CHAPTER

4

Exercise and Core Temperature

C. BRUCE WENGER

The views, opinions, and findings in this chapter are those of the author and should not be construed as an official Department of the Army position, policy, or decision unless so designated by other official documentation. Approved for public release; distribution is unlimited; this chapter in public domain.

Temperature changes affect biologic processes through configurational changes that alter the function of protein molecules such as enzymes, receptors, and membrane channels, and through a general effect on chemical reactions rates as described by the law of Arrhenius. Within the physiologic range of temperatures, most chemical reaction rates vary approximately as an exponential function of temperature, and raising temperature by 10°C increases the reaction rate two- to threefold. A familiar clinical consequence of this effect is described by the rule that each 1°C of fever increases fluid and calorie needs 13%.[1] The thermoregulatory responses of homeotherms keep internal or body core temperature within a narrow range, thereby providing a more stable physicochemical environment for their biologic processes.

Normal human body temperature is conventionally said to be 37°C (98.6°F), a figure that may be misleadingly precise. Core temperature at rest undergoes a daily or circadian rhythm with an amplitude of about 1°C, and is lowest in the early morning and highest in the late afternoon.[2–4] In women of childbearing age, this circadian rhythm is superimposed on another rhythm, with a somewhat smaller amplitude, associated with the menstrual cycle.[5–7] These rhythms are produced by underlying rhythms in the control of the thermoregulatory responses, in what we may think of as the setting of the body's "thermostat." These rhythms, plus other factors such as individual variation and acclimatization to heat, account for a range of core temperatures of healthy subjects at rest (Fig. 4–1). In addition, heavy exercise or fever may raise core temperature several degrees, and more extreme disturbances of core temperatures may result from neurologic disease or from heat or cold stress that overwhelms the capacity of the thermoregulatory system.

Adverse effects of heat stress include impairment of physical and mental performance,[8,9] heat-related illnesses and syndromes,[10–12] aggravation of preexisting illnesses,[13–15] and direct injury caused by high tissue temperature. Apart from burns, direct thermal injury may include some of the tissue injury associated with heat stroke. In healthy individuals, the physiologic defenses against heat are ordinarily so powerful and effective that tissue temperature rarely reaches harmful levels during heat stress, and most adverse effects of heat stress owe much more to secondary consequences of thermoregulatory and other homeostatic responses than to direct thermal injury to tissue. With the exception of local tissue injury, adverse effects of cold are chiefly those associated with hypothermia, ie, clinically significant lowering of core temperature, which include depression of central nervous system function, cardiac output, and respiration, and electrical disturbances of the heart. Because of the high rates of metabolic heat production associated with exercise, heat stress is a much more frequent threat than cold stress during exercise. Nevertheless, hypothermia may be a significant problem during marathons and other prolonged exercise performed in cold or

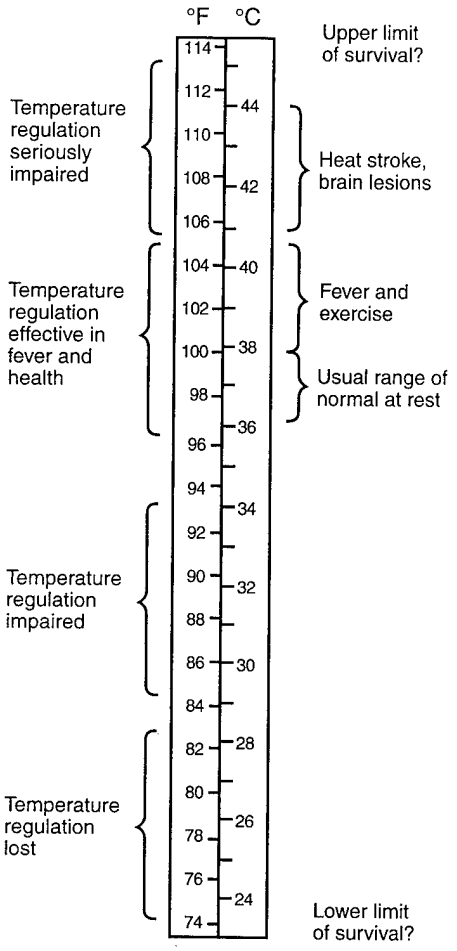

FIGURE 4–1. Ranges of rectal temperature in healthy persons, patients with fever, and persons with impairment or failure of thermoregulation. (Modified from Du Bois EF: Fever and the Regulation of Body Temperature. Charles C. Thomas, Springfield, IL, 1948.)

wet weather.[16–18] This chapter discusses normal physiologic responses to heat and cold, especially in combination with exercise; events that lead to deterioration of performance or frank illness during heat or cold stress; and factors that affect tolerance to heat and cold. In addition, clinical aspects of heat and cold stress are briefly summarized.

BODY TEMPERATURE AND HEAT TRANSFER IN THE BODY

Thermal physiologists divide the body into a warm internal core and a cooler outer shell. The regulated internal body temperature is the temperature of the vital organs inside the head and trunk. The core includes these organs, along with a variable amount of other more superficial and peripheral tissue. The amount of the body included in the core is greater in a warm environment and when metabolic heat production is high. Within the core, temperature is relatively uniform and close to the temperature of the central blood.

Shell temperature is strongly influenced by the environment and thus is not regulated within narrow limits, as core temperature is, even though thermoregulatory responses strongly affect the temperature of the shell and especially its outermost layer, the skin. The thickness of the shell depends on the environment and the body's need to conserve heat. In a warm environment, the shell may be less than 1 cm thick, but in a subject conserving heat in a cold environment, it may extend several centimeters below the skin.

Heat is lost to the environment only from tissues in contact with the environment, chiefly from skin but to a lesser extent from the respiratory passages also. Therefore, body heat balance depends on the flow of heat from the sites of heat production to the skin. Heat is transported within the body by two means: conduction through the tissues and convection by the blood, a process in which flowing blood carries heat from warmer tissues to cooler tissues. Heat flow through tissue by conduction depends on the thermal conductivity of the tissue, whereas heat flow by convection depends on the rate of blood flow through the tissues. Changes in skin blood flow in a cool environment change the thickness of the shell. When skin blood flow is reduced in the cold, the affected skin becomes cooler, and the underlying tissues, which may include the more superficial muscles of the neck and trunk and most of the volume of nonexercising limbs, become cooler as they lose heat by conduction to cool overlying skin and ultimately to the environment. In this way, these underlying tissues, which in a warm environment were part of the body core, now become part of the shell. Since the shell lies between the core and the environment, all heat leaving the body core via the skin passes through the shell before being given up to the environment, and thus the shell insulates the core from the environment. In a cool subject, skin blood flow is low, and core-

to-skin heat transfer is dominated by conduction, and since the shell is thicker under these conditions, it provides more insulation to the core. Thus changes in skin blood flow, which directly affect core-to-skin heat transfer by convection, also indirectly affect core-to-skin heat transfer by conduction, by changing the thickness of the shell.

