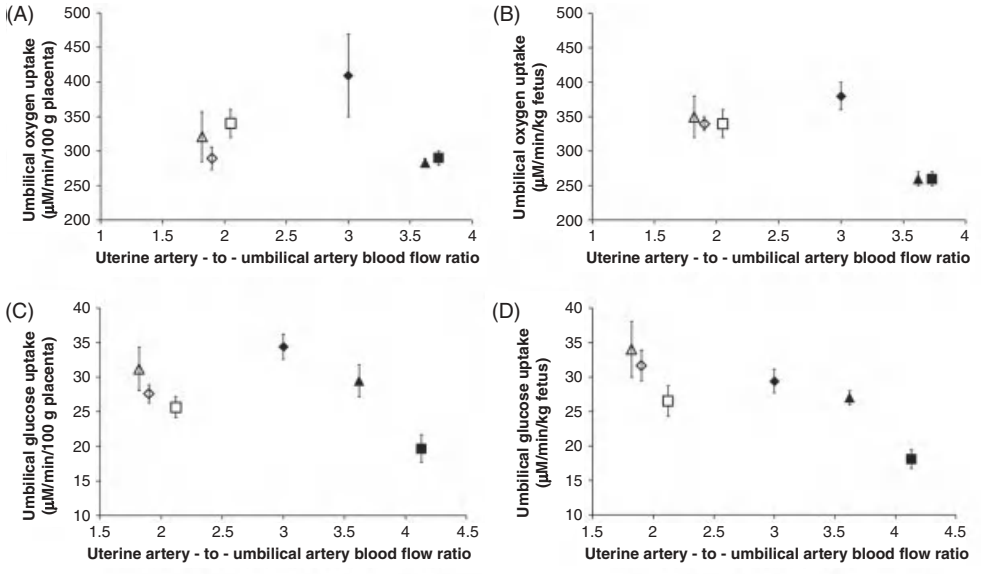

Figure 12.6. Umbilical oxygen (A, B) and glucose (C, D) uptakes per 100 g placenta or kg fetal weight (y-axis) are plotted against the uterine to umbilical blood flow ratio (x-axis). Increased uterine-to-umbilical blood flow ratios appear to partially compensate for the placental insufficiency and maintain umbilical oxygen and glucose uptakes between thermoneutral gestation (white symbols) and prenatal heat stress (black symbols). Data are from Thureen et al. (1992; diamonds), Limesand et al. (2004; squares, C and D), and de Vrijer et al. (2004; triangles).

ethanol is a blood-flow limited molecule (Wilkening et al., 1985). This leads to an eventual state of chronic hypoxemia and hypoglycemia in the fetus.

Amino acid flux across the placenta is also compromised by reduced placental size and transport capacity. Branch-chain amino acid transport falls short by 23% in absolute terms and by 58% after adjustment for placental mass (de Vrijer et al., 2004). For most amino acids, fetal blood concentrations are greater than maternal amino acid concentrations and therefore must be actively transported across the placenta against their concentration gradient. The rate of transfer depends not only on surface area of the maternal-fetal interface, which is reduced, but also on the concentrations of placental transport proteins and amino acids themselves (Regnault et al., 2005). Although amino acid transporters have not yet been measured in the hyperthermic ruminant placenta, physiological studies indicate that amino acid fluxes are reduced in heat-stressed animals (Anderson et al., 1997; de Vrijer et al., 2004; Ross et al., 1996). Moreover, activity and expression of multiple transporters are reduced in the rat placenta on both the maternal and fetal interface (Jansson et al., 2006; Malandro et al., 1996). Interestingly, amino acid transport does not always reduce fetal plasma concentrations because they can be mobilized from fetal tissues to compensate for reduced placental transport (Limesand et al., 2007, 2009). Again, these data show that placental insufficiencies created by heat stress during gestation are not only restricted to a smaller placenta but also decreased permeability or transport, even though compensatory mechanisms were in place to assist with the deficiencies.

Heat-Stressed Fetal Growth Profile during Gestation

Asymmetric fetal growth is a hallmark of placental insufficiency and shows that the fetus is attempting to adapt to its nutrient-deprived environment by altering its metabolism and blood flow (Regnault et al., 2002). Cranial and skeletal growth is depressed by placental insufficiency but to a lesser extent than muscle and visceral organ growth (Regnault et al., 2002a). At term, sheep fetuses exhibit reduced heart girth, head length, and trunk length as well as shorter metacarpus, metatarsus, and femur bones (Alexander and Williams, 1971).

Ultrasound data demonstrate that biometric differences in fetal parameters emerge after the midpoint of gestation and continue to diverge thereafter. Abdominal circumference and femur and tibia length are lower at the middle of the second trimester, and decreased biparietal (skull) circumference occurs before the start of the third trimester (Barbera et al., 1995). In heat-stressed sheep fetuses that were collected for weights during gestation, a similar profile is observed. Average fetal weights were not different between controls and hyperthermic fetuses at the start of the second trimester (55 dGA), but were 25% lower at the end of it (de Vrijer et al., 2006; Regnault et al., 2002a). By the midpoint of the third trimester, growth was restricted by almost 50% (Galan et al., 2005), and near term restriction exceeded this mark (Regnault et al., 2007). A similar pattern was reported in heat-stressed cattle (Reynolds et al., 1985, 2005). Together, these data indicate that fetal weights are unaffected by the initial stress but the impact to placental function causes the divergence to increase as gestation progresses and coincides with increasing nutritional demands for fetal growth and maintenance.

Placental Insufficiency Causes Fetal Adaptations in Metabolism

From our previous discussion it is apparent that heat-stressed induced placental insufficiency alters the fetal milieu. Two primary outcomes already discussed are hypoxemia and hypoglycemia, and both conditions can lead to fetal hypoinsulinemia (Limesand et al., 2006; Leos et al., 2010). These conditions worsen over the final trimester in hyperthermic sheep fetuses, culminating in a 50% or greater reduction at 0.9 of gestation (Leos et al., 2010). It is apparent, therefore, that the chronic development of fetal hypoxemia, hypoglycemia, and hypoinsulinemia contributes to a fetal adaptive response in metabolism.

In the fetus, hypoglycemia triggers metabolic adaptations designed to spare glucose for utilization in critical tissues (Hales and Barker, 1992, 2001). Enhanced glucose uptake from circulation by fetal tissues may help maintain intracellular glucose availability despite hypoglycemia. In chronically hypoglycemic sheep fetuses produced by lowering maternal glucose concentrations with an insulin infusion, GLUT-1 is up-regulated in the brain and down-regulated in the liver, which supports preferential uptake of glucose by the brain (Das et al., 1999). Similar increases in GLUT-1 expression occur in the brain of heat-stressed sheep fetuses, but decreased expression in the liver and skeletal muscle has not been reported (Limesand et al., 2007). Surprisingly, glucose utilization in heat-stressed fetuses is similar to that in non-stressed fetuses, indicating that glucose uptake by skeletal muscle is also improved. This is most likely a product of improved insulin sensitivity, because GLUT-1 and GLUT-4 are not changed (Limesand et al., 2007), but insulin receptor concentrations are increased (Thorn et al., 2009). Despite normal glucose utilization, the fraction of glucose that is oxidatively metabolized is less, which may indicate that fetuses are taking advantage of the Cori

cycle and shuttling lactate from the skeletal muscle to the liver to produce glucose (Limesand et al., 2007).

De novo glucose production is nonexistent in normal sheep fetuses (Hay et al., 1988, 1989), and gluconeogenic pathways are usually only activated after large spikes of catecholamines and cortisol during parturition (Fowden et al., 2005; Sperling et al., 1984). However, high catecholamine concentrations are seen in hypoglycemic/hypoxic fetuses and stimulate enzymes for hepatic glucose production (Limesand et al., 2007). Greater concentrations of catecholamines and glucagon appear to be the primary promoters of fetal gluconeogenesis in heat stressed animals, as cortisol concentrations may not increase (Limesand et al., 2006). This differs from sheep fetuses made chronically hypoglycemic for two weeks, as cortisol appears to be the primary inducer of gluconeogenic enzyme up-regulation (Limesand and Hay, 2003; Narkewicz et al., 1993; Rozance et al., 2008). Although cortisol concentrations are increased by hypoxemia and hypoglycemia, chronic stimulation of the adrenal cortex desensitizes it to adrenocorticotropic hormone, reducing the cortisol response (Fowden et al., 2005).

The primary role of catecholamines in the sheep fetus is suppression of insulin secretion (Bassett and Hanson, 2000; Jackson et al., 2000), which in turn increases glucose production and restricts fetal growth. Chronic adrenergic stimulation causes some tissues to become desensitized to catecholamines (Chen et al., 2010). However, catecholamines continue to suppress insulin secretion in heat-stressed fetuses, even though β-cells appear to be hypersensitized to glucose stimulation after chronic exposure (Leos et al., 2010). Furthermore, catecholamine suppression of insulin secretion may augment asymmetric fetal growth, as anabolic actions would only affect insulin-responsive tissues (Bassett and Hanson, 1998, 2000). Therefore, alterations between glucose metabolism and tissue accretion may manifest downstream from the insulin receptor. Like insulin, IGF-1 is greatly suppressed in the second half of gestation (Thorn et al., 2009).

In addition to altered GLUT concentrations and hypoinsulinemia that favor neuronal tissue development, blood flow to the brain and heart also increases, while flow to other tissues and visceral organs becomes limited. In near-term sheep fetuses, blood flow to the brain and heart increases by 50% and 8%, respectively, while at the same time, blood flow decreases noticeably to the liver, lungs, small intestine, pancreas, and adipose tissue (Alexander et al., 1987; Walker et al., 1995). This adaptive mechanism helps maintain nutrient and oxygen supply to vital organs, promoting their growth and development. To illustrate, brain-weight to liver-weight ratio is increased in most instances of placental insufficiency, which is indicative of preferential growth by the brain (Bell et al., 1989; Regnault et al., 2007). Interestingly, the adrenal glands do not suffer vasoconstriction or blood flow restriction. The fetus in fact increases blood flow to both the medulla and cortex of the adrenal (Buchwalder et al., 1998; Morrison, 2008; Walker et al., 1995) by splanchnic nerve activation as part of the fetal stress response.

Prevention of Intrauterine Growth Restriction

Exposure to hyperthermic conditions negatively impacts placental function, which then restricts fetal growth causing developmental alterations that appear to compromise the lifelong productivity of the animal. Thus, abatement of elevated ambient temperatures is the best strategy to avoid intrauterine growth restriction. When abatement is not possible, hormonal therapy as well as nutritional and antioxidant supplementation may be mildly to moderately effective

if implemented early (Wu et al., 2006). In a porcine model of inanition-induced placental insufficiency, maternal administration of progesterone and estradiol benzoate once daily over the last third of the first trimester partially restored weight and nitrogen content of the placenta (Anderson, 1975), while daily progesterone in ewes over the first third of pregnancy resulted in a 1.5-fold increase in lamb birth weight after placental insufficiency (Wallace et al., 2003). Administration of human chorionic gonadotropin within the first two weeks of pregnancy increased progesterone (Yates et al., 2010) and resulted in greater cotyledonary and fetal weight at the end of the first trimester (Cam and Kuran, 2004). Growth hormone administered to ewes at breeding or during rapid placental proliferation also increased fetal growth (Costine et al., 2005; Wallace et al., 2004) but not in all situations (Wright et al., 2008). Arginine supplemented to gilts toward the end of the third trimester increased live piglet weight by 24% (Mateo et al., 2007), however doubling dietary energy in late gestation did not affect birth weight (Pond et al., 1981).The benefit of supplemental antioxidants is less clear. Although deficiencies of vitamin E can impair fetal development, dietary supplementation of vitamin E to heat-stressed rats throughout gestation did not rescue fetal weight near term (Ashworth and Antipatis, 2001; Yates et al. unpublished). Therefore, endocrine and nutrient supplementation can improve fetal outcomes, but more work is needed to fully elucidate their attributes and return on producer investment.

Other Forms of Environmental Stress

Like heat stress, altitude and cold stress can affect placental and fetal development. In ewes born, raised, and maintained at an altitude of 4,267 meters, the weight, but not number, of placentomes was reduced near term (Metcalfe et al., 1962) and placental blood vessels exhibited decreased in number but lumen diameter increased (Krebs et al., 1997). Data on fetal development in ruminants at various altitudes are scarce, but human findings indicate that birth weight and placental weight at term are proportionately diminished with progressively higher altitudes (sea-level to 3,100 meters; Tissot van Patot et al., 2009), and reduced birth weight at altitude (3,600 meters) is a result of poor placental oxygen diffusion (Mayhew, 1991). The predominant changes in placental structure involve blood vessel appearance and orientation and are most likely due to lower maternal oxygen levels (Espinoza et al., 2001). Altitude stress can cause similar postnatal conditions to heat stress, including pulmonary hypertension (Xue et al., 2008).

Information regarding the impact of cold stress on the ruminant fetus is minimal. As with other prenatal stressors, cold stress elicits certain fetal adaptations that are advantageous to survival. In lambs, cold stress during late gestation slightly increased birth weight due to a 21% increase in adipose tissue. These lambs also exhibited greater non-shivering thermogenesis and increased core body temperature to aid cold tolerance immediately after birth. Most of these metabolic advantages disappeared within a few days of birth, but greater fat deposition persisted and may increase to as much as 53% by 1 month of age (Symonds et al., 1992). Hypertension (Kanayama et al., 1997) and a pre-eclampsia-like condition (Khatun et al., 1999) have been observed in cold stressed rats. Vasoconstriction of uterine (but not fetoplacental) vessels alters the fetal/maternal heat gradient and slows fetal heat loss, which helps to preserve fetal core body temperature (Laburn et al., 2002). Therefore, the influence of cold stress on the fetus is less severe than the influence of heat stress because cold stress does not alter the fetal thermal environment to the same extent as heat (Laburn et al., 1992). However, fetal

adaptations exist and appear to persist showing that, like heat stress, other environmental factors can cause lifelong complications.

Summary

Heat stress alters maternal physiology, which has implications on the developing conceptus. Increased maternal core body temperature and changes in placental mass and vasculature lead to dysfunction. The compromised placenta is unable to support the appropriate rate of fetal growth after mid-gestation, and thus the fetus must adapt to the worsening hypoxemic and hypoglycemic conditions. It does so by rerouting blood flow patterns, sparing metabolic substrates, and increasing glucose uptake to its most critical organs at the expense of less-vital organs. However, these adaptations result in a plethora of postnatal complications that may lower animals' production and commercial value.

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Chapter 13

Effects of Photoperiod on Domestic Animals

Geoffrey E. Dahl and Izabella M. Thompson

Introduction

Photoperiod is defined as the alternating exposure to light and dark on a daily basis. Lighted periods are termed the photophase, whereas darkness is the scotophase. Physiologically, the pattern of light exposure, particularly the relative duration of light and dark, affects a number of endocrine pathways to culminate in daily, monthly, and annual shifts in functions related to growth, reproduction, pelage, and immune function. From an evolutionary perspective, adoption of photoperiod as an ultimate driver for annual changes in physiological function is predictable because it is the most consistent environmental signal over extended periods of time (Gwinner, 1986). But photoperiod can also be harnessed to improve production in all farmed domestic species, especially in today's intensive systems.

Light

One of the most frequent questions with regard to photoperiod concerns the relative difference between light and dark. Put another way, how dark is "dark" and how much light registers as a signal? Light intensity is measured and reported in footcandles (FC; English) or lux (Lx; metric), with a conversion ratio between the two of about 10 lux to 1 footcandle. Although there are limited data on domestic species in regard to the minimal intensity of light that is perceived as "light," an illumination as low as 5 footcandles registers as light. This does not mean, however, that an intensity of less than 5 FC is "dark," as animals may acclimate to lower intensities over time. In fact chickens can respond to intensities as low as 1 FC. The American Society of Agricultural and Biological Engineers (ASABE) recommends that all housing for domestic animals achieve an intensity of 15 footcandles or more. The maximum intensity

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measured under natural conditions exceeds 1,000 FC on a sunny day and even a cloudy day will routinely provide an intensity of 200 to 300 FC. Thus it is clear that animals have a wide, dynamic range of light perception, and the only true measure of darkness appears to be the absence of light.

One exception to the foregoing discussion is that of low intensity red lamps. Although FC intensity is not measured per se in this single wavelength lamp source, the use of 7 to 15 W lamps during the scotophase does not register as light. This observation is consistent for cattle, sheep, chickens, and swine, and the use of low intensity red lamps is a management tool for observation and manipulation of animals during periods of darkness.

Type of light provided is also of practical interest in the production setting. The spectral qualities of incandescent, fluorescent, metal halide, and sodium vapor lamps vary particularly in the color-rendering index, which is a measure of the "white" quality of the light transmitted. However, responses appear to be consistent in farmed species for all those lamps. Because the lamps also vary in the relative efficiency, it is to the producer's advantage to use the most efficient lamp type appropriate to each setting.

Endogenous Rhythms and Light Signal Reception

Photoperiod signals modify the endogenous rhythms present in animals that occur on a daily or annual basis. The most obvious of these rhythms are the circadian (i.e., around a day) and circannual (i.e., around a year) rhythms that drive physiological systems that underlie acute and long-term functions. An example of a circadian event is the daily fluctuation in body temperature between an apex in the afternoon and a nadir in the early morning hours of a subjective day. The most widely adapted circannual rhythm is that which times seasonal reproductive events to optimize the chances for neonatal survival. These rhythms are innate to the animal and oscillate in the absence of any external cues or "zeitgebers" (e.g., time givers), although the period or time between each physiological event will drift from a consistent 24 hour or 365 day interval. Photoperiodic signals then serve to synchronize the endogenous rhythms to the day or year (Gwinner, 1986).

Light energy in the form of photons causes a conformational shift in photoreceptors found in photoreceptor cells of the retina that in turn open sodium channels to alter the membrane potential of those cells. In the absence of light (i.e., dark), stimulation of the photoreceptors is absent. Thus, photoreception is a transduction of the physical energy of light waves to the chemical energy of neuronal stimulation. Subsequent to photoreceptor action, signals are propagated through a series of interneurons to a collection of neurons within the hypothalamus known as the suprachiasmatic nucleus (SCN; see Fig. 13.1). The SCN is termed the master pacemaker for circadian events through expression of a group of transcription factors known as "clock" genes.

Within the SCN neurons, four genes form a transcription-translation feedback loop that influences neuronal signaling. On one side of the loop are CLOCK and BMAL1, which encode transcription factors that heterodimerize and initiate the transcription of the Period (PER) and Cryptochrome (CRY) genes that form the other side of the loop. As PER:CRY gene products accumulate, they form heterodimers that translocate to the nucleus and repress the expression of CLOCK and BMAL1 (Ko and Takahashi, 2006). A complete cycle of the loop occurs at roughly 24 hour intervals, a duration that is consistent with circadian oscillation. Expression of the clock genes, however, is not limited to the SCN and numerous other tissues

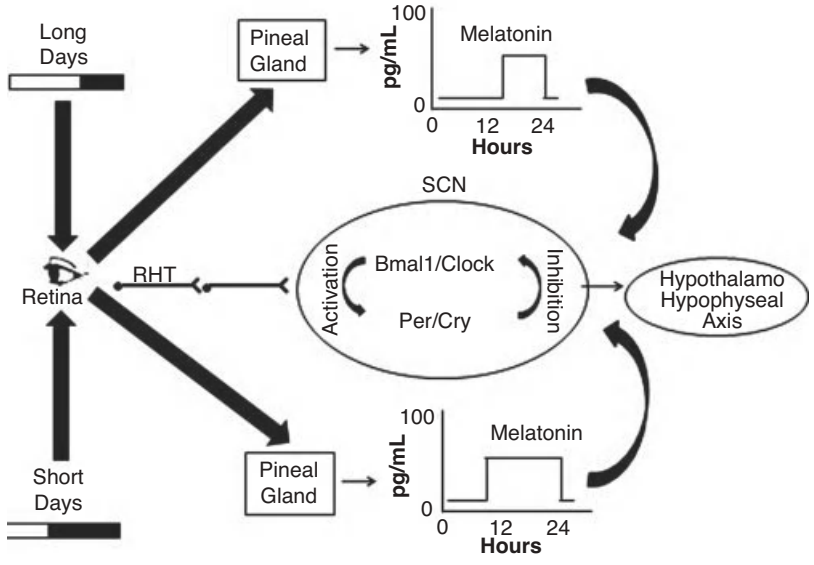

Figure 13.1. A model of photoperiodic input to the endogenous timing mechanism in animals. Light impacting the eye is perceived and transduced as a nervous signal along the retino-hypothalamic tract to the suprachiasmatic nucleus (SCN) and directly to the pineal gland. Within the SCN, the light signal impacts the transcription-translation feedback loop of the "clock" genes *BMal1, Clock, Period, and Cryptochrome,* which ultimately determine the timing of daily and annual events via outputs to the hypothalamus and pituitary. Additional input from the daily pattern of melatonin release from the pineal influences the relative timing of the clock gene expression such that the timing is synchronized with the geophysical day under natural conditions.

express these genes as well, including the liver, mammary gland, and intestinal tissue. Whereas clock gene expression is constitutive in the SCN, they are not necessarily in other tissues and thus may be under the control of the master circadian oscillator.

Photoperiodic signals integrated at the SCN then modulate the expression of clock genes. Long days induce PER expression patterns quite different than exposure to short days in rodents (Naito et al., 2008), and it is likely that this is a conserved response across mammalian species. The rapid adjustment to altered photoperiodic input, and the eventual development of refractoriness to those inputs (Buchanan et al., 1992; Tournier et al., 2009), provides further evidence that photoperiodic cues modulate the endogenous rhythm of the SCN. The master clock then affects other physiological systems, in particular endocrine systems related to reproduction, growth, immune responses, and lactation.

Endocrine Effects of Photoperiod

Melatonin is the primary indoleamine secreted by the pineal glands of birds and mammals (reviewed in Rieter, 1991; Rieter et al., 2010). Photic input from the eye is transduced in a similar manner to that previously described to a sympathetic pathway innervating the pineal gland. Pinealocytes absorb tryptophan from the circulation and convert it to serotonin, which

is then converted to N-acetylserotonin in a reaction catalyzed by N-acetyltransferase (NAT). This action of NAT is the rate-limiting step in melatonin synthesis, and NAT activity is the only process that exhibits a circadian rhythm in the production of melatonin (Illnerová and Sumova, 1997). The enzyme hydroxyindole-O-methyltransferase then converts the N-acetylserotonin into melatonin. Melatonin diffuses freely across cell membranes and thus the circulating concentrations increase dramatically as synthesis accelerates upon exposure to dark conditions.

Pinealectomy of domestic mammals and birds eliminates the daily pattern of melatonin and the ability to track photoperiodic changes in mammals in particular. In the absence of photic input, animals continue to display endogenous rhythms of activity on a daily and annual basis, but those rhythms become uncoupled and drift from the daily and yearly patterns of expression, a process termed "free-running" (Gwinner, 1986). In fact, free-running activities are hallmarks for endogenous rhythms and emphasize the importance of external cues – in this case photoperiod – in aligning endogenous rhythms with the daily and seasonal patterns of physiological events.

It is important to understand that the photic control of melatonin secretion is separate from that of inputs to the SCN, yet the two systems interact to provide an output that is synchronized to the external environment under natural conditions (Lincoln et al., 2003). For example, the decreasing day length observed in the autumn means that melatonin is present during phases of the circadian fluctuation of the clock genes when it would not be present during the long days of summer. Relative presence or absence of melatonin then impacts the level of clock gene expression and ultimately affects the observed output of the SCN to peripheral tissues.

After melatonin, the impact of photoperiod on prolactin (PRL) secretion is the most consistent endocrine response across birds and mammals. Long days (i.e., a short duration of elevated melatonin) drive an increase in PRL, whereas short days (i.e., extended duration of elevated melatonin) are associated with decreases in PRL in chickens, cattle, sheep, and horses (Sreekumar and Sharp, 1998; Peters et al., 1981; Mikolayunas et al., 2007; Johnson, 1987). In cattle, an inverse relationship between the circulating PRL concentration and PRL-receptor (PRL-R) expression is observed in a number of tissues, including the mammary gland, liver, and leukocytes (Auchtung et al., 2003), such that high concentrations of PRL associated with long days reduce PRL-R mRNA expression, and this is associated with a reduction in responsiveness to PRL (Auchtung and Dahl, 2004).

Altered day length induces shifts in circulating insulin-like growth factor I (IGF-1) in cattle (Dahl et al., 1997). Similar effects of long days are observed in farmed red deer, which suggests a common response among ruminants to extended light (Suttie et al., 1992). The increase in IGF-1, however, is not due to an increase in growth hormone (GH), as there is no evidence that photoperiod alters GH release or clearance in cattle or other domestic animals (Dahl et al., 2000). In addition, photoperiod does not affect expression of hepatic GH receptors (Kendall et al., 2003). One possibility is that long days increase circulating concentrations of IGF binding proteins (IGFBP) that then alter clearance of IGF-1. Evidence to support the hypothesis that photoperiod affects IGFBP is indirect in that elevated PRL decreases IGFBP-5 in bovine mammary cultures, an observation consistent with greater effective IGF-1 action (Accorsi et al., 2002). Further, summer season increased IGF-1 in both bST and non-bST treated cattle relative to winter conditions (Collier et al., 2008).

Reproductive Responses

Sheep have been used extensively as a model for study of circannual rhythms and have provided evidence that photoperiod modifies the expression of those rhythms via the pattern of

melatonin release from the pineal gland (Karsch et al., 1984). The seasonal waxing and waning of reproductive competence observed in many sheep breeds results from a rhythm of altered sensitivity to estradiol at the level of hypothalamic gonadotropin-releasing hormone (GnRH) secretion (Karsch et al., 1993). During the breeding season, GnRH release is stimulated by the increasing estradiol secretion from developing follicles on the ovary, and that stimulation ultimately causes the preovulatory surge of GnRH and, in turn, luteinizing hormone (LH) and release of the ova from the follicle. In contrast, ewes in anestrus are exquisitely sensitive to the negative feedback effects of estradiol, such that as small follicles develop on the ovary and steroid secretion increases, there is a profound suppression of GnRH release and no surge of LH develops – therefore ovulation is absent (see Fig. 13.2).

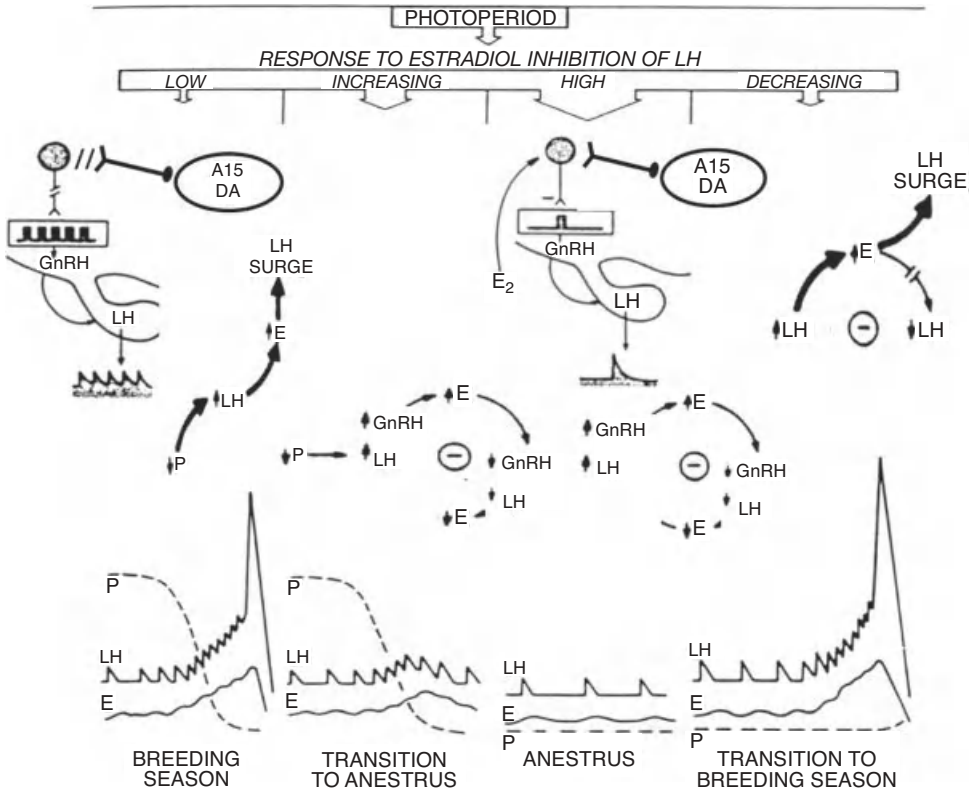

Figure 13.2. A summary model of the impact of photoperiod on reproduction in the ewe, a seasonal breeder. The melatonin signal resulting from photoperiodic inputs synchronize the expression of the endogenous circannual rhythm of responsiveness to the negative feedback effects of circulating estradiol. During anestrus, naturally longer days emphasize the profound negative feedback response to estradiol, observed in the GnRH neurosecretory system, to limit GnRH and LH release to a low frequency pulse pattern characterized by an inability to mount a preovulatory LH surge. In the breeding season, this inhibitory impact of estradiol is blunted such that rising concentrations of estradiol from the waves of follicular development eventually induce a preovulatory surge of GnRH, LH, and ovulation. The inhibitory inputs to the GnRH neurosecretory system are actively induced and retract on a seasonal basis, as the induction is a thyroxine-dependent process, through extension of an inhibitory dopaminergic input from the A15 region of the hypothalamus. Adapted from Karsch et al. (1984).

The seasonal change in sensitivity to estradiol results from a shift in neuronal inputs to the GnRH neurosecretory system. A dopaminergic pathway, projecting from the A15 area of the hypothalamus, extends and retracts from synaptic association with GnRH neurons depending on the season. The neuronal synapses from the A15 neurons inhibit the secretory activity of GnRH neurons and thus releases GnRH to a level that achieves a preovulatory surge (Goodman et al., 2000). It is of interest that thyroid hormones are required for the initiation of anestrus, as they act in a permissive manner in the neuronal extension of the inhibitory inputs to the GnRH neurosecretory system (Karsch et al., 1995). Photoperiod is not required for the shift in responsiveness to estradiol, as seasonal changes occur in ewes kept on a constant long or short day (Woodfill et al., 1991). That is, an endogenous circannual rhythm of reproductive activity drives the cycle of breeding season and anestrus. However, the natural shifts that occur in day length do synchronize the timing of the rhythm such that parturition occurs at the optimal time for neonatal survival. This is characterized by increasing temperatures and greater food availability for the dam. Chickens, turkeys and ducks are all photoresponsive and photoperiod management was first exploited to improve productivity in these species (Payne and Simmons, 1934). As with mammals, light exposure affects the onset of reproductive activity, i.e., seasonality, and the daily event of ovulation in females. Ovulation is driven by a circadian oscillation in the secretion of FSH and LH, likely driven by a surge of GnRH, which causes ovulation and oviposition to occur (Johnson, 2000). Long days of 12 to 14 hrs of light are used to extend the productive period of egg laying under typical management conditions.

Of interest the photoperiodic effect in galliforms does not appear to be mediated by pineal secretion of melatonin. Pinealectomy eliminates circulating melatonin in chickens (Pelham, 1975). But, neither pinealectomy nor orbital enucleation of turkeys alter photoperiodic influences on gonadotropin and prolactin secretion (Siopes and El Halawani, 1986). There is evidence that photoreceptors that perceive light signals are deep within the brain rather than the eye or pineal, and those receptors then influence GnRH secretory neurons in the hypothalamus (Kuenzel, 1993).

Light management of chickens varies based on production outcome, be it growth or egg laying (North and Bell, 1990). Because egg size is directly related to the age of the hen, pullets will often be managed to reach sexual maturity at a later age and larger size to avoid small egg size in the initial production cycle. Light exposure is reduced as the pullets are growing to delay sexual maturity (North and Bell, 1990). This does not affect overall productivity of the hen, but small eggs are more difficult to market, although they are no different from a nutritional perspective.

Consistent with other farm species, the most noticeable impact of light on equine performance is linked to reproduction, and there are effects on puberty and the breeding season. The primary effect on puberty appears to be a negative impact of long days to ensure that foals do not reach reproductive competence to foal at a time of year less compatible with survival of the foal (Wesson and Ginther, 1982). Because horses have a gestation length of 11 months, the timing of reproductive events dictates a long-day breeding linkage to ensure that foaling occurs at the time most advantageous to survival. Light manipulation for mares involves an increase in day length during the autumn to induce early reproductive activity, and this treatment results in a breeding season of extended duration, as horses begin to ovulate sooner under a long-day photoperiod in autumn than under natural day length (Sharp et al., 1975). Subsequent studies indicated that the earlier resumption of reproductive activity did not reduce the length of the breeding season, providing evidence that long days drive the onset of ovulatory cycles and short days result in anestrus (Kooistra and Ginther, 1975).

