Chapter 1
Comparative Physiology of Thermoregulation

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Introduction

From single-cell organisms to the largest animals, the thermal environment challenges both performance and survival. Whether it is the honeybee or the thoroughbred race horse, organisms constantly adapt to the temperatures around them to maintain homeostasis. In athletic, military and occupational settings, thermoregulation is often secondary to the goals of the sport, mission, or job. Similarly, in the animal kingdom thermoregulation is seldom the primary obstacle to survival. Instead, the ability to respond to the thermal environment is controlled via subconscious physiological and behavioral systems. These thermoregulatory systems across species have developed in response to the environments these animals have been exposed to throughout their anagenesis.

The purpose of this chapter is to overview the similarities and differences between a variety of animal species and humans which allow them to adapt and thrive in a given environment. Throughout the mechanisms and systems presented in this chapter, it is important to not dismiss one species' adaptation as superior to another, but rather evaluate the advantages and disadvantages afforded by each system or behavior. We will pay particular attention to the concepts of thermoregulation in animals that apply to human thermoregulatory challenges; as the quest for higher, faster, and stronger performances not only drives our understanding of the

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limitations of physiology but also generates creative solutions to further enhance athletic performance. Finally, we discuss the use of animal models and how multiple approaches can be used to relate this information to exertional heat illnesses.

Comparative Physiology Informs Animal Models of Hyperthermia

Our search of the scientific literature revealed that numerous animal models have been studied to gain insights into human temperature regulation and hyperthermia. Working under the auspices of animal protection committees, which ensure humane treatment of laboratory animals at universities and hospitals, this research has focused on various aspects of thermoregulation including, skin anatomy, organ function, physiological responses, and heat gain/loss/balance. Humans are homeothermic (i.e., constantly attempting to maintain body temperature at a stable set-point), endothermic (i.e., producing considerable internal heat via metabolism) animals that release heat to the environment via dry heat loss (i.e., convection, conduction and radiation) and wet heat loss (i.e., sweat evaporation, respiration).

In addition to these physiologic factors, the design of an animal model of hyperthermia and the resulting clinical complications of heatstroke requires that scientists consider the methods to induce increased body temperature and to measure temperature [1]. Regarding the former, hyperthermia can be induced by viral or bacterial toxins, drugs, exercise, and exposure to a hot environment. Toxins, however, induce unwanted pathologies and increase the risk of investigator infection. Drugs that induce hyperthermia also may induce unwanted side effects and irrelevant compensatory responses. Exercise-induced hyperthermia in an animal model, therefore,

1. must induce natural compensatory responses
2. must mimic human hyperthermia
3. can be generated using commercially available animal treadmills

Therefore, no single animal model is perfect to describe human responses to exercise in the heat and heatstroke. Instead, animal models must be selected to study the responses and adaptations that most mimic human responses for the variables of interest.

Classification of Thermoregulatory Systems

The most basic method of classifying species' thermoregulation considers the methods by which temperature is regulated. While *homo sapiens* and nearly all mammals and birds represent one end of the spectrum as homeothermic endotherms, other