REGULATION OF BODY TEMPERATURE

Physiologic and Behavioral Temperature Regulation

Two distinct control systems, physiologic and behavioral, operate in parallel to regulate body temperature. Physiologic thermoregulation utilizes involuntary responses. In humans the most important responses involved in physiologic thermoregulation are changes in skin blood flow, which controls flow of heat from the interior of the body to the skin; sweating, which increases heat loss by evaporation, in the heat and during exercise; and shivering, which increases metabolic heat production, in the cold. The physiologic control system is capable of fine adjustments to these responses, and enables homeotherms to achieve fairly precise regulation of their core temperature. Behavioral thermoregulation involves the conscious use of any means available and operates primarily to reduce the level of thermal discomfort. Since thermal discomfort is closely related to the underlying physiologic strain,[19] behavioral thermoregulation reduces the demand on the physiologic thermoregulatory responses. Familiar behavioral responses include adding or removing clothing, seeking a more comfortable environment, and drinking hot or cold liquids, and reducing physical activity in hot environments. Behavioral thermoregulation is strongly influenced by learned responses, and may be compromised or overridden when there is enough motivation to persist in a situation that produces a high degree of thermal stress, as during intense physical training or athletic competition or in the performance of certain jobs. In healthy young persons, harmful effects of heat and cold are most often the result of failure to make the appropriate behavioral responses, owing to excessive motivation, improper supervision, or lack of foresight.

Balance Between Heat Production and Heat Loss

Although the body exchanges some energy with the environment in the form of mechanical work, most is exchanged as heat, by conduction, convection, and radiation, and as latent heat through evaporation or, rarely, condensation of water (Fig. 4–2). If the sum of energy production and energy gain from the environment does not equal energy loss, the extra heat is "stored" in or lost from the body. This is summarized in the following heat balance equation:

$$M = E + R + C + K + W + S \qquad \text{Eq 1}$$

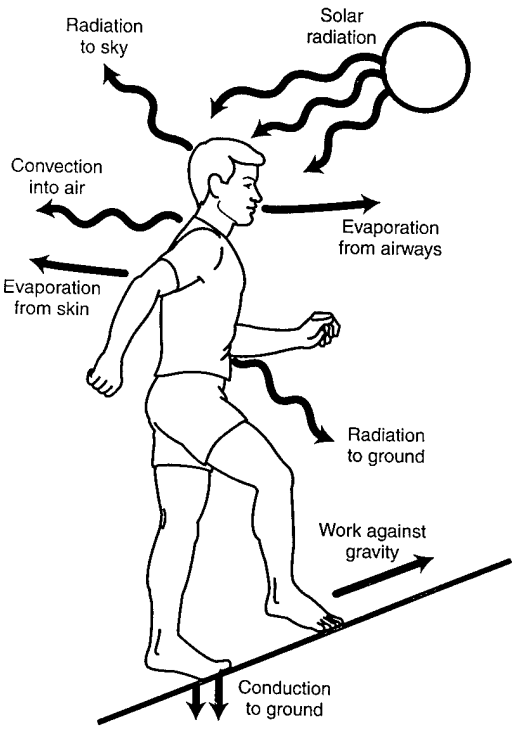

FIGURE 4–2. Exchange of energy with the environment. This hiker gains heat from the sun by radiation, and loses heat by conduction to the ground through the soles of his feet, by convection into the air, by radiation to the ground and sky, and by evaporation of water from his skin and respiratory passages. In addition, some of the energy released by his metabolic processes is converted into mechanical work, rather than heat, since he is walking uphill. (Redrawn from Wenger CB: The regulation of body temperature. In: Rhodes RA, Tanner GA [eds]: Medical Physiology. Little, Brown & Co, Boston, 1995, pp. 587–613. Used with permission.)

where M is metabolic rate, E is rate of heat loss by evaporation, R and C are rate of heat loss by radiation and convection, respectively, K is the rate of heat loss by conduction (only to solid objects, in practice, as explained later), W is rate of energy loss as mechanical work, and S is rate of heat storage in the body,[20,21] which is positive when mean body temperature is increasing.

Metabolic Rate and Sites of Heat Production

At thermal steady state, the rate of heat production in the body is equal to the rate of heat loss to the environment and can be measured precisely by direct calorimetry, a cumbersome technique in which all heat and water vapor leaving the body are captured and measured with special apparatus. More usually, metabolic rate is estimated by indirect calorimetry[22] from measurements of oxygen consumption, since virtually all energy available to the body depends on oxygen-consuming chemical reactions. The heat production associated with consumption of 1 L of oxygen varies somewhat according to the proportions of carbohydrate, fat, and protein that are oxidized. An average value of 20.2 kJ (4.83 kcal) per liter of oxygen is often used for metabolism of a mixed diet. Since the ratio of carbon dioxide produced to oxygen consumed varies according to the fuel, indirect calorimetry can be made more accurate by also measuring carbon dioxide production and calculating the amount of protein oxidized from urinary nitrogen excretion.

Metabolic rate for a fasting young man at rest is about 45 W/m^2 of body surface area, or 81 W (70 kcal/h) for a surface area of 1.8 m^2. At rest, the trunk viscera and the brain account for about 70% of energy production, even though they comprise only about 36% of the body mass (Table 4–1). During exercise, however, the muscles are the chief site of energy production and may account for 90% during heavy exercise (Table 4–1). A healthy but sedentary young man performing moderate exercise may reach a metabolic rate of 600 W, and a trained athlete performing intense exercise, 1,400 W or more. The overall mechanical efficiency of exercise varies enormously, depending on the activity; but, at best, no more than one fourth of the metabolic energy is converted into mechanical work outside the body, and the remaining three fourths or more is converted into heat within the body.[23] Since exercising muscles produce so much heat, they may be nearly 1°C warmer than the core. They warm the blood that perfuses them, and this blood, returning to the core, warms the rest of the body.

TABLE 4–1. Relative Mass and Rate of Metabolic Heat Production of Various Body Compartments During Rest and Strenuous Exercise

	BODY MASS (%)	HEAT PRODUCTION (%)	
		REST	EXERCISE
Brain	2	16	1
Trunk viscera	34	56	8
Muscle and skin	56	18	90
Other	8	10	1

Modified from Wenger CB, Hardy JD: Temperature regulation and exposure to heat and cold. In: Lehmann JF (ed): Therapeutic Heat and Cold. Williams & Wilkins, Baltimore, MD, 1990, pp. 150–178.

Biophysics of Heat Exchange with the Environment

Radiation, convection, and evaporation are the dominant means of heat exchange with the environment. In humans, respiration usually accounts for a minor part of total heat exchange and is not predominantly under thermoregulatory control, although hyperthermic subjects may hyperventilate. Humans, therefore, exchange most heat with the environment through the skin, and the rate of heat exchange between the body and the environment depends on the surface area of the skin.

Every surface emits energy as electromagnetic radiation with a power output that depends on its area, reflectivity, and temperature, and every surface absorbs electromagnetic radiation from its environment at a rate that depends on its area and reflectivity and on the radiant temperature of the environment (T_r). Radiative heat exchange (R) between the skin and the environment is proportional to the difference between the fourth powers of the respective absolute temperature of the surfaces; but if the difference between skin temperature (T_{sk}) and T_r is much smaller than the absolute temperature of

the skin, R is approximately proportional to $(T_{sk} - T_r)$. At ordinary tissue and environmental temperatures, virtually all radiant energy is in the far infrared range, where nearly all surfaces except polished metals have low reflectivity. However, bodies such as the sun that are hot enough to glow emit large amounts of radiation in the near infrared and visible range, in which light-colored surfaces have higher reflectivity than dark surfaces do. The practical importance of this is that skin and clothing color have little effect on heat exchange except in sunlight or intense artificial light.