While an effect of season on reproductive performance is apparent in swine, and photoperiodic mechanisms are likely at play, the impact on overall reproduction is less than that of other domestic species (Peltoniemi and Virolainen, 2006). The effects of photoperiod on puberty attainment vary with some studies indicating a positive effect of short days (Dufour and Bernard, 1968), whereas others report an advantage of long days (Ntunde et al., 1979). It is likely that other environmental factors such as the season in which the study commenced, nutritional regime, and the effects of other management tactics may affect the response to photoperiod in animals to a greater extent than photoperiod.

Effects on Growth

Despite the fact that cattle are not typically considered to be seasonal breeders, the effects of photoperiod on other physiological endpoints are profound. Growth, especially in prepubertal calves, is stimulated by exposure to long days and the composition of that increase in mass favors leaner components and height relative to short days (Osborne et al., 2007; Petiticlerc et al., 1983; Rius et al., 2005). This growth improvement persists until calving even when photoperiod conditions are not controlled after puberty, with calves that developed during long days calving in at heavier bodyweights and taller stature. Long days also increase mammary parenchymal growth (Petitclerc et al., 1984; 1985), which appears to improve the lactation performance in the first lactation (Rius and Dahl, 2006). Exposure to long days also hastens the onset of puberty relative to shorter days (Hansen et al., 1983; Petiticlerc et al., 1983), but the effects on growth appear to be independent of the earlier achievement of reproductive competency. In general, exposure to long days is beneficial to calf growth and long-term productivity. Similar effects of photoperiod on lean body growth are observed in other ruminants including lambs and kids.

Photoperiod manipulation can accelerate growth in poultry, and this is exploited to improve the efficiency of gain in birds destined for slaughter. In contrast to mammals, however, a strict long day is not associated with the optimal growth pattern in chickens (Classen et al., 1991). Broiler chicks reared under an increasing photoperiod from 6 to 23 hours between day 4 and 35 of life had improved performance relative to controls raised under a constant 23 hours of light. This observation is consistent with earlier work that lean body growth was depressed at an almost constant photoperiod of 23L:1D (Robbins et al., 1984). Turkey growth efficiency shows a similar advantage of intermittent lighting versus a near continuous photoperiod (Noll et al., 1991).

Like reproduction, the effect of photoperiod on swine growth is variable and less robust than in other farmed animals. Young piglets respond positively to a 23L:1D after weaning relative to an 8L:16D regimen, and, in particular, feed intake and average daily gain benefit from the extended lighting (Bruininx et al., 2002). The impact of the light:dark cycle in older pigs, however, is absent or subtly related to the season of observation (Ntunde et al., 1979; Diekman and Hoagland, 1983), and thus of less consequence to the overall management of pig growth.

Impact on Lactation

Photoperiod manipulation of mature cows has substantial impact on lactational performance, both during established lactation and during the dry period. During an established lactation,

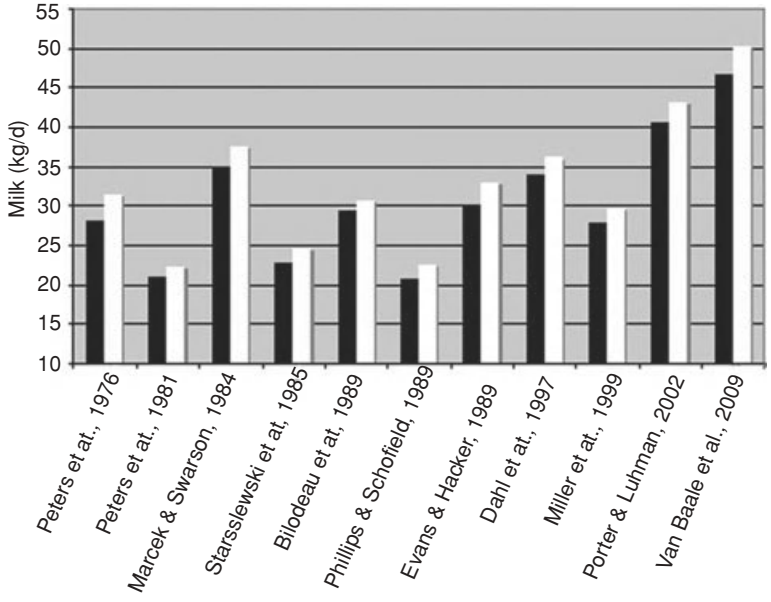

Figure 13.3. Summary figure of the effects of long day exposure on milk yield in cows. White bars represent cows under 16 to 18 hrs of light/day, whereas black bars represent yields of cows under common management of approximately 12 hrs of light/day. The studies represent a range of initial production levels, days in milk, and management conditions, as well as a broad geographic base where the experiments were conducted.

cows receiving 16 to 18 hours of light each day produce 2 to 3 kg more milk than those on a 12 light:12 dark photoperiod regardless of stage of lactation or production level (Dahl et al., 2000; see Fig. 13.3).

The greater yield during long days does not affect milk composition, as protein, lactose and fat content are all unchanged. During long days, cows will increase dry matter intake to accommodate the increase in yields, although the increase in milk output precedes the milk response. Similar increases in milk yield have been observed in sheep and goats exposed to long days when lactating. Evidence points to the aforementioned increase in IGF-1 as an endocrine mechanism underlying this response (Dahl et al., 1997).

The effect of melatonin has variable impact with regard to lactation in cattle. Feeding of melatonin to mimic a short day did not affect milk yield in early or mid-lactation cows (Dahl et al., 2000). However, melatonin implants did accelerate the decline in milk yield in late lactation cows on pasture (Auldist et al., 2007). The discrepancy in responses may be related to the relative difference in production and the nutrition of the cows in the two studies. But response variability does suggest that melatonin may explain only a portion of the observed responses to photoperiod during lactation.

During the dry period, exposure to short days improves immune status and milk yield in the subsequent lactation relative to long days (Aharoni et el., 2000; Miller et al., 2000; Dahl and Petitclerc, 2003; Velasco et al., 2008). The endocrine basis for responses at the mammary gland and circulating leukocytes is related to PRL secretion, wherein the elevated PRL during long days reduces PRL-R expression in target tissues and depresses responses to PRL (Auchtung et al., 2004, 2005). At the mammary gland, long days during the dry period are

associated with lower mammary cell uptake of tritiated thymidine, indicating lesser mammary cell division relative to cows on short days (Wall et al., 2005). These observations are further supported by examination of seasonal effects on milk yield and disease. Cows with calving dates in the winter months, (characterized by short days and cooler temperatures), produce more milk relative to herd mates that calve in summer months (characterized by long days and higher temperatures). Of interest, increases in ambient temperature have a direct relationship to circulating PRL, similar to the effect of photoperiod. Ultimately the exposure of dry cows to short days improves their capacity to produce milk and resist pathogens in the next lactation. Figure 13.4 presents a unified model of the effects of photoperiod during the life cycle of the dairy cow.

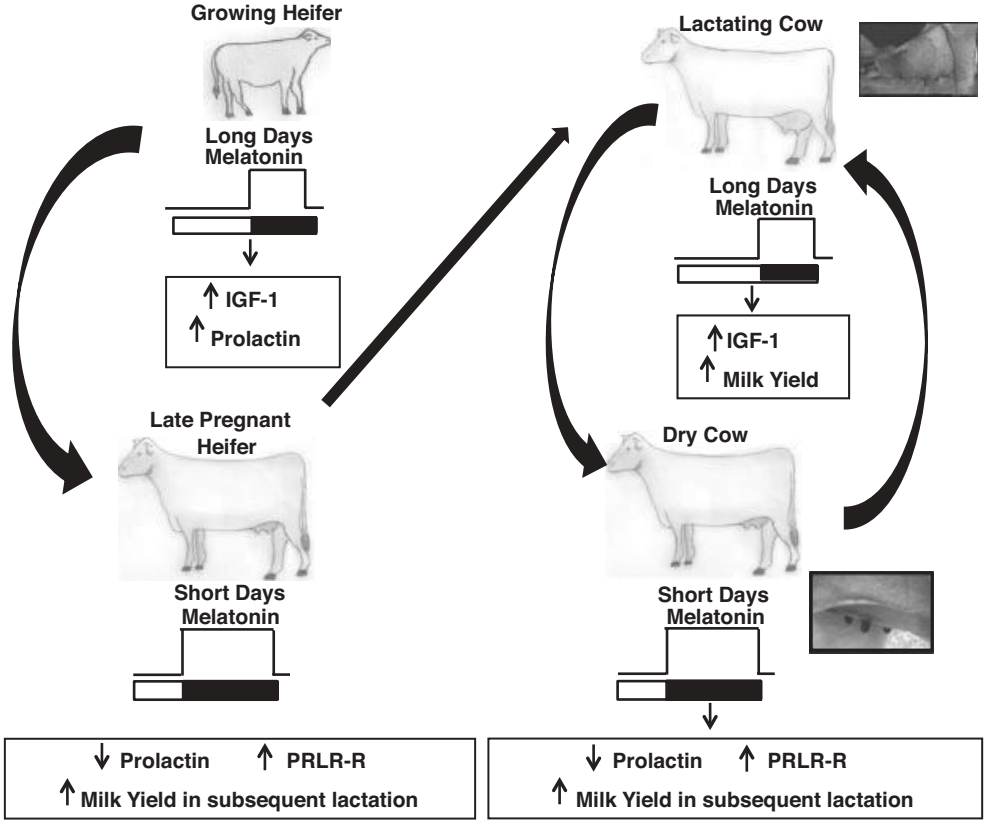

Figure 13.4. Summary model of the physiological effects and management outcomes of photoperiod manipulation of dairy cattle. Exposure to long days promotes lean body and mammary growth and accelerates puberty in growing heifers relative to short days. These effects are associated with increases in circulating IGF-1 and prolactin, which are both associated with altered melatonin profiles in cattle. During the latter stages of pregnancy in both pregnant heifers and dry cows, exposure to short days is recommended to reduce circulating prolactin and increase expression of prolactin receptor at mammary, immune, and hepatic tissues. Cows and heifers exposed to short days during pregnancy subsequently produce more milk than those to long days when dry. Lactating cows should be exposed to long days as there is an increase in circulating IGF-1 and prolactin, and an increase in milk yield during established lactation.

Other Effects

Hair, feather, and other pelage changes are some of the most readily observed effects of changes in photoperiod in birds and mammals. The short hair coat noted during summer months in cattle and horses results from the increasing day length after the spring equinox and not from higher temperatures associated with the summer (Kooistra and Ginther, 1975; Dahl et al., 2000). Moulting in birds, characterized by a loss of and subsequent regrowth of feathers is also driven by photoperiod. This is consistent with the adaptation of photoperiod signaling as a proximate cue to predict the need to alter physiological processes and adapt to environmental conditions.

An emerging area of research on the effects of photoperiod has a focus on immune function. Whereas seasonal fluctuations in disease have long been noted, the potential relationship to host immune function is a more recent observation. Some of the first evidence that photoperiod may alter immune status was generated in poultry (Skwarto-Sonta et al., 1983; Kirby and Froman, 1991), and observations in seasonal mammals soon followed (Brainard et al., 1987).

The physiological mechanisms that underlie the effect of photoperiod on immune status are related in part to changes in PRL secretion rather than other hormones affected by light. Melatonin treatment limits mammary epithelial cell loss to neutrophil-induced damage observed in response to pathogen infiltration (Boulanger et al., 2002), but this results from the innate antioxidant action of melatonin rather than an endocrine effect. In contrast, long days induce a depression of immune status in cattle relative to short days (Auchtung et al., 2004), and there is an inverse relationship between immune status and circulating PRL concentrations in cattle (Auchtung et al., 2003). Further, bovine lymphocytes express PRL-receptors and lymphocytes harvested from calves on short days are more responsive to PRL than those from calves exposed to long days (Auchtung and Dahl, 2004). Sows exposed to short days during pregnancy have improved immune function relative to those pregnant during long days, and piglets from short day sows also benefit immunologically, relative to those from long-day sows (Niekamp et al., 2006). Therefore, multiple lines of evidence suggest that seasonal cycles of disease may be related to both pathogen and host physiology, and that photoperiod is an environmental signal to adjust immune status in domestic animals.

Summary

Photoperiod is the primary cue used by farm animals to time seasonal events to optimize successful outcomes. Knowledge of the species-specific effects of light manipulation can be used to improve management efficiency, production, and health of farmed animals. This is particularly apparent in intensive housing systems used for dairy and poultry production.

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Chapter 14

Rethinking Heat Index Tools for Livestock

J. B. Gaughan, T. L. Mader, and K. G. Gebremedhin

Introduction

Climate change models predict an increase in the number of extreme weather events, including an increase in the severity and duration of heat waves. These events are likely to have a negative impact on animals that are used for food and fiber. Climate change is seen as major threat to the viability of livestock production systems in many parts of the world. Studies have suggested that severe economic and production losses are likely if management systems are not modified to account for changing climatic conditions – especially changes in heat load (St-Pierre et al., 2003). Livestock managers must be in a position to adapt quickly to climatic change, and they need to be preparing for change now (ILRI, 2006; Gaughan, 2010). In particular, high producing animals, such as modern dairy cows, are highly susceptible to heat stress due to their high level of metabolic heat production, which is required to meet the high levels of milk output.

Having the ability to predict the response of animals to heat load will allow for improvement in management strategies that may be used to ameliorate heat load. Predictive models will allow the impact of climate change scenarios to be modeled. This will then provide forecasts, which will help with regional development planning of livestock industries and livestock buildings. Modeling the impact of climate change on livestock production will allow planners to determine the economics of building modifications if animals are to be managed in potentially harsh environments and determine the feasibility of developing or maintaining livestock in certain regions and locations.

The most common empirical model of heat load is the temperature-humidity index (THI), which exists in a number of formats. The THI may not adequately describe the effect of hot climatic conditions on livestock, and it does little to predict the effects of cold conditions. The major limitation of the THI is that it does not account for solar load or wind speed (Hahn et al., 2003). In addition, it does not take into account genotype, breed, or other animal differences

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(e.g., age, level of production). The reliability of using THI (and other models) to predict animal responses to thermal stress has been examined (Bohmanova et al., 2007; Dikmen and Hansen, 2009; Hahn et al., 2009; Li et al., 2009).

In this chapter we will explore the development of heat indices, outline their limitations, and discuss attempts to modify existing indices, and discuss the development of new indices.

Defining Stress

Stress is difficult to define, partly because there has been a tendency to use stress, which is an input, to define an output. Selye (1973) defined stress as "the non-specific response of the body to any demand made upon it." Basically, this is the initiation of adaptive functions to re-establish normalcy (Lee, 1965; Selye, 1973). It may be more appropriate to use the terms stress and strain. Stress is a measure of the forces external to the body that disrupt homeostasis, whereas strain is the internal displacement brought about by the stressor (Lee, 1965). For example, we assess the impact of heat stress by measuring or observing specific responses (strain; e.g., increased rectal temperature or decreased growth rate). Furthermore, individuals will not respond to a given stressor in exactly the same manner.

There may be production changes as a response to increased heat load, but the animal may not necessarily be heat stressed, (i.e., its well-being may not be compromised). For example, a feedlot steer may reduce feed intake to a level where metabolic heat production is reduced enough so that the animal can re-establish homeostasis. The animal is no longer stressed, but growth performance has decreased.

There is also a need to define heat load and heat stress. In the context of this chapter, heat stress is the result of an animal's heat load such that the animal is not able to maintain homeostasis.

Heat balance is complex and is affected by climatic factors (e.g., ambient temperature, relative humidity, wind speed, radiant heat); animal factors (e.g., metabolic heat production, genotype, hair coat characteristics, degree of acclimatization, health status, physical activity, level of performance, reproductive state, age); and management factors (e.g., housing, provision of shade, fans and sprinkler, nutritional management). Other factors such as altitude may also play a role (Muller et al., 1994).

Heat loss or gain from an animal is a function of convection (sensible heat exchange – this may add to heat gain if environmental temperature exceeds body temperature), conduction (contact with a surface such as ground or water – this may be added to heat gain if the temperature of the contact surface exceeds body temperature), evaporation (latent heat exchange), radiation (long- and short-wave), and respiration (sensible and latent heat exchange). These factors need to be considered in any new model development.

Heat indices need to model the effect of climate on physiological factors (e.g., body temperature, milk production). They also need to account for differences between animals (e.g., genotype, age, level of production), and they may need to be species-specific. The term biological response function was termed by Hahn and McQuigg (1970) to describe these relationships.

Development of Heat Indices: The Last 70 Years

Heat-load research has focused on animal responses to heat, management strategies to alleviate heat load, and predictive tools (e.g., THI). These are not new areas of research. Indeed two publications in the 1950s: *The Effects of Temperature, Humidity, Air Movement and Solar Radiation on The Behaviour and Physiology of Cattle and Other Farm Animals* by Findlay

(1950) and *Manual of Field Studies on the Heat Tolerance of Domestic Animals*, by Lee (1953) provided comprehensive detail on the then current knowledge and future research directions.

The development of heat-load or heat-stress indices to predict animal responses began in the 1940s (Lee, 1965). Early heat index tools include but are not limited to the Iberian heat tolerance test (Rhoads, 1944), coefficient of adaptability (Benezra, 1954), biochemical index of heat tolerance (Kamal et al., 1962), discomfort index (Cargill et al., 1962), and milk production decline index (dairy cows; Berry et al., 1964).

Some of these will be discussed in more detail in the following sections.

Predicting the Effect of Heat Stress on Animals

In livestock and poultry an increase in respiration rate is an important means of increasing heat loss and is usually the first visible sign of heat stress (Bianca, 1963; McDowell, 1972). Amakiri and Funsho (1979), using tropically adapted African cattle, European cattle, and an African × European cross reported that respiration rate was a better indicator of heat tolerance than rectal temperature. However, Eyal (1963a) reported that respiration rate of Awassi sheep could not be used as the sole criterion for assessing heat tolerance. Furthermore, Bianca (1963) suggested that respiration rate either separately or in combination with rectal temperature was an inadequate measure of heat tolerance. Reporting that the actual rectal temperature after five hours of exposure to various temperature and humidity was a better indicator of heat tolerance than the magnitude of change or rate of change. Bianca (1963, p. 320) went on to say, based on laboratory studies conducted on heat tolerance, that "deep body temperature, if properly used is the best single physiological criterion of heat tolerance in cattle." The majority of the studies undertaken since 1963 would agree with this. The major obstacle to routine use of body temperature in the field has been the inability to obtain data. Field studies have been undertaken where body temperature (rectal or tympanic) has been obtained from sensors implanted in cattle over short time periods (usually less than 10 days; Davis et al., 2003; Mader and Kreikemeier, 2006; Gaughan et al., 2009), with very few studies undertaken in which body temperature was obtained over prolonged periods (Lefcourt and Adams, 1996; Hillman et al., 2003; Brown-Brandl et al., 2005a). More recently, temperature transmitters placed in the rumen have been used to obtain body temperature (Gaughan et al., 2010; Scharf et al., 2010). All of these are invasive and are not, as of yet, a realistic tool for commercil operations. The inability to reliably obtain body temperature data under field conditions has restricted the development of new heat index tools until recent times.

One of the first indices of heat stress developed was the Iberian heat tolerance test (HTC), which was used to assess the heat tolerance of cattle (Rhoad, 1944; Eq. 1 in Table 14.1). The HTC assesses heat tolerance by measuring the amount by which rectal temperature exceeds the normal rectal temperature of 101.0°F. Heat tolerance is determined by the value of HTC. The higher the HTC value the more heat tolerant the animal is perceived to be. The HTC equation was later adapted by Bianca (1963) to accommodate °C (Eq. 2 in Table 14.1). In Bianca's study, the mean rectal temperature of four Ayrshire bull calves recorded at five-minute intervals over a five-hour period when exposed to an ambient temperature of 30, 35, 40, 45, or 50°C were used to calculate heat tolerance. The HTC values fell from 94 to 49 as ambient temperature increased from 30 to 50°C (Bianca, 1963).

Heat tolerance values of 89 to 90 were reported by Rhoads (1944) for Brahman cattle. HTC values of 75.5 to 87.4 were reported by Gaalaas (1947) for Jersey cows, and values of 79 to 92 were reported for African breeds by Walker (1957).

Table 14.1. Various heat indices developed between 1944 and 1965.

Number	Equation	Source
14.1	[1]$HTC = 100 - [10 \times (BT - 101.0)]$	Rhoad (1944)
14.2	[2]$HTC = 100 - [18 \times [Tr - 38.3)]$	Bianca (1963)
14.3	[3]$HT = (BT/38.33) + (RR/23.0)$	Benezra (1954)
14.4	[4]$DI = [8.3 + (0.4 \times T_{db}) + (0.4 \times T_{wb})]$	Thom (1959)
14.5	$RT = [T_{db} \times 0.35] + [T_{wb} \times 0.65]$	Bianca (1962)
14.6	$THI = 0.4 \times (T_{db} + T_{wb}) + 15$	Johnston et al. (1962)
14.7	$THI = (T_{db} \times 0.55) + (T_{dp} \times 0.2) + 17.5.$	Johnson (1965)
14.8	[5]$DEC\ (ABS) = 2.370 - 1.736 \times NL + 0.02472 \times NL \times THI$	Berry et al. (1964)
14.9	[6]Absolute decline (lb/d) $= (3.009 + NL) \times (6.404 - (0.08008 \times T_{db}) - (0.1005 \times T_{wb}) + (0.001281 \times T_{db} \times T_{wb})$	Berry et al. (1964)

[1]Where BT = average rectal temperature (°F) based on readings at 1000 h and 1500 h.
[2]Where Tr was the mean rectal temperature of four Ayrshire bull calves.
[3]Where BT is body temperature (°C) and RR is breaths per minute.
[4]Temperature is in °F.
[5]Where DEC (ABS) is milk decline (lb/d) during periods of heat stress from that recorded under thermoneutral conditions, NL is the actual milk production (lb/d) under thermoneutral conditions, and $THI = 0.4 \times (T_{db} + T_{wb}) + 15$.
[6]Where NL is the actual milk production (lb/d) under thermoneutral conditions, and temperature is in °F.

In a much later study, Amakiri and Funsho (1979) used the difference between body temperature at 1600 h and 0800 h to predict HTC. They reported little difference between tropically adapted breeds and temperate breeds (White Fulani = 90.7; Friesian = 89.8). This was not surprising given that Vernon et al. (1959) reported that the HTC was not a useful aid for selection of heat tolerant cattle. They concluded that selection on the basis of productivity "automatically includes sufficient selection for necessary heat tolerance." Bianca (1963) came to a similar conclusion stating that high heat tolerance "goes hand in hand with a high gain of body weight." Amakiri and Funsho (1979) concluded that the lack of difference between the breeds they assessed was due to environmental adaptation. These results suggest that there is a need to account for adaptation when developing heat index tools.

Further, Benezra (1954) developed a heat tolerance index (HT) based on respiration rate (RR) and rectal temperature (RT; Eq. 3 in Table 14.1). Respiration rate was included to give recognition to its importance in body temperature control. In the equation, the denominator 38.33 (BT/38.33) is defined as the normal body temperature of cattle (°C), and the denominator 23 (RR/23) is considered to be the normal respiration rate of cattle (breaths/minute) under ideal conditions (Benezra, 1954). The lower the value determined by the equation the higher the degree of adaptability.

In 1959, Thom developed a heat index for human comfort (Discomfort Index; DI) based on dry-bulb and wet-bulb temperature (both °F; Moran, 2001; Eq. 4 in Table 14.1). The DI was used as the basis for the development of animal-based heat indices.

In a seminal study published in *Nature,* Bianca (1962) used the rectal temperature of four Ayrshire bull calves exposed to combinations of dry- and wet-bulb temperatures (°C) to develop weighting factors for wet and dry bulb temperatures (Eq. 5 in Table 14.1). The equation is generally shown using THI rather than rectal temperature.

One of the first applications of THI to livestock performance was reported in 1962. Johnston et al. (1962) studied the effects of temperature (°F) and humidity on Holstein cows. They reported a strong relationship between temperature and humidity on milk production and cow comfort (Eq. 6 in Table 14.1).

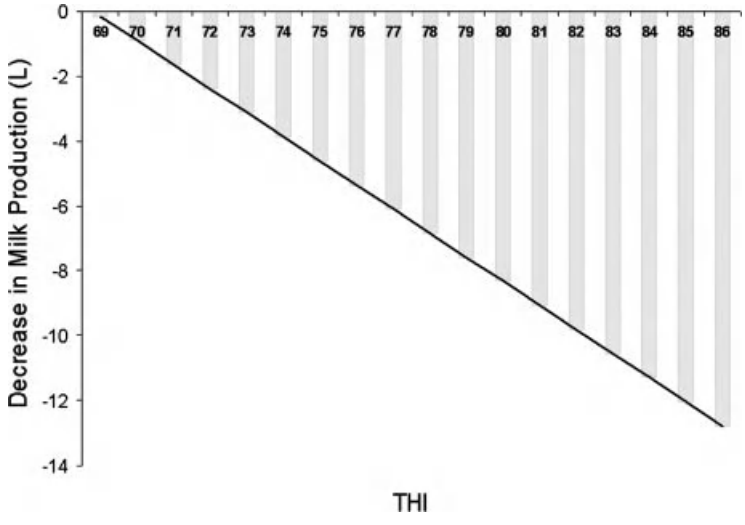

Figure 14.1. The linear decline (L/d) in milk production from a base of 30 L/d as THI increases from 69 to 86 (adapted from Berry et al., 1964).

This study formed the basis for the use of THI as an indicator of livestock heat stress. The index was later refined based on a number of studies (Johnson, 1965; Eq. 7 in Table 14.1).

In 1964, Berry et al. produced a new index which incorporated both THI and milk production (Eq. 8 in Table 14.1). The milk decline equation was recalculated and the THI component removed (Berry et al., 1964). The new equation incorporated dry bulb temperature (°C; T_{db}) and wet bulb temperature (°C; T_{wb}; Eq. 9 in Table 14.1). Equation 9 predicts that as heat load increases there will be a linear decline in milk production (see Fig. 14.1).

The THI (in its various forms) has become the de facto indicator of animal stress (Hahn et al., 2003), and is widely used to assess the response of animals to heat stress (Table 14.2). The THI has been used as the basis for the Livestock Weather Safety Index (LWSI; LCI, 1970) to describe categories of heat stress for livestock exposed to extreme hot-weather conditions and can be utilized to define thresholds where the potential for heat stress in livestock exists (FASS, 2010).

Although THI is widely accepted for evaluating the effects of the climatic environment on livestock, it has some limitations. One of the major problems with many of the previously mentioned indices is that there is an underlying (although not explicitly stated) assumption

Table 14.2. Some forms of THI[1] developed for various species.

Species	THI Equation	Source
Swine	$(0.65 \times T_{db}) + (0.35 \times T_{wb})$	Ingram (1965)
Swine	$(0.75 \times T_{db}) + (0.25 \times T_{wb})$	Roller and Goldman (1969)
Laying hens	$(T_{db} \times 0.60) + (T_{wb} \times 0.40)$	Zulovich and DeShazer (1990)
Turkeys	$(T_{db} \times 0.74) + (T_{wb} \times 0.26)$	Xin et al. (1992)
Dairy cows	$T_{db} + (0.36 \times T_{dp}) + 41.2$	Johnson and Vanjonack (1976)
Beef cattle	$(0.8 \times T_{db}) + [rh \times (T_{db} - 14.3)] + 46.3$	NOAA (1976)

[1]All temperatures in °C, rh in decimal form.

that all animals respond to an environmental stressor exactly the same way. This is, of course, an unrealistic assumption. For example, it is generally accepted that low producing cows (e.g., 20 L milk/d) are less affected by heat stress than high producing cows (e.g., 45 L milk/d). Variation in animal response to climatic variables is well documented. For example, Thwaites (1967) reported that young lambs are more susceptible to heat than older sheep, and Xin et al. (1994) reported that broilers are more susceptible to heat during the first three weeks of growing period, and males are more affected by heat than are females. Brown-Brandl et al. (1997) found an age response (regarding RR and RT) in turkeys exposed to high heat load, but no set relationships for respiration rate or rectal temperature were determined.

The THI does not take into account the effects of thermal radiation (solar and long-wave), wind speed, duration of exposure, or differences in age or genotype. Furthermore, the usefulness of a specific index may be a function of the conditions under which it was developed. Seven variations of the THI were evaluated in a hot, humid environment and a hot, semi-arid environment by Bohmanova et al. (2007). They reported that there were differences in milk-decline threshold among the indices and between the two regions. They concluded that the "indices with higher weights on humidity were best in humid climates, whereas indices with higher weights on temperature were the best in the semiarid climate." Attempts to rectify some of the perceived deficiencies in the THI have resulted in the development of new indices.

Modifications to THI and New Indices

In recent times the need to use a biological approach for assessing susceptibility to heat stress has been emphasized (Hahn et al., 2003). However, this is not a new approach. As we have already seen Johnston et al. (1963) used THI to explain changes in milk production, and much earlier, Rhoad (1944) used rectal temperature as an indicator of heat tolerance.

Over the past 60 years, many new indices have been proposed (Bohmanova et al., 2007). Most have focused on ambient temperature and relative humidity, and their use is somewhat limited (Bohmanova et al., 2007). In regards to a thermal stress model for livestock, Mader et al. (2010) suggested that a multi-factor approach would be superior to a single factor index for determining environmental effects on animals. Technological advances have improved the ease of data collection while the reliability and accuracy of data collection have also improved. Studies that incorporate physiological factors such as skin temperature, sweating rate, respiration rate, core body temperature, and blood profiles are now possible under controlled laboratory conditions and in the field (e.g., Li et al., 2009; Gebremedhin et al., 2010; Scharf et al., 2010).

In an attempt to account for solar load, Buffington et al. (1981) developed the black globe humidity index (BGHI) to explain reductions in milk production for dairy cows exposed to hot conditions (Eq. 14.1). The BGHI is essentially the same as the one developed by Johnson and Vanjonack (1976), with black globe temperature replacing ambient temperature.

$$BGHI = T_{bg} + (0.36 \times T_{dp}) + 41.5 \tag{14.1}$$

Where:

T_{bg} = black globe temperature (°C)
T_{dp} = dew point temperature (°C)

A black globe temperature is obtained by using a matte black copper ball approximately 12.5 to 15 cm diameter with a temperature sensor inside (Lee, 1953). The black globe integrates

the effects of ambient temperature, solar radiation, and convective cooling of wind into a temperature value (Li et al., 2009).

A more comprehensive index for lactating dairy cows was developed by Baeta et al. (1987). The equivalent temperature index (ETI) was derived from the analysis of milk production and heat-loss rates. The ETI incorporates ambient temperature, relative humidity, and wind speed into a single index. The index is applicable for ambient temperature between 16 and 41°C, relative humidity from 40 to 90%, and air velocity from 0.5 to 6.5 m/s (Baeta et al., 1987; Eq. 14.2). This index demonstrated the importance of air movement in ameliorating the effects of high temperature and humidity (see Fig. 14.2)

$$\begin{aligned} ETI = 27.88 &- 0.456 \times t_{db} + 0.010754 \times t_{db}^2 - 0.4905 \times rh + 0.00088 \times rh^2 + 1.15 \times ws \\ &- 0.12644 \times ws^2 + 0.019876 \times t_{db} \times rh - 0.046313 \times t_{db} \times ws \end{aligned} \quad (14.2)$$

Where:

t_{db} = dry bulb temperature (°C)
rh = relative humidity
ws = wind speed (m/s)

Zhou and Yamamoto (1997) developed a respiration rate index for broilers (Eq. 14.3). The index developed is a function of the heat produced by the birds and the associated ambient temperature. This study demonstrated the importance of including heat production in a predictive model of heat stress. The inclusion of heat production in a predictive model will not be an easy task, due to differences in feed ingredients, feed intake, and feed utilization by the animal.

$$RR = -777.0 + 5.0 \times HP + 26.0 \times T_{db} \quad (14.3)$$

Where:

RR = respiration rate (breaths per minute, bpm)
HP = heat production ($KJ/kgW^{0.75}h$)

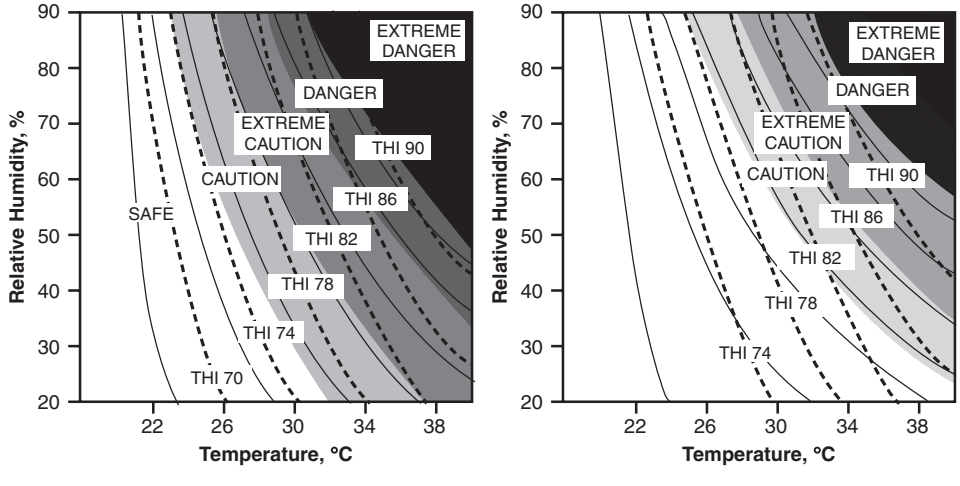

Figure 14.2. Equivalent Temperature Index (ETI) as a function of ambient temperature and humidity at wind speeds of 0.5 m/s (left) and 6 m/s (right), with associated categories of potential impact on dairy cows (Baeta et al., 1987). Values of THI are superimposed for comparison.