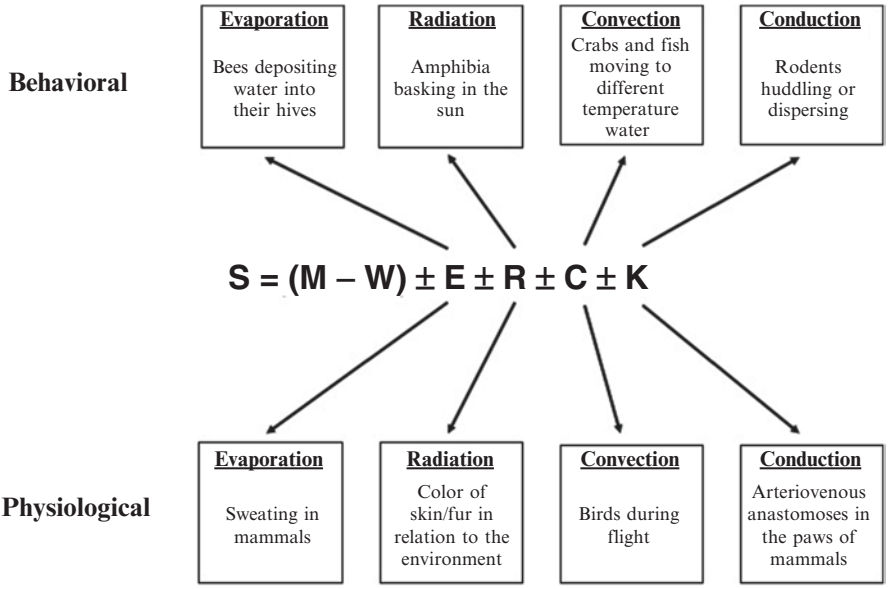

Fig. 1.1 Theoretical representation of the Q_{10} effect. Adapted from [2]

species do not regulate their temperature as closely or utilize environmental sources of heat rather than metabolic heat. Most fish, amphibians, and reptiles can be classified as poikilotherms because their internal temperature is strongly influenced by environmental conditions [2]. Poikilothermy is often coupled with ectothermy, in that heat energy from the environment is necessary for some species to maintain normal body temperature [3]. It is important to note that these categorizations are not exclusive. Endotherms may allow for substantial fluctuation in their body temperature, for example, in the case of hibernation.

While maintaining an internal body temperature that is different from the external environment provides evidence of thermoregulation and classification as a relative homeotherm, evaluation of Q_{10} offers a more nuanced approach. The Q_{10} is defined as the change in metabolic activity of a given organism or system that results from a temperature increase of 10°C [2]. For example, the Q_{10} effect of 2.3 in muscle physiology, following the Law of Aerrhenius [4], is typically the reasoning behind "warming-up" in athletics, with a slight increase in muscle temperature leading to increased athletic performance [2].

In the absence of homeostatic control of internal temperature, a twofold to threefold increase of metabolic activity (i.e., a Q_{10} of 2–3) is observed in response to an increase of environmental temperature [5]. A theoretical uncompensated Q_{10} response (~2.3), such as that in the true poikilothermic ectotherm, is illustrated in Fig. 1.1. Meanwhile, in a perfect homeotherm, a Q_{10} of 1 would be expected because the animal is able to isolate its body temperature responses from changes in the environmental temperature. However, most species are not able to totally isolate

their internal temperature responses, a criterion Q_{10} of < 2 is often used to classify species as homeotherms or poikilotherms [5]. Further, a diurnal rhythm of internal body temperature exists in most mammals [6].

Behavioral Thermoregulation

While homeothermy is defined as the ability to physiologically regulate body temperature in response to environmental changes, nearly all species possess the ability to thermoregulate behaviorally. In poikilotherms, behavioral change is the predominant manner by which they cope with changes in their environments. Metabolically, behavioral thermoregulation is very efficient [3]. This explains why nearly every species has a series of behaviors that alter the effect of the environment, even if they possess highly functioning physiological systems. For some animals, changing posture or moving to a new location is an adequate method of thermoregulation. For reptiles and amphibia, sunning or basking is a typical behavior by which the animal exposes its body to as much solar radiation as possible, leading to internal heat gain [7].

In many animals, activity levels are closely tied to ambient temperature. A Gaussian distribution of activity has been widely observed; as ambient temperatures increase or decrease beyond an animal's thermal preference, it decreases activity to minimize heat gain or loss [8]. For example, cattle decrease rumination as ambient temperature increases [9]. This distribution of varying activity levels corresponding to ambient temperatures is widely conserved across species, suggesting widespread effectiveness.