Convection is transfer of heat via moving fluid, either liquid or gas. In thermal physiology the fluid is usually air or water in the environment or blood inside the body. Fluids conduct heat in the same way as solids do, and a perfectly still fluid transfers heat only by conduction. Since air and water are not good conductors of heat, perfectly still air or water is not effective in heat transfer. However, it is rare that a fluid is perfectly still, and slight movement produces enough convection to have a large effect on heat transfer. Thus, although conduction contributes to heat transfer by moving fluids, convection so dominates the overall heat transfer that we refer to the entire process as convection. The conduction term (K) in equation 1 is therefore, in practice, restricted to heat flow between the body and other solid objects, and usually represents only a small part of the total heat exchange with the environment. Convective heat exchange between the skin and the ambient air is proportional to the skin surface area and the difference between skin and air temperature. Convective heat exchange depends also on geometric factors that affect heat exchange with moving air and on the degree of air movement. It is approximately proportional to the square root of air speed, except at very low air speeds.

A gram of water that is converted into vapor at 30°C absorbs 2,425 J (0.58 kcal) in the process. In subjects who are not sweating, evaporative water loss is typically about 13 to 15 g/($m^2 \cdot h$), corresponding to a heat loss of 16 to 18 W for a surface area of 1.8 m^2. About half of this amount is lost through breathing, and half as insensible perspiration[24,25] (ie, evaporation of water that diffuses through the skin). Insensible perspiration is independent of the sweat glands and is not under thermoregulatory control. These modes of water loss, however, are quite small compared with what is possible during sweating. Evaporation of sweat is proportional to the skin surface area that is wet with sweat, and depends also on air movement, since water vapor is carried away by moving air, and on the temperature of the skin and the moisture content of the air. The most familiar way of representing the moisture content of air is as relative humidity, the ratio between the actual moisture content of the air and the maximum moisture content that is possible at the temperature of the air. However relative humidity is not the most useful measure of the evaporative cooling power of the environment for thermal physiology, and may be misleading. A more useful index is the wet bulb temperature, which is the temperature of a completely wet ventilated surface that is not artificially heated or cooled. Wet bulb temperature is measured with a psychrometer, a device that includes a thermometer, a water source with a wick to keep the thermometer bulb wet, and some means of blowing ambient air across the wick. The temperature inside a closed vehicle or poorly ventilated building in direct sunlight may easily reach 50°C (122°F), and if there are sources of moisture inside, the relative humidity may reach 37%, which may not sound particularly high; however, the wet bulb temperature in such an environment is 35°C (95°F), the same as in a 35°C environment at 100% relative humidity.

Tissue Blood Flow and Heat Transport in the Body

Heat travels within the body by two parallel means: conduction through the tissues and convection by the blood, the process by which flowing blood carries heat from warmer to cooler tissues. Heat flow by conduction is proportional to the change of temperature with distance in the direction of heat flow and to the thermal conductivity of the tissues. Heat flow by convection depends on the rate of blood flow through the tissue and the temperature difference between the tissue and the blood supplying it. The power of the body to transport heat through a layer of tissue by conduction and convection combined is expressed as conductance, C, defined as $C = HF/(\Delta T)$, where HF is the rate of heat flow through the tissue layer, and ΔT is the temperature difference across the tissue layer.

The most important conductance for thermal physiology is that involved in heat transfer from body core to skin. The skin and other superficial and peripheral tissues are, in general, cooler than the core. These cooler tissues, lying between the core and the skin surface, compose the shell. The shell is defined functionally, rather than anatomically, and is thinnest when the body is warm and skin blood flow is high. Since all heat leaving the body via the skin passes through the shell, the shell insulates the core from the environment. In a cold subject, vasoconstriction reduces skin blood flow so much that the conductance of the shell, and thus core-to-skin heat transfer, is dominated by conduction. A representative value for shell conductance of a lean man under these conditions is 8.9 W/(m^2 · °C), or about 16 W/°C for a whole body with a typical surface area of 1.8 m^2. The subcutaneous fat layer adds to the insulation value of the shell of a vasoconstricted subject, because it increases the thickness of the shell and because its thermal conductivity is only about 0.4 times that of dermis or muscle; thus it is a more effective insulator. In a warm subject, however, the shell is relatively thin and provides little insulation. Furthermore, a warm subject's skin blood flow is high, so heat flow from the core to the skin is dominated by convection. In these circumstances the subcutaneous fat layer, which affects conduction but not convection, has little effect on heat flow. Obese persons do tend to be less heat-tolerant than thinner persons, for two main reasons. First, the obese are at a relative disadvantage for dissipating heat because they have less skin surface area in proportion to their weight than do their thinner counterparts. Second, obese individuals tend to be less physically fit and therefore to have less well-developed heat-dissipating responses, as discussed later.

Let us return to our vasoconstricted man with a shell conductance of 16 W/°C. Under these conditions, a temperature difference between core and skin of 5°C allows a typical resting metabolic heat production of 80 W to be conducted to the skin surface. In a cool environment, T_{sk} may be low enough for this to occur easily; however, in a warm environment or especially during exercise, shell conductance must increase substantially to allow all the heat produced to be conducted to the skin without at the same time causing core temperature to rise to dangerous or lethal levels. For example, without an increase in shell conductance, T_c would have to be 30°C higher than T_{sk} to allow heat production of 480 W during moderate exercise to be carried to the skin. Fortunately, under such circumstances, increases in skin blood flow occur that can raise shell conductance 10-fold or more. Thus a crucial thermoregulatory function of skin blood flow is to control the conductance of the shell and the ease with which heat travels from core to skin. A closely related function is to control T_{sk}. In a person who is not sweating, an increase in skin blood flow tends to bring T_{sk} toward T_c, and a decrease allows T_{sk} to approach ambient temperature. Since convective and radiative heat exchange (R + C) depend directly on skin temperature, the body can control heat exchange with the environment by adjusting skin blood flow. If the heat stress is so great that increasing R + C through increasing skin blood flow is not enough to maintain heat balance, the body secretes sweat to increase evaporative heat loss. Once sweating begins, skin blood flow continues to increase as the person becomes warmer, but now the tendency of an increase in skin blood flow to warm the skin is approximately balanced by the tendency of an increase in sweating to cool the skin. Therefore, after sweating begins, further increases in skin blood flow usually cause little change in skin temperature or R + C. The increases in skin blood flow that accompany sweating are important to thermoregulation, nevertheless, since they deliver to the skin the heat that is being removed by evaporation of sweat and facilitate evaporation by keeping the skin warm. Skin blood flow and sweating thus work in tandem to dissipate heat that is produced in the body.

Physiologic Heat-Dissipating Responses

Humans have two physiologic responses for dissipating heat, dilation of the cutaneous vasculature and sweating. Each of these may affect cardiovascular homeostasis.