Table 14.3. Respiration rates associated with temperature-humidity index thresholds (Eigenberg et al., 2005).

Threshold	THI	Respiration Rate, Breaths min^{-1}
Normal	74 or less	<90
Alert	74 to <79	90 to 110
Danger	79 to <84	110 to 130
Emergency	84 and above	>130

Eigenberg et al. (2005) developed an algorithm (Eq. 14.4) to predict the respiration rate of unshaded cattle based on ambient temperature (°C), relative humidity, wind speed, and solar radiation. As previously mentioned, respiration rate is the first visual symptom of heat stress, and, therefore, it is logical to use changes in respiration rate to assess animal welfare (Table 14.3).

$$RR = 5.1 \times T_{db} + 0.58 \times rh - 1.7 \times ws + 0.039 \times sr - 105.7 \quad (14.4)$$

Where:

sr = solar radiation (W/m^2)

Using data from three cattle studies, Mader et al. (2006) developed wind speed and solar radiation adjustments for THI (Eq. 14.5). The adjustments were made on the basis of changes in panting score (0 = no panting to 4 = severe panting) of feedlot cattle (>2,000 observations). Over the three studies, the animals were exposed to a temperature range of 17.2 to 36.0°C.

$$THI_{ADJ} = 4.51 + THI - (1.992 \times ws) + (0.0068 \times sr) \quad (14.5)$$

Where:

The THI used is $THI = \{(0.8 \times T_{db}) + [rh \times (T_{db} - 14.4)] + 46.4\}$

In addition to the effects of ambient temperature and relative humidity, these new models also include the effects of wind speed and solar load. Furthermore, new approaches have attempted to categorize animals based on biological differences (e.g., breed type, coat color, health status, etc.).

Brown-Brandl et al. (2005b) developed five respiration rate models using statistical and non-statistical modeling techniques. The models were based on weather parameters including dry bulb temperature (T_{db}), dew point temperature (T_{dp}), sweating rate (sr) wind speed (ws), and breed (Angus, Charolais, Gelbvieh, and a composite consisting of Pinzgauer, Red Poll, Hereford, and Angus (MARC III). Four of the models performed well and were able to account for 59 to 68% of the variation in the respiration rate data. It was evident from this study that breed differences in thermal tolerance need to be taken into account.

The Heat Load Index (HLI; Gaughan et al., 2008) was developed for feedlot beef cattle. The index accounts for biological differences (panting score, respiration rate, body temperature, and feed intake), breed differences, and management factors (e.g., access to shade). The HLI combines the effects of relative humidity, wind speed, and black globe temperature on the panting score of feedlot cattle into a single index. The model was developed within an ambient temperature range of 8 to 45°C. Within this index, low wind speed results in the greatest change, leading to an increase in the HLI.

The HLI algorithm consists of two parts based on a black globe temperature threshold of 25°C (Eqs. 6 and 7 in Table 14.1).The HLI can provide a spot measure of thermal stress. However, its main function is in the determination of accumulated heat load (accounting for intensity × duration). The HLI is also used as the basis for a Web-based risk assessment program and heat stress prediction service.

$$HLI_{TBG>25} = 8.62 + 0.38 \times rh + 1.55 \times T_{BG} - 0.5 \times ws + e^{(2.4-ws)} \quad (14.6)$$

Where e is the base of the natural logarithm.

$$HLI_{TBG<25} = 10.66 + 0.28 \times rh + 1.30 \times T_{BG} - ws \quad (14.7)$$

All of the above livestock indices are relevant only under hot conditions. None of them incorporates major environmental components that are experienced over a range of both hot and cold conditions. Also, most of the models are not tied or linked to physiological responses of livestock.

To determine which of the thermal index models are good predictors of stress levels of cattle, the Pearson correlation coefficient between the calculated indices and measured physiological responses of each model were calculated (Li et al., 2009). The correlation coefficient is a measure of the strength of the linear relationship between two variables and is independent of the respective scales of measurement. Two data sets were used for the analyses. The first data set was from a study on sweating rate of cows by Gebremedhin et al. (2008). The data were collected at five different sites (Ona, Florida; Oahu, Hawaii; Starkville, Mississippi; Clay Center, Nebraska; and Tucson, Arizona) with different breeds of dairy cows (Holsteins, Gir-Holstein cross, Jersey) and feedlot heifers (Black Angus, Charolais, MARC I and MARC III from Clay Center, Nebraska; Angus White from Ona, Florida; Black Angus, a genetic strain of black Angus from Brooksville, Florida; Kansas Black, a genetic strain of black Angus from Northern climates that were not a acclimated to hot conditions).

The measured physiological parameters include sweating rate, skin temperature, rectal temperature, and respiration rate, and the environmental parameters measured were air temperature, relative humidity, solar radiation, and wind speed.

The second data set was taken at the University of Arizona Parker Agriculture Research Complex during August of 2008; air temperature, relative humidity, air velocity and solar radiation were controlled, and skin temperature, rectal temperature, respiration rate, and sweating rate were measured (Gebremedhin et al., 2010).

The Pearson correlation coefficients were calculated using the CORR procedure of SAS (SAS Institute Inc., 2004). The basic descriptive statistics for the two datasets is given in Tables 14.4 and 14.5. The environmental conditions cover what most dairy production systems would experience, and the physiological responses also cover from the zone of least thermoregulation (thermoneutral) to highly stressful conditions (in which respiration rate = 148 times/minute, sweating rate = 1101 g/m^2/hr, skin temperature = 46.9°C, and rectal temperature = 41.9°C). These peak responses did not occur in one cow simultaneously, however.

The correlation coefficients among the environmental indices (THI, THI_{adj}, BGHI, ETI, HLI, and RR) and the physiological responses (skin temperature, respiration rate, and sweating rate) calculated using the first dataset is given in Table 14.6. The results show that skin temperature is correlated with the all of the previously mentioned environmental indices but not strongly so, whereas respiration and sweating rates are not correlated with THI, THI_{adj}, BGHI, ETI, and HLI.

Table 14.4. Descriptive statistics of Dataset 1, where measurements were taken at five sites across the United States from 2000 through 2007.

		N	MEAN ± SD	MIN	MAX
Environmental factors	T_{db}, (°C)	269	32.7 ± 3.7	25.0	41.1
	rh, (%)	269	52.1 ± 17.5	24.0	81.6
	sr, (W/m^2)	269	759.0 ± 216	126.0	1120
	ws, (m/s)	269	0.86 ± 0.34	0.1	1.8
Thermal indices	THI (Eq. 14.6)	269	81.9 ± 2.5	73.6	86.4
	BGHI (Eq. 14.1)	269	89.9 ± 3.6	80.9	98.3
	ETI (Eq. 14.2)	269	34.1 ± 2.3	27.0	37.4
	RR (Eq. 14.4)	269	120 ± 1.5	79.7	151.1
	THI_{adj} (Eq. 14.5)	269	89.8 ± 3.0	81.1	94.9
	HLI (Eqs. 14.6 and 14.7)	269	96.6 ± 4.4	84.4	106.5
Physiological responses	RR, (bpm)	184	102 ± 19.1	60.0	148
	SK, (°C)	263	39.3 ± 2.96	31.5	46.9
	RT, (°C)	269	40.1 ± 0.92	38.2	41.9
	SW, (g/m^2 h)	269	329.0 ± 163.0	6.0	1101

Table 14.5. Descriptive statistics of Dataset 2 where measurement was taken at the University of Arizona in 2008.

		N	MEAN ± SD	MIN	MAX
Environmental factors	T_{db} (°C)	403	32.0 ± 3.9	26.2	38.6
	rh (%)	405	51.3 ± 22.5	20.6	80.7
	sr (W/m^2)	405	388.9 ± 298	0.0	850.0
	ws (m/s)	405	0.863 ± 0.61	0.1	1.8
Thermal indices	THI (Eq. 14.6)	405	80.5 ± 1.5	75.1	83.6
	BGHI (Eq. 14.1)	403	85.2 ± 5.1	73.7	94.5
	ETI (Eq. 14.2)	403	32.6 ± 1.7	27.6	35.0
	RR (Eq. 14.4)	403	101.0 ± 15.7	61.1	137.9
	THI_{adj} (Eq. 14.5)	405	85.9 ± 3.1	77.6	93.6
	HLI (Eqs. 14.6 and 14.7)	403	89.8 ± 9.6	62.9	103.3
Physiological responses	RR, (bpm)	386	104.0 ± 20.5	40.0	132.0
	SK, (°C)	358	36.93 ± 2.46	31.4	43.2
	RT, (°C)	405	39.6 ± 0.75	38.2	40.9
	SW, (g/m^2 h)	405	213.8 ± 168	0.0	993.0

Table 14.6. Correlation coefficients between environmental indices and physiological responses of cattle using Dataset 1.

Index	Skin Temperature, °C	Respiration Rate, bpm[1]	Sweating Rate
THI	0.40	0.16	0
THI_{adj}	0.52	0.19	−0.07
BGHI	0.42	0.02	0.15
ETI	0.30	0.34	−0.25
HLI	0.36	0.22	−0.31
RR	0.48	0.10	0.07

Table 14.7. Correlation coefficients between environmental indices and physiological responses of cattle using Dataset 2.

Index	Skin Temperature	Respiration Rate	Sweating Rate
THI	0.10	0.39	0.26
THI_{adj}	0.49	0.65	0.03
BGHI	0.56	0.73	0.24
ETI	−0.29	0.23	−0.08
HLI	0.31	0.68	−0.05
RR	0.54	0.68	0.23

Similarly, the correlation coefficients for the second dataset are given in Table 14.7. The results show that respiration rate is reasonably well correlated with THI_{adj}, BGHI, and HLI but skin temperature is not strongly correlated with any of the environmental indices. Sweating rate is again poorly correlated with all environmental indices. The poor correlation of sweating rate can be explained by the fact that sweating response of cattle is cyclic in nature (Gebremedhin et al., 2010). Therefore, a measured sweating rate can be anywhere in the cycle, which inherently produces inconsistency in the data.

The two datasets were pooled together and further statistics were performed to determine the R^2 values between skin temperature and each of the three indices (THI_{adj}, BGHI, and RR) that showed some correlation. The calculated adjusted R^2 values are 0.36, 0.36 and 0.38, respectively, which again illustrate that a better index tool that accurately predicts physiological responses of cattle is necessary, thus the need for development of the Comprehensive Climate Index (CCI) discussed further on in this chapter. The linear regression curves between skin temperature and the three indices are shown in Figures 14.3 through 14.5.

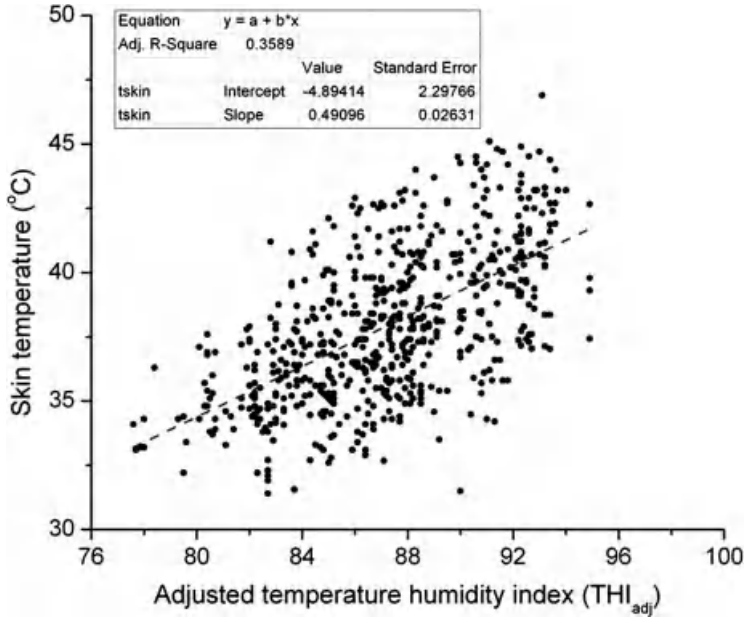

Figure 14.3. Regression of skin temperature versus adjusted temperature humidity index (THI_{adj}).

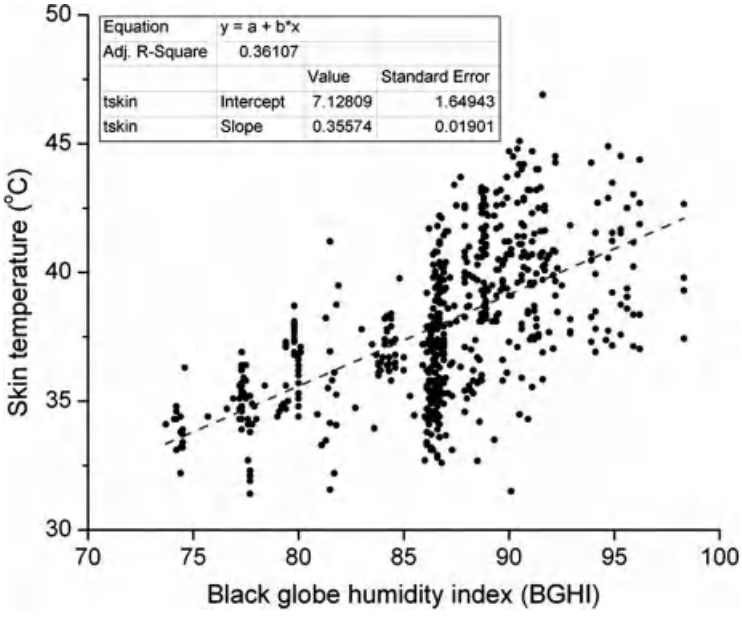

Figure 14.4. Regression of skin temperature versus black globe humidity index (BGHI).

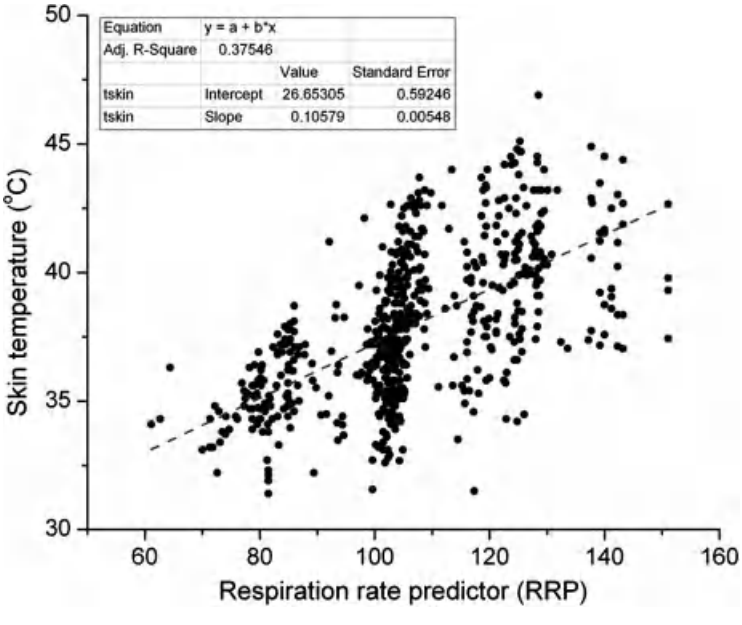

Figure 14.5. Regression of skin temperature versus respiration rate predictor (RR).

Table 14.8. Arbitrary comprehensive climate index thermal stress thresholds (adapted from Mader et al., 2010).

		Cold Conditions	
		Animal Susceptibility	
Environment	Hot Conditions	High	Low
No stress	<25	>5	>0
Mild	25 to 30	0 to 5	0 to −10
Moderate	>30 to 35	<0 to −5	<−10 to −20
Severe	>35 to 40	<−5 to −10	<−20 to −30
Extreme	>40 to 45	<−10 to −15	<−30 to −40
Extreme danger	>45	<−15	<−40

The Comprehensive Climate Index

The Comprehensive Climate Index (CCI) was developed within a temperature range of –30 to 45°C (Mader et al., 2010). The CCI builds on the HLI by taking into account a much broader range of climatic conditions and incorporates major environmental components that are experienced over a range of both hot and cold conditions. In addition, environmental stress thresholds have been developed (Table 14.8). The CCI, with designated thresholds, incorporates into a single index the combined effects of temperature, relative humidity, wind speed, and solar radiation. The purpose of the CCI was to provide a relative indicator of the environmental conditions surrounding an animal and to quantify how solar radiation, wind speed, and relative humidity interact with ambient temperature to produce an "apparent temperature" that adjusts ambient temperature for the effects of respective environmental variables. Thus, equations were derived to allow adjustments to ambient temperature due to the effects of relative humidity, wind speed, and solar radiation. From this analysis, three general algorithms were developed to define the relationship between ambient temperature and relative humidity (see Fig. 14.6), ambient temperature and wind speed (see Fig. 14.7) and ambient temperature and solar radiation (see Fig. 14.8). With this index, low wind speed results in the greatest change in apparent temperature per unit of wind speed.

For strategic decision-making, the goal should be to have an index that is broadly applicable across life stages and species in order to maximize the utility of probability information (Hahn et al., 2003). Indices are needed that are comprehensive in nature and allow for greater application across a range of conditions. Both the HLI and the CCI have developed a variety of thresholds to indicate the intensity of climatic stress experienced by the animal (see Tables 14.8 and 14.9).

Accounting for Intensity × Duration

It has been recognized for some time that there is a need to assess heat load on the basis of diurnal variations in an animal's physiological responses (Amakiri and Funsho, 1979). For example, Eyal (1963b) stated that heat tolerance needs to be assessed by taking into account animal responses both during the hot part and the cool part of the day.

To account for intensity × duration impacts of heat stress, Hahn et al. (1999) derived a two-stage classification scheme (THI-hrs) that categorized heat stress based on the amount of

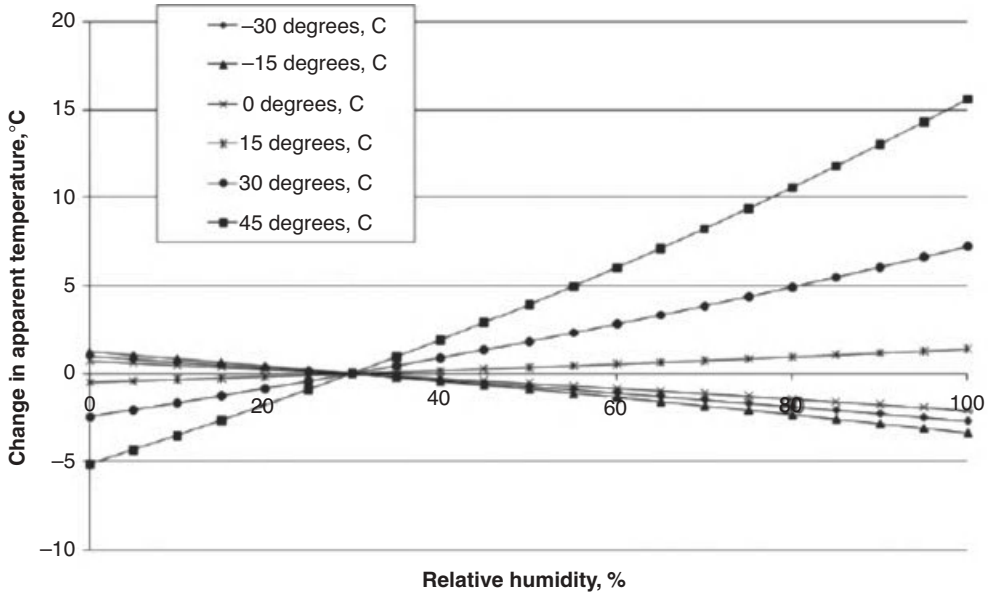

Figure 14.6. Temperature adjustments for the Comprehensive Climate Index, based on percent relative humidity at different ambient temperatures.

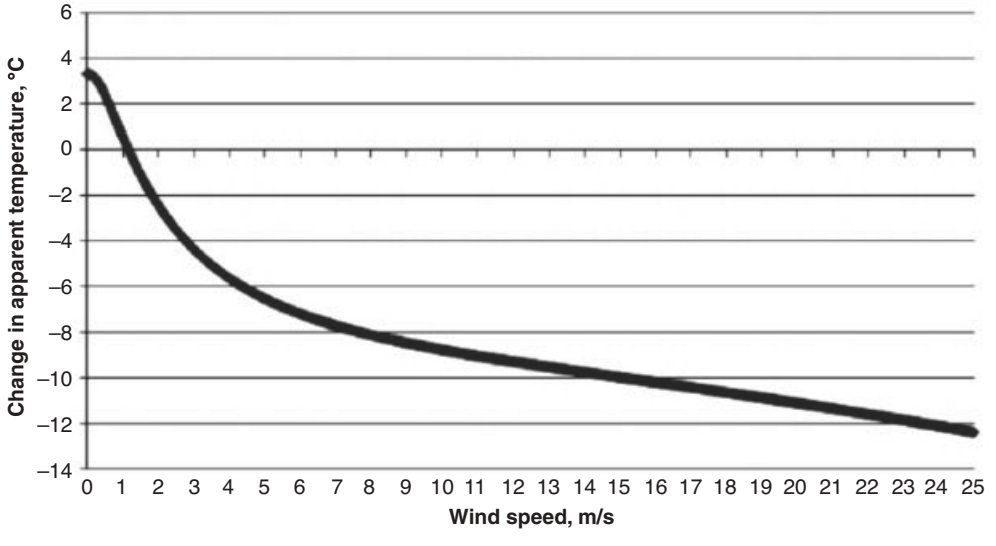

Figure 14.7. Temperature adjustments for the Comprehensive Climate Index based on wind speed.

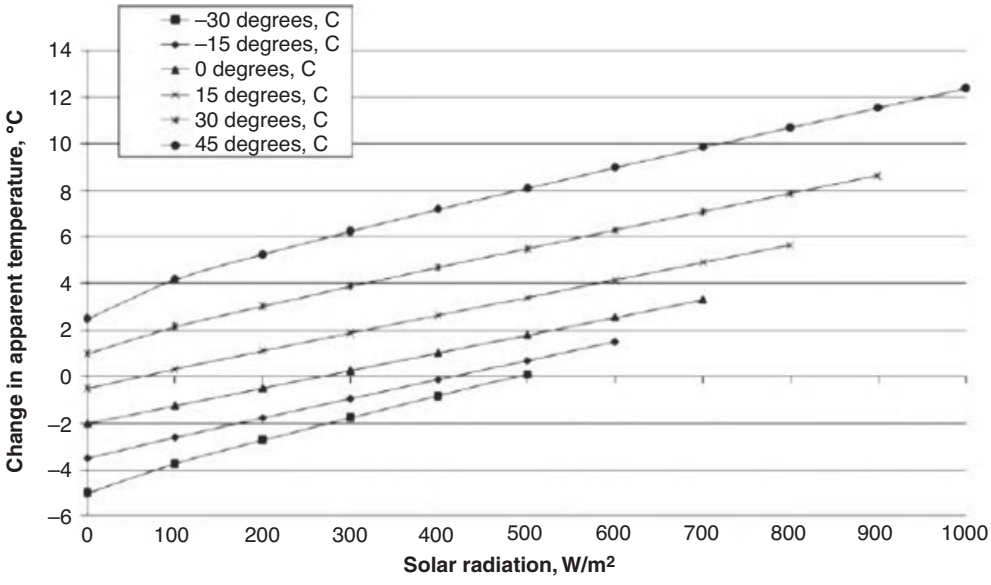

Figure 14.8. Temperature adjustments for the Comprehensive Climate Index based on solar radiation at different ambient temperatures.

time (hours) feedlot cattle were exposed to THI>79 and THI>84, and the effects of nighttime recovery (hours <72). The THI thresholds of 79 and 84 are the Danger and Emergency categories of the Livestock Weather Safety Index (LCI, 1970). This was an important step forward in classifying the impact of heat load on cattle. However, Hahn et al. (1999) acknowledged that the THI-hrs model did not account for the effects of solar radiation, wind speed or biological factors such as genotype. In an attempt to rectify this, Gaughan et al. (2008) used the THI-hrs concept to develop an accumulated heat load model (AHL) based on the HLI discussed previously. When an animal is exposed to a HLI above its threshold, there is a rise in core body temperature. The greater the amount of time (hours) an animal spends above the threshold the greater the AHL and the greater the stress on the animal. The standard AHL threshold (HLI = 86) is based on a reference animal (healthy Black Angus steer without access to shade). Adjustments to the threshold (+ or −) are then made on the basis of animal type, health status, and management (Table 14.9).

The HLI thresholds are also used in a Web-based risk assessment model. The risk assessment model provides an analysis of the susceptibility of feedlot cattle to high heat load based on historical weather data for a specific location, genotype, phenotype, access to shade, days on feed, and various management strategies (see Fig. 14.9).

Early Warning Systems

Paramount to any early warning system is animal observation. Management tools such as thermal stress models should be used in conjunction with animal response and should not be used in place of sound animal management. The panting score system for cattle (Mader et al., 2006) provides an easy-to-use visual assessment of cattle response to climatic conditions

Table 14.9. Animal characteristics (genotype, coat color, health status, acclimatization), management adjustments (access to shade, days on feed, manure management, and drinking water temperature), and their effects (+ and −) to the heat load index (HLI) threshold of the reference steer (healthy, unshaded Angus, 100 days on feed; Gaughan et al., 2008).

Item	Number of Cattle[1] Used to Determine the Specific Threshold	Relative Effect on on Upper HLI Threshold of the Reference Steer (HLI = 86)
Genotype:		
Bos taurus (British)	9,075	0[2]
Bos taurus (European)	429	+ 3 (i.e. 86 + 3)
Bos indicus (25%)	451	+ 4
Bos indicus (50%)	1,345	+ 7
Bos indicus (75%)	1,039	+ 8
Bos indicus (100%)	666	+ 10
Coat Color:		
Black	2,859	0
Red	1,158	+ 1
White	293	+ 3
Health Status:		
Healthy	15,623	0
Sick/recovering	1,987	− 5
Acclimatization:		
Acclimated	6,200	0
Not acclimated	2,920	− 5
Shade:[3]		
No Shade	3,467	0
Shade (>1.5 to 2 m^2/animal)	1,336	+ 3
Shade (>2.0 to 3 m^2/animal)	6,473	+ 5
Shade (>3.0 m^2/animal)	4,761	+ 7
Days on Feed: [4]		
0–80 d	2,672	+ 2
80–130 d	8,385	0
130+ d	1,239	− 3
Manure Management: [5]		
Max. depth of manure pack = 50 mm	3,224	0
Max. depth of manure pack = 100 mm	704	− 4
Max. depth of manure pack = 200 mm	220	− 8
Drinking Water Temperature:[6]		
15 to 20 °C	224	+ 1
21 to 30 °C	2,035	0
31 to 35 °C	399	− 1
>35 °C	201	− 2

[1]Not all cattle have been assessed within each threshold trait. For example, coat color was only assessed in *Bos taurus* cattle, manure management was assessed at five feedlots and drinking water temperature was assessed at three feedlots.
[2]The values for the reference steer are presented as "0," i.e., no change from the threshold of 86.
[3]For shade that provides 70% block-out (includes shade cloth and also steel structures with gaps in the roof). Unshaded *Bos indicus* cattle >25% not included.
[4]Not all cattle were assessed for this trait.
[5]Mean depth over 54 d.
[6]Only unshaded Angus cattle were assessed for this trait.

MLA Risk-Analysis Program—Results
RAP Version 1.0
Effective from 10 December 2006
Results calculated on Thu Oct 21 08:42:12 2010

Parameter	Value
Site	Amberley (Qld)
Period analyzed	January
Cattle type	Bos taurus
Coat color	Black
Health status	Healthy
Number of days on feed	80–130
Amount of shade	No shade
Trough water temperature	20–30 degrees
Pen class	Class 1
Extra water troughs installed	No
Heat load ration fed	No
Wet manure removal	No

HLI value that stock begin to accumulate heat stress: 86

Event duration	High-event frequency	Extreme-event frequency
2 days	1–2 events in 4 years	1–2 events in 45 years
3 days	1–2 events in 3 years	1–2 events in 5 years
4 days	1–2 events in 3 years	1–2 events in 10 years
5 days	1–2 events in 4 years	1–2 events in 10 years
6 days	1–2 events in 5 years	1–2 events in 10 years
7 or more days	1–2 events in 5 years	Less than 1 event in 9 years

Figure 14.9. Parameters entered into the risk assessment program and the subsequent outcome. A high event frequency represents a dangerous situation, and an extreme event is an event in which cattle (healthy, unshaded Black Angus) deaths due to heat stress are possible.

(Table 14.10). Panting scores are used to assess individual animals and can then be combined to give a mean panting score for a group of cattle (e.g., a feedlot pen; Gaughan et al., 2008). Panting scores give an indication of an animal's thermal load, which livestock managers can then use in strategic decision-making. For example, if feedlot cattle have a panting score ≥ 2 at 0600 h, and the day is predicted to be hot then it may be necessary for managers to implement strategies to reduce the heat impact on the animals. This could, for example, constitute a change in dietary components in the ration.

The primary limitation in the design and implementation of an efficient early warning system of impending thermal stress is the dissemination of weather predictions to those that need the information (Gaughan and Hahn, 2010).

A number of open access Web-based early warning forecast systems for pending high heat load (and cold stress) have been developed (Table 14.11). Access to a number of other sites is available via subscription. The forecasts are usually based on spatial distribution of weather data (e.g., temperature variation across 5 km grids) determined from official weather stations which may be many km apart. Modeling the differences in ambient temperature and humidity

Table 14.10. Panting score[1] and breathing condition (adapted from Gaughan et al., 2008).

Panting Score	Level of Stress	Breathing Condition
0	No stress	No panting.
1		Slight panting, mouth closed, no drool, easy to see chest movement.
2	Moderate stress	Fast panting, drool present (from nose and mouth), mouth closed.
2.5		As for 2, but occasional open mouth, tongue not extended.
3	High stress – dangerous conditions	Open mouth for prolonged periods and excessive drooling, neck extended, head held up, tongue not extended.
3.5		As for 3 but with tongue out slightly, and occasionally fully extended.
4	Extreme stress – emergency condition	Open mouth with tongue fully extended for prolonged periods with excessive drooling. Neck extended and head held up.
4.5		As for 4 but head held down, cattle may "breath" from the flank, drooling may cease.

[1]Modified from Mader et al. (2006).

in the area between weather stations is generally very good (although it is only as good as the reliability of the forecast).

The Web-based models provide a one- to five-day forecast of weather conditions. The predictions are updated at least every 24 hours, although more frequent updates are available. For example, Figure 14.10 shows the 24-hour forecast for the United States on the July 27, 2010, and Figure 14.11 shows a five-day forecast for Gatton Australia from October 22 to 27, 2009. The accuracy of the predictions appears to have a high degree of reliability for three days (Gaughan and Hahn, 2010). However, there appears to be an inability to adequately model wind speed. Furthermore, natural and built structures can have profound effects on wind speed and direction.