This idea of a thermal preference has also been studied in fish, which exhibit a distribution of metabolic rates that are proportional to the temperature of water [10]. This thermal preference is not uniform across species. Nocturnal reptiles have been observed to tolerate lower temperatures than similar diurnal species [7]. In fact, even within the same species, thermal preferences can vary greatly. For example, fiddler crabs adapt to different water temperatures, depending on whether they come from temperate or tropical waters [5].

The animal kingdom also utilizes group dynamics to behaviorally cope with a changing environment. Annelids and arthropods in the desert have been observed to burrow underground when ambient temperatures increase and to aggregate in groups when temperatures decrease [8]. Burrowing decreases the radiant load from the sun, while aggregation increases the thermal inertia of a group. The same huddling and dispersion can be seen in rodents [11]. Meanwhile, bees can collectively cool their hive with water from pollinated plants, one drop at a time [8].

In humans, behavioral thermoregulation is considered primarily in terms of thermal comfort [12]. When you sense that you are cold, you may look to add a layer of clothing; if you sense that you are hot, you may remove a layer or you may change the room temperature by adjusting the thermostat [13]. This is based upon integration of information in the pre-optic area of the hypothalamus from cutaneous and

visceral temperature sensors [3]. Instead of a measured physiological response, you are able to use another strategy to better achieve thermal comfort. This same neural pathway exists in vertebrates and demonstrates the importance of the hypothalamus in both physiological and behavioral thermoregulation [3, 14].

In athletics, changing the time of outdoor training to the morning or evening from the middle of the day is another example of behavioral thermoregulation. Just as many animals may seek shade in the middle of the day, smart coaches also alter activities to protect their athletes. Whether this involves moving practice to an air-conditioned facility, increasing rest breaks, or altering the time/location of training, these changes likely will have a greater impact than relying on thermoregulatory responses in an uncompensable environment.

Physiologic Thermoregulation

In homeotherms, physiological mechanisms must compensate for changes in the thermal load placed upon the organism. There must be a constant balance of heat gain and dissipation to maintain the narrow homeostasis of body temperature. Birds and mammals are the typical focus of this phylogeny; however, fish, reptiles, and amphibia also possess some of the same components of temperature regulation.

One of the most basic methods of physiologic thermoregulation involves the countercurrent exchange of heat. In this system, opposing channels of fluid in close proximity allow for rapid exchange of heat between the body's tissues and the external environment. Unsurprisingly, fish utilize this method of thermoregulation very efficiently [10]. In humans, an expanded cavernous sinus, compared to other primates, facilitates countercurrent exchange of heat in the skull [15]. This direct exchange occurs in a continuous manner. However, it relies on the presence of a local heat gradient which can be problematic in animals that have a large tissue mass that does not directly interface with the environment.

Heat Balance Equation

The fundamental methods of heat gain and dissipation in homeotherms can be modeled through the heat balance equation. While other chapters in this book will focus on the specific human aspects of the heat balance equation, it is important to understand that the same principles govern the flow of heat in a variety of organisms.

$$S = \left(M - W\right) \pm E \pm C \pm R \pm K$$

where S is the amount of heat storage in the body, M is the metabolic heat production, W refers to external work (which at rest has a nearly negligible effect on heat