Responses of Skin Vascular Beds, and Pooling of Blood. Blood vessels in human skin are under dual vasomotor control, involving separate nervous signals for vasoconstriction and for vasodilation.[26–28] Reflex vasoconstriction, occur-

ring in response to cold and also as part of certain nonthermal reflexes such as baroreflexes, is mediated primarily through adrenergic sympathetic fibers distributed widely over most of the skin.[29] Reducing the flow of impulses in these nerve fibers allows the blood vessels to dilate. In the so-called acral regions ie, lips, ears, nose, palms of the hands, and soles of the feet,[27,29] and in the superficial veins,[27] vasoconstrictor fibers are the predominant vasomotor innervation, and the vasodilation occurring during heat exposure is largely a result of withdrawal of vasoconstrictor activity.[30] Reflex control of skin blood flow in these regions, unlike that in the rest of the skin,[30] is sensitive to small temperature changes in the thermoneutral range, ie, the range of thermal conditions in which the body is neither chilled nor sweating, and may "fine tune" heat loss to maintain heat balance in this range.

In most of the skin, the vasodilation occurring during heat exposure depends on sympathetic nervous signals that cause the blood vessels to dilate, and is prevented or reversed by regional nerve block.[31] Since it depends on the action of nervous signals, such vasodilation is sometimes referred to as active vasodilation. Active vasodilation occurs in almost all the skin outside the acral regions.[30] In skin areas where active vasodilation occurs, vasoconstrictor activity is minimal in the thermoneutral range, and as the body is warmed, active vasodilation begins near the point of onset of sweating.[27,32] The neurotransmitter or other vasoactive substances responsible for active vasodilation in human skin is not known.[29] However, since sweating and vasodilation operate in tandem in the heat, there has been considerable interest in the notion that the mechanism for active vasodilation is somehow linked to the action of sweat glands.[27,33] Active vasodilation is impaired or absent in the skin of patients with anhidrotic ectodermal dysplasia,[34] even though their vasoconstrictor responses are intact, implying that active vasodilation either is linked to an action of sweat glands or is mediated through nerves that have not developed or are nonfunctional in these patients.

The superficial venous beds receive blood from the skin. Dilation of these beds, which is complete at mild levels of heat stress, enhances transfer of heat from blood to skin. However, in regions below the level of the heart, these veins readily become engorged with blood, especially when skin blood flow is high, and the resulting peripheral pooling of blood impairs venous return, reduces central blood volume and compromises diastolic filling of the heart, and limits cardiac output, especially during exercise. Compensatory responses that maintain cardiac function in the face of peripheral pooling are discussed later in the chapter.

Sweating and Loss of Fluid and Electrolytes. Humans can dissipate large amounts of heat by secretion and evaporation of sweat. When the environment is warmer than the skin, usually when the environment is warmer than about 35°C, evaporation is the only way to lose heat. Human sweat glands are controlled through postganglionic sympathetic nerves that release acetylcholine,[35] rather than norepinephrine like most other sympathetic nerves. Human skin contains 2 million to 3 million functional eccrine sweat glands,[35] the histologic type most important in thermoregulation. Their secretory capacity can be increased by aerobic exercise training and heat acclimatization. A fit man well acclimatized to heat can achieve a peak sweating rate greater than 2.5 L/h.[36,37] Such rates cannot long be maintained, however, and the maximum daily sweat output is probably about 15 L.[38]

Eccrine sweat is formed from a precursor fluid in the secretory coil of the gland. This fluid is initially isotonic with plasma; but as it moves along the duct, Na^+ is reabsorbed from the fluid by active transport. When it emerges from the duct as sweat, it is the most dilute body fluid, with $[Na^+]$ ranging from less than 5 to 60 mEq/L.[39] As the rate of sweat secretion increases, the precursor fluid moves through the duct more quickly, and a smaller fraction of its initial sodium content is reabsorbed, and $[Na^-]$ in the resulting sweat is higher. Thus salt losses through sweating increase disproportionately as sweat production rises.

Large amounts of water and salt can be lost in a few hours of profuse sweating, and the consequent reduction in plasma volume may compromise cardiovascular homeostasis and cardiac output. In addition, since sweat is hypotonic to plasma, loss of sweat progressively increases the osmolality of the bodily fluids if the water is not replaced. Both the reduction in plasma volume and the increase in osmolality will compromise

thermoregulation by shifting the thresholds for sweating and vasodilation in the skin toward higher core temperature. If large amounts of salt are lost, and only the water but not the salt is replaced, plasma volume will not return to normal because the loss of salt reduces the total number of osmoles in the extracellular fluid, and a disproportionate amount of the water that is replaced goes into the intracellular space.

During prolonged (several hours) heat exposure with high sweat output, sweat rates often gradually diminish, and the response of the sweat glands to locally applied cholinergic drugs is reduced also. The reduction of sweat gland responsiveness is sometimes called sweat gland "fatigue." One mechanism involved is hydration of the stratum corneum, which swells and mechanically obstructs the sweat duct, causing a reduction in sweat secretion, an effect called hidromeiosis.[40] The glands' responsiveness can be at least partly restored if the skin is allowed to dry, eg, by increasing air movement,[41] but prolonged sweating also causes histologic changes in the sweat glands.[42]

Compensatory Cardiovascular Responses

During heat stress, peripheral pooling of blood and decreased plasma volume due to unreplaced fluid losses combine to impair venous return and diastolic filling of the heart. Several compensatory mechanisms help to defend cardiac filling, cardiac output, and arterial blood pressure under such circumstances. The most important compensatory reflexes are constriction of the renal and splanchnic vascular beds. Reduction of blood flow through these beds increases the fraction of cardiac output that is available to perfuse exercising muscle. In addition, the splanchnic vascular bed is very compliant; thus, reduction in splanchnic blood flow reduces the volume of blood contained in the splanchnic vascular bed, allowing a partial restoration of central blood volume and cardiac diastolic filling. The effect of pooling of blood in the skin on central blood volume and the compensatory effect of splanchnic vasoconstriction are shown schematically in Figure 4–3. The degree of splanchnic vasoconstriction is graded according to the levels of heat stress and exercise