There is a need therefore for livestock managers to have access to onsite weather data. Although onsite data may be of little use as a prediction tool it will allow managers to determine site variations in ambient temperature, relative humidity and wind speed from the official weather stations. This will allow managers to modify the predicted weather conditions to their particular site. It is likely that software will be developed that will allow managers to

Table 14.11. Web-based weather forecast sites for livestock (adapted from Gaughan and Hahn, 2010).

Country	Species	Web Address
AUS	Dairy cows	www.coolcows.com.au
AUS	Feedlot beef	www.katestone.com.au/mla
USA	Feedlot beef	http://www.ars.usda.gov/Main/docs.htm?docid=19896
USA*	Dairy and beef cattle	http://agweather.mesonet.ou.edu/models/cattle/default.html
USA	Livestock	http://wwwagwx.ca.uky.edu/mrf_lsi.htm
USA**	Livestock	http://www3.abe.iastate.edu/livestock/heat_stress.asp

*Assumes no difference between beef and dairy cattle.
**This site only provides THI thresholds it does not provide a predictive service.
AUS = Australia.

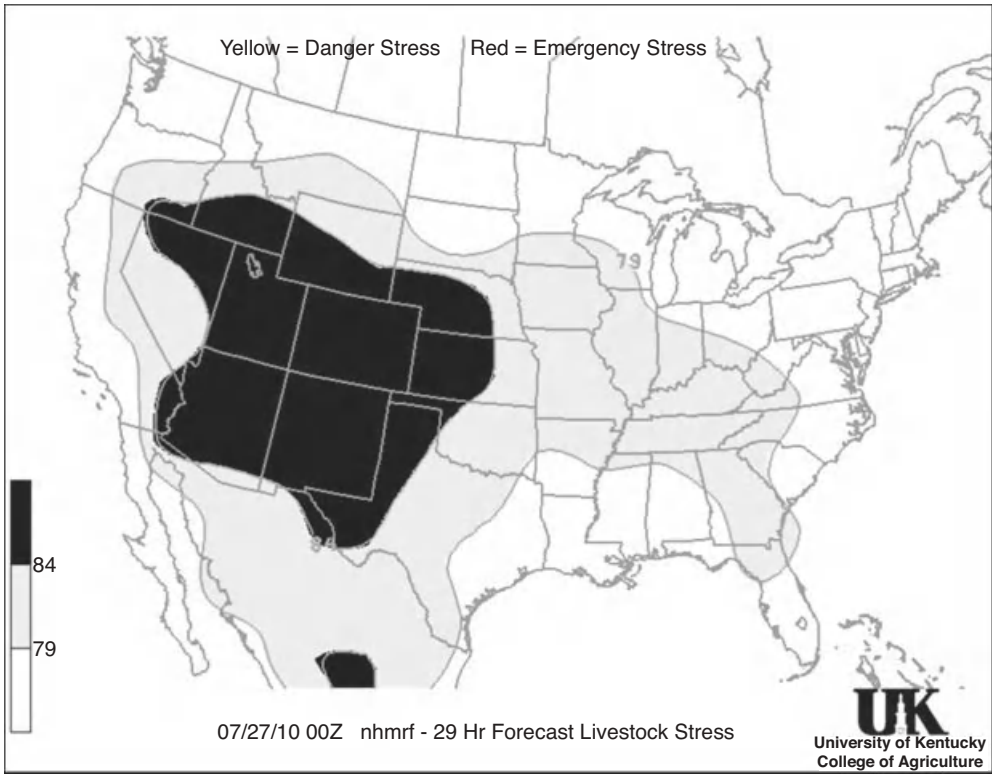

Figure 14.10. A 24-hour heat stress forecast based on THI covering the United States for July 27, 2010 (http://wwwagwx.ca.uky.edu/mrf_lsi.htm).

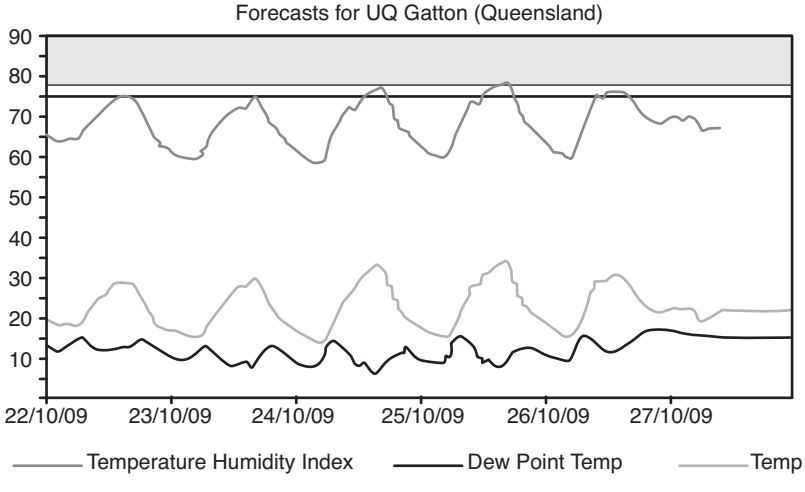

Figure 14.11. A five-day heat stress forecast based on THI for a specific location (Gatton, Australia) from October 22 to 27, 2009 (www.coolcows.com.au).

integrate their onsite data with Web-based services. Commercially available weather stations are now cheap, and reliable enough to allow this. However, there is a need to ensure that sensors are calibrated and that the weather station is placed in the "best" position in relation to the location of the animals. For example, there is little value in placing the weather station 400 m from the animals to be assessed.

High-speed computers and software packages are allowing us to work with more expansive climate models on a farm. However, there is still a need to assess animals in the field. The use of sentinel animals has been suggested (i.e., placing body temperature sensors in one or two animals and using these to estimate the effect of climate on all animals). However, there is considerable animal variation, and if the wrong animals are chosen the results will not be truly representative. Using the available data is still somewhat problematic in that you manage for the average effect, or on the basis of the most affected animals.

Conclusions

Model development is problematic in that the models must account for the complexities in the relationship between climatic and animal variables. To do this, models will need to be tested under a wide range of environmental and management conditions. There is also a need to consider genotypic and phenotypic variations between various species of interest. The newer, complex models (e.g., HLI and CCI) include the important climatic variables, and more importantly, have developed environmental stress thresholds which can be applied to take into account animal differences.

Intensity $\times$ duration effects of exposure to thermal stress must be accounted for in model development. The accumulated heat load model has attempted to do this; however, there is a need for further research to define the rate of heat accumulation and heat loss from livestock.

The available Web-based sites use animal stress models to predict thermal stress events. Access to this information will allow managers to plan strategies to ameliorate the impact of these events. However, the value of these sites may be limited when they do not account for animal or management differences. Furthermore, there needs to be a method by which livestock managers can integrate the predictive services with on-farm data.

What Will the Future Hold?

- Models will become more complex in an attempt to account for climate variables, animal variables, and management variables.
- Software will allow animal managers to input data that is relevant to their location and management.
- Models need to be dynamic. There will be ongoing development of models as more information, particularly field information, becomes available.
- Models are not an instant fix, they are a management tool and must be used in conjunction with animal observations and local knowledge.

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Chapter 15

Strategies to Reduce the Impact of Heat and Cold Stress in Dairy Cattle Facilities

John F. Smith and J. P. Harner, III

Introduction

In modern dairy facilities dairy producers strive to achieve consistently high milk production, feed efficiency, and reproductive efficiency while maintaining the health of the dairy cows. Heat stress reduces intake, milk production, health, and reproduction of dairy cows. Spain et al. (1998) showed that lactating cows under heat stress decreased intake 6 to 16% compared to cows in thermal neutral conditions. Holter et al. (1996) reported heat stress depressed intake of cows more than heifers. Other studies have reported similar results. In addition to a reduction in feed intake, there is also a 30 to 50% reduction in the efficiency of energy utilization for milk production (McDowell et al., 1969). In many parts of the world, milk production and reproductive performance drastically decline during periods of heat stress. Heat stress also has a negative impact on a dairy farm's future by reducing the peak milk production of cows that go through the transition period during periods of heat stress. The impact of reduced peak milk production often lingers into late fall or early winter. Cows can be managed and cooled to minimize the impact of heat stress. The method used will vary depending on the severity of the climate and the ambient relative humidity. In modern dairy facilities it is essential to minimize variation in the cow's core body temperature during periods of heat stress to maximize milk production and reproductive performance.

In recent years, more emphasis has been put on reducing the impact of cold stress in dairy cattle. This has been driven by the increased interest in mechanically ventilated freestall facilities. Cold stress typically has little impact on milk production and reproductive performance; however, it can have a negative impact on feed efficiency. If feed efficiency is reduced, an increase in manure production occurs. If the cow's environment is maintained above −6.7°C (20°F), the negative impacts on feed efficiency and manure production caused by cold stress can be reduced or eliminated.

Environmental Physiology of Livestock, First Edition. Edited by R. J. Collier and J. L Collier.

Dairy facilities are being constructed throughout the world. Producers must carefully select the appropriate facility for the local climate. Facility options vary depending on the severity of heat and cold stress.

How Cows Dissipate Heat

A cow may exchange heat to the environment through conduction, convection, evaporation, and radiation. Heat exchange via conduction is dependent upon a temperature differential between the surface of the cow and the surrounding environment. Convection results from air movement and a temperature differential. Cows seek shade to avoid incoming solar rays striking their bodies and to minimize increases in heat load due to radiation. Evaporation or evaporative cooling is the main mechanism of heat exchange during heat stress. This form of heat exchange utilizes body heat to evaporate moisture from the surface of the body. The phase change of the moisture from a liquid on the body surface to a vapor requires energy. The energy utilized to evaporate moisture lowers the cow's body temperature. Evaporative cooling may occur due to moisture evaporating from the cow's body surface or through the respiratory track and panting.

The total heat production of a dairy cow ranges from 4,220 to 5,275 kJ (4,000 to 5,000 BTU) per hr. Figure 15.1 illustrates the relationship between temperature and body heat dissipation. Conduction, convection, and radiation are the primary methods a cow uses for heat dissipation when the temperature is below 21.1°C (70°F). Once temperatures exceed 21.1°C (70°F), evaporative cooling becomes the primary method of heat dissipation. Figure 15.1 shows that as temperature increases above 21.1°C (70°F), a cow depends more on evaporative cooling from its body than breathing. Panting or increased respiration is a form of evaporative cooling, however, a cow can only dissipate so much heat through its respiratory tract. Brouk et al. (2003)

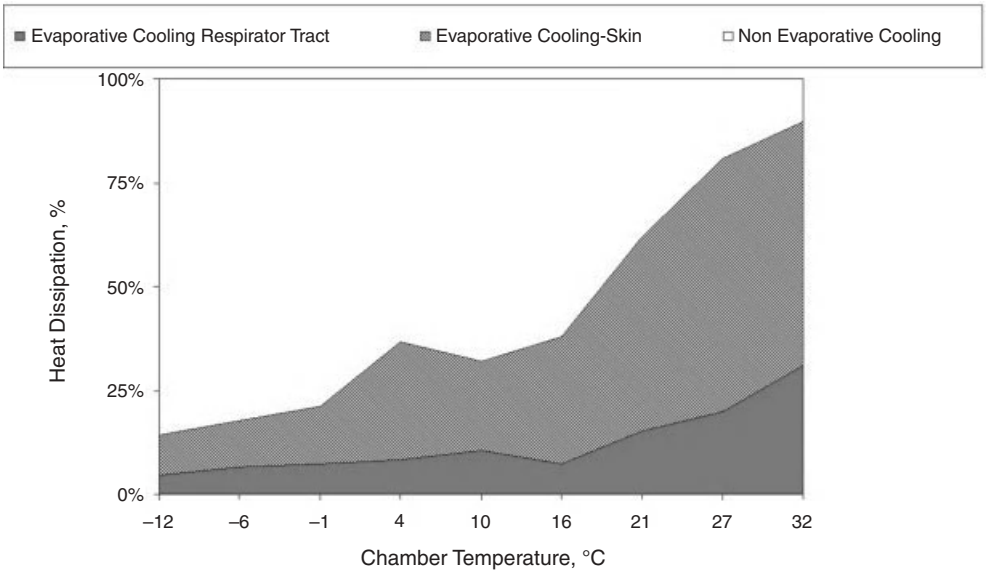

Figure 15.1. Impact of temperature on cow's ability to dissipate heat through evaporative and non-evaporative cooling (adapted from Kibler and Brody, 1952).

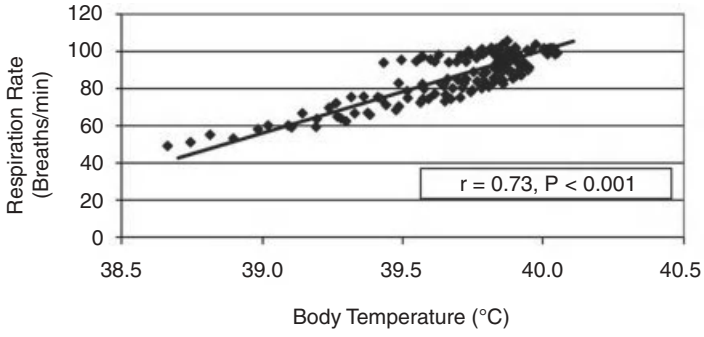

Figure 15.2. Impact of core body temperature on respiration rates (Brouk et al., 2003).

correlated the relationship between core body temperature and respiration rate. Figure 15.2 illustrates that core body temperatures continue to increase in spite of increased respiration rates.

Evaporative Cooling

The theoretical equation for evaporative cooling is (Esmay et al., 1969):

$$q = k \times A \times V^n \times (p_s - p_a) \tag{15.1}$$

Where:

q is evaporative heat loss
k is evaporative constant
A is effective wetted area
V^n is velocity component to exponential power
P_s and p_a are vapor pressure of skin and air, respectively

Equation 15.1 shows that two manageable factors influencing the evaporative cooling from a cow are wetted surface area and air velocity. Hillman et al. (2001) confirmed this relationship as shown in Figure 15.3. As temperature or frequency of wetting increases, the total heat loss per unit area increased. It is this author's opinion that during periods of intense heat stress a cow probably needs to be able to dissipate a minimum of 24.5 kJ/hr/m^2 (250 BTUs/hr/sq ft) of surface area assuming a wetted surface area of 1.86 m^2 (20 sq ft). Heat stress is overcome by a combination of increasing the air speed and wetted surface area. Hillman et al. (2001) noted that only increasing the air speed does not provide enough benefit to the cow to overcome heat stress.

Heat stress audits were conducted in several dairies in New York during the summer of 2006. Figure 15.4 shows the core body temperatures in cows from two dairies from July 14 to 18, 2006. The cows' core body temperatures were lower on the dairy that used fans and soakers compared to the cows cooled with only air movement. This limited field trial supports the laboratory study of Hillman et al. (2001). Cows housed on the dairy with only air movement had core body temperatures 0.6 to 1.1°C (1 to 2°F) higher than those housed on the dairy utilizing air movement and surface wetting.

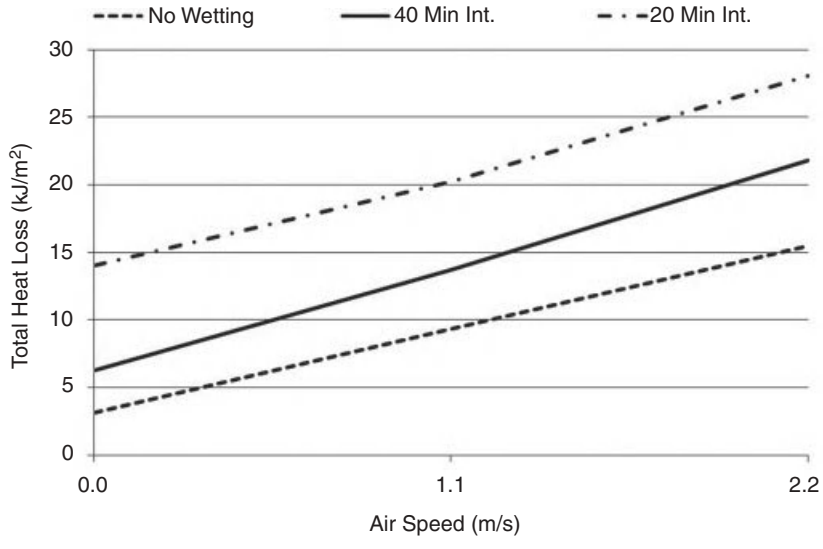

Figure 15.3. Impact of air velocity and wetting cycle on total heat loss (Hillman et al., 2001).

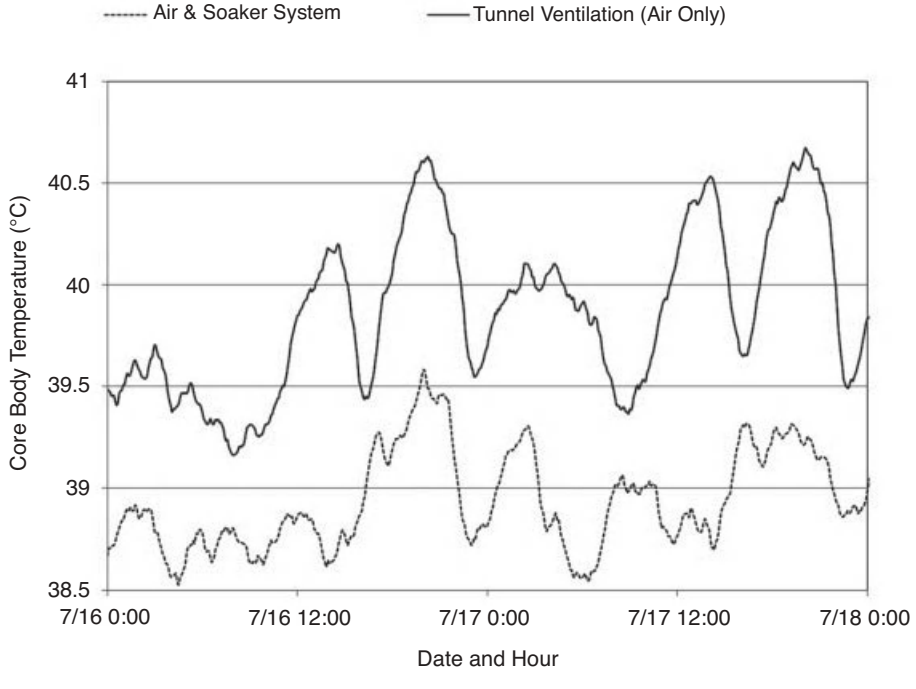

Figure 15.4. Comparison of core body temperatures on two New York dairies with different heat abatement systems in the summer of 2006 (Perkins, 2006).

Cooling the Cow or Changing the Environment

The use of low-pressure sprinklers, soakers, and fan systems to effectively wet and dry cows will increase heat loss from the cow. Dairy cows can be soaked in the holding pen, exit lanes, and at the feed lines. The goal should be to maximize the number of wet and dry cycles per hour.

Brouk et al. (2002) conducted an 8 × 8 replicated Latin Square experiment in which eight cows were exposed to each of eight different cooling strategies. The THI during the study was 80. Each cow was exposed to treatments involving no cooling, fan-only cooling, soaking 1 minute out of every 5 minutes, soaking 1 minute out of every 10 minutes, soaking 1 minute out of every 15 minutes, or a combination of a fan with each of the soaking strategies. The results of this study are shown in Figures 15.5 and 15.6. Respiration rates at the beginning of each trial were near 100 breaths per minute (bpm). The combination of air and soaking cows 1 minute out of every 5 minutes resulted in respiration rates decreasing to 50 bpm after 80 minutes. Respiration rates dropped to only 95 bpm after 80 minutes when only air was used to cool cows. Figure 15.6 shows a corresponding reduction in core body temperature.

These data suggest that different cooling strategies could be developed for different levels of heat stress. Under severe heat stress soaking every 5 minutes with air movement may be the most effective. Under periods of moderate stress, soaking every 10 minutes with air movement may be adequate. Reducing soaking frequency when temperatures are lower could significantly reduce water usage. Data indicate that the combination of soaking and supplemental air movement is superior to either single treatment. If used singularly, soaking cows potentially has more impact than the use of only air for cow cooling. These data indicate that about one-third of the total reduction in respiration rates was due to airflow and the remainder was due to soaking. Under periods of severe heat stress, soaking every 15 minutes with airflow may not be adequate and soaking frequency must be increased.

Cooling the Cow's Environment

The temperature-humidity index (THI) is used as an indicator of heat stress. Cows begin to experience heat stress at a THI value of 70. Figure 15.7 shows the THI values for different

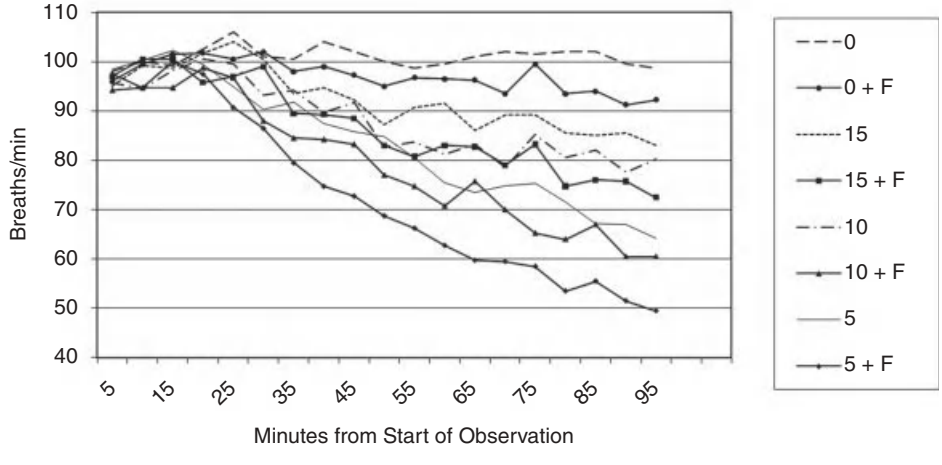

Figure 15.5. Respiration of cows cooled using different cooling strategies including: no airflow; airflow only; and soaking one minute in every 5, 10, or 15 minutes (Brouk et al., 2002).

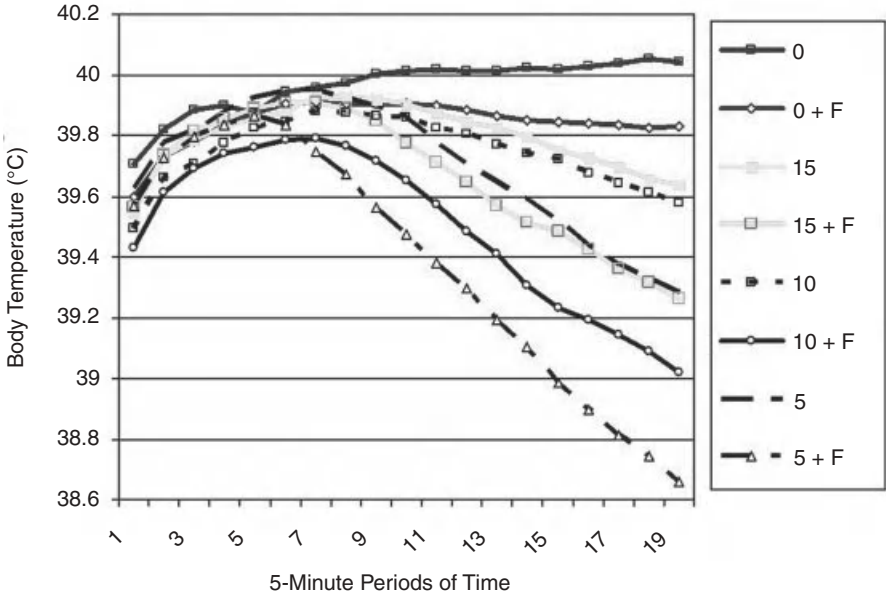

Figure 15.6. Core body temperatures of cows cooled using different cooling strategies including: no airflow; airflow only; and soaking one minute in every 5, 10, or 15 minutes (Brouk et al., 2002).

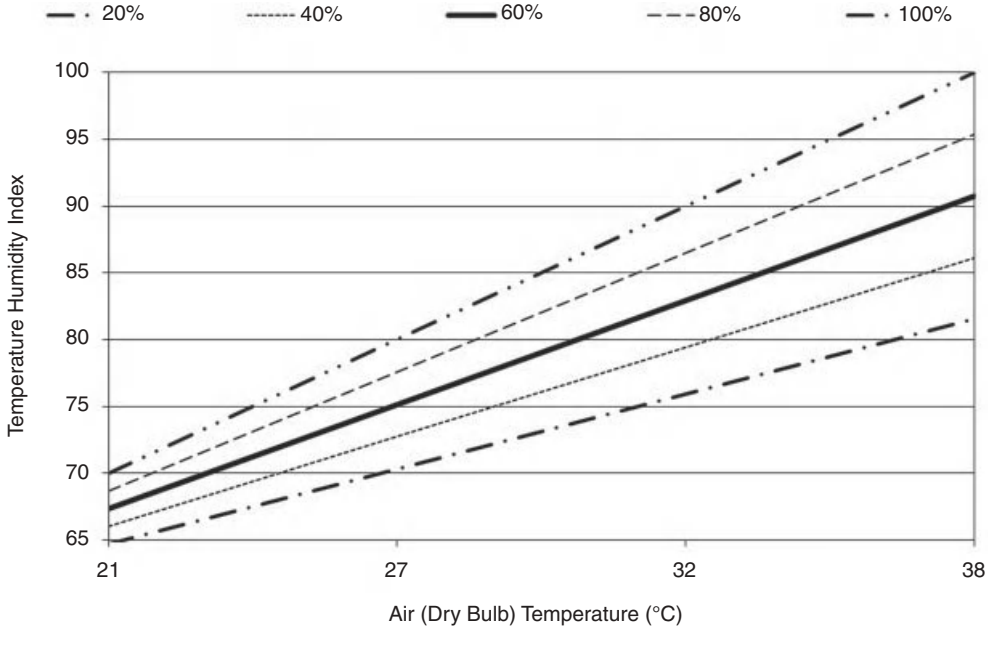

Figure 15.7. Impact of air temperature and relative humidity on temperature-humidity index (THI).

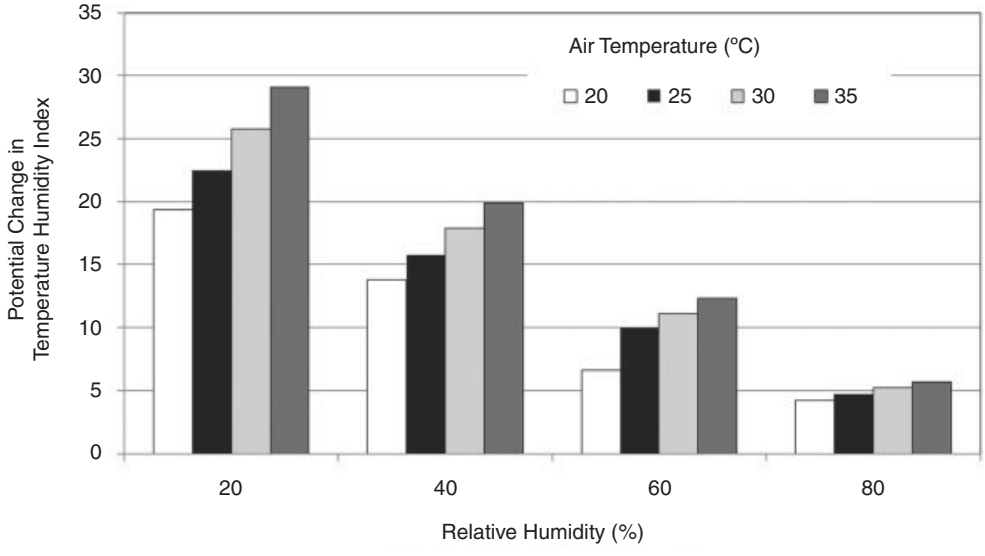

Figure 15.8. Potential THI change due to water evaporation at 20, 25, 30, and 35°C (68, 77, 86 and 95°F, respectively) in a low relative humidity environment. Assuming 100% efficiency of the evaporative cooling system.

temperatures and relative humidities. The THI index exceeds 70 any time air temperatures exceed 26.7°C (80°F), irrespective of relative humidity. Relative humidity begins to influence the THI index when temperatures are between 21.1°C (70°F) and 26.7°C (80°F).

Evaporative cooling can be used to cool the air around the cow. Dairy producers have used tunnel or cross ventilation with evaporative pads and combinations of fans and high-pressure sprayers to cool the air around the cow. These methods work well in arid climates. Temperature declines and humidity increases as water is evaporated into the air. The expected changes in THI using evaporative cooling are presented in Figure 15.8, as humidity increases it becomes more difficult to change the environment in which the cow is housed.

Outdoor air temperature, relative humidity, and the evaporative cooling system all affect the indoor temperature of the buildings. Because air temperature decreases and humidity increases as moisture is added to the air, the lowest temperature occurs when the air is saturated, or at 100% humidity.

Mechanical versus Natural Ventilation

Dairy housing systems utilize natural and mechanical ventilation. Figure 15.1 shows that as ambient temperatures increase above 21.1°C (70°F) cows primarily depend upon evaporative cooling to dissipate body heat to the environment. Minimizing the impact of heat stress with either natural or mechanical ventilation facilities requires supplementing the natural ability of a cow's evaporative cooling mechanism. Neither ventilation system provides adequate heat-stress relief without some additional moisture to cool the air or soak the body surface as the temperature differential between the ambient environment and a cow's normal body temperature decreases below 16.7°C (30°F). Research by Hillman et al. (2001) showed increases in heat loss in cows exposed to increases in air speed and more frequent wetting.

Properly designed naturally ventilated dairy housing systems work well when the outdoor air temperatures are below 21°C (70°F). Armstrong et al. (1999) reported afternoon respiration rates were lower when cows were housed in freestall buildings with a 4/12-pitch roof and an open ridge compared to cows housed in buildings with 2/12 or 3/12-pitched roofs with equal sidewall heights. They also observed that eave heights of 4.3 m (14 ft) resulted in lower increases in cow respiration rates as compared to shorter eave heights. During the winter months, it is necessary to allow adequate ventilation to maintain air quality while providing adequate protection from cold stress.

Another ventilation consideration is the width of the barn. Six-row barns are 4.9 to 6.1 m (16 to 20 ft) wider than four-row barns. This additional width reduces natural ventilation. Chastain et al. (1997; Chastain, 2000) indicated that summer ventilation rates were reduced 37% in six-row barns compared to four-row barns. In hot and humid climates, barn choice may increase heat stress resulting in lower feed intake and milk production. A trial completed in northwest Iowa indicated that respiration rates were higher in six-row versus four-row barns (Smith et al., 2001a). Generally, naturally ventilated housing systems will require supplemental mechanical ventilation as part of the heat-stress abatement management strategy.

Three methods are utilized in supplementing natural ventilation in the cow housing area. These include high-volume low-speed fans (HVLS), low-volume high-speed fans (LVHS), and tunnel ventilation. Some dairies are utilizing the high-volume, low-speed fans with the main benefit being reduced electrical energy cost. These fans typically have a diameter of 3.7 to 7.3 m (12 to 24 ft) and are spaced 12.2 to 18.3 m (40 to 60 ft) through the center feed alley. Studies done at three dairies in Wisconsin showed that air speed within the housing area was typically less than 1.34 meters per second (m/s; 264 feet per minute, fpm). These fans are utilized in manufacturing facilities where there are enclosed side walls. As the air impacts the floor, the sidewalls cause the air to turn upward creating turbulence. In naturally ventilated freestalls, the sidewalls are open and therefore the turbulence is not created. The studies in Wisconsin showed that the highest airflow in the facility corresponded with wind direction and speed. The HVLS fans are much quieter than high speed fans, which some producers feel is a benefit. However, these authors are not aware of any data that reveal correlations among reduced noise and milk production or cow comfort.

Most heat abatement research has focused on the low-airflow high-speed fans. Some refer to these fans as axial, basket, or cage fans. Meyer et al. (1998) evaluated the performance of heat-stress abatement using LVHS fans and sprinklers on a commercial dairy. The study involved a low pressure sprinkler system over each of the feed lines with varying fan configurations. Pen 1 had two rows of fans placed over the freestalls, pen 2 had a single row placed over the freestalls and a row placed over the feed line; pen 3 involved two rows of fans over the freestalls and one row over the feed line. Cows with similar milk production and days in lactation were randomly assigned to each pen. The authors reported that cows housed in pens 2 and 3 with fans over the feed line had 1.4 to 2.3 kg (3 to 5 lb) more milk production than those housed in pen 1. No additional benefit was observed by placement of the second row of fans over the freestalls. Another study (Brouk et al., 2000) compared performance of cows housed in a pen with a row of fans over the freestalls and a row over the feed line versus cows housed in another pen with just fans over the feed line. Cows housed in the pen with a row over freestalls and feed line had a 2.7 kg (6 lb) increase in milk production as compared to the other cows. Based on these studies and other field trials, most have come to accept that a row of fans is required over the freestalls with another row over the feed line as shown in Figure 15.9. In tail-to-tail stall configuration, additional fans may be needed over the stalls located near the sidewalls.