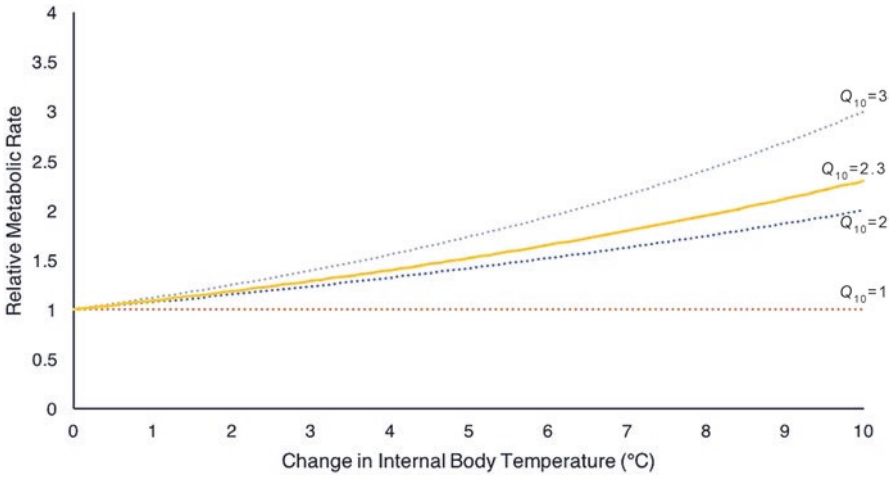

Fig. 1.2 Examples of behavioral and physiological methods of heat balance across species

balance), *E* is evaporation, *C* is convection, *R* is radiation, and *K* is conduction; *E*, *C*, *R*, and *K* usually refer to heat exchange between skin and air [16]. For each component of this heat balance equation, there exists a unique animal adaptation that illustrates the interplay between different avenues of heat flow (Fig. 1.2).

Metabolic Heat Production

Most endotherms maintain a body temperature greater than the ambient environment, which requires a large amount of heat gain [3]. Metabolic heat production is subdivided into either shivering or non-shivering thermogenesis. Shivering thermogenesis occurs primarily as a result of cold exposure and is one of the few thermoregulatory responses observed in snakes [3]. Non-shivering thermogenesis is further classified into four components: thyroid hormone induced increases in metabolic rate, oxidative phosphorylation, muscular work, and brown adipose tissue [3]. Humans are considered relatively efficient with 20–25% of metabolic energy being converted to locomotion during exercise [17]. The remaining energy is released as heat to the tissues. By contrast, the cheetah approaches 10% efficiency when running at 17 km/h [18]. Therefore, due to the excessive heat production, many animals are limited by overheating during exercise [19].

Convection

Convection is the heat exchange between a surface and a fluid, typically air. In free convection, the fluid density determines the rate of heat transfer, whereas forced convection is dependent on the velocity of fluid [12]. In humans, the most common

example of convective cooling is the difference between running indoors on a treadmill and performing the same exercise outdoors. During outdoor exercise, forced convection occurs as a result of both wind and body movements. Meanwhile, indoor exercise at the same intensity is typically considered more difficult from a thermoregulation standpoint because the only convection that occurs is a result of free convection.

For most exercising animals, convective cooling is very similar to humans. An illustrative example of the effects of convection can be found in birds. Despite the fact that most physiologists have identified predominant evaporative cooling methods, the heat balance of a bird while flying could not be achieved without the great amount of convection that occurs during flight [20]. In furred mammals, convection also plays an interesting role in cooling. In the air space between individual hairs, convection loops form as small circular movements of air that gradually bring heat from the skin to the outside environment [6]. While this may not be as efficient as evaporative cooling methods on the skin, these convective loops contribute to some cooling of an otherwise well-insulated animal. However, it is important to note that convection relies on a heat gradient between the body's surface and the environment. When the ambient temperature is greater than the surface, convective cooling is impossible.

Conduction

Conduction is the heat exchange between two solid objects [12]. Physiologically, this occurs within the body as heat transfers between tissues; as a method of heat loss, it appears in limited circumstances because most animals have limited direct contact with a surface that allows heat transfer. Birds and mammals all share fairly similar thermal conductance, which increases in response to increases in blood flow [11, 21]. Meanwhile, poikilothermic lizards possess up to ten times the thermal conductivity of mammals [21].

Thermal conductivity of skin is great in two areas. First, arteriovenous anastomoses provide conductive heat exchange. These pre-capillary blood vessels densely populate the palms and feet of humans and the paws of mammals [22]. Second, similar areas of great cooling potential exist in some animals' tails [23]. Therefore in both humans and animals, the skin surface serves as a target for cooling modalities.