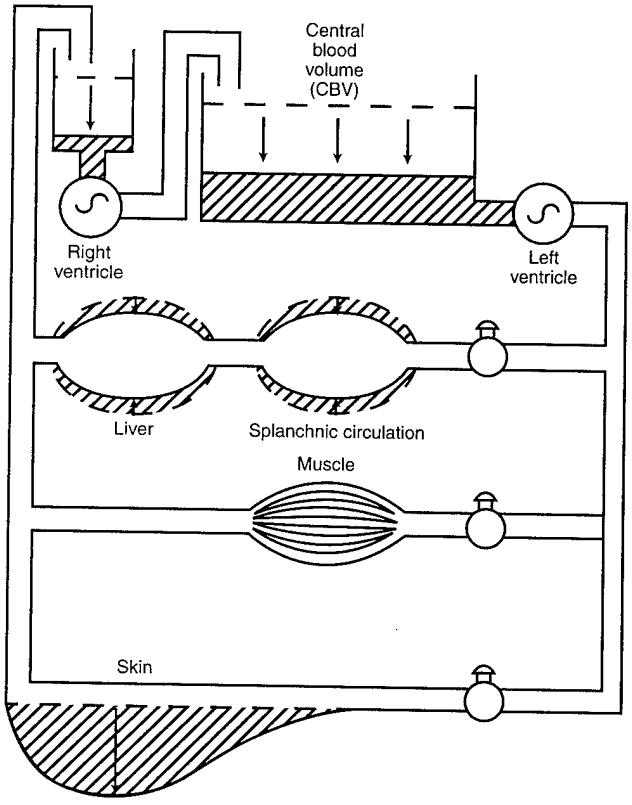

FIGURE 4–3. Schema of the effects of skin vasodilation on peripheral pooling of blood and the thoracic reservoirs from which the ventricles are filled, and the effects of compensatory vasomotor adjustments in the splanchnic circulation. The valves drawn at the right sides of liver–splanchnic circulation, muscle, and skin vascular beds represent the resistance vessels that control blood flow through those beds. *Arrows* show the direction of the changes during heat stress. (Redrawn from Rowell LB: Cardiovascular adjustments to thermal stress. In: Shepherd JT, Abboud FM [eds]: Handbook of Physiology, Section 2: The Cardiovascular System, Vol 3: Peripheral Circulation and Organ Blood Flow. American Physiological Society, Bethesda, MD, 1983, pp. 967–1023; and Rowell LB: Cardiovascular aspects of human thermoregulation. Circ Res 52:367–379, 1983.)

intensity. During strenuous exercise in the heat, renal and splanchnic blood flow may decrease to 20% of their values in a cool resting subject.[27,43] Splanchnic vasoconstriction may help to explain nausea and vomiting accompanying heat exhaustion, and gastrointestinal symptoms that some athletes experience after endurance events.[44]

In addition, the superficial veins, which drain the skin, constrict during exercise and thus reduce the volume of blood pooled in them. Because of the essential thermoregulatory function of skin blood flow during exercise and heat stress, the body preferentially compromises splanchnic and renal flow to maintain cardiovascular homeostasis[45]; but above a certain level of cardiovascular strain, skin blood flow too is compromised to maintain cardiac filling. Another important mechanism that opposes pooling of blood in dependent veins during leg exercise is the so-called muscle pump. Since the valves in the veins of the limbs permit blood flow only toward the heart, rhythmic contraction of skeletal muscle assists the movement of venous blood toward the heart. Exhausted runners often collapse only after finishing a race, partly because they lose most of the effect of the muscle pump.

Despite these compensatory responses, heat stress markedly increases the thermal and cardiovascular strain that exercise produces in subjects unacclimatized to heat. In Figure 4–6, a comparison of responses on the first day of exercise in the heat with those on cool days shows some effects of unaccustomed environmental heat stress on the responses to exercise. On the first day in the heat, heart rate during exercise reached a level about 40 beats/min higher than in the cool environment, to help compensate for the effects of impaired cardiac filling and to maintain cardiac output, and rectal temperature during exercise rose 1°C higher than in the cool environment.

Responses to Cold

The body maintains core temperature in the cold by minimizing heat loss and, when this is not sufficient, by increasing heat production. In humans, constriction of peripheral blood vessels to reduce core-to-skin thermal conductance is the chief physiologic means of conserving heat in the cold. Skin blood flow is the principal determinant of conductance, and constriction of cutaneous arterioles reduces conductance by reducing skin blood flow. In addition, constriction of the superficial limb veins further improves heat conservation by diverting venous blood to the deep limb veins, which lie close to the major arteries of the limbs and do not constrict in cold. (Since many penetrating veins connect the superficial veins to the deep veins, venous blood from anywhere in the limb potentially can return to the heart via either superficial or deep veins.) In the deep veins, cool venous blood returning to the core can take up heat from the warm blood in the adjacent deep limb arteries. Thus some of the heat contained in the arterial blood as it enters the limbs takes a "short circuit" back to the core, and when the arterial blood reaches the skin, it is already cooler than the core and so loses less heat to the skin than it otherwise would. (When the superficial veins dilate in heat, most venous blood returns via superficial veins to maximize core-to-skin heat flow.) The transfer of heat from arteries to veins by this short circuit is called countercurrent heat exchange, and it can cool the blood in the radial artery of a cool but comfortable subject to as low as 25°C by the time it reaches the wrist.[46]

Once skin blood flow is near minimal, metabolic heat production increases. In human adults, nearly all of this increase occurs in skeletal muscles, as a result first of increased tone and later of frank shivering. Shivering may increase metabolic rate at rest by more than fourfold, eg, to 350 to 400 W, comparable to mild-to-moderate exercise. It is frequently stated that the shivering response diminishes substantially after several hours and is impaired following exhaustive exercise, but these effects have not been studied systematically and are not well understood. In a reasonably fit athlete exercising in cold air, exercise rather than shivering would ordinarily be expected to account for most of the metabolic heat production. Since warm clothing tends to restrict movement, an athlete will improve his or her competitive advantage by wearing the lightest clothing that will maintain heat balance with the expected rate of heat production. Thus an athlete who cannot maintain the expected pace due to exhaustion or musculoskeletal injury may be at increased risk of hypothermia during competition in a cold environment.

The shell's insulating properties increase in the cold, as its blood vessels constrict and its thickness increases. In the cold the shell includes a substantial amount of skeletal muscle, whose blood flow is reduced by direct cooling. The resulting reduction of blood flow through muscle in the shell of a cool subject increases the shell's insulating properties.[47] This effect limits the ability of skeletal muscle activity to warm the core, since peripheral or superficial exercising muscles will be warmed by their own heat production and by the blood flow required by aerobic exercise and thus may lose large amounts of heat to the environment through the overlying skin, especially when the overlying skin is very cold,[48] as during immersion in cold water.

Control of Thermoregulatory Responses

Integration of Thermal Information. Temperature receptors in the body core and the skin transmit information about their temperatures through afferent nerves to the brain stem, and especially the hypothalamus, where much of the integration of temperature information takes place. Core temperature receptors involved in thermoregulation have been found in several sites, including the spinal cord and medulla,[49] but they are concentrated especially in the hypothalamus,[49] and in experimental mammals temperature changes of only a few tenths of 1°C in the anterior preoptic area of the hypothalamus elicit changes in the thermoregulatory effector responses.

Most physiologic control systems produce a response that is graded according to the disturbance in the regulated variable. In many such systems, changes in the effector responses are proportional to displacement of the regulated variable from some threshold value.[24] Such control systems are called proportional control systems. Changes in the heat-dissipating responses are proportional to displacement of core temperature from some threshold value (Fig. 4–4). Each response has a core temperature threshold, a temperature at which the response starts to increase. These thresholds depend on mean skin temperature; thus, at any given skin temperature, the change in each response is proportional to the change in core temperature, and increasing the skin temperature lowers the threshold level of core temperature and increases the response at any given core temperature. Control of the heat-dissipating responses is more complicated than the most simple proportional control systems, since the heat-dissipating responses are controlled according to both core and skin temperature. The sensitivity of the thermoregulatory system to core temperature enables it to adjust heat loss so as to resist disturbances in core temperature, and the system's sensitivity to skin temperature enables it to respond appropriately to moderate changes in the environment with little or no change in body core temperature. For example, the skin temperature of someone who enters a hot environment rises and may elicit sweating even if there is no change in core temperature. On the other hand, an increase in heat production due to exercise elicits the appropriate heat-dissipating responses through an increase in core temperature.