LVHS fan spacing is critical within the housing area. Current recommendations limit fan spacing to ten times the fan diameter. Thus, maximum spacing for 0.9 m (36 in) fans is 9.1

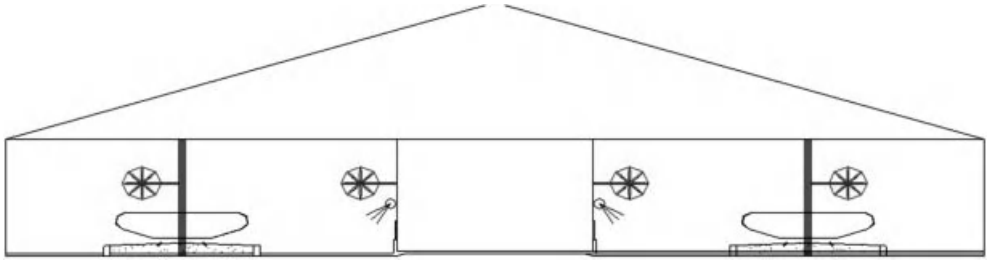

Figure 15.9. Current recommendations for fan placement in a naturally ventilated freestall barn with head-to-head stalls.

(30 ft) and 12.2 m (40 ft) for 1.2 m (48 inch) fans. The air speed declines rapidly in the stall area as distance from the fan increases (see Table 15.1). For a 0.9 m (36 in) fan, the air speed reduces below 0.89 m/s (176 fpm) at a distance 9.1 m (30 ft) from the fan. These are theoretical airflow rates because in freestall housing the open sidewalls, cow body interference, and natural air currents all affect fan performance. Spacing the fans further apart than recommended reduces the effectiveness of the fans. Figure 15.3 shows that total heat loss declines proportionally to a reduction in airflow.

Figure 15.9 demonstrates current recommendations on fan placement in freestall housing based on repeated field trials showing that summertime milk production increased 2.3 to 2.7 kg (5 to 6 lbs) per cow per day when fans were located on both the feed line and the freestalls versus only locating fans on the feed line or over the stalls.

Fans should be tilted down 15 to 30 degrees from the vertical plane. This directs the air currents down into the stall area rather than over the cows' backs or into the area above the stalls. There is a tendency to tilt the fans upward if stalls are bedded with sawdust or dried manure. High air velocities directed into the stalls cause the smaller particles to become suspended in the air creating dust or respiratory problems. Fans are operated by a thermostat with the on-temperature being 20 to 22.2°C (68 to 72°F). Normally, fans are operated based on temperature rather than humidity and are on anytime the setpoint temperature is exceeded.

Many dairies tunnel-ventilate freestall buildings. Tunnel ventilation requires enclosing the sidewalls and moving air the length of the building or parallel to the ridge. Air inlets are located at one end of the building and fans are located on the other end. In the past, the design air velocity through the building was 2.2 to 2.7 m/s (440 to 528 fpm). The challenge with tunnel ventilation is maintaining air flow in the freestall area. Air tends to move toward the alleys, ceiling, or feed lane where there is minimal interference with cows. The air speed in

Table 15.1. Maximum theoretical velocity m/s (fpm) of air perpendicular to the fan as a function of distance.

Distance from Fan m (ft)	Fan Diameter		
	0.6 m (24 in)	0.9 m (36 in)	1.2 m (48 in)
4.6 m (15 ft)	1.08 mps (211 fpm)	1.50 mps (290 fpm)	2.00 mps (396 fps)
9.1 m (30 ft)	.53 mps (106 fpm)	.75 mps (150 fpm)	1.03 mps (202 fpm)
13.7 m (45 ft)	.36 mps (70 fpm)	.44 mps (88 fpm)	.67 mps (132 fpm)

the alleys may be 0.89 to 1.33 m/s (176 to 267 fpm) higher than the air speed in the freestall area. Some dairies have installed baffles to redirect air into the cow space. Other dairies have installed ceilings to reduce the cross section area and fan requirements. The bottom of the baffle or ceiling cannot interfere with normal operation of the bedding and feeding equipment. The ceiling height or bottom of the baffles must be at least 3.7 to 4.0 m (12 to 13 ft) above the floor for equipment allowances. Another option is increasing the air velocity through the building. Design air speeds have increased in recent years to 3.58 to 4.47 m/s (704 to 880 fpm). This results in a 1.78 to 2.69 m/s (352 to 528 fpm) air speed in the cow space. The size of the air inlet is based on the total volume of air moving through the building. If an evaporative pad is used, then the inlet is based on 1.5 to 2.0 $m^3/sec/m^2$ (300 to 400 cfm per sq ft) of pad area. The air speed through the inlet may be increased to 3.0 to 4.0 $m^3/sec/m^2$ (600 to 800 cfm per sq ft) if no evaporative pad is used. Increasing the air speed through a building requires adjusting the inlet accordingly. Some dairies utilize tunnel ventilation during the summer months and natural ventilation the remainder of the year. Natural ventilation requires adjusting the sidewall curtains. Often the curtains are not tight and air enters along the sidewalls when tunnel ventilating. When this occurs, there will be an increase in air speed from the inlet to the fans. The airflow near the air inlet may be less than 2.25 m/s (440 fpm) even though the designed ventilation system indicates an average speed of 3.58 m/s (704 fpm) or higher. The reduction depends on the volume of air entering along the sidewalls.

Freestall buildings may be totally mechanically ventilated using tunnel ventilation or cross ventilation. The goal during summer months is to maintain a minimum air velocity in the stall area of 2.25 m/s (440 fpm). The building air exchange rate will be 1 to 4 minutes during the summer depending on building dimensions. The winter air exchange rate is 10 to 15 minutes depending on weather and management strategies.

Water Availability

Water availability is a critical component in minimizing the impact of heat stress on dairy cattle. The water intake of lactating dairy cattle can increase 1.5-fold to 2-fold during periods of heat stress. Water should be provided in housing areas and at the milking center. Cows will drink approximately 10% of their daily water intake as they exit the milking parlor (Brouk et al., 2001). Current recommendations for the housing area suggest a range of 3 to 9 linear cm (1.2 to 3.6 linear in) per cow (Smith et al., 2000). Many of these recommendations were developed before an emphasis was put on minimizing heat stress. Producers should strive to provide 9 cm (3.6 linear in) per cow during summer months. This will allow 15% of the cows in a pen to drink at the same time. Water troughs should be located in multiple locations in each pen to avoid the impact of dominant cows monopolizing access to water.

Providing adequate water space in freestall housing can be difficult to accomplish. In freestall housing located in climates where curtains are used on the sidewalls water troughs are located at each crossover. Typically pens with two rows of freestalls (head-to-head configuration) or three rows of freestalls have the same number of crossovers. Thus, water access in a pen with three rows of stalls is reduced by 37.5% compared to a two-row configuration (Table 15.2). When overcrowding is considered (Table 15.3), water access is greatly reduced and the magnitude of reduction is greater in pens with three rows of stalls. Producers choosing to build facilities with two rows of freestalls per pen tail-to-tail will have to increase the number of crossovers or widen crossovers to accommodate two water troughs per crossover. This occurs because

Table 15.2. Average pen dimensions, number of stalls, and allotted space per animal. Adapted from Smith et al. (1999).

					Per Cow		
Rows Stalls Pen	Pen Width m (ft)	Pen Length m (ft)	Stalls Per Pen	Cows Per Pen	Area Cow m^2 (ft^2)	Feedline Space Cow cm (in)	Linear Water Space Cow cm (in)
2	11.9 (39)	73.2 (240)	100	100	8.5 (94)	73.7 (29)	9.1 (3.6)
3	14.3 (47)	73.2 (240)	160	160	6.5 (71)	45.7 (18)	5.7 (2.25)

shorter water troughs have to be used in a tail-to-tail configuration. In climates where curtains are not used on the sidewalls or in mechanically ventilated barns with two rows of stalls per pen in a head-to-head configuration, additional water troughs can be located on the outside walls. When freestall housing is constructed care should be taken to provide 9 cm (3.6 linear in) of water space per cow based on the actual stocking rate of the facility.

Providing access to drinking water at the milking center gives cows another opportunity to drink. Research has shown that when water troughs are located at the parlor, cows will consume approximately 10% of their water intake leaving the milking center. In parallel and herringbone parlors water space should be provided to allow all the cows on one side of the parlor to drink at one time. In rotary parlors, water trough space should be provided so that the number of cows exiting the parlor in 12 minutes can drink at one time. Ideally these water troughs should be sized to provide 61 cm (24 in) of space per cow.

Importance of Shade

Providing shade in housing areas and in the holding pen of the milking parlor is an essential component in minimizing heat stress to reduce the impact of solar radiation. Research from Florida, California, Australia, and Arizona indicates that when high-producing cows were exposed to a THI greater than 80 and provided shade, they produced an additional 1.8 to 4.1 kg (4 to 9 lb) of additional milk per day than cows not having access to shade (Armstrong, 2000). Natural shading provided by trees is effective, but most often shade is constructed from solid steel or aluminum. Using more porous materials such as shade cloth or snow fence is not

Table 15.3. Effect of stocking rate on space per cow and feed and water area in pens with 2 or 3 rows of freestalls.

	Area Per Cow M^2 (ft^2)		Linear Feedline Space Per Cow cm (in)		Linear Water Space Per Cow cm (in)	
Stocking Rate (%)	2-Row	3-Row	2-Row	3-Row	2-Row	3-Row
100	8.7 (94)	6.6 (71)	73.7 (29)	45.7 (18)	9.1 (3.6)	5.7 (2.25)
110	7.9 (85.5)	6.0 (64.5)	66.0 (26)	40.6 (16)	8.3 (3.27)	5.2 (2.05)
120	7.3 (78.3)	5.5 (59.2)	61.0 (24)	38.1 (15)	7.6 (3.0)	4.8 (1.88)
130	6.7 (72.3)	5.1 (54.6)	55.9 (22)	35.6 (14)	7.0 (2.77)	4.4 (1.73)
140	6.2 (67.1)	4.7 (50.7)	53.3 (21)	33.0 (13)	6.5 (2.57)	4.2 (1.66)

Table 15.4. Shade material listed in descending order of effectiveness, as compared with new corrugated aluminum Bond et al. (1961).

Material	Description	Effectiveness
Hay	15 cm thick	1.203
Wood	Unpainted	1.060
Galvanized Steel	Top white, bottom natural	1.053
Aluminum	Top white, bottom natural	1.049
Neoprene Coated Nylon	White, both sides	1.037
Aluminum	Standard	1.000
Galvanized Steel	Standard	0.992
Asbestos Board	Natural color	0.956
Shade Cloth	90% solid	0.839
Shade Cloth	30% solid	0.819
Slatted wood	5 cm solid −5 cm open	0.589

as effective as solid shades. Table 15.4 lists the effectiveness of different shade materials in descending order (Bond et al., 1961; Kelly and Bond, 1958).

Cooling the Milk Center

Cows may spend 10 to 25% of their time in a holding pen prior to milking. Current designs of holding pens create significant heat stress since space per cow is about only 1/5 of that in the housing area and many have solid fences limiting air flow. Space limitations impede the ability of the cow to exchange heat through much of their body surface area. Solid fences hinder the ventilation system from exhausting heat from the holding pen area in particular the heat exchanged between the lower portion of the body (udder area) and the environment. Therefore, heat abatement in the holding pen is primarily dependent upon respiratory evaporative cooling and evaporative cooling from the surface of the cow's back. The holding pen should be cooled with fans and sprinkler systems and an exit lane sprinkler system may be beneficial in hot climates. Holding pen time should not exceed one hour. Fans should move 0.47 cubic meters per second (m^3/sec; 1,000 cfm) per cow. Most 76.2 to 91.4 cm (30 and 36 in) fans will move between 4.7 to 5.7 m^3/sec (10,000 to 12,000 cfm) per fan. If one fan is installed per ten cows or 13.9 m^2 (150 ft^2) adequate ventilation will be provided. If the holding pen is less than 7.3 m (24 ft) wide with 2.4 to 3.0 m (8 to 10 ft) sidewall openings, fans may be installed on 1.8 to 2.4 m (6 to 8 ft) centers along the sidewalls. For holding pens wider than 7.3 m (24 ft), fans are mounted parallel to the cow flow. Fans are spaced 1.8 to 2.4 m (6 to 8 ft) apart and in rows spaced either 6.1 to 9.1 m (20 to 30 ft) apart from 91.4 cm (36 in) fans or 9.1 to 12.2 m (30 to 40 ft) apart for 121.9 cm (48 in) fans (Harner et al., 2000). In addition to the fans, a sprinkling system should deliver 1.25 l of water per m^2 (0.03 gal/ft^2) of area. Cycle times are generally set to soak cows every 5 to 7 minutes.

Additional management strategies to consider include reducing the group size to minimize time in holding pens, altering milking times if the parlor is not used at full capacity, milk low-producing heifers during hottest part of the day, and enhancing natural ventilation by opening the sidewalls and ridge vents. Sidewalls should have a minimum 75% opening with an open ridge cap or vents. A minimum ridge row opening of 5.1 cm (2 in) per 3.0 m (10 ft) of building width is recommended.

Reducing Heat and Cold Stress in Different Types of Housing

Naturally Ventilated Freestalls

Naturally ventilated freestalls are used in many regions of the world. The first design criteria to consider should be the orientation of the structure. Barns with a north-to-south orientation have a greater solar radiation exposure than barns with an east-to-west orientation (see Figs. 15.10 and 15.11). Sunlight can directly enter north-to-south oriented barns both in the morning and afternoon. While the afternoon sun is the most detrimental, during hot summer weather, morning sun can also modify cow behavior. Because cows seek shade during the summer, direct sunlight will reduce stall usage. Thus, utilization of stalls located on east and west outside walls of north-to-south oriented barns are greatly impacted when in the direct sunlight. It is also important to consider that with greater sidewall heights, afternoon sunlight can reach much of the west half of the structure. Protection from direct sunlight is vital for effective heat-stress abatement. A trial in California showed an increase in morning and afternoon respiration rates when barns were orientated north-to-south versus east-to-west (Smith et al., 2001b). Barns with an east-to-west orientation provide greater protection from solar radiation than a north-to-south orientation.

Cow cooling in naturally ventilated freestall barns is typically a combination of low-pressure feed-line soakers and axial fans. Fans should be mounted as low as possible and out of the reach of the cattle in a manner that will not obstruct equipment movement. Fans should create airflow of 0.38 m^3/sec to 0.42 m^3/sec (800 to 900 cfm) per stall or headlock, with a minimum air velocity of 2.7 m/s (528 fpm). Feed-line soakers should be utilized in addition to the fans and feed-line sprinkling systems should be installed to soak cows. Cows should be soaked every 5 to 15 minutes depending on the severity of heat stress. Application rate per cycle should be 1.3 to 1.5 l (0.35 to 0.4 gal)/cow/cycle and sprinklers should operate when the temperature exceeds 21.1 to 23.9°C (70 to 75°F). In tail-to-tail four-row barns and six-row barns, an additional row of fans per pen may be needed over the stalls located near the sidewalls.

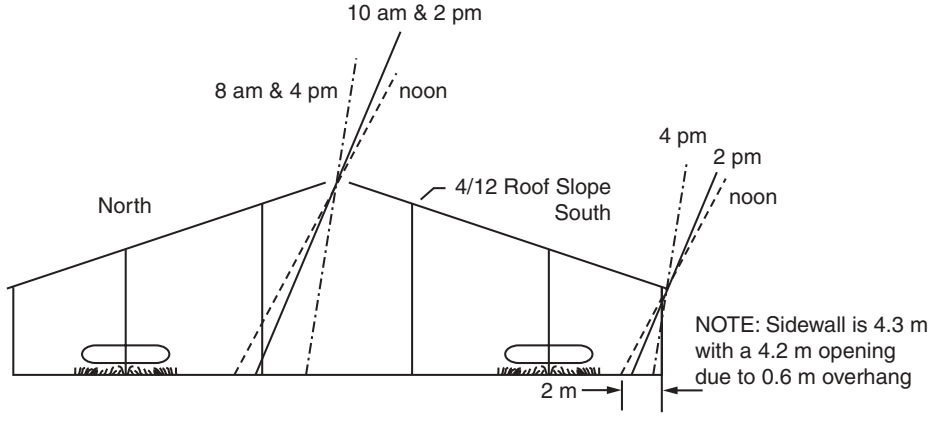

Figure 15.10. Sun angles of an east-to-west oriented freestall barn.

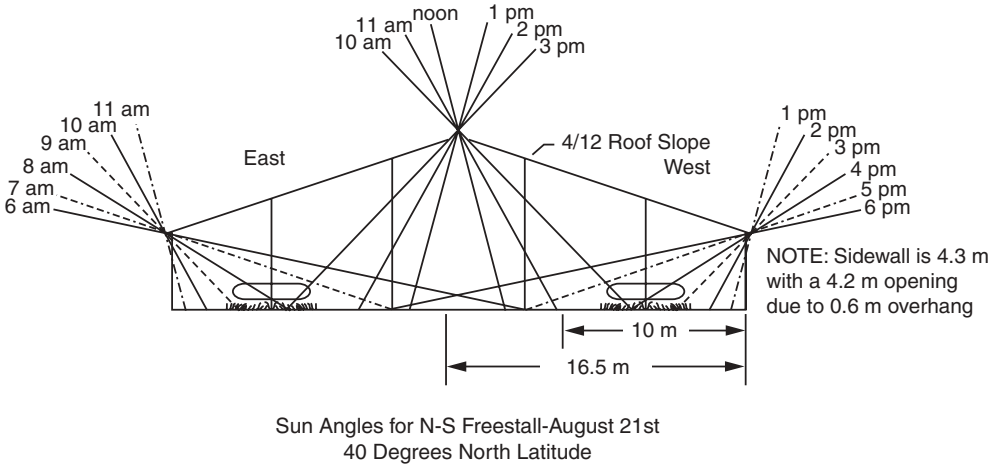

Figure 15.11. Sun angles of a north-to-south oriented freestall barn.

In climates where cold stress is a concern sidewall curtains can be used to reduce wind chill. It is important to leave an opening above the curtains to facilitate natural ventilation in the winter months, which is important in maintaining air quality. An opening above the curtains equal to 2.54 cm (1 in) per every 3.1 m (10 feet) of building width is recommended.

Dry Lot Facilities

Typically, dry lot facilities are constructed where the moisture deficit (annual evaporation rate minus annual precipitation rate) is greater than 50.8 cm (20 in) annually (Sweeten et al., 1993). Dry lot facilities provide 46.5 to 65.0 m^2 (500 to 700 ft^2) per lactating cow depending on the evaporation rate. Pens are constructed with 2 to 3% side slope and 0.5 to 1% down slope. Pens generally have a double slope with the shade located at the high point of the pen. Constructing a dry lot dairy so the water drains outside of the pens is ideal; however, this is often avoided due to the cost of additional fencing. The slope of pens will have a dramatic impact on how fast the earthen surface will dry. Mud can have a significant negative impact on dry matter intake. Fox and Tylutki (1998) suggested that every centimeter of mud reduced DMI of dairy cattle 2.5%. Feed lines are constructed with a north-to-south orientation and the shades are constructed parallel to the feed line. This allows the shade to move throughout the day causing the cows to use different sections of the lot surface. Shade is essential to minimize heat stress in dry lot facilities. Typically shades have a minimum height of 4.3 m (14 ft) and provide 4.2 to 4.6 m^2 (45 to 50 ft^2) of shade per cow (Wiersma, 1982). Installing gutters on shades and removing the water from the pens will allow the lot surface to dry faster after inclement weather. Depending on the severity of heat stress, additional steps can be taken. In some areas low-pressure feed-line soakers are used. It is important that the cow platform be constructed with a curb or that the cow pad slopes back to the stem wall if a fence line soaker is installed. This prevents runoff from the soakers reaching the earthen surface of the pen. In areas with more severe heat stress, high pressure evaporative cooling systems and curtains are installed on the shades to change the environment that the cow experiences.

Windbreaks are constructed in areas where the potential for severe winter weather exists. Windbreaks should be constructed to allow 20% of the air to pass through. This helps to prevent the turbulence behind the windbreak that occurs when solid structures are used. The snow dump generally occurs at four times the windbreak height and wind protection is ten times the windbreak height. Ideally 9.3 m^2 (100 ft^2) of protected area per cow should be provided. It is important to realize that dry lot housing does not allow managers the luxury of managing the risk Mother Nature can present in the form of rain, snow, and severe wind chill. The advantage of dry lot facilities is the lower capital investment per cow as compared to freestall housing.

Desert Barns

A desert barn is a dry lot dairy where a gable roof is constructed over the feed lines and part of the lots of both sides of the feed alley. The shaded area over the lots provides a resting area that is protected from solar radiation. These structures are typically 32 m (105 ft) wide, have a sidewall height of 3.4 to 4.3 m (11.2 to 14 ft), and a roof pitch of 2/12 to 4/12. In the lots outside of the covered area 56 sq m (600 sq ft) is provided. In climates with severe heat stress, the sidewall height is typically 3.4 m (11.2 ft) and a roof pitch is 2/12. Due to the low sidewall height the roof is insulated (Martin, 2010). The orientation of structures is dependent upon the climate and use of curtains on the sidewalls. In climates with severe heat stress the bedding area is cooled via evaporation and curtains are used on the sidewalls to keep the cooled air over the resting area. In this situation these structures are typically oriented with a north-to-south orientation that allows sunlight to keep both sides of the barn dry. In recent years additional cooling has been provided in climates with severe heat stress on the feed line using low-pressure soakers. In milder climates producers are choosing to eliminate the curtains and evaporative cooling. In this situation the orientation should be east-to-west to protect the cows from solar radiation. Additional cow cooling would be in the form of low pressure soakers and axial fans. If the climate has the potential for cold stress, windbreaks are constructed on the fences dividing the pens. The guidelines for windbreaks would be the same as those used for dry lot facilities.

Low-Profile Cross-Ventilated Freestall Buildings (LPCV)

Recently there has been significant interest in constructing freestall facilities that are mechanically ventilated. These facilities allow producers to have control over a cow's environment during all seasons of the year. As a result, an environment similar to the thermoneutral zone of a dairy cow is maintained in both the summer and winter, resulting in more stable core body temperatures.

The latest mechanical ventilation design is the low profile cross-ventilated freestall buildings. The LPCV building moves air perpendicular to the ridge or across the building. Traditional tunnel ventilation moves air parallel to the ridge. By moving air across the building, baffles may be strategically located to move air into the cow space without interfering with equipment. The bottom of the baffle is 1.8 to 3.0 m (6 to 10 ft) above the floor, depending on the number of baffles and desired air velocity. Evaporative cooling pads are placed along one side of the building and fans are placed along the opposite side. There is more space available for placement of fans and evaporative pads are parallel to the ridge rather than perpendicular because the equipment doors are located in the end walls. One potential advantage of the LPCV or tunnel ventilated buildings is cows are exposed to near constant wind speeds. Inside

the building the air velocity or wind speed is normally less than 3.6 m/s (704 fpm) during peak airflow. The ventilation rate is reduced during cold weather with wind speed reducing to less than 0.9 m/s (176 fpm).

The description of "low profile" results from the roof slope being changed from a 3/12 or 4/12 pitch common with naturally ventilated buildings to a 0.5/12 or 1/12 pitch. Contractors are able to use conventional warehouse structures with the LPCV building, but the interior components and space per cow for resting, socializing, and feeding in an LPCV building is similar to a naturally ventilated four-row structure. Figure 15.12 shows an end view of an eight-row LPCV building. An evaporative cooling system is located along one side of the building. Fans are placed on the opposite side. More space is available for fan placement and the cooling system is parallel to the ridge rather than perpendicular because the equipment doors are located in the end walls.

Baffles are placed over the freestalls creating the maximum air velocity over the freestalls. These facilities are typically designed to create a 3.13 m/s (616 fpm) wind speed over the freestalls. Since the airflow is parallel to the cow's resting area, cows experience an increase in wind speeds when lying in the stalls. LPCV facilities allow for buildings to be placed closer to the parlor, thus reducing time cows are away from feed and water. Other advantages include a smaller overall site footprint than naturally ventilated facilities and less critical orientation since naturally ventilated facilities need to be oriented east-to-west to keep cows in the shade. Some of the other benefits of controlling the cow's environment include increased milk production, improved feed efficiency, increased income over feed cost, improved reproductive performance, ability to control lighting, reduce lameness, and reduce fly control costs.

Cold Stress and Warming Effect with LPCV Buildings

LPCV freestall buildings allow producers to have control over a cow's environment during all seasons of the year. In the winter the interior of an LPCV building is 5.5 to 16.7°C (10 to 30°F) warmer than outside air temperatures. Dairy cows housed in an environment beyond their thermoneutral zone alter their behavior and physiology.

Compared to research on the impact of heat stress, little attention has been spent on cold stress in lactating dairy cattle. The high metabolic rate of dairy cows makes them more susceptible to heat stress; as a result, the lower critical temperature of lactating dairy cattle is not well established. Estimates range from as high as 10°C (50°F; NRC, 1981) to as low at −73°C (−100°F; NRC, 2001). Regardless, there is evidence that the performance of lactating cows decreases at temperatures below 6.7°C (20°F; NRC, 1981). One clear effect of cold stress is an increase in feed intake. While increased feed intake often results in greater milk production, cold-induced feed intake is caused by an increase in the rate of digesta passage through the gastrointestinal tract. An increased passage rate limits the digestion time and results in less digestion as the temperature drops (NRC, 2001). In cold temperatures, cows also maintain body temperature by using nutrients for shivering or metabolic uncoupling, both of which increase maintenance energy costs. These two mechanisms decrease milk production by more than 20% in extreme cold stress. However, even when cold stress does not negatively impact productivity, decreased feed efficiency can hurt dairy profitability.

Smith et al. (2008) assessed the effects of environmental stress on feed efficiency and profitability using a model incorporating the temperature effects on dry matter intake, diet

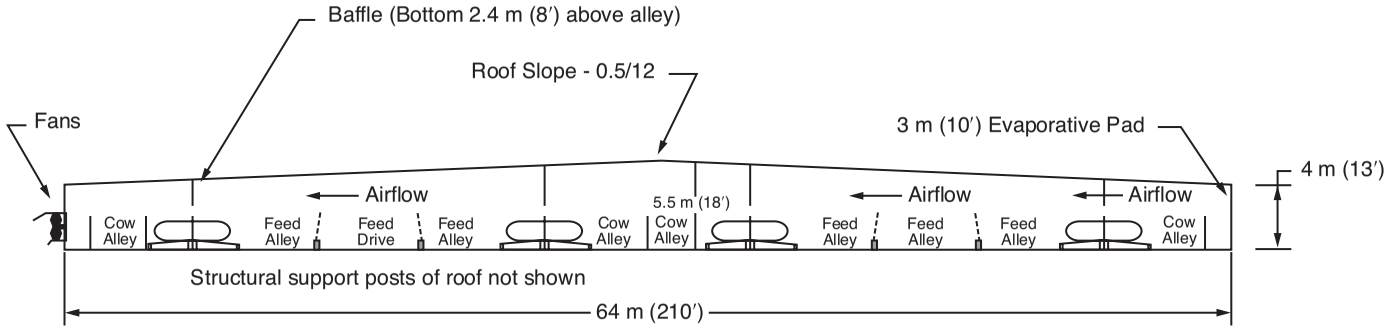

Figure 15.12. End view of an eight-row LPCV freestall building.

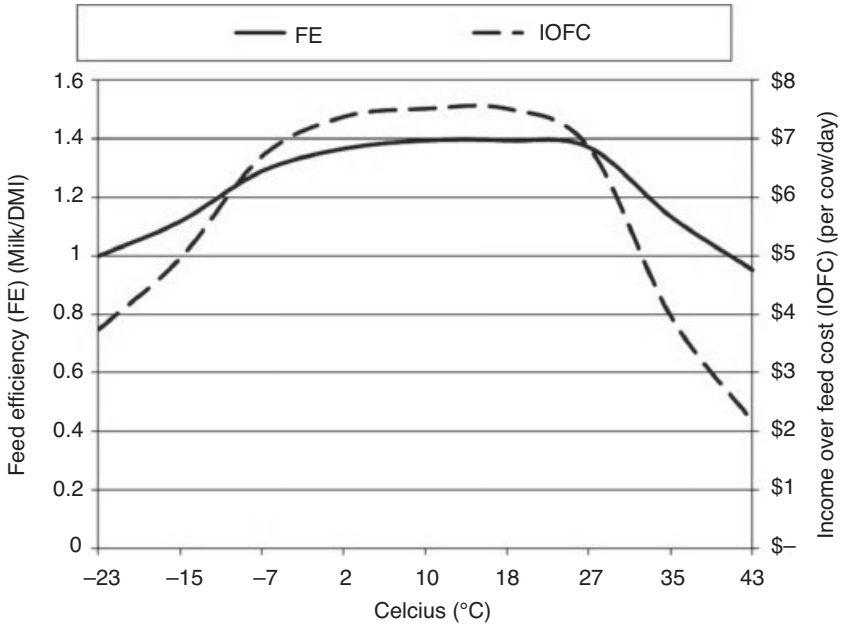

Figure 15.13. Responses to environmental stress (thermoneutral production of 80 lbs/day, TMR cost of $0.12/lb dry matter, and milk value of $18/cwt).

digestibility, maintenance requirements, and milk production. Figure 15.13 shows the expected responses of a cow producing 36.4 kg (80 lbs) of milk per day in a thermoneutral environment. The model was altered to assess responses to cold stress if milk production did not decrease. In this situation, the decrease in diet digestibility results in an 48% decrease in income over feed cost as temperatures drop to −23.3°C (−10°F).

There are different management strategies during cold weather. The first mode of action decreases the air exchange rate (e.g., turning off fans) to prevent frozen manure on the alleys. This strategy prevents potential lameness and injury problems but probably leads to an increase in ammonia and moisture levels inside the building. The second mode of action utilizes a controller to operate fans based on temperature along the inlet side of the building. As outdoor air temperature declines, the number of fans operating remains constant, resulting in a colder temperature inside the building, potential frozen manure problems, and employees exposed to colder temperatures. There appears to be some agreement that an 8 to 16 minute air exchange rate is adequate during winter months. A 16 row facility will require twice as many fans (assuming equal number of fans) operating as an eight-row facility under the same winter conditions. This additional ventilation requirement during the winter months in a 16-row facility results in the sidewall inlet opening having to be twice as large to exchange twice the volume of air as compared to an eight-row building. In 16-row facilities, having to mix larger volumes of cold air with warm air may result in the first 61 m (200 ft)of building being colder than other parts of the building because more cold air must be pulled through the inlets to obtain the desired air exchange rate. The cold air entering the building will not warm as rapidly in a 16-row facility compared with an eight-row facility during the winter months if

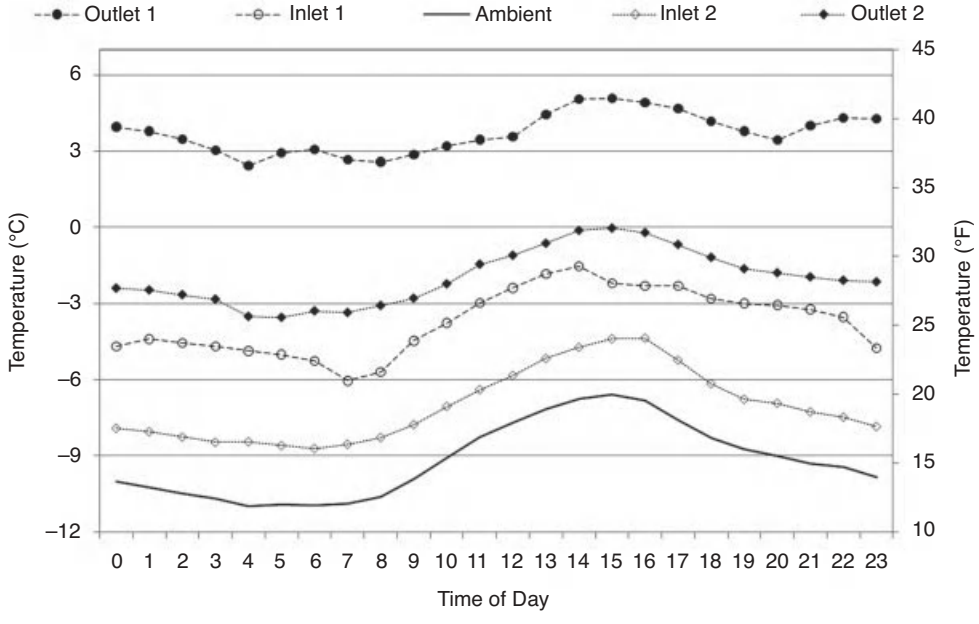

Figure 15.14. Summaries of temperatures from January 18 to February 17, 2008, inside two 400-ft-wide LPCV buildings located in Iowa.

the air exchange rate is equal. During extremely cold weather, more manure may freeze on the alleys closest to the air inlet in a 16-row LPCV.