Radiation

Radiation is typically considered a method of heat gain through solar radiation, like the basking of amphibia on a sunny day [21]. While it is not explicitly physiologically controlled by animals, the color of their skin or fur in relation to the environment can impact radiant heat load. Furthermore, the different densities of mammal coats throughout the year can either increase radiant heat load for heat gain during cold weather or minimize radiant heat load during warm weather [24].

When modeling radiative heat and the body, there are six terms to consider regarding net radiation balance: five are the environment's influence on the body and one the body releases to the environment [12]. For example, the color of skin, fur, or feathers can alter the emissivity of a surface, either minimizing heat loss or maximizing heat gain [9].

When compared to other species, humans are notably successful at minimizing solar radiation. Only 7% of the skin surface is exposed to maximal radiation when standing upright [25]. Contrast this to quadrupedal animals that expose a much greater area to the sun, greatly increasing the radiant heat load.

Evaporation

Evaporation as a method of heat dissipation is of particular interest when examining physiologic thermoregulation. For birds and mammals, this is by far the predominant method of heat dissipation. Evaporation relies on the energy required for the phase change of water from liquid to vapor [12] and occurs in a variety of methods across the animal kingdom, as illustrated by the following examples. First, the honeybee regurgitates its stomach contents onto its body [19]; when the fluid from the contents evaporates, the bee cools. Second, rats and kangaroos spread saliva on their skin to dissipate heat via evaporation [3, 23, 26]. Third, storks and vultures defecate on their legs to cool [19]. Most other birds rely predominantly on the evaporation of fluid from mucosal surfaces to cool [20]. This is similar to the respiratory cooling in dogs, typically referred to as panting [27]. Respiration in dogs is linked to stride patterns; thus, the cooling capacity of these animals is limited by the speed of their legs and stride rate [15]. However, in an example of divergent evolution, African hunting dogs have been shown to rely less on evaporative cooling than their domestic counterparts [18].

Sweat glands exist only in the skin of mammals; their density varies greatly, from 20 to 30 glands·cm^{-2} in pigs to >2000 glands·cm^{-2} in some species of cattle [28]. Two types of sweat glands exist, apocrine and eccrine. Apocrine sweat glands are typically found with fur or hair [4], while eccrine glands are predominantly used for thermoregulation [15]. Chimpanzees and gorillas possess approximately two-thirds eccrine sweat glands and one-third apocrine sweat glands, while humans possess nearly 100% eccrine sweat glands [29].

Not all vertebrates have similar sweat glands; for example, cats, dogs, and pigs have eccrine glands only in their foot pads and/or snout; these animals rely more on respiratory panting to release heat to the surrounding air. Bedouin black goats are an interesting counterexample, as they possess a relatively large number of apocrine sweat glands, perhaps to help keep themselves cool despite possessing black fur [15].

Horses, one of the closest thermoregulatory counterparts to humans, possess a very large mass in comparison to their surface area, making cooling difficult. However, horse sweat contains a protein, latherin, that acts as a dispersant for sweat [30].

Their sweat is also slightly hypertonic to blood plasma, which makes electrolyte replacement following exercise a particular concern [28].

One of the downsides to sweating as a means of evaporative cooling is that it requires the loss of body water. In humans, hypohydration becomes a serious concern during prolonged, intense exercise in the heat. Camels demonstrate a unique countermeasure to this phenomenon. Contrary to popular belief, the hump of a camel is fat rather than water. However, during prolonged bouts of sweating, the camel is able to use this fat to yield metabolic water, providing great resistance to hypohydration [19].

What Do Animal Models Reveal About Human Heatstroke?