Both sweating and skin blood flow participate in reflexes other than thermoregulatory responses. For the purposes of this chapter, the most important nonthermoregulatory reflexes are those that involve the blood vessels of the skin in responses that help to maintain cardiac output, blood pressure, and tissue oxygen delivery. During heat stress, thermoregulatory requirements usually dominate the control of these responses, but in conditions of high cardiovascular strain, thermoregulatory requirements for skin blood flow may be overridden to support circulatory function. An important and dramatic example is the reduction in skin blood flow that accounts for the cool, ashen skin characteristic of heat exhaustion.

Thermoregulatory Responses During Exercise. At the start of exercise, metabolic heat production increases rapidly, but there is little change in heat loss initially, so heat is stored in the body and core temperature rises. The increase in core temperature, in turn, elicits heat-loss responses, but core temperature continues to rise until heat loss has increased enough to match heat production; thus heat balance is restored and core temperature and the heat-loss responses reach new steady-state levels. The rise in core temperature that elicits heat-dissipating responses sufficient to reestablish thermal balance during exercise is an example of a load error,[24] which occurs when any proportional control system resists the effect of some imposed

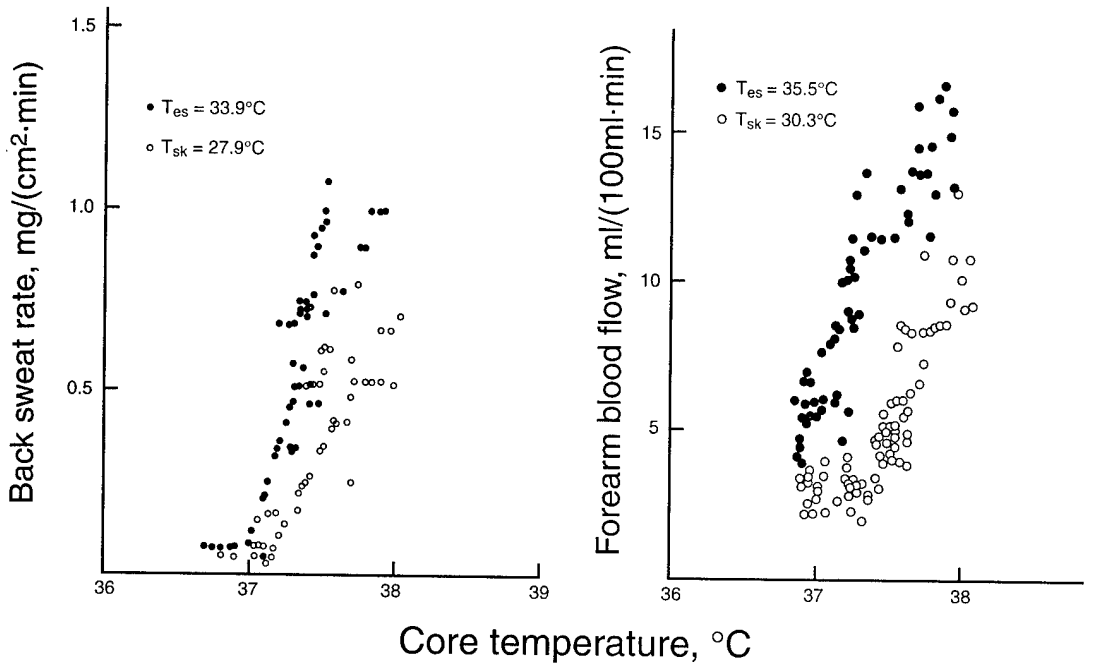

FIGURE 4–4. The relations of back sweat rate (*left panel*) and forearm blood flow (*right panel*) to esophageal (T_{es}) and mean skin temperatures ($\overline{T}_{sk}$). Sweating data are from four subjects performing cycle exercise at an oxygen consumption rate of 1.6 L/min; blood flow data are from one subject. During measurements of blood flow, forearm temperature was kept at 36.8°C to eliminate a difference in local temperature between experiments. Local temperature was not controlled independently during measurements of sweating; thus the difference between conditions includes a small effect of local skin temperature, appearing as a difference in slope. (*Left panel* drawn from data of Sawka MN, Gonzalez RR, Drolet LL, Pandolf KB: Heat exchange during upper- and lower-body exercise. J Appl Physiol 57:1050–1054, 1984; *right panel* modified from Wenger CB, Roberts MF, Stolwijk JAJ, Nadel ER: Forearm blood flow during body temperature transients produced by leg exercise. J Appl Physiol 38:58–63, 1975.)

disturbance or "load." In a proportional control system, the load error is proportional to the load, and indeed the magnitude of core temperature elevation at steady state during exercise is proportional to the metabolic rate[50] and thus to the rate of heat production. Although the elevated core temperature during exercise superficially resembles that during fever due to resetting of the body's thermostat, there are some crucial differences. First, although heat production may increase substantially (through shivering) at the beginning of a fever, it does not need to stay high to maintain the fever but returns nearly to prefebrile levels once the fever is established; during exercise, however, an increase in heat production not only causes the elevation in core temperature but also is necessary to sustain it. Second, the rate of heat loss while core temperature is rising during a fever, is, if anything, lower than before the fever began; but the rate of heat loss during exercise starts to increase as soon as core temperature starts to rise and continues to increase as long as core temperature is rising. Because of the role of skin temperature in thermoregulatory control, the steady-state core temperature during exercise is largely independent of ambient temperature and humidity[51] over a range of environmental conditions called the "prescriptive zone," whose limits depend on exercise intensity.[52] Figure 4–5 shows steady-state rectal temperatures during exercise at three intensities in a broad range of environmental conditions. The higher the metabolic rate during exercise, the lower the upper limit of the prescriptive zone.

During prolonged exercise there is a gradual "drift" in several cardiovascular and thermoregulatory responses. This may include a continuous rise in heart rate, accompanied by a fall in stroke volume and reductions in aortic, pulmo-

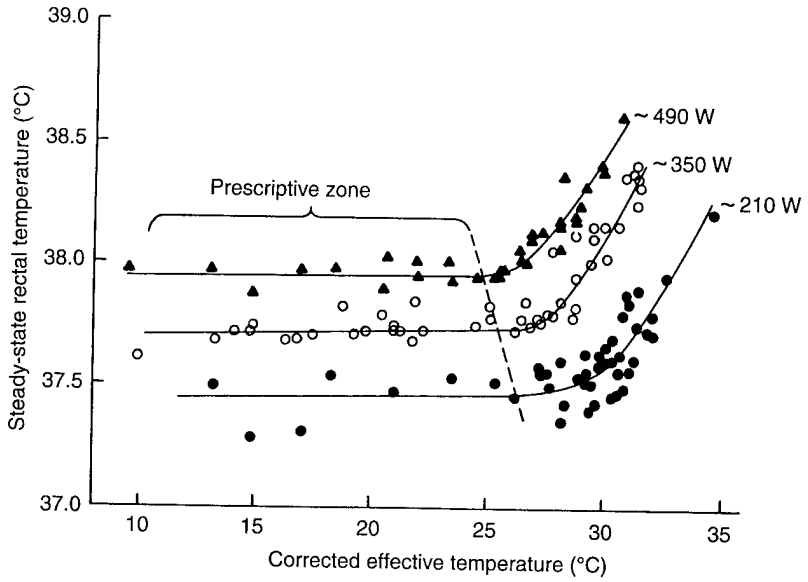

FIGURE 4–5. Relation between environmental conditions and steady-state rectal temperature during exercise at three metabolic rates. The abscissa is "corrected effective temperature," a function of globe temperature (which combines air temperature and radiant temperature), wet-bulb temperature, and air speed, chosen to be an index of environmental stress. (Redrawn from Lind AR: A physiological criterion for setting thermal environmental limits for everyday work. J Appl Physiol 18:51–56, 1963.)