Hourly ambient, inlet, and exhaust temperature data were collected in two LPCV buildings from January 18 to February 17, 2008 (see Fig. 15.14). Figure 15.14 shows a rapid warming of the air between the inlet and first baffle in the LPCV facilities. The air continued to warm until exhausted from the building. The ambient temperature during the winter period averaged −6.7°C (20°F) colder than barn conditions. Figure 15.15 shows a correlation between temperature rise across the building and the outdoor air temperature. Temperature rise is defined as the difference between the exhaust and outdoor air temperature. There is less variability in the temperature rise when ambient temperatures are above −6.7°C (20°F) since there are more consistent strategies in fan operation and less concern about freezing alleys.

Monitoring Heat Stress on Commercial Dairies

Recently, a technique called heat-stress audit has been developed to evaluate the effectiveness of heat abatement strategies on an individual dairy (VanBaale et al., 2006). Because of the typical location of cooling equipment relative to animals and the large variety of animal positions (i.e., location within a pen), there is a wide range of microenvironments present within a facility. As a consequence, cows experience differing levels of heat stress within a day. Thus, accurately determining the degree of heat stress a cow is experiencing over time is a challenge. During heat stress audits eight cows in a pen are fitted with temperature logging

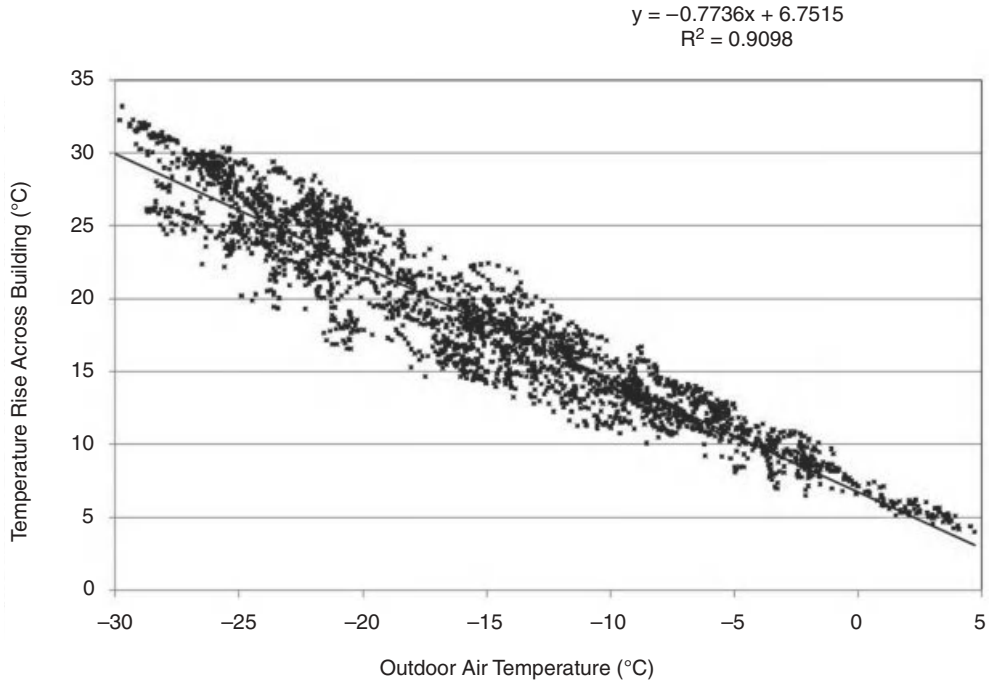

Figure 15.15. Correlation between outdoor air temperature in a low-profile cross-ventilated freestall building and the temperature rise across a 500-ft-wide building in Minnesota during winter 2008.

devices (e.g., Hobo® U12 Stainless Temperature Data Logger, Onset Computer Corporation; Bourne, MA) attached to a blank controlled internal drug release device (CIDR; not containing hormones). After cows have been acclimated, vaginal temperatures are recorded for 72 h at 5 min intervals. This information can be used to determine if core body temperatures are elevated and if deficiencies in the dairy's cooling system exist. Critical groups of cows can be evaluated including pre-fresh cows, fresh cows, and cows eligible to be bred. Heat-stress audits have proven to be a valuable technique in evaluating how effective cooling strategies are working in an individual dairy.

Summary

Heat stress reduces intake, milk production, health, and reproduction of dairy cows. The dairy cow can be managed and cooled to minimize the impact of heat stress. Listed below are the priorities for reducing heat stress in dairy facilities:

1. Improve water availability
2. Provide shade in the housing areas and holding pen
3. Reduce walking distance
4. Reduce time in the holding pen
5. Improve holding pen ventilation

6. Add holding pen cooling and exit lane cooling
7. Improve ventilation in cow housing areas (freestalls)
8. Cool close-up cows (three weeks prior to calving)
9. Cool fresh cows and early lactation cows
10. Cool mid and late lactation cows.

If these priorities are implemented, incremental improvements in milk production (assuming all else is equal) can be made over time to minimize the impact of heat stress.

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Chapter 16

Genotype by Environment Interactions in Commercial Populations

Ignacy Misztal and Peter Lovendahl

Introduction

Genotype by environment interaction (G×E) is different performance of genotypes in different environments (Falconer and Mackay, 1996). The environment may be defined by geography, type of management, type of nutrition, or seasonal attributes. Genotypes refer to breeds or individuals within a breed. Large G×E indicates that genotypes exhibit rank change in different environments.

Two terms related to G×E are phenotypic plasticity, or an environmental sensitivity, and homeostatis. High plasticity means large phenotypic changes are observed in response to different environmental conditions (Bradshaw, 1965; Piglucci, 2001). Homeostasis means small phenotypic changes (or small undesirable changes) are observed under small deviations in an optimal environment (Waddington, 1942). Genetic variation in plasticity results in genotypes that have variable sensitivities to different environments. An optimal genotype for a given environment should maintain homeostasis (de Jong, 1995). For a given environment, homeostasis can be achieved by the majority of animals in other breeds adapted to or selected for that environment, or by a fraction of animals in another breed.

The terms above are very general. While they refer to a phenotype, animals are, in fact, selected for a variety of traits at a time. In this case, a phenotype would mean an index of traits with the weights of that index also possibly being a function of the environment. Also, an environment may be multi-dimensional. While various genotypes can react differently to environmental changes, the important question is whether ranking of genotypes changes with environments.

Falconer (1990) defines selection upward in a bad environment or downward in a good environment as antagonistic, with the selection and the environment acting in opposite directions on the genotype. Synergistic selection is the reverse, upward in a good environment

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or downward in a bad, with selection and environment acting in the same direction. The antagonistic selection reduces environmental sensitivity and synergistic selection increases environmental sensitivity.

Artificial selection in farm animals is usually synergistic. It favors higher productivity at the expense of fitness, which is compensated by an improved environment. It is assumed that benefits of increased productivity outweigh extra costs of the improved environment. Continuous selection requires continuous improvement of the environment to maintain homeostasis. Thus, if at one time a genotype functions well in a variety of environments (low plasticity, or small G×E), intensively selected animals may not perform well in environments that failed to improve, generating larger G×E (Frankham, 2008).

The antagonistic selection would lead to (increased) homeostasis in a wide range of environments or robustness (Veerkamp et al., 2009). Robustness may be desirable from the view of adaptability to varying environments. However, it may be less commercially desirable, as robust animals may not be the most productive ones in the best environments.

Genetic Improvements and Environmental Changes in Farm Animals

A dramatic effect of selection over the past 50 years can be observed in broiler chicken (Eitan and Soller, 2002). As a result of selection, time to harvest has been reduced from almost a year to a few weeks while feed consumption dropped to about 1.5 kg consumed per 1 kg of growth. However, the dramatic improvements were associated with problems. First, the rate of maturity among sexes became different, requiring separation of sexes. Further drops of fertility in both sexes were addressed by artificial lightning. Early fatigue by males necessitated male supplementation. Finally, decrease in disease resistance was circumvented by antibiotic additives. Thus, all negative aspects of selection were addressed by environmental changes.

Leading poultry companies have successful operations worldwide including in the tropics. This means that it is possible to create environments in a variety of geographical locations that use efficient genotypes developed elsewhere. Success could be partially attributed to final products in tightly controlled environments and chicken being crossbred, which have hybrid vigor and thus better fitness than purebreds (Muir and Agrey, 2003).

In swine, development and production systems are similar to those in poultry (Rothschild and Ruvinsky, 1998). A specific issue in swine breeding is high mortality caused partly by selection for larger litters and decreasing sow survival. One of the hot topics in pig breeding is limited transfer of genetic progress in breeding purebreds to commercial crossbreds (Wei and van der Werf, 1994; Lutaaya et al., 2001). This issue may be due to several reasons, including different environments in breeding and commercial populations as well as insufficient modeling of genetic effects. Thus G×E in crossbred animals is a complicated issue as data recording beyond purebreds is limited and more accurate models of genetic analysis for crossbreds are complex (Lo et al., 1995).

In pigs, and particularly in chicken, the generation interval is relatively short and animals are relatively inexpensive. Thus maintaining a few selection lines is economically feasible. This is not the case in cattle, where the cost per animal is high and the generation interval long.

Beef uses both purebred and crossbred systems, with crossbreds being either F1 or composites. Many purebred animals are in fact crosses of upgrading populations (Field and Hagan, 2007). In general, G×E for major breeds may be larger within one country (e.g., the United

States) than across countries (de Mattos et al., 2000). One of the specific issues in beef is crossing *Bos Indicus* and *Bos Taurus* for production in tropical or semi-tropical systems. While F1 may have good performance, the other crosses could be worse despite the same breed percentage (Rutledge, 2001). This is caused by epitasis, which is ignored in routine models for multibreed evaluation (Pollack and Quaas, 1998; Legarra et al., 2007). Therefore, like in pigs, the issues of G×E and quality of modeling are confounded.

Dairy breeding in developed countries is driven by Holsteins, arguably the most productive dairy breed (Tyler and Ensminger, 2005). Although the genetic evaluation of the major dairy breeds is national, the national EBVs are combined by Interbull (www.interbull.org) to provide evaluations on the scales of many countries. Because bulls ranked as best by Interbull are used globally, the selection for Holsteins is mostly global forming a de facto single line. Slight exceptions could be New Zealand, which selects for production on pasture, and Israel, which indirectly selects for production in hot areas. The selection is dominated by phenotypes mainly from developed countries in temperate climates. Exceptions could be successful only if the exchange of genetics with other countries is restricted.

Side effects of intensive selection in Holsteins and the other dairy breeds are reduced fertility and high levels of culling (Dechow and Goodling, 2008; Madalena, 2008). More productive but less fertile cows can be more profitable up to a threshold (Lawlor et al., 2006). While fertility can be improved by increasing the weight on fertility at the expense of additional production, environmental changes to improve fertility such as timed AI, or timing of breeding are seen in many countries as more profitable (Caraviello et al., 2006).

Even though Holsteins are selected for the temperate market, many Holsteins (or their semen) are imported with varying success by developing and tropical countries (Costa et al., 2000; Madalena, 2008). Holsteins seem to function well in controlled environments (confinement, high-quality consistent feeding, cooling devices, high-quality labor) where the effect of tropical conditions (tick or disease resistance, unequal feed quality and quantity) are minimized. In less controlled environments, Holsteins do not fare well, although their crosses do.

Effects of Selection across Species

Decrease in fertility with increase of mortality has been observed across species for strongly selected populations (Rauw et al., 1998; van der Werf et al., 2008). This decrease may be due to higher fraction of energy spent on production with corresponding lower fraction of energy spent on maintenance, which includes fertility and disease resistance (van der Waaij, 2004). For example, Holsteins use more energy that can be metabolized on production than the more fertile Norwegian cattle (Yan et al., 2006). The more productive a genotype the more sensitive it is to deviation from its optimal environment. Van der Waaij (2004) postulated that the reduction of maintenance below a threshold of homeostasis induces problems and eventually causes mortality. The threshold is environment dependent, with the threshold being higher in challenging environments. Assuming that this theory is valid, there is an upper limit to efficiency above which the benefit of extra production is offset by costs of low welfare, including culling, low fertility, morbidity, and mortality. Even if the threshold is not reached normally, periodic disruptions in the environment like cold stress, heat stress, or disease challenge can lead to serious problems including high mortality.

If the genotype can no longer maintain homeostasis in important environments and environmental modifications are too costly or implausible, several choices are possible. A breeding

goal may be modified for more robust performance across environments (Veerkamp et al., 2009). While this would mean improved performance in challenged environments, it also could mean reduced performances in better environments. Another option is the creation of one or more lines. Creation of a line could be very expensive in cattle due to a long generation interval; although, as argued further on, the use of genomic selection can reduce costs and the generation interval dramatically.

The profit per genotype is a function of many traits including production, feed efficiency, reproduction, disease resistance, mortality, etc. It is desirable to have all economically important traits recorded. It is also desirable for models of genetic evaluation to correctly partition genetic and environmental factors and to take into account genetic correlations. Another issue is accounting for selection bias due to incompleteness of data. For instance, if culling in dairy cows is intense so that only few cows have records in later parities, the selection for production may result in sires with faster aging. Alternatively, selection for growth in mature pigs disregarding losses when growing up may result in selection of boars causing with high mortality of piglets on the commercial side.

Models to Measure G×E

Many strategies exist to measure G×E interactions (James, 2008). The obvious measures of G×E seem to be genetic correlations of a genotype among the environments. However, environments may be plentiful and variable over time, recording incomplete, and management may be hard to discern from genetics. This section describes models used for determination of G×E in specific situations.

Multiple Trait Model

The simplest model to measure G×E is a multiple trait model, wherein each environment is treated as a separate trait (Falconer, 1952). While systematic effects are particular to each trait, genetic effects in each environment are assumed to be correlated. The multiple trait model allows for different variances and heritabilities per environment, and it allows for varying genetic correlations among the environments. However, for reliable estimates of variance components, several conditions need to be fulfilled. First, the number of animals per environment should be sufficient. Second, animals among environments need to be sufficiently tied by ancestors. Third, environments need to be stable. Bias can occur if animals for some environments are pre-selected and the data on pre-selection is not part of the model. If the number of environments is too high, similar environments can be clustered, or "meta" environments can be created (Rekaya et al., 2003; Zwald et al., 2003).

Multiple Trait Model for Crossbreds

A different amount of G×E may occur in purebreds and in crossbreds. Accurate modeling of purebred and crossbred animals is difficult (Lo et al., 1995). When crossbred animals are limited to F1, a model for terminal cross can be applied (Lo et al., 1997). In this model each purebred has a single genetic effect, and each F1 has two genetic effects: one corresponding to the purebred sire and one corresponding to the purebred dam. Such a model allows for differential genetic variance and genetic correlations for each parental breed and their cross in different environments (Bloemhoef et al., 2010).

Interaction Model

When the number of environments is high, an interaction model can be used (Buchanan and Nielsen, 1979). In this model, the genotypes and environments are fitted as separate effects and as an interaction with all effects being treated as random. The relative value of variance of the interaction provides an indication of the magnitude of G×E. This model is best used with the sire model, e.g., as by DeMattos et al. (2000).

Reaction Norm

A reaction norm allows for a continuous change of an environment (Schlichting and Pigliucci, 1998; Strandberg et al., 2000; Kolmodin et al., 2002). With q being a variable that quantifies an environment, q can vary from −1 for the lowest producing herd to 1 for the highest producing herd. Then breeding values (BV) can be estimated by a linear reaction norm model (Eq. 16.1).

$$BV(q) = BV_{gen} + qBV_{sp} \tag{16.1}$$

BV_{gen} is generic breeding value and BV_{sp} is specific breeding value; these values are assumed correlated. Thus, BV is a function of the environmental variable q. A small variance of BV_{gen} relative to the variance of BV_{sp} indicates large G×E relative to the specific environmental variable q. Large positive correlations between BV_{gen} and BV_{sp} indicates that the selection on BV_{gen} improves performance in environments with large q but reduces performance in environments with low q. The negative correlation means the opposite. Low BV_{sp} means that an animal performs similarly across environments, or is robust.

The environmental variable q can be selected based on known or estimated data. Known data could be an average level of production (standardized), latitude or longitude, average rainfall, temperature-humidity index, etc. The variable q can be estimated from solutions to least square equations, e.g., solutions to heat-year effect, however, this may lead to biases (Su et al., 2006).

The reaction norm model as shown above assumes that changes in the environment are linear. Also, its performance depends on details. For instance, artifacts in estimates can be expected if changes in environments also change environmental variances and these changes are not modeled. One way to expand this model is to allow a nonlinear response to an environmental variable as well model environmental variances using a random regression model (Schaeffer, 2004). In such a model, changes in effects across the environmental values are modeled as functions, e.g., polynomials or splines. However, these models are of higher complexity, and estimation of their parameters requires large data sets.

Genetics of Heat Tolerance in Holsteins: A Case Study

One limiting factor in dairy production in hot climates is heat stress (St-Pierre et al., 2003). During heat stress, production and fertility decline while health problems increase (Kadzere et al., 2002). Heat stress can be managed by physical modification of the environment such as shade, sprinklers and fans (Collier, 1982). Cooling is very effective in dry environments but less so in humid conditions. When humidity reaches 100% at night, evaporative cooling loses efficiency. Also, not all production systems can afford the cooling management.

One particular challenge for Holsteins is declining performance under heat stress. Under high temperatures, milk yield and fertility decline while mortality increases. Although the decline in milk yield over the summer can be greatly reduced under good heat management, the decline in fertility under heat stress is still strong (Her et al., 1988; Flamenbaum and Ezra, 2007). The effect of heat stress on fertility is currently observed not only in the southern United States but also as far north as Alberta, Canada (Brouk et al., 2007). If heat tolerance in Holsteins is decreasing as a correlated response of selection for production, Holsteins may no longer be profitable in hot climates including the southern United States.

Higher heat tolerance can be achieved by selecting or crossbreeding more heat-tolerant animals. Crossbreds in dairy cattle have been successful under extensive, but not intensive, management because of lower production levels than purebreds (McDowell et al., 1996). Also, while the F1 may be heat-tolerant, the more complex crossbreds may be less so (Rutledge, 2001). Therefore, the remaining option is to select more heat-resistant purebreds, which are predominantly Holsteins.

For the selection to be successful, several conditions need to be met. First, the genetic component of heat stress should be high enough to create a potential for improvement. Second, heat tolerant animals must be identified with sufficient accuracy. Third, the existing selection must be against heat tolerance so selection for heat tolerance will become increasingly more important in the future. Last, the environmental modifications must be unable or too expensive to address the problem of heat tolerance in the long run, in comparison to genetic selection. One of the issues here is whether heat tolerance is single- or multi-dimensional. For example, whether improving heat tolerance for production also improves the heat tolerance for reproduction and longevity.

One way to study genetics of heat stress is via multi-trait models where phenotypes from different environments are treated as different although correlated traits (Ojango and Pollott, 2002; Rekaya et al., 2003; Hayes et al., 2003). However, this leads to confounding of environment and management. Also, the effects of more extreme climates cannot be accounted for while the number of animals from "hot" environments could be too small for a successful genetic evaluation. Therefore it would be desirable to have a methodology based on reaction norms where the magnitude of heat stress associated with specific records can be accounted for. The following sections will present such a methodology and its applications to several traits.

Model for Analysis of Heat Stress

Ravagnolo and Misztal (2000) presented a methodology for genetic analyses of heat tolerance using inexpensive weather information. The basic assumption of this methodology is illustrated in Figure 16.1. It is assumed that a trait is influenced by a temperature-humidity index (THI) around the day of recording. That influence is only above a threshold t_0 (THI > t_0), and the slope past the threshold is assumed to be linear. Individual variation exists for both for the value of the trait at low THI, which is called a regular effect, and for the slope, which is called a heat-tolerance effect. The variation is partly environmental and partly genetic. These assumptions correspond to the model in Equation 16.2

$$y_{ijklmn} = \text{"fixed"} + a_m + f(i)^* v_m + p_m + f(i)^* q_m + e_{i..mn} \qquad (16.2)$$

where y_{ijklmn} = records of an animal (m) in herd-year-day (i) and a set of "fixed" effects; a_m = regular additive effect of cow (m); f(i) = heat stress function for herd-year-day (i);

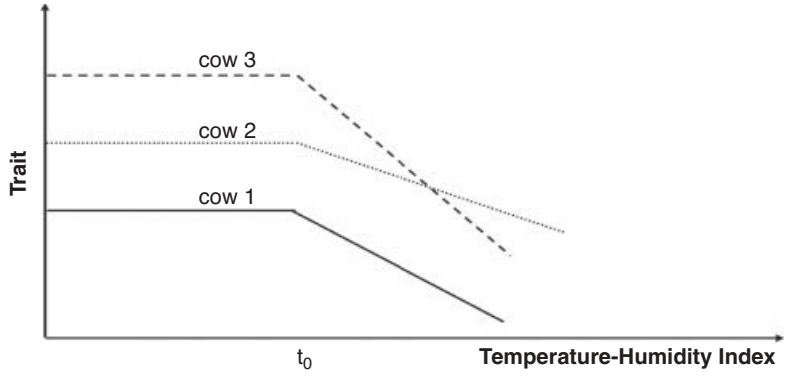

Figure 16.1. Assumed value of a trait as a function of THI where t_0 is threshold of sensitivity to heat stress.

v_m = additive effect of heat tolerance of cow (m); p_m = regular permanent environmental effect of cow (m); and q_m = permanent environmental effect of heat tolerance of cow (m). The permanent environmental effects are present only if there are repeated observations per animal. Regular and heat tolerance effects are assumed to be correlated with variances:

$$Var\begin{bmatrix} a \\ v \\ p \\ q \\ e \end{bmatrix} = \begin{bmatrix} A\sigma_a^2 & A\sigma_{av} & 0 & 0 & 0 \\ A\sigma_{av} & A\sigma_v^2 & 0 & 0 & 0 \\ 0 & 0 & I\sigma_p^2 & I\sigma_{pq} & 0 \\ 0 & 0 & I\sigma_{pq} & I\sigma_p^2 & 0 \\ 0 & 0 & 0 & 0 & I\sigma_e^2 \end{bmatrix} \tag{16.3}$$

where subscripts in the formula correspond to (co)variances for respective effects. Under the heat-stress model, the genetic merit at heat-stress level f(i) for animal (m) is a function of heat stress:

$$u_m[f(i)] = a_m + f(i)\,{}^*v_m \tag{16.4}$$

and the total genetic variance under heat stress level f(i) is:

$$\text{var}(a_m + f(i)\,{}^*v_m) = \sigma_a^2 + 2f(i)\sigma_{av} + f(i)^2\sigma_v^2 \tag{16.5}$$

The genetic correlation between regular and heat-tolerance additive values can be computed as:

$$\text{corr}(a, v) = \frac{\sigma_{av}}{\sigma_a \sigma_v}, \tag{16.6}$$

and the genetic heritability for heat stress under heat stress level f(i) is:

$$h_v^2\,[(f(i)] = \frac{f(i)^2\sigma_v}{\sigma_a^2 + 2\mathrm{f}(i)\sigma_{\mathrm{av}} + f(i)^2\sigma_v + \sigma_a^2 + 2\mathrm{f}(i)\sigma_{\mathrm{av}} + f(i)^2\sigma_{\mathrm{v}} + \sigma_{\mathrm{e}}^2} \tag{16.7}$$

Also, the genetic correlation between cold and hot environments is a function of f(i):

$$\mathrm{corr}(\mathrm{a_m},\ \mathrm{a_m} + \mathrm{f(i)}\,{}^{*}\mathrm{v_m}) = \frac{\sigma_a^2}{\left(\sigma_a^2 + 2\mathrm{f}(i)\sigma_{\mathrm{av}} + f(i)^2\sigma_v\right)^{0.5}\sigma_a} \tag{16.8}$$

Analyses for Test-Day Milk and Non-Return Rate

Ravagnolo and Misztal (2002) analyzed first-parity test-day records for production from Holsteins in Georgia and Florida and first-parity non-return (NR) information from Florida. Daily temperature and humidity information was available from over 21 public weather stations in GA and FL. Farms were matched to the closest weather station, first manually then automatically based on zip codes. THI was computed as:

$$\mathrm{THI(t,\,h)} = \mathrm{t} - (1 - \mathrm{h})\,(\mathrm{t} - 15) \tag{16.9}$$

where t = maximum daily temperature in °C and h = minimum relative humidity. The heat stress function was defined as:

$$f(i) = \begin{cases} \mathrm{THI}(t_i,\,\mathrm{hum}_i)\text{-}\mathrm{THI}(t_0,\,100) & \text{if } \mathrm{THI}(t_i,\,\mathrm{hum}_i) > \mathrm{THI}(t_0,\,100) \\ 0 & \text{otherwise} \end{cases} \tag{16.10}$$

Following Ravagnolo and Misztal (2000), the threshold point for the onset of heat stress was set to $t_0 = 22$, which would be equivalent to 22°C at 100% humidity (see Fig. 16.2). A similar curve was obtained for NR except that the threshold was lower at $t_0 = 20$.

For milk, protein, and fat the genetic correlations between regular and heat tolerance effects were between -0.3 and -0.4 (Ravagnolo and Misztal, 2000, 2002). This indicates that selection under temperate climates reduces heat tolerance in terms of sharper decline under high THI.

Heritability of NR90 increased with THI indicating good selection potential for reproduction under hot temperatures. Similarity in performance across environments is usually shown by high genetic correlations. The correlation between milk yield in mild and hot environments was 1.0 for THI below the threshold but decreased to 0.8 at THI corresponding to 30°C. High correlations reported in the literature (Zwald et al., 2003) could be due to cows exposed to heat stress for only part of the year and because cows may be managed to avoid production during the hottest period. Genetic effect of heat stress is high at higher temperatures indicating possibility of genetic selection.

Variable Threshold of Heat Stress

Studies by Ravagnolo and Misztal (2002) assumed a constant threshold of heat stress for different animals. This assumption was easy to model although it was not realistic. Sanchez et al. (2009) developed a Hierarchical Bayes model where also the threshold of heat stress could be estimated. Their model was computationally intensive. Based on Holstein data, they

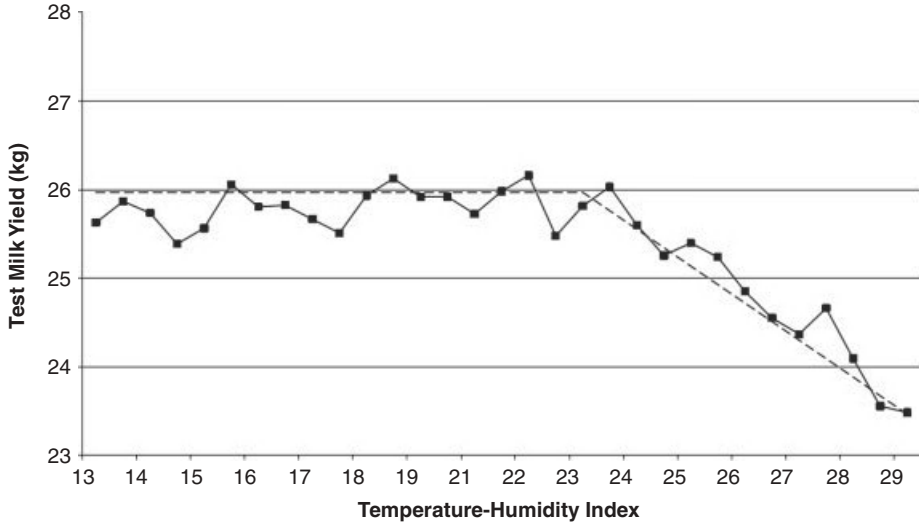

Figure 16.2. Least square means of test day milk yield as a function of Temperature-Humidity Index.

found that both effects have large genetic components; however, their correlation was −0.9. This means that animals with a higher threshold of heat stress have lower rates of decline under increasing temperatures. Thus, animals identified as having a lower rate of decline would almost automatically have a higher threshold of response to heat stress. Therefore, a simple model assuming a constant threshold is sufficiently accurate.

Loss of Information with Weather Stations

Important questions are whether public weather stations provide accurate information and whether more genetic variance may be captured with on-farm measurement of THI. West et al. (2003) studied rates of decline in milk yield at high THI based on on-farm measurements. Cows were at a similar lactation stage for the same parity. Daily THI was recorded over three months during the summer. Decline in milk yield was about 0.9 kg/THI unit (based on Fahrenheit temperature) over the THI threshold for heat stress compared with the decline of 0.2 kg/THI unit reported by Ravagnolo et al. (2000), who used test-day records from cows at different lactation stages on different farms and weather data from public weather stations. Freitas et al. (2006a) reanalyzed the data of West et al. (2003) with added information from public weather stations that were 3 to >400 km from the farm (see Fig. 16.3). The decline in milk yield relative to THI based on data from the nearest weather station was 1.1 kg/THI unit, which was larger than the decline relative to THI from on-farm measurements. Decline based on data from more remote weather stations were all >0.7 kg/THI unit. If the terrain is flat, data from well-managed weather stations can be as (or more) informative as data from on-site measurements. Data from Freitas et al. (2006a) were expanded to include test days over 10 years and test days from a cluster of farms. In both cases, the decline in milk yield was <0.5 kg/THI unit. Only a fraction of response to heat stress is captured with test days as opposed to more frequent measurements, especially if cows are in different lactation stages. Test days provide only a few observations per year per herd, and accounting for past events that

influence test-day milk yield, including daily heat fluctuations, is difficult. Consequently, the estimates of genetic correlations between cold and hot environments derived from tests days are likely inflated.

Heat Stress and Management

Freitas et al. (2006b) analyzed data from states with seasonal heat stress, such as South Dakota and parts of California. Milk yield of small herds (<100 cows) declined with increasing THI; however, smaller or no decline was found for large herds. In regions with less heat stress, usually only larger farms have cooling devices. In regions with low humidity, such devices are so efficient that the effect of heat stress on milk yield is difficult to detect.

National Genetic Evaluation for Heat Stress

Bohmanova et al. (2005) developed a national genetic evaluation for heat stress. The U.S. national data set consisted of 57 million first-parity test-day records of 7 million Holsteins that calved from 1993 to 2004. Hourly temperature and relative humidity records were available from 202 public weather stations across the United States. Herds were assigned by distance to the nearest weather station. Records were analyzed by a test-day repeatability model with random regression on a function of THI. Heat-tolerance predicted transmitting abilities (PTA) of sires ranged from −0.9 to 0.8 kg milk/THI unit > 22/day; general milk-yield PTA for sires was between −8.9 and 7.9 kg/day. Official U.S. genetic evaluations from February 2005 were compared for the 100 most and 100 least heat-tolerant sires based on estimated PTA for heat tolerance (see Table 16.1). Sires that were most heat tolerant transmitted lower milk yields with higher fat and protein contents than did sires that were least heat tolerant. Daughters of the most heat-tolerant sires had better type, worse dairy form, better udder and body composites, higher Type-Production Indexes, longer productive life, and higher daughter pregnancy rates than did daughters of the least heat-tolerant sires.

Many dairy producers in the southeastern United States are paid based on fluid milk. This pricing scheme provides incentives to select for cows with high milk yield without an

Table 16.1. Mean official February 2005 predicted transmitting abilities and Type-Production Indexes for the 100 most and 100 least heat-tolerant U.S. Holstein bulls based on estimated predicted transmitting ability for heat tolerance.