Physiologists employed a rat model of exertional heat stroke for more than 15 years, at the U.S. Army Research Institute of Environmental Medicine, Natick MA, USA [31]. This model acknowledged that rats spread saliva on fur and skin, across a wide range of ambient temperatures, as an important element of heat dissipation. In fact, evaporation of saliva accounts for approximately 90% of the heat lost by male rats, in a 40 °C/104 °F environment [26]. Similarly, in a hot-dry environment, evaporation of sweat from human skin accounts for >80% of all heat loss during treadmill running. Despite the viscosity and compositional differences between saliva and sweat, many rat physiological responses and compensations are similar to those of humans [1]. For example, the rat model provided the following insights regarding human exertional heatstroke: hepatic ultrastructural changes, acidosis, hyperkalemia, and membrane damage are similar to those observed in humans; individual factors (e.g., age, body weight) influence heat sensitivity, mortality, and survival time; passive and exercise-induced hyperthermia resulted in unique serum enzyme profiles of alanine aminotransferase, aspartate aminotransferase, creatine kinase, and lactate dehydrogenase; low potassium and low sodium diets (versus adequate dietary intake) increased the rate of heat storage and reduced total treadmill work accomplished; gut-derived bacterial endotoxins appeared in plasma after hyperthermia; and endurance training influenced exercise tolerance time, ability to sustain thermal load, and susceptibility to work-induced thermal fatality [31–34].

Researchers in South Africa are widely known for their primate simulations of human classical heatstroke, published during the years 1986–1988. During exposure to a hot environment, the internal body temperature of monkeys and baboons rose to ≥43 °C/109.4 °F, well above the often-cited 40 °C/104 °F threshold of human exertional heat stroke. Due to the taxonomic similarities (i.e., thermoregulatory, cardiovascular) of primates and humans, the primate model of heatstroke resulted in relevant findings regarding cardiovascular responses (e.g., heart rate, mean arterial pressure, peripheral resistance), hyperthermia-induced increases of gut-derived bacterial endotoxins (i.e., lipopolysaccharide, LPS), and

Table 1.1 Factors that influence investigator choice of species to model human hyperthermia and exertional heat stroke

Species	Availability	Cost-effectiveness	Convenience of handling and housing	Similarity to human responses
Baboon	+	+	+	++++
Monkey	+	+	+	++++
Dog	++	++	++	+
Sheep	+++	++	+++	++++
Rabbit	++++	+++	+++	+++
Rat	++++	++++	++++	++++

Adapted from [1]
+, lowest or poorest; ++++, highest or greatest

the relationship between morbidity–mortality and Gram-negative bacterial shock [35, 36]. Because LPS plays an important role in heatstroke symptomatology (e.g., hypotension, shock), South African investigators also studied the protective effects of administering intravenous compounds to primates whose rectal temperature reached 43.5–44.5 °C/110.3–112.1 °F. They observed improved survival times and lower mortality rates following administration of a corticosteroid (i.e., reducing inflammation), an antibiotic (i.e., decreasing bacterial infection), and the antibody to LPS (i.e., counteracting increased plasma LPS concentration) [37–39]. Few or none of the above studies could have involved human subjects, due to the current ethical standards involving human research.

Several other animal models of severe hyperthermia and heatstroke have been developed, with limited success and a smaller number of resultant publications. These models include dogs, chicks, rabbits, sheep, and cows [40]. Sheep are reserved for large-scale experiments in which several variables and functions are studied concurrently [1]; rabbits are seldom utilized in such studies. As shown in Table 1.1, numerous other practical and scientific factors encourage and/or discourage involvement of these animal families.

Summary

The animal kingdom offers unique insights into the complex responses that different species employ to regulate internal body temperature. Whether these involve altering behavior or physiological responses, to better cope with heat stress, humans are not alone in their efforts to thrive in hot environments. It is in light of comparative physiology that we appreciate the thermal load experienced by humans during exercise or occupational labor, and develop strategies, techniques, and products to ameliorate thermal strain and avoid illness or death.

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