nary arterial, and right ventricular end-diastolic pressures.[43] Rowell[43] named these changes "cardiovascular drift," and thought of them as appearing as early as after 15 minutes of exercise. He[43] and Johnson and Rowell[53] emphasized the role of thermoregulatory increases in skin blood flow in producing cardiovascular drift. However, later authors[54–56] described, as part of the picture of cardiovascular drift, an upward creep in core temperature, which may begin only after a period of apparent thermal steady state (eg, after 30–60 minutes of exercise). In some of these studies, most but not all of the changes in cardiovascular and thermoregulatory responses could be prevented by replacing fluid lost in sweat, suggesting that these changes were mostly secondary to changes in plasma volume and osmolality due to sweating. Other factors that may affect cardiovascular and thermoregulatory function during prolonged exercise include changes in myocardial function,[57] changes in baroreceptor sensitivity or peripheral α-adrenergic receptor responsiveness,[58] or an upward adjustment of the thermoregulatory set point,[59] presumably due to some sort of inflammatory response and perhaps elicited by products of muscle injury.[59] These effects have not been investigated extensively, and little is known about the underlying physiologic or pathologic mechanisms. Some of these effects have been reported only after several hours of exercise or near exhaustion, and little is known about the conditions of exercise duration and intensity required to produce them, or their persistence after the end of exercise. Although their functional significance is, as yet, only poorly understood, these changes may be important in limiting performance during prolonged strenuous activity, such as forced marches, marathons, and other endurance athletic events.

ADVERSE EFFECTS OF HEAT AND COLD STRESS

Heat Disorders

Exercise is often an important factor in heat disorders because of both the metabolic heat produced during exercise, and the combined effects of thermoregulation and exercise on several physiologic systems, particularly the circulatory system. Although hyperthermia is often associated with heat disorders and may be involved in their pathogenesis, the relation between body

temperature and clinical manifestations is complex,[60] and levels of core temperature that are typically associated with heat stroke have been observed in athletes who apparently suffered no ill effects.[61,62] For convenience, the heat disorders may be divided into two groups: those with primarily local manifestations and those with more general manifestations. This division is not absolute, however; for example, extensive miliaria rubra, a skin disorder, may impair thermoregulation. For more detailed discussion of pathogenesis and clinical management, the reader is referred elsewhere.[10,11] The heat disorders are discussed in brief.

Disorders with Primarily Local Manifestations

Heat edema, a dependent edema of the hands, legs, and feet, typically occurs within the first week of adaptation to tropical heat, and is worsened by prolonged standing. Heat edema is probably due to the retention of salt and water, which is a normal part of acclimatization to heat, and peripheral vasodilation probably has a contributory role. Heat edema is benign and self-limiting. Treatment with diuretics is not indicated and will impair development of acclimatization by interfering with retention of salt and water.

Miliaria rubra, commonly called heat rash or prickly heat, is characterized by blockage of the sweat ducts with plugs of keratin debris, and typically occurs following repeated or prolonged exposure to heat. The resulting rash is irritating, but the most serious effect is marked impairment of sweating in the affected skin, which may precede the appearance of the rash by up to a week and may persist for some time after the rash clears.[63] Some patients may be unable to sweat below the neck. The impairment of sweating, if extensive, substantially limits the ability to tolerate exercise in heat.

Heat Syncope

Heat syncope is a temporary circulatory failure due to pooling of blood in the peripheral veins and a consequent decrease in diastolic filling of the heart. The primary cause of the peripheral pooling is the large increase in skin blood flow that is part of the thermoregulatory response to heat exposure, but an inadequate baroreflex response may be an important contributing factor. Heat syncope usually occurs in individuals who are standing with little activity. Symptoms may range from lightheadedness to loss of consciousness. Core temperature typically is no more than slightly elevated, except when an attack follows exercise, and the skin is wet and cool. Recovery is rapid once the patient sits or lies down, though complete recovery of blood pressure and heart rate often take an hour or two. Heat syncope affects mostly those who are not acclimatized to heat, presumably because the expansion of plasma volume that occurs with acclimatization compensates for the peripheral pooling of blood. Patients being treated for hypertension with diuretics or medications that impair the baroreflexes are at particular risk and should exercise care when standing in crowds or lines in hot surroundings.

Continuum of Heat Cramps, Heat Exhaustion, and Heat Stroke

Traditionally, heat cramps, heat exhaustion, and heat stroke were considered three distinct clinical entities. However, these disorders have overlapping features, and the concept that they are syndromes representing different parts of a continuum[64,65] has gained favor. In keeping with this concept, some recent literature describes a syndrome called exertional heat injury, intermediate in severity between heat exhaustion and heat stroke. However, there does not seem to be a consensus on diagnostic criteria for distinguishing exertional heat injury from heat exhaustion, on one hand, or from heat stroke, on the other; compare, for example, Petersdorf[66] and Kark and Ward.[67]

Water loss from the sweat glands can exceed 1 L/h during exercise in the heat. The amount of salt lost in the sweat is quite variable, and persons who are well acclimatized to heat can often secrete very dilute sweat. However, those who are less well acclimatized may lose large amounts of salt in their sweat and become substantially salt depleted. Consider the following conditions.

Heat Cramps. Heat cramps is an acute disorder consisting of brief, recurrent, and often agonizing cramps in skeletal muscle of the limbs and trunk. The cramp produces a hard lump in the affected muscle, which typically has recently been used in intense exercise. Although the

cramps are brief, generally lasting only a few minutes, they may recur for many hours in severe, untreated cases. Patients are characteristically physically fit men, well acclimatized to heat, who have been drinking adequate amounts of water but not replacing salt lost in the sweat. They usually have hyponatremia, which is thought to be involved in the pathogenesis of heat cramps, though the mechanism is obscure. Hyponatremia is common, however, whereas heat cramps are an unusual accompaniment. Intravenous infusion of 0.5 to 1 L of normal saline solution or, alternatively, somewhat smaller amounts of hypertonic saline solution is the treatment of choice in severe cases. However, oral administration of 0.1% salt in water is also effective,[11] somewhat unexpectedly, given the usual association of heat cramps with hyponatremia. The immediate goal of treatment is relief of the cramps, not restoration of salt balance, which takes longer and is best achieved by giving salted food or fluids by mouth.