Trait	Most Heat Tolerant	Least Heat Tolerant	Difference between Most and Least Heat Tolerant
Milk yield (kg)[A]	−751	373	−1124
Fat (%)[A]	0.08	−0.02	0.10
Protein (%)[A]	0.03	−0.03	0.06
Type[B]	0.11	−0.46	0.57
Dairy form[B]	−0.49	0.96	−1.44
Udder composite[B]	0.15	−0.58	0.73
Body composite[B]	0.07	−0.25	0.32
Type-Production Index[B]	984	948	35
Productive life (mo)[A]	−0.22	−1.12	0.90
Daughter pregnancy rate (%)[A]	0.14	−1.49	1.62

[A]Official source: Animal Improvement Programs Laboratory, USDA, Beltsville, MD.
[B]Official source: Holstein Association USA, Brattleboro, VT.

advantage for high protein content. Based on results of Bohmanova et al. (2005), sires of such cows would be expected to transmit the least tolerance for heat stress. In a separate analysis, regional distribution of bulls was examined based on heat tolerance. Sires used in the southeastern United States had lower heat tolerance than the average U.S. average. Problems of heat stress in hot climates may be compounded by selection of less heat-tolerant sires.

Genotype by Environment Interaction Due to Heat Stress in the United States

Bohmanova et al. (2008) calculated separate breeding values for milk for the northeastern and southeastern United States. Breeding values for mild conditions (northeast) were calculated with and without the effect of heat stress. For bulls with more than 300 daughters in each region, genetic correlation between regional evaluations was 0.86 when heat stress was not considered for northeastern evaluations, and 0.87 when heat stress was considered. Therefore, regions with short heat stress but many records also provide useful information to rank sires for heat tolerance. Although evaluations were slightly more accurate when the effect of heat stress was included in the model, probably less than a quarter of the variation due to heat stress was accounted for in the evaluations. Also, the correlation of <1.0 resulted partly from reduced evaluation accuracy because information was available only from a limited number of daughters. In reality, heat stress may account for a large part of genetic variation between the regions.

Heat Stress in First Three Parities in Holsteins

Studies by Ravagnolo and Misztal (2002) involved only the first parity. Aguilar et al. (2009) looked at the genetics of heat stress in three parities. Their estimates of genetic parameters are summarized in Table 16.2. While the regular genetic variance increased from parity 1 to 3 by up to 50%, the variance due to heat stress increased up to five times. Much higher sensitivity of later lactations due to heat stress may be a reason for strong culling from parity to parity; in the analyzed data, only 25% of first parity cows had third parity records. Intensive selection in moderate climates decreases heat tolerance. Drops in productivity due to decreased heat tolerance may intensify due to increased heat stress, particularly during heat waves.

Trends for Heat Stress for Milk

Aguilar et al. (2010a) applied the same model to a U.S. national data set for Holsteins. Trends for regular and heat-stress effects are in Figure 16.3. While the trends for the regular effect are all favorable, the trends for heat stress are flat in the first parity and declining in the subsequent

Table 16.2. Parameter estimates for the three parities of test-day milk, fat, and protein.

	Milk (kg)			Fat (kg*100)			Protein (kg*100)		
Parameter	1	2	3	1	2	3	1	2	3
REG	5.6	7.5	6.5	74.0	93.9	109.0	42.5	56.8	52.2
HEAT	3.7	7.2	8.9	37.0	74.9	141.7	21.7	47.8	107.8
CORR	−0.46	−0.38	−0.47	−0.39	−0.39	−0.30	−0.43	−0.36	−0.50

REG = regular genetic variance; HEAT = heat tolerance variance at 5°C over the threshold; CORR = genetic correlation between the regular and heat-stress effects.

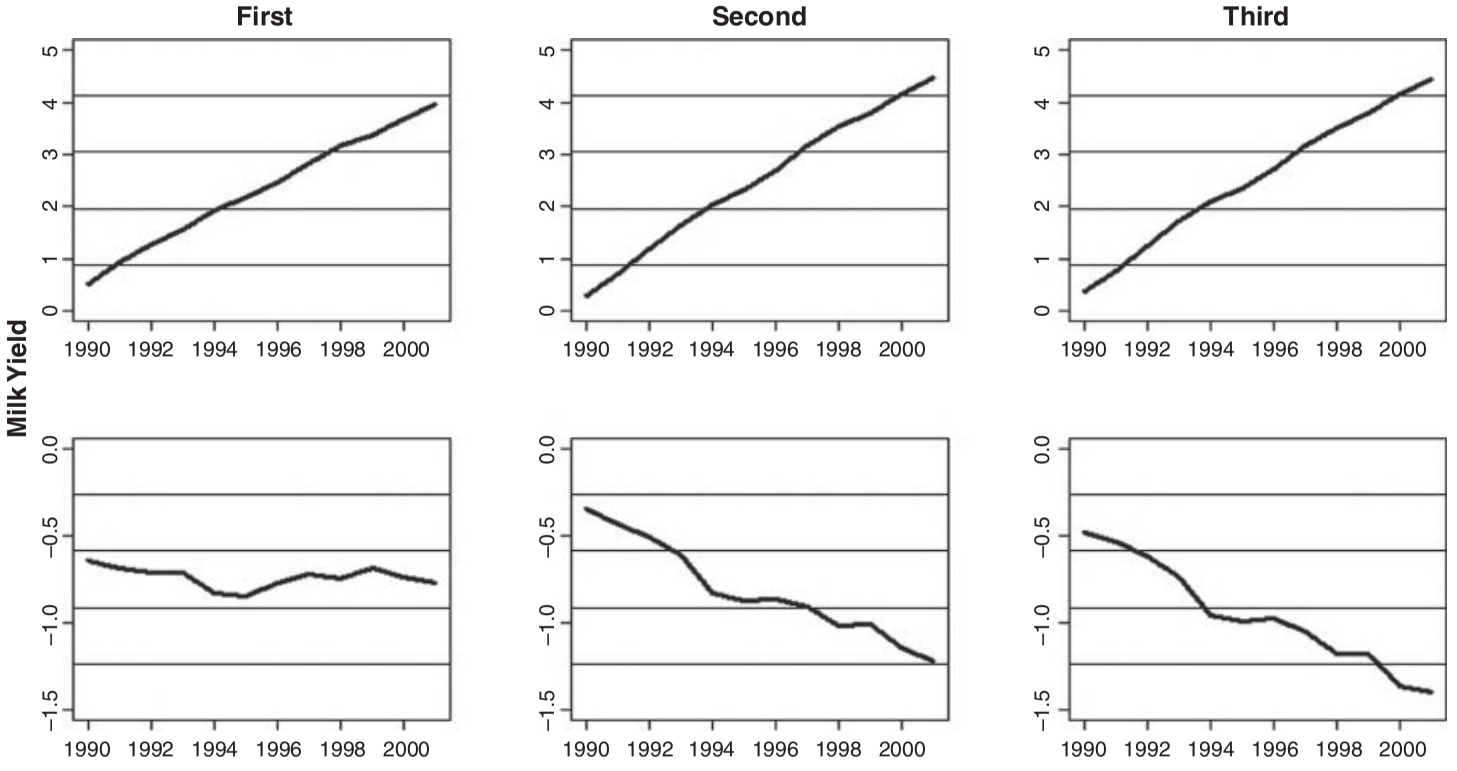

Figure 16.3. Trends in milk yield in the first three parities for the regular component (upper) and the heat stress component (lower).

parities. While negative selection for heat stress in the first parity is compensated by selection for fertility and survival in the first parity, such compensation is insufficient in later parities due to higher genetic component for heat stress.

Heat Stress and Days Open

Oseni et al. (2004) looked at genetics of heat stress for days open. The highest days open were from inseminations during the summer times. A monthly index was constructed that had a value of 0 corresponding to the month with the lowest days open and 1.0 for the months with the highest days open. Such an index was used in the reaction norm model. The heritability for the index value of 1.0 was twice as high as the value of 0. Thus the selection for shorter days open under heat stress can be successful. Pszczola et al. (2009) extended the model of Oseni et al. (2004) to include all regions of the United States by creating indices specific to each region. Trend for days open was negative (i.e., desirable) for the colder season and positive for the hot season. Sires selected as most heat tolerant were mostly low for production and type reflecting reality that expensive semen is not used during periods of low fertility. Such management of heat stress for reproduction can cause underestimation of the real effect of heat stress for fertility.

Seasonal Trends in Conception Rate

Huang et al. (2009) looked at monthly conception rates defined as success of an insemination. Cows from the Southeast were grouped in three classes of year-of-birth. For all groups, the conception rate in winter was very similar. The lowest conception rates occurred in August or September and were also similar for all the groups. However, the onset of decline was about a month earlier for the youngest cows. Therefore, the genetic changes make the cows more susceptible to lower levels of heat stress, despite continued improvement in management. Assuming that homeostasis means good fertility, the fraction of the year when cows are in homeostasis is decreasing.

Heat Stress and Genomic Information

If only first-parity records are available, only old bulls with a large number of daughters can be accurately evaluated for heat tolerance (Bohmanova et al., 2008). Use of later parities may increase accuracies due to a higher genetic component for heat stress in these parities; however, these accuracies may be insufficient for practical use, especially for young bulls. A dramatic improvement in accuracy could be obtained by the use of genomic information. The simplest and perhaps most efficient methodology in such a case would be the enhancement of pedigree-based relationships based on the genomic information (Aguilar et al., 2010b).

Effect of Heat Stress on Growth

Heat stress has a negative effect not only on milk production but also on growth. However, modeling that effect is complicated because only the final weight is usually available and the animal grows continuously over various phases of heat stress.

Zumbach et al. (2008) assumed that pigs are affected by heat stress only during the last weeks of growth and that each degree of THI over a threshold reduced average daily gain by a

proportionate amount. With field data they estimated 10 weeks and a threshold of 20°C. Based on such assumptions, heat loads were constructed as a function of month of harvesting.

The heritability of carcass weight under the maximum heat load was twice as high (0.28) as under the minimum heat load (0.14), and the correlations between performances under the two extremes were only 0.4. Therefore, growth rates under mild and hot conditions are different traits, and selection for performance under hot conditions is likely to be efficient.

Summary of Research on Heat Stress

With genetic parameters as derived here, it is possible to partially predict relative profitability of dairy operations at different levels of heat stress, e.g., using the methodology of de Vries et al. (2005). Assuming ongoing trends, one can predict changes in profitability in the future. More comprehensive analyses would require access to more traits effecting profitability under heat stress, such as culling and mortality. In the end, one may be able to decide whether a) the current selection is profitable, b) heat tolerance should be included in the current selection indices, or c) it is beneficial to create a separate line of heat-tolerant Holsteins

Genetic Selection and Genomics

The genetic selection via progeny testing is efficient but costly and with a long generation interval, particularly in cattle. Also, unless progeny sizes are large, the accuracy of evaluations and thus the genetic gain are low for low heritability traits. In dairy or beef, high accuracy for fertility or survival is achieved only for old proven bulls. Therefore, there is a limited interest in creating additional lines for specific environments.

Genetic evaluations could be obtained immediately after genotyping if major genes useful for specific environments are identified (Collier et al., 2008; Lillehammer et al., 2009). However, it seems that the number of genes affecting major traits is too large to be correctly identified. Therefore, new methodologies focus on large number of SNP markers without identifying individual genes (Meuwissen et al., 2001). In genomic selection, genotypes based on large SNP panels are used to enhance the accuracy of evaluations especially for young animals (VanRaden et al., 2009). Using these animals without progeny testing can decrease the generation interval, increase the genetic progress per year, and drastically reduce costs of genetic selection (Schaffer, 2006). Under selection, the accuracy of genomic prediction decays with each generation if new phenotypes are no longer used (Muir, 2007). Therefore, phenotypes still need to be collected and utilized although the best genomically tested animals can be used immediately without waiting for the result of the progeny test.

New Lines with Genomic Selection

The genomic selection makes it possible to select multiple lines from the same initial population at a low cost. Assume that a non-genomic genetic evaluation provides breeding values to create indices for several lines but only for old bulls. With the genomic selection, these indices can also be accurately predicted for the next generation of bulls, and selection for multiple indices would be possible without extra phenotyping. Phenotypes available when selected animals or their progenies mature can be used for "recalibration."

When genotyping involves only a fraction of animals, current procedures (e.g., VanRaden, 2008) involve several steps and are difficult to use for complicated models. However, the

genomic information is equivalent to improved animal relationships (Hayes et al., 2009; VanRaden, 2008). Aguilar et al. (2010b) developed a method to combine pedigree and genomic relationships. This procedure called "single-step" can utilize all phenotypic, pedigree, and genomic information. The single step procedure can be applied directly to complicated models, including those mentioned previously.

For specialized environments EBVs of even low accuracy cannot be obtained. For instance, the trait of "tick resistance" or resistance to tsetse fly cannot be recorded in developed countries. In such situations, phenotypes need to be obtained in environments of interest.

Conclusions

In farm populations, G×E is a dynamic concept because both genotypes and environments are evolving. Undesirable correlated responses of selection for production are compensated by improved environment. When environmental changes to maintain homeostasis are too expensive or impossible, one solution is selecting a specific line. In large animals, such a selection by progeny testing is likely to be very expensive and have too long a lag time. A much more attractive option could be by genomic selection, where costs are drastically decreased and lag time minimized. Either selection requires a refined genetic evaluation system for traits important in the desired environment.

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Chapter 17

Responses of Poultry to Environmental Challenges

J. Brake and S. Yahav

Introduction

Poultry display characteristics of both poikilotherms and homeotherms during their lives. During the perinatal period following hatching it has become common practice to provide supplemental heat to "brood" the neonate until a complete coat of insulating feathers can be grown and the bird becomes an efficient homeotherm. Brooding requires excellent husbandry skills to be uniformly successful in providing an external environment that will keep a bird warm, comfortable, and consuming feed and water at this early age. However, it is after the bird becomes an efficient homeotherm that even greater challenges develop. Poultry are fast-growing animals that consume significant quantities of feed rapidly. With more rapid feed consumption comes greater generation of body heat. Given the excellent insulating value of feathers, regulation of body temperature has become an overarching concern in poultry husbandry systems.

Modern poultry housing has not become universal and certainly has not solved all husbandry problems associated with regulation of environmental temperature. Nevertheless, the surface temperature of the world has increased in the past few decades and is expected to continue to do the same over the next few decades (U.S. National Climatic Data Center, 2001). In order to better design management schemes for poultry, a thorough understanding of the basic mechanisms of how birds cope with hot, as well as cold, thermal conditions would be helpful. In many cases, the realities in poultry differ somewhat from the more heavily studied experimental animal models such as mice and rats (Horowitz 1998, 2002); this is probably due to the previously mentioned genetic selection for productive performance that contributes to the difficulties that highly productive fowl have in maintaining a dynamic steady state under semi to extreme environmental conditions (Yahav et al., 2009).

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This chapter will focus on physiological and molecular responses elicited in response to changes in ambient temperature as well as management and nutritional strategies that enable poultry to cope.

Hypothermia

There is a range of temperatures within which the bird minimizes resting heat production, and body temperature is regulated by various physical means. This range is called the zone of thermoneutrality and includes ranges between the upper critical temperature where hyperthermia ensues and the lower critical temperature where hypothermia develops.

The negative effects of acute cold exposure in the adult domestic fowl are clearly limited due to an established metabolism, skin fat deposits, small surface-to-volume ratio, and feather cover. As long as feed consumption is adequate and feather cover remains intact, any reduction in body temperature would simply approach the lower range of normothermia. However, in juvenile fowl the large surface-to-volume ratio and the lack of a complete cover of feathers can result in high heat loss during exposure to cold and high-energy expenditure in an attempt to increase thermogenesis. Thus, there will be a lower fat accumulation needed for insulation and energy storage such that there will be longer-term consequences. Juveniles lack fat deposits and have a high surface-to-volume ratio with a developing insulation provided by feathers that may take up to 35 days to be complete in some cases. Physiological immaturity (Dunnington and Siegel, 1984; Modrey and Nichelmann, 1992) with respect to the integration of thermal information in the hypothalamus (Rothwell, 1992) and maturation of the body-to-brain temperature difference (Arad and Itsaki-Glucklish, 1991) during the first 10 days post-hatching also creates difficulties. Hypothermia due to post-hatching exposure to cold has been documented (Wekstein and Zolman, 1971; Freeman and Manning, 1984; Arad, 1991; Shinder et al., 2002). These circumstances provide the basis for the standard husbandry practice of providing supplemental heat during the "brooding" period that can last from 21 to 35 days of age, depending upon feather cover and temperatures external to the brooding facility.

Birds minimize heat loss by decreasing cutaneous blood flow (vasoconstriction), initiated by a sympathetic neural action, in parallel with direction of greater blood flow to the viscera to enhance heat production. Both shivering thermogenesis (Hillman et al., 1985) and non-shivering thermogenesis are employed (Duchamp and Barre, 1999) to maintain body temperature at extremely cold temperatures. Non-shivering thermogenesis involves the avian uncoupling protein (avUCP) in the skeletal muscle of chickens (Duchamp and Barre, 1999; Collin et al., 2003) and ducklings (Raimbault et al., 2001).

Shinder et al. (2007) exposed broiler chicks at 3 and/or 4 days of age to 15, 10, and 5°C for 3 or 1.5 h/day and found that the chicks could not maintain an adequate body temperature for longer than 90 minutes due to the heavy demand imposed. Importantly, a second exposure enhanced the capacity of the chick to maintain body temperature. During this study the dynamics of sensible heat loss from the face and legs, the two non-feathered body areas, differed somewhat. The face, being a major sensory organ as well as a major route for blood supply to the brain, maintained vasomotor response flexibility in order to maintain these crucial functions, whereas the legs being a secondarily important organ resisted a dramatic reduction in blood supply using the vasoconstriction mechanism (see Fig. 17.1). Furthermore, as legs have direct contact with the surface, it is important to have the vasomotor response in this organ in order to lose heat during thermal challenge.

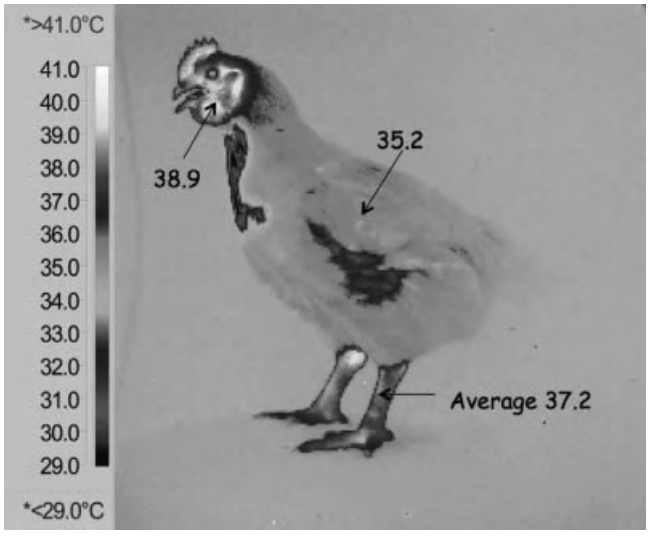

Figure 17.1. Thermal image of a broiler chicken exposed to 35°C. The frame on the leg demonstrates a section of surface area for which minimum, average, and maximum surface temperatures were determined.

Obviously, during hypothermia the objective is to increase thermogenesis and conserve heat, while in hyperthermia the objective is to reduce thermogenesis and increase heat loss in order to maintain body temperature. Thermogenesis encompasses basal metabolism, feeding, digestion, egg production, and activity. However, the factor that is most likely to alter body temperature is ambient temperature, especially high temperature. This is due to the fact that at lower ambient temperatures poultry can simply consume more feed to increase thermogenesis and generate more heat. However, the processes of thermolysis (heat loss) are not as effective for a well-feathered bird that is trying to consume significant quantities of feed at an ambient temperature that may approach body temperature.

In cold acclimation, changes in the cardiovascular system act mainly to accommodate an increased need for oxygen to fuel increased metabolism. The changes observed in birds that were adapted to low ambient temperature included peripheral blood flow vasoconstriction, increased blood volume as a result of increased erythropoiesis that affected hematocrit level and hemoglobin concentration, and compensatory changes in heart muscle weight (Olsen, 1937; Deaton et al., 1969; May et al., 1971; May and Deaton, 1974; Carey and Morton, 1976; Palomeque and Planas, 1978; Julian et al., 1989; Shlosberg et al., 1992,1996; Yahav et al., 1997b; Yahav, 1999, 2000a) followed by increased cardiac output. An increased red blood cell volume (i.e., increased oxygen carrying capacity) to accommodate greater oxygen demands also results in an increased blood viscosity (Fedde and Wideman, 1996) that precipitates an increased cardiac workload (Owen et al., 1995, Wideman and Tackett, 2000), blood pressure (Owen et al., 1995), and blood flow resistance (Wideman et al., 1998), which may account for the compensatory change in heart muscle weight.

One of the main post-hatching hazards faced by the fast-growing broiler is related to their inability to satisfy the body's oxygen demands when exposed to low ambient temperatures (Olkowski et al., 2005). Therefore, cold acclimation has been observed to fail often and, as a

result, the ascites syndrome may develop (Julian, 1993; Wideman, 2000; Luger et al., 2003; Baghbanzaden and Decuypere, 2008). This syndrome, also called the pulmonary hypertension syndrome, has been characterized by hypoxemia, increased workload of the cardiopulmonary system, central venous congestion, fluid exudation mainly into the body cavity, and, ultimately, death (Julian, 1993; Maxwell et al., 1995; Olkowski and Classen, 1998) so that this syndrome has been a main reason for significant economic losses under cold conditions (Wideman and French 1999; Luger et al., 2001; Druyan et al., 2007a, 2007b).

Ascites was first observed at high altitude and low oxygen gas tension was thought to play a major role in the development of the syndrome. However, it is now known that eggs become hotter than normal when incubated at high altitude because the air that enters the incubators from the surrounding room is too cold, such that the incubators do not ventilate optimally. Indeed, ascites can be observed at sea level when the incubator room temperatures are colder than about 20°C (Brake, unpublished observations) and the eggs become hot. This is typically in winter when it is often the case that the chicks will also be exposed to lower than ideal temperatures during brooding or subsequent growth. Low incubation temperature can be used in order to facilitate epigenetic temperature adaptation. Indeed, Shinder et al. (2009) demonstrated that acute short cold exposures during the last phase of embryogenesis (the endothermic phase) improved the ability of the growing broiler to cope with low ambient temperatures after hatching and reduced the development of ascites syndrome in the prenatal manipulated chickens.

Hyperthermia

All birds become homeotherms and are able to maintain their body temperatures within a narrowly regulated range as long as there is no exposure to excessively hot conditions and/or excessive metabolic heat production, which can precipitate a cascade of potentially lethal irreversible thermoregulatory events. Poultry, as all birds, have developed certain responses to avoid the deleterious consequences of thermal stresses. These direct responses that are elicited have been characterized as the rapid thermal stress response-RTSR (Parsell and Lindquist, 1994; Yahav et al., 1997b), acclimation/acclimatization (Yahav et al., 1997a; Horowitz, 2002), and embryonic or post-hatch thermal manipulation, based on epigenetic temperature adaptation during the perinatal period (Yahav and Hurwitz, 1996; Nichelmann et al., 1999; Tzschentke et al., 2001; Janke et al., 2002; Tzschentke and Basta, 2002; Piestun et al., 2008b).

The Rapid Heat Stress Response (RHSR)

The rapid heat stress response (RHSR) is an immediate response to heat stress that initiates the utilization of body resources to support homeostasis in a manner that is similar to the Alarm Reaction of the General Adaptation Syndrome, often termed Physiological Stress (Selye, 1936, 1973). This short-term response allows an animal to escape an adverse situation, i.e., similar to the "fight or flight" scenario of Physiological Stress. This short-term response has been characterized by massive release of adrenomedullary hormones and sympathetic neural transmitters that provide an immediate means to mobilize body resources to support heightened cardiovascular, pulmonary, metabolic, and muscular activity. An animal can survive an acute thermal challenge as long as it can mobilize the scarce resources that are immediately available, but when subject to a continuous and severe heat stress, an uncontrollable cascade

of events will ensue that will lead to heat stroke (irreversible heat prostration and acute adrenocortical insufficiency). Ascorbic acid supplementation has been shown to reduce heat stress related mortality in broilers (Pardue, 1983) through inhibition of the 21-hydroxylase and 11 beta-hydroxylase enzymes in the corticosterone biosynthetic pathway. This causes reduced synthesis of corticosterone and prevents adrenal cortical depletion.

Comparison of studies with experimental animal models, i.e., rats and mice (Horowitz, 1998, 2002), versus domestic fowls (Siegel, 1980) suggests that highly productive agricultural fowl, such as chickens and turkeys, differ to some extent from other homeotherms in their abilities to maintain homeostasis in the presence of severe environmental challenges (Yahav, 2000a), due to their enhanced genetic development for economically important production traits, which include enhanced carcass meat characteristics without parallel increases in the size and functional efficiency of the cardiovascular and respiratory systems (Havenstein et al., 2003).

One of the disadvantages of being a homeotherm is that the thermoregulatory system must be quite sensitive and operate at a very high gain in order to control body temperature within a relatively narrow range wherein metabolic processes have become adapted. During thermal challenge the thermoregulatory system utilizes the cardiovascular system to alter blood flow in such a manner that an augmented supply is directed to tissues and organs important for heat loss. Respiratory-evaporative mechanisms (Richards, 1968, 1970, 1976; Seymour, 1972; Marder and Arad, 1989), an evaporative cutaneous mechanism (Webster and King, 1987; Ophir et al., 2002), and sensible heat loss via radiation, convection (Yahav *et al.*, 2005), and conduction (Wolfenson et al., 2001) have been shown to be utilized to dissipate heat in birds. However, the respiratory-evaporative mechanism (panting) can be both energy consuming and heat producing, so any increase in sensible heat loss that diminishes the demand on the respiratory-evaporative mechanism will contribute to better thermotolerance in the presence of high ambient temperatures.

Dehydration can adversely affect evaporative heat loss via panting and passive cutaneous evaporation, so a certain amount of water consumption during thermal challenge must be required to replenish daily water losses not generated from metabolism. Panting also induces a mild to acute respiratory alkalosis, which may affect the efficacy of respiratory evaporation (Yahav et al., 1995). However, atrial smooth muscle that circumscribes the entrance to the pulmonary air capillaries has been shown to limit excessive gaseous diffusion, while allowing evaporation to proceed, and thus limit the development of respiratory alkalosis (for review, see Fedde, 1980). This is an anatomical adaptation that is unique to birds.

Although sodium bicarbonate has been added to feed and water of heat-stressed birds for many years, the product does not appear to consistently affect blood pH in heat-stressed broilers (Teeter et al., 1985; Branton et al., 1986). Improvements in performance obtained with this supplement do appear frequently in the presence of wide arginine-to-lysine ratios (e.g., high protein diets) and environmental temperatures sufficient to induce continuous panting (Balnave and Brake, unpublished data and observations). One possible way by which sodium bicarbonate could act at high temperatures in combination with wide arginine-to-lysine ratio diets would be to supply bicarbonate ions to buffer the increased concentrations of arginine, a strongly charged cation, in the blood. The pKa of the guanidinium group of arginine is 12.48. Sodium bicarbonate has the additional merit of improving the eggshell quality from heat-stressed laying hens (Balnave and Muheereza, 1997) if the dietary bicarbonate was consumed during the period of eggshell formation by using suitable lighting patterns (Balnave and Muheereza, 1997, 1998) that provided periods of light during the normal night hours, and therefore feed intake, in light-proof houses. This would be during the period of increased

carbonate ion production required for calcium carbonate deposition in the eggshell. The hens also consumed more protein daily when allowed to eat during the cooler night hours.

The development of hyperthermia (Etches et al., 1995) as a result of thermal challenge enhances the flow of blood flow to the skin, particularly to the non-feathered areas (Wolfenson et al., 1981; Wolfenson, 1986; Yahav et al., 1998a, 2004b, 2005) and to the upper respiratory passageways (Wolfenson et al., 1981) in order to enhance the first stage of heat dissipation, i.e., transport of heat from the viscera in the body core to the body surface. The first step is influenced by prevailing temperature gradients, thermal conductance of tissues involved, proportionality of body surface to body size, and flow of blood. The subsequent elevation of skin temperature increases the thermal gradient between the animal and surrounding air and facilitates more efficient heat loss by radiation, convection, and conduction. Radiation is the process of emitting energy in the form of electromagnetic waves. The bird can also gain considerable heat this way since it is a virtual "black body" in the infrared region, which is the type of energy generated beneath an un-insulated metal roof or from a heat lamp. Conduction is the direct transfer of heat by contact. Since air is a good insulator, little heat is lost from birds in this manner except from the feet, which can be well insulated. Poultry will bury into the litter to increase conductive heat loss and birds may be cooled from the outside or from the inside. Glatz (2001) reported that laying hens at 30°C that consumed cool drinking water also consumed more feed and produced eggs with better eggshell quality.

Convection is the process of heating air and having it rise from a hot surface as it expands. In this way air moving at reasonable velocity removes heat from a bird as it increases this process. Ruffling of the feathers and drooping of the wings allows air to move among the feathers and contact the skin to increase convective loss. Evaporation is the transfer of heat by using sensible heat to vaporize water and create latent (insensible) heat due to the energy trapped in the water vapor. The bird does not have sweat glands but can evaporate water from the lungs and skins. Birds will splash water on themselves to increase evaporative loss.

Broiler chickens acutely exposed to 35°C for 2 h exhibited a facial surface temperature of approximately 2°C less than core body temperature (Yahav and Giloh, 2010). Enhanced cutaneous blood flow is responsible for an increase in cutaneous water evaporation that desert species (Smith and Suthers, 1969, Arieli et al., 2002; Ophir et al., 2002) use as their main cooling mechanism and functions to some extent in poultry. Sensible heat loss consumes little energy and generates little heat, but passive water loss from the cutaneous surfaces depends on the rate of ventilation around the birds as moisture must be removed from the "halo" that develops around each bird in order for more moisture to absorb heat from (and thus cool) the body surface in the process of evaporation (Yahav et al., 2005). The microenvironment is the very limited area immediately adjacent to each bird. This area is what we intend to manage. This is often difficult since our ventilation systems do a poor job of mixing the meso-environment of the poultry house with the microenvironment. During acute thermal challenge, evaporative cooling plays a pivotal role (Hillman et al., 1985) but birds may suffer from dehydration as a result of excessive panting (Etches et al., 1995). This may negatively impact blood viscosity and thus the functioning of the blood system, leading to heat stroke. These circumstances point out the necessity to activate emergency husbandry practices to limit the necessity for excessive panting in a timely manner when faced with acute heat stress. In some cases, not feeding at all provides a suitable alternative to avoid mortality because of the associated decrease in excessive heat production.

In general, the initial reaction to high temperature is increased water consumption that in laying hens later decreases when egg production and feed intake decrease. Water-to-feed intake ratios increase from about 2:1 at thermoneutral temperatures to 5:1 during acute heat

stress in an attempt to increase heat loss. Environmental temperature has a pronounced effect on appetite. Reduction in feed intake is estimated to be 1% for each 0.6°C rise in ambient temperature between 21°C and 30°C and 3% per degree rise from 32°C to 38°C (Smith and Oliver, 1972).

The blood supply to the skin and the upper respiratory passageways is elevated during the early stages of the response to acute heat stress but no impairment of blood supply to essential tissues initially occurs as the increase in cardiac output that results from an increased heart rate and stroke volume is coupled with a redistribution of blood flow away from certain non-vital tissues. The increased heart rate and enhanced venous return support an overall increase in cardiac output that more rapidly refills the arterial pressure reservoir and prevents a severe reduction in arterial pressure (Whittow et al., 1964; Sturkie, 1967; Darre and Harrison, 1987; Zhou, 2000). However, depletion of blood volume as a result of dehydration has been found to cause a reduction in venous pressure that will diminish blood flow to the skin and the upper respiratory tract, severely affecting the efficacy of these two routes of sensible heat loss, possibly leading to a severe hyperthermia that can reach 46°C prior to death (Yahav, unpublished data). Death has been found to be preceded by detrimental changes at the cellular and molecular levels that lead to decreased blood pressure, brain hypoxia, neuronal dysfunction, cell fatigue, etc. (Hales et al., 1996) that are characteristic of heat stroke. The level of hyperthermia from which a sufficient recovery can occur was found to be between 44.0 and 44.5°C for broilers and turkeys (Yahav et al., unpublished data). This is the point where heavy panting will be observed.

Obviously, thermolysis must be maximized during the response to thermal challenge but a decreased thermogenesis can also remove some of the strain on the thermoregulatory system. Thermogenesis is an expression of the overall metabolic rate and has been shown to be regulated by the neuronal sympathetic system and thyroid hormones. It has been found to be able to decline in a manner proportional to the level and duration of heat stress (Silva, 2006). Metabolic rate is subject to control by the hormone thyroxine (T_4) that is secreted by the thyroid gland and is peripherally deiodinated to triiodothyronine (T_3), which exerts considerable control over metabolism (McNabb and King, 1993; Gabarrou et al., 1997) and temperature regulation (McNabb and King, 1993; Carew et al., 1998; Gonzáles et al., 1999; Yahav, 2000a). When exposed to acute thermal challenge the body immediately activates mechanisms to reduce the peripheral deiodination of T_4 to T_3, in what can be characterized as an emergency first step that is in concert with the initial stages of Physiological Stress that will mobilize required energy. The significant reduction in heat production as a result of longer- term acclimation in broilers (Yahav et al., 1996) and turkeys (Yahav, 1999) has been shown to be accompanied by a significant reduction in plasma T_3 concentration, mainly as a consequence of reduced thyroid gland activity. Feed intake was found to be significantly related to plasma T_3 and will also decline. Although frequently mentioned in the scientific literature as a means to help poultry control body temperature in hot climates, the strategy of lowering dietary protein while adding essential amino acids such as lysine, methionine, and threonine to reduce the dietary heat increment and combat heat stress has been found to be flawed (Alleman and LeClercq, 1997). These findings were consistent with personal observations that birds receiving nutritionally dense diets typically perform well in tropical countries. These diets typically had a wide arginine-to-lysine ratio, which led to research that demonstrated the value of higher arginine levels in hot climates (Brake et al., 1998; Balnave and Brake, 1999). Part of this benefit may be derived from the fact that nitric oxide (NO) is a natural vasodilator produced from the amino acid arginine that will reduce blood pressure (Wideman et al., 1995) and may contribute to an efficient peripheral vasodilatation.

Cells are protected for up to approximately 1 h during the initial phase of acute heat stress by activation of pathways that involve the adenosine receptor, mitochondrial $_{k}$ATP-dependent channels, and various kinases (Bogin et al., 1996, 1997; Hausenloy and Yellon, 2006). The expression of heat shock genes and their encoded heat shock proteins (HSPs; reviewed by Lindquist and Craig, 1988; Gething and Sambrook, 1992; Jaattela and Wissing, 1992; Welch, 1993) comprises the delayed but long-lasting second phase response (Jaattela and Wissing, 1992; Parsell and Lindquist, 1994). The HSPs have been demonstrated to be so-called molecular chaperones that bind to other cellular proteins, support intracellular transport and folding, prevent or ameliorate the effects of protein denaturation, and facilitate their renaturation (Feige and Polla, 1994). Proteins of various families of HSPs (HSPs 110, 90, 70, 60, 47, and small HSPs ranging from 16 to 40 kDa) that are both present prior to, and synthesized in response to, thermal challenge have been termed constitutive HSPs, while HSPs that are detectable only following stress have been termed inducible HSPs. The HSP-70 family, in particular, has been recognized for its prominent cytoprotective function (Volloch and Rits, 1999). The HSP-90 and HSP-27 families also appear to be involved (Yahav et al., 1997b). A close correlation between the induction of these proteins and increased thermotolerance has been demonstrated (Li and Laszlo, 1985; Wang and Edens, 1998; Yahav et al., 1997b). Furthermore, a small HSP of apparent molecular weight 29 kDa appeared in broilers after 3 h of heat stress, which suggested that it may be some sort of "second-stage defense protein" (Friedman-Einat et al., 1996). Heat stress is thought to be sensed thermally at the cell membrane level and subsequently triggers an induced transcription of HSPs in avian cells that is mediated by heat-shock transcription factors (HSF; Morimoto, 1998) 1 and 3 (Naki, 1999; Shabtay and Arad, 2006). Collectively, an immediate increase in heat loss by evaporation and sensible heat loss, coupled with changes in the cardiovascular system and a significant reduction in heat production form the physiological response that enables the chicken to cope with acute exposure to heat stress.

Acclimatization/Acclimation

Acclimatization refers to the lifelong natural physiological or behavioral processes of an organism that reduce the strain or enhance the tolerance to the strain caused by stressful climatic changes. The process whereby these changes are simulated experimentally has been termed acclimation (IUPS Thermal Commission, 2001). Husbandry strategies must take into consideration that there are two types of heat stress normally encountered by poultry, acute and chronic. Increased sensitivity combined with episodic acute heat stress has become a major problem in temperate climates, while chronic heat stress remains problematic in tropical regions. Heat acclimation and acclimatization involve an expansion of the autonomically controlled thermoregulatory range of the bird (Horowitz, 2002). Expanded body core temperature safety margins, increased heat loss, and decreased heat production comprise the heat acclimation/acclimatization processes that lead to a new level of homeostasis. Acclimation/acclimatization to heat initiates long-acting changes in response to persistent or repeated challenge by moderate rather than acute heat. Mildly efficient control of body temperature may be accomplished in broilers (Yahav et al., 1996), turkeys (Yahav, 1999), and laying hens (Yahav et al., 2000) exposed to moderately hot environmental conditions in 4 to 7 d but essential changes in the cardiovascular system of broilers appear to require 2 to 3 wk (Yahav et al., 1997a), depending upon physiological and genetic circumstances (Shannon and Brown, 1969;

Davis et al., 1972). As a practical example, Deaton et al. (1986) allowed birds to be exposed to 35°C daytime temperatures, as compared to 29°C, for six days prior to exposure to 41°C temperature. Mortality was reduced from 41% to 15%. This procedure would allow birds grown in evaporative-cooled houses to be prepared for transport in hot weather.

A moderate, rather than extreme, level of hyperthermia has been observed in broilers during acclimation as compared to an acute thermal stress. In turkeys, however, a marked hyperthermic response has been difficult to demonstrate even though both species belong to the same order (Yahav, unpublished data). Turkeys may possess more efficient cooling mechanisms (i.e., evaporative and sensible heat losses) and/or an ability to more efficiently reduce heat production. It can also be speculated that the relatively large unfeathered neck and facial areas of turkeys account for greater heat loss via convection and radiation. Less than a full feather coat has been found to improve the performance of laying chickens during hot weather as heat is dissipated more easily and more feed is consumed (Romijn and Lokhorst, 1961; Peguri and Coon, 1993). This would not be the case during cold weather.

The thermoregulatory features of acclimation include changes that may be characterized as milder than those of RHSR due to the less acute nature of the response. For example, skin vasodilatation coincides with vasoconstriction in the visceral organs, but the blood flow to these organs can continue as during pre-acclimation as a consequence of less severe systemic blood pressure adjustment. The cooler temperature of the visceral organs in such a case contributes to improved heat endurance through more sustained function. The obligatory peripheral vasodilatation observed during acclimation moved blood and heat to the periphery where significant advantage was accomplished when optimal ventilation was applied with broilers (Yahav et al., 2005), turkeys (Yahav et al., 2008), and laying hens (Ruzal and Yahav, 2010). The improvement due to optimal ventilation was largely due to increased sensible heat loss but it must be kept in mind that the extent of vasodilatation during acclimation is relatively low compared with that associated with the RHSR.

It should be noted that the livability and production of laying hens and broiler breeder hens during prolonged periods of hot weather may be improved by supplementing their diets with antioxidants such as ascorbic acid or vitamin E (Peebles and Brake, 1985; Njoku and Nwazota, 1989; Cheng et al., 1990; Bollengier-Lee, 1999; Puthpongsiriporn et al., 2001). Also, the lower concentrations of plasma inorganic phosphate in hens exposed to 30°C as compared to 18°C (Usayran and Balnave, 1995) can be taken as evidence of an increased requirement for energy metabolism.

Heat acclimation/acclimatization results in a reduced heart rate (Forrest et al., 1968; Sturkie et al., 1970) and greater stroke volume that improves cardiac efficiency. However, increased cardiac output requires increased venous return that is dependent upon an increased plasma volume (Senay et al., 1976). There is a significant expansion of broiler plasma volume during acclimation to constant or diurnal cyclic high ambient temperature that supports altered cardiovascular function while also providing fluid for respiratory evaporation (Marder and Arad, 1989). Plasma volume expansion as a result of acclimation, which has been mainly attributed to an increased plasma protein concentration that alters the balance between capillary hydrostatic pressure and colloid osmotic pressure and attracts additional fluid into the vascular space, has been demonstrated in birds (Whittow et al., 1964; May et al., 1971; Yahav et al., 1997a). More importantly, chickens have been shown to be capable of maintaining plasma volume following dehydration (Koike et al., 1983), such as might be associated with increased evaporative heat loss via respiratory and cutaneous routes during a prolonged acclimation.

Heat acclimation/acclimatization can obviously serve as an efficient means to develop thermotolerance in a slow-growing or long-lived animal such as a laying hen, turkey, or

broiler breeder. However, the early marketing age of broilers when combined with the need to provide heat for brooding during the initial poikilothermic portion of life has precluded such an approach. Nevertheless, such an approach can induce transient negative effects on growth and egg production of turkeys and laying hens, respectively, but the longer productive periods of these types of poultry provide more time for recovery and the opportunity to employ such an approach. One of the most efficient means to improve performance of laying hens during hot weather when feed intake may be reduced is to allow the birds to consume additional feed prior to the onset of lay and thereby accumulate greater body reserves (for a review, see Balnave and Brake, 2005).

Modulation of heat production during acclimation to either high or low ambient temperature is crucial as low ambient temperature will induce an increase in heat production while high ambient temperature will produce an opposite response. The thyroid hormones, T_4 and T_3, have considerable influence over metabolism and growth (McNabb and King, 1993; Tsukada et al., 1998; Vasilatos-Younken et al., 2000). Ambient temperature and T_3 move in a divergent manner in broiler chickens (Yahav et al., 1996) and turkeys (Yahav, 2000a), i.e., T_3 levels are higher when ambient temperature is lower. The levels of T_3 also increase as the level of nutrition improves, obviously to facilitate efficient utilization of the available nutrients (Gabarrou et al., 1997; Gonzales et al., 1999; Buyse et al., 2000). Nevertheless, acclimation to either cold or hot conditions will always cause control of body temperature to take precedent over growth and development and decrease performance and production of poultry.

Utilization of Ventilation to Control Body Temperature

Maximizing the efficiency of the major component of sensible heat loss, i.e., convection requires appropriate management of ventilation. Sensible heat loss has been assumed by some to not be very important when ambient temperature exceeds the upper limit of the zone of thermoneutrality (for review see Hillman et al., 1985) but a number of studies in poultry have demonstrated the beneficial effect of ventilation (see Fig. 17.1) on performance at high ambient temperatures (Drury, 1966; Wathes and Clark, 1981; Mitchell, 1985; Lacy and Czarick, 1992; Timmons and Hillman, 1993; Phillip and Sanborn, 1994; Tzschentke et al., 1996; Simmons et al., 1997, 2003; Lott et al., 1998; May et al., 2000; Czarick et al., 2000; Tzschentke and Nichelmann, 2000; Yahav et al., 1998a, 2001, 2004c, 2005, 2007). However, there is no single optimal ventilation rate. The necessity of using mechanical ventilation is a function of body weight, growth rate, and feather coat. Generally, this means that air velocity will need to begin to increase about 28 days of age, depending upon when the birds complete their feather growth and become more fully insulated. Excessive air speed will prematurely increase feed consumption without an associated increase in growth rate (i.e., poorer feed conversion due to excessive heat loss).

Birds lose heat at 29°C in still air at a rate roughly equivalent to the situation where they would be exposed to a wind speed of 2.55 meters per second at 35°C (Donald, 2001). This beneficial "wind chill" effect works relatively well as long as the air temperature does not exceed body temperature and there is a tendency for birds to allow their body temperature to increase during hot weather in order to maintain an adequate thermal gradient.

In order to modify air velocity, fans installed within poultry houses need to have the ability to alter their direction of airflow relative to ambient temperature after the brooding period has been completed. As the ambient temperature increases and the broilers become more heavily

feathered, the fans need to gradually blow more directly onto the birds, which will increase air velocity, rather than just stir the air above the birds as has been typically the case with horizontally directed fans (Czarick, 1989; Bottcher et al., 1993b).

Maximum six-week-old broiler performance at an ambient temperature of 35°C was at an air velocity of 2.0 m/s while 2.5 m/s performed better at 30°C. However, at 25°C the air velocity had to be reduced to 0.8 m/s in order to obtain maximum performance. These data suggest that at lower temperatures, high ventilation rates removed too much heat and caused a chilling effect, which would have increased energy expenditures for maintenance and reduced growth. At 25°C and 30°C in broilers the range of body temperatures observed when ventilation was varied from 0.8 m/s to 2.5 m/s was only from 40.4°C to 41.1°C, which suggested that body temperature per se could not be directly related to productive performance. However, a significant bell-shaped response of ventilation rate on body temperature was observed when broilers were exposed to 35°C as they exhibited hyperthermia as expressed by a body temperature of 43.9°C at 0.8 m/s and 43.2°C at 3.0 m/s, while at 1.5 and 2.0 m/s body temperature was approximately 42.85°C (Yahav et al., 2004c). Hyperthermia at a low ventilation rate was logical but was somewhat paradoxical at the higher ventilation rate. In both cases it was speculated that hyperthermia developed as a result of body water deficit. However, while the deficit at high air velocity resulted mainly from passive loss of water from the skin, the deficit observed at low air velocity most probably resulted from a high panting rate. Nevertheless, a similar bell-shaped response of ventilation rate on performance and body temperature was observed at 35°C in 6-wk-old turkeys. Ventilation rates between 1.5 and 2.5 m/s produced the best performance at 30°C but there was no effect of ventilation rate at 25°C. However, a significant increase in feed intake at 25°C and 20°C was taken to indicate that significant ventilation at these temperatures caused an increase in maintenance requirements (Yahav et al., 2007). During the studies outlined above, a significant linear ($r^2 = 0.998$) increase in convective heat loss at an ambient temperature of 35°C with increasing ventilation rate was observed as air velocity increased from 0.8 m/s to 3.0 m/s (Yahav et al., 2004c). No effect on heat loss due to radiation was noted, as that would have required a change in the surface temperature of the surroundings of the bird. The increased convective heat loss had a dramatic effect on the ratio of sensible heat loss to maintenance energy. While the ratio was only 29% in broilers exposed to air velocities of 0.8 and 1.5 m/s, it exceeded 44% of the energy expended for maintenance in birds exposed to 3.0 m/s. These data clearly demonstrated that sensible heat loss, as influenced by ventilation rate, had a major role in heat loss at high ambient temperature.

Greater air speed that increased convective heat loss during hot weather probably accounts for most of the benefit of modern "tunnel-ventilated" poultry housing (Czarick and Tyson, 1989). The combination of evaporative cooling systems (pads or foggers) with the high air speed created in such "tunnel" houses can greatly reduce the "effective" air temperature and maximize sensible heat loss by increasing the thermal gradient between the bird and the surrounding house environment as well as by increasing convective heat loss.

Advanced ventilation systems to control heat stress may be needed for only a limited amount of time each year in temperate climates, which can create an economic dilemma between the costs of such systems and sporadic heat-stress problems (Bottcher et al., 1993b). Downward directed high-speed fans will produce high air velocity at bird level and have been shown to produce effects equal to those reported for tunnel-ventilated houses when combined with foggers (Bottcher et al., 1991, 1993a). This approach increased sensible heat loss due to greater air velocity with cooler air and increased evaporation from the facial area when those areas became wet with the fog. It has been found that it is important to allow the birds to gradually become accustomed to these systems as they age and complete feathering so as to not create

a situation where the birds rush to a suddenly appearing zone of cool air during an acute thermal challenge.

Furthermore, the opportunity to dissipate body heat during the cool night period has been shown to allow birds to better withstand heat-stress temperatures (Smith and Oliver, 1972). Cyclic versus constant temperatures for commercial layers have been shown to be better (Smith and Oliver, 1971; Wilson et al., 1972). Typically, commercial poultry housing utilizes ventilation strategies that attempt to reduce the daily high temperature when it would appear that a greater focus on taking advantage of the diurnal changes in ambient temperature might be advantageous. Indeed, utilization of a cycling temperature has allowed some commercial enterprises to operate at a higher average temperature and thus have more feed efficient egg production (Brake, personal observations). This approach is based upon the premise that the average daily temperature determines the daily energy requirement while the low temperature determines appetite. Further, an average temperature that approaches the upper end of the zone of thermoneutrality, without inducing extreme panting, will require less feed for maintenance requirements. One simple option during very hot weather is to operate fans more at night, when the ambient temperature is cooler, by lowering fan thermostats and utilizing low priced off-peak electricity.

The Effects of the Interaction of Relative Humidity and Ambient Temperature on Body Temperature

Studies that have examined the effect of relative humidity on poultry have been limited, and most have focused on performance effects. Relative humidity from 50% to 90% did not affect growth rate or feed intake in an early study (Prince et al., 1965). Further, the range from 25% to 90% did not affect growth rate at an ambient temperature of 32.2°C (Winn and Godfrey, 1967), but at 29°C Adams and Rogler (1968) reported better performance at a relative humidity of 40% than at 80%. In tropical climates there has always been a reliance on evaporative heat loss due to panting by the birds to minimize losses. The influence of relative humidity on evaporative heat loss was studied by Romijn and Lokhorst (1966) who demonstrated that birds increase sensible heat loss (e.g., convective) and heat storage when evaporative heat loss is limited, due to high relative humidity. These data also suggest that the poor feathering that can cause problems with ascites in cold weather may be beneficial in hot weather, particularly in hot, humid environments. However, while Canton et al. (1983) concluded that body temperature was affected only by ambient temperature, Yahav et al. (1995) and Yahav (2000b) found that by acclimation of broilers to high ambient temperatures at varying levels of relative humidity produced maximal growth rate and feed intake at 60–65% relative humidity. The combination of high temperature and high relative humidity that is typical in tropical countries is of particular concern, as it appears that the greater breast meat of the modern yield-strain broiler contributes to heat production.

The reason for the variation in the broiler growth response to relative humidity is not clear but differences in relative humidity might affect the energy expenditure required for maintenance (i.e., energy needed to control body temperature) at high ambient temperature. This energy expenditure was assessed by plotting energy intake against growth with the intercept of the plot assumed to be an estimate of maintenance energy expenditure (for details, see Hurwitz et al., 1980). The maintenance energy requirement was calculated to be lowest at a relative humidity of 60–65% at all ambient temperatures measured. Maintenance requirements declined as a

percentage of total energy expenditure as ambient temperature declined (Yahav, 2000a), which suggested that broilers had greater thermoregulatory efficiency at this relative humidity. Indeed, a subsequent study demonstrated that broilers developed hyperthermia at both high (70–75%) and low (40–55%) relative humidity (Yahav et al., 1995) but were able to maintain their body temperature in the normothermic range only at 60–65% relative humidity.

Laying hens maintained at a constant 31°C and exposed to an increase in relative humidity (RH) from 40% to 60% for three months exhibited symptoms of respiratory alkalosis as well as small, but significant, adverse effects on egg production, feed conversion, mortality, and egg quality (Cheng et al., 1990). Hens housed at a higher, compared with a lower, cage density exhibited more detrimental effects on egg weight and shell quality as compared to hens at a lower cage density, probably due to localized ventilation deficiencies. It must be remembered that this was a constant and not cycling temperature. Allowing laying hens to be exposed to typically lower ambient temperatures at night allows them to dissipate heat that was stored during the hottest part of the afternoon and prevents many of the adverse effects of high ambient temperature (Smith and Oliver, 1971, 1972).

The performance response to relative humidity has been found to be age-dependent in turkeys (Yahav et al., 1995, 1998b; Yahav, 2000a). Maximal growth and feed intake in male turkeys from 4 to 8 weeks of age were obtained at 40–45% relative humidity at an ambient temperature of 35°C when studying a relative humidity range from 40 to 75%, but no effect was observed at 30°C. Turkeys from 10 to 19 weeks of age at 35°C exhibited a bell-shaped pattern of response to relative humidity, with maximum body weight and feed intake at 70–75%. Obviously, the response of turkeys to relative humidity differs from that of broilers, probably for somewhat similar reasons as stated previously for differences in the response to ambient temperature.

The Effects of Ammonia on Body Temperature Regulation

Ammonia gas, formed from uric acid and undigested protein in the manure by aerobic or anaerobic bacteria (Groot Koerkamp, 1994; Kristensen and Wathes, 2000), can have effects on thermoregulation of chickens and turkeys. The mechanical defense components and dead space of the respiratory system (Oyetunde et al., 1978) play a significant role during panting and have been reportedly affected by high levels of ammonia (Hillmann et al., 1985; Marder and Arad, 1989). Yahav (2004) found that broilers exposed to 16 ppm ammonia at 32°C maintained a lower body temperature than broilers exposed to 54 ppm. Arterial pH was also observed to increase, and arterial CO_2 decreased, with increasing ammonia concentration, which suggested a higher rate of panting in the presence of higher concentrations of ammonia, but with less control of body temperature. Exposure to 39 ppm of ammonia or more increased body temperature into the range expected with mild hyperthermia; so, in the absence of other information, a negative effect on the efficacy of panting as a mechanism of heat loss must be suspected.

The Epigenetic Approach: The Broiler Chicken Model

Given that the obligatory heat production that accompanies rapid growth rate and feed consumption will continue to increase as genetic improvement continues in broilers, and that the present physiological situation has already begun to test the economically feasible limits of

modern environmentally modified housing, a new approach to aid rapidly growing broiler chickens in dealing with high ambient temperature has begun to be developed. This new approach has been termed "epigenetic temperature adaptation" and has been based on the assumption that ambient temperature and other environmental factors can be used to modulate the "setpoint" for physiological control systems during "critical developmental phases" in the life of an animal. This was first described by Dörner (1974) as the "determination rule." This can also be described as a long-lasting physiological memory. Epigenetic adaptation takes place within critical developmental phases during embryogenesis and/or early post-hatching development and affects gene expression throughout the life of an animal. This research takes into consideration the accumulated knowledge of the "imprinting" of physiological control systems, such as the thermoregulatory system (Nichelmann et al., 1994, 1999; Tzschentke and Basta, 2002; Tzschentke et al., 2004; Tzschentke and Plagemann, 2006).

Physiological systems generally evolve during early development from an open-loop without feedback system to a closed control system with feedback according to the "transformation rule" described by Dörner (1974). Thermal manipulation during critical phases of such a developmental process of an appropriate centrally located system has been shown to permanently alter the thermoregulatory control system. The pre-optic anterior hypothalamus (PO/AH) has been found to possess thermosensitive neurons that receive afferent temperature signals from throughout the body and integrate these signals in order to direct appropriate thermoregulatory responses (Boulant, 1996). These responses include physiological, endocrinological, and behavioral actions intended to maintain a relatively constant core body temperature. This approach may affect the development of stress responses in a similar manner.

The control of body temperature in poultry begins during incubation as incubation temperature – among other factors such as turning, water loss, and gaseous exchange – is the most important controlling factor involved in incubation. Incubation temperature, in combination with other microenvironmental parameters such as relative humidity, air speed, and airflow, determine the temperature of the egg (Meir and Ar, 1987; Swann and Brake, 1990a, 1990b, 1990c). The body temperature of the embryo will be determined by the balance between the exchange of heat between the egg and its microenvironment and embryo heat production (Van Brecht et al., 2005). Embryo temperature can be measured non-invasively and accurately based upon eggshell temperature (Southerland et al., 1987; Joseph et al., 2006; Leksrisompong et al., 2007), which largely reflects embryo temperature through changes in the blood flow in the chorioallantoic membrane (Reizis et al., 2005).

Post-Hatching Thermal Manipulations

The body-to-brain temperature differential of broiler chicks has been shown to be maintained at a lower level than that of adult chickens for the first 10 days of life, when the development of temperature regulation has been reported to be completed (Arad and Itsaki-Glucklish, 1991). Thereafter, with increasing age and body weight, body temperature continues to incrementally increase relative to that of the brain. The epigenetic principle was initially demonstrated by exploiting the plasticity of the incomplete thermoregulatory system in the young broiler chick. Yahav and Hurwitz (1996) reported that exposure of three-day-old broilers to 37–38°C at 60–80% relative humidity for 24 h imparted the ability to efficiently reduce heat production during acute thermal challenge more than 30 d later. This enhanced ability was accomplished by increased sensible heat loss through convection and radiation (Yahav et al., 2005), a

reduction in the production of the stress hormone corticosterone, and increased quantities of the 27-, 70-, and 90-kDa heat-shock proteins (HSPs) in the heart muscle and lung tissue of broilers heated at 3 d of age (Yahav et al., 1997b). Increased sensible heat loss had the advantage of requiring less energy expenditure and heat production than would be the case for increased heat loss through respiratory evaporation ("panting"). This slowed the development of hyperthermia. The reduction in the production of corticosterone probably also helped avoid frequently observed mortality in a manner somewhat similar to that described above for ascorbic acid (Pardue, 1983), i.e., by maintaining a sustained production of corticosterone the birds were able to better adapt to the acute stressor.

In the chick PO/AH, R-Ras3 (Labunskay and Meiri, 2006), brain-derived neurotrophic factor (BDNF; Katz and Meiri, 2006), and 14-3-3ε (Meiri, 2008) were expressed to a greater degree during post-hatching thermal manipulation, which suggested that these genes might be involved in this epigenetic adaptation. The R-Ras3 belongs to the small GTP-binding protein subfamily and plays essential roles at the transcriptional level in cell proliferation, differentiation, and survival, as well as modulation of synaptic functions. The BDNF binds specifically to the TrK-B receptor and initiates tyrosine phosphorylation that activates the phosphotyrosine-binding site. This initiates the internal cellular pathway of RAS and results in transduction of genes involved in neuronal growth and maintenance. Thermal manipulation at 3 days of age also resulted in proliferation of skeletal muscle satellite cells (Halevy et al., 2001) that resulted in compensatory muscle growth. Uni et al. (2001) have subsequently reported a positive effect on gastrointestinal development. These latter two findings suggest potentially broad and economically important effects of post-hatching thermal conditioning. However, uniform post-hatch temperature manipulation would be difficult to manage on a commercial scale given the number of animals involved and the size of the facilities within which they have to be managed.

Pre-hatching Thermal Manipulations

As incubators for chicken eggs have been shown to be more uniform than poultry housing, it was thought that thermal manipulations during incubation would be possibly more efficacious. However, the interactions between the mechanics of incubation and timing of key phases of embryological development have to be adequately understood. Firstly, natural incubation conditions have been reported to not always be under exact control, as a result of searching for food, escaping from predators, and non-uniform nest insulation (Webb, 1987). This has certainly led to eggs incubated in natural conditions being exposed to episodic periods of heat or cold, which may have aided in development of mechanisms to adapt to environmental extremes post-hatching. Indeed, it was previously reported that exposing chicken embryos to low or high temperatures during incubation improved their capacity to adapt to cold or hot environments, respectively, during the post-hatching growing phase (Nichelmann et al., 1994; Tzschentke and Basta, 2002; Moraes et al., 2003; Yahav et al., 2004a). This was certainly in contrast with the normal commercial industry paradigm of uniform temperature during commercial incubation.

Broiler egg temperature increases with length of incubation. Initially the egg temperature is lower than the air temperature of the incubator that surrounds the egg. This situation persists up to about the tenth to thirteenth day of incubation, depending upon the incubator temperature, which may typically range between 37 and 38°C, and the rate of development of the embryo.

Even small changes in incubation temperature (0.3°C) during this time have the potential to change the overall length of incubation by several hours (Whittow and Tazawa, 1991). During the next phase of incubation, egg temperature will begin to increase above incubator air temperature by as much as 1°C, as embryogenesis produces an increasing amount of heat while the thermal conductance of the egg remains unchanged (Van Brecht et al., 2005). From the beginning of about the nineteenth day of incubation, when the chick begins to pip into the air cell of the egg with its beak and the shift from respiration via the eggshell to pulmonary respiration begins, egg temperature will remain higher than the incubator air temperature. The extent of this elevated egg temperature will depend upon the incubator air temperature and airflow.

While exposure to continually elevated temperature during prolonged periods of incubation has been shown to lead to reduced hatchability and poor chick quality (under developed chicks could be characterized as "premature" in mammalian terms; Piestun et al., 2008a; Leksrisompong et al., 2007), the use of intermittent periods of elevated temperature have not produced similarly adverse effects (Piestun et al., 2008a) probably because the embryo retains the innate ability to deal with incubation temperatures that may vary between 30 and 40°C (Webb, 1987) under natural scenarios. Broiler chicks that were less than fully developed due to extended periods of elevated incubation temperature appeared to be quite sensitive to cool house temperatures immediately post-hatching, but this could be managed by utilizing hotter than normal brooding temperatures for the first two days following hatching (Leksrisompong et al., 2009). The elevated brooding temperature encouraged greater feed consumption, which led to improved residual yolk sac utilization. After the initial two-day period during which the chicks adapted to the brooding environment and apparently experienced a maturation of their thermoregulatory systems, normal management schemes could be resumed. However, if these chicks were exposed to a cool brooding environment they would often exhibit the initial steps in the development of ascites, (also called pulmonary hypertension syndrome due to extension of the right ventricle of the heart; Julian, 1993). Once initiated, the cascade of events leading to death has been very difficult to stop. These chicks were also found to be more susceptible to acute heat stress from 28 to 35 days of age.

In an effort to demonstrate that the post-hatching tolerance to cold could be improved, episodes of 15°C lasting 30 or 60 min during the eighteenth and nineteenth days of incubation were employed (Shinder et al., 2009). The timing of this experimental exposure was based on findings that in the chicken, endothermic responses could be detected from E18 onwards, which suggested that heat production increased as a result of relatively lower incubation temperatures (Nichelmann et al., 1994; Tzschentke and Nichelmann, 1999; Tazawa et al., 2001; Loh et al., 2004; Nichelmann, 2004). It was thought that exposure to cold may modulate the metabolic response capability of the chicks regarding subsequent environmental demands (Decuypere, 1984; McNabb, 2006; Walter and Seebacher, 2007). Indeed, a dramatic decline in egg temperature ensued as a result of increased sensible heat loss via convective and radiative means. Embryo temperature also declined but recovered to a level above that observed prior to the cold episodes, which suggested a subsequently increased metabolic rate that would be better able to endure cold exposure post-hatching (Josef et al., 2006). Indeed, the incidence of ascites syndrome was observed to diminish (Shinder et al., 2009). Although these data were impressive, a sharp decline in incubation temperature during the hatching process would be somewhat difficult to accomplish with current incubation technology. However, this does not preclude the use of modified approaches to induce tolerance to cool post-hatching temperatures.

Early attempts at thermal manipulation pre-hatching had demonstrated an improvement in thermotolerance during the first 10 d post-hatching, as evidenced by lower body temperature that persisted up to 35 d, but thermal challenge at 42 d of age revealed that the initial thermal

advantages of these chickens was no longer evident (Collin et al., 2007; Tona et al., 2008). It was logical that the hypothalamus-hypophyseal-thyroid axis (thermoregulation) and/or the hypothalamus-hypophyseal-adrenal axis (stress) would be intimately involved in post-hatching thermoregulation and resistance to heat stress and that the "set point" or "response threshold" of these systems involved in the development of thermotolerance could be altered most efficiently during their development/maturation. This period had been reported to be from the seventh to the sixteenth day of incubation, inclusive. Piestun et al. (2008a, 2008b, 2009) demonstrated for the first time that adopting this period as the "critical phase" for thermal manipulation of chick embryos significantly enhanced thermotolerance with an intermittent application of 39.5°C and 65% RH for 12 h per day to broiler embryos during this embryonic period, which did not negatively affect hatchability and chick quality. The chicks were then raised under standard conditions to 35 d of age before exposing them to a thermal challenge (35°C for 2.5 to 4 h). Chicks that had been exposed to this in ovo thermal manipulation exhibited a lower metabolic rate, reduced body temperature, and reduced plasma T_4 and T_3 concentrations (Piestun et al., 2008a). The fact that the plasma T_4 concentration was reduced in the thermally manipulated chicks suggested that thyroid gland activity was reduced, which would contribute to a fundamentally reduced metabolic rate (Yahav et al., 2004a, 2004b). Of course, a lower T_3 level also helped reduce the metabolic rate of the chick. There was also a significantly lower level of stress, as indicated by the level of plasma corticosterone, and by a mortality rate that was half that of the control chickens during the subsequent thermal challenge at 35 days of age.

Summary

The accumulating evidence has demonstrated that the epigenetic adaptation approach, used either during incubation or immediately post-hatching can provide broiler chickens with an effective means to adapt to high ambient temperatures such that rapid genetic progress can continue and existing growing facilities can be effectively and economically utilized. However, it is clear that much more work is needed in order to fully exploit this approach. In conclusion, poultry, being homeotherms, can be managed with several strategies when dealing with environmental challenges. However, the contradictory goals of high productivity and thermotolerance create continuing challenges for poultry husbandry and poultry science.

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