Heat Exhaustion. Heat exhaustion is characterized by circulatory collapse occurring after prolonged or repeated exercise-heat stress. Most patients have lost both salt and water, but heat exhaustion may be associated predominantly with either salt depletion or water depletion. Salt-depleted patients have hypovolemia out of proportion to the degree of dehydration and are hypovolemic even if not greatly dehydrated, since their body water is distributed preferentially to the intracellular space to maintain osmotic balance between the intracellular and extracellular spaces. Salt-depleted persons tend either to be unacclimatized to heat or to be consuming small amounts of salt in their diet, and they have replaced at least some of their water loss. Heat exhaustion due primarily to water depletion tends to develop more rapidly than that due to salt depletion, and is characterized by greater thirst. In addition, hypovolemia occurring during water-depletion heat exhaustion is associated with less hemoconcentration, since water is lost from both the red blood cells and the plasma.

Heat exhaustion spans a clinical spectrum, from fairly mild disorders that respond well to rest in a cool environment and fluid replacement by mouth, to severe forms with collapse, confusion, and hyperpyrexia. Loss of consciousness is uncommon, but there may be vertigo, ataxia, headache, weakness, nausea and vomiting, pallor, tachycardia, and orthostatic hypotension. The patient usually is sweating profusely. Muscle cramps indistinguishable from heat cramps may occur, especially if salt depletion is part of the pathogenesis. Treatment consists primarily of laying the patient down away from the heat, and replacing fluid and salt, as needed. In severe cases, intravenous administration of normal saline solution may be required. Active cooling measures may be called for if the patient's core temperature is 40.6°C (105°F) or higher, since water-depletion heat exhaustion may lead to heat stroke.

Restoration of Fluid Loss. As $[Na^+]$ in the extracellular fluid is reduced, water moves from the extracellular fluid into the intracellular fluid to maintain osmotic balance, causing the cells to swell. Since the brain occupies most of the space within a rigid case, even a modest degree of cerebral edema can increase intracranial pressure, leading to encephalopathy and brain stem herniation in extreme cases. By removal of interstitial fluid and by loss of solutes from within the cells, the brain can protect itself from osmotic swelling if plasma $[Na^+]$ changes slowly enough.[68] Although osmotic swelling of the brain is usually associated with hyponatremia, its occurrence is related to the rate of change of plasma $[Na^+]$ rather than the level of $[Na^+]$. For this reason, care should be taken to prevent reducing plasma $[Na^+]$ too rapidly when replacing water in water-depleted patients.[11] In addition, a few individuals who are drinking large amounts of fluid during sustained exercise in the heat may become hyponatremic if they lose excessive amounts of salt in their sweat or drink and retain more fluid than is required to replace their losses.[69–71] Although hyponatremia is far less common than water-depletion heat exhaustion, it may be difficult to differentiate the two conditions in the early stages without laboratory tests. Patients with water-depletion heat exhaustion respond quickly to fluid replacement, whereas hyponatremia is aggravated by administering hypotonic fluids, and may progress to life-threatening cerebral edema. Therefore, in a patient presumed to have heat exhaustion but who does not improve quickly in response to administration of hypotonic fluids, such treat-

ment should not be continued without further medical evaluation. A rule suggested for field use is that a patient with presumed heat exhaustion should be given 2 quarts of water to drink over the course of an hour and needs medical evaluation if noticeable improvement has not occurred by the end of the hour.

Heat Stroke

Heat stroke is the most severe heat disorder and as such deserves special attention.

Heat stroke is characterized by hyperthermia, which often develops rapidly, and severe neurologic disturbances, frequently including convulsions. Although these disturbances typically are characteristic of a nonfocal encephalopathy, some patients may show abnormalities of cerebellar function, which may be transient or may persist. Heat stroke may be divided into two forms depending on the pathogenesis. In the classic form, the primary pathogenic factor is environmental heat stress that overwhelms an impaired thermoregulatory system, whereas in exertional heat stroke the primary factor is metabolic heat production (see Knochel and Reed[11] for a more extensive discussion). Consequently, victims of exertional heat stroke tend to be younger and more physically fit (typically, soldiers, athletes, and laborers) than victims of the classic form. Heat stroke may be complicated by liver damage, electrolyte abnormalities, and, especially in the exertional form, by rhabdomyolysis, disseminated intravascular coagulation, or renal failure.

Loss of consciousness may occur suddenly or may be preceded by up to an hour of prodromal symptoms including headache, dizziness, drowsiness, restlessness, ataxia, confusion, and irrational or aggressive behavior. The physiologic pathology is not well understood, and there is evidence that factors other than hyperthermia contribute to the development of heat stroke. The traditional diagnostic criteria of heat stroke—coma, hot dry skin, and temperature above 41.1°C (106°F)—reflect experience primarily with the classic form. Rigid adherence to these criteria will lead to underdiagnosis, since cessation of sweating may be a late event, especially in exertional heat stroke. Moreover, patients may come to medical attention either in the prodromal phase or after they have had a chance to cool somewhat and regain consciousness, especially if they still are sweating.

Measurement of rectal temperature or other deep body temperature is essential for clinical evaluation of hyperthermia and for observing response to treatment. A diagnosis of heat stroke must not be excluded on the basis of either oral temperature or temperature measured at the external auditory meatus or tympanic membrane. Because of hyperventilation, oral temperature may be 2° to 3°C lower than rectal temperature in heat stroke, and the temperature of the external auditory meatus or tympanum may be as much as 5°C lower than rectal temperature in collapsed hyperthermic athletes.[72] Low temperature of the tympanum may be due in part to cooling of its blood supply, which comes mostly from branches of the external carotid artery and thus follows a superficial course. It is sometimes asserted that since the tympanum is so close to the cranium, tympanic temperature represents intracranial temperature, and thus the temperature of the brain, more accurately than any other noninvasive temperature measurement. Thus tympanic temperature measurements that are appreciably lower than measurements of trunk core (eg, rectal or esophageal) temperature in hyperthermic human subjects are sometimes adduced to argue for the existence of physiologic heat exchange mechanisms that protect the human brain during hyperthermia by cooling it below the temperature of the central blood. However, there is little empirical support either for the claims made for tympanic temperature or for the existence of special mechanisms to cool the human brain (see Sawka et al[33] and Brengelmann[73] for further discussion).

Heat stroke is an extreme medical emergency, and prompt appropriate treatment is critical in reducing morbidity and mortality. Cooling the patient to lower the core temperature is the cornerstone of early treatment and should begin as soon as possible. The patient should be removed from hot surroundings without delay, excess clothing and any equipment that obstructs free flow of air should be removed, the patient's skin should be wetted if water is available, and the patient should be fanned to promote evaporative cooling. Although helpful, these measures are no substitute for more vigorous cooling once appropriate means are available, and cooling is accomplished most effectively by immersion in

cold water. Costrini et al[74] lowered the rectal temperature of patients with heat stroke at a mean rate of 0.18°C/min by immersing them in ice water. There is some disagreement as to the optimal water temperature, since lowering the temperature not only increases the core-to-skin thermal gradient for heat flow but also reduces skin blood flow. Observations in dogs with heat stroke suggest that while water at 15° to 16°C (59°–61°F) is more effective than warmer water, little further advantage is gained with lower water temperature.[75]

However, there is no empirical support for the superiority of cooling methods, such as tepid baths or evaporation of sprayed water, that achieve only modest skin cooling. Some arguments in favor of such cooling methods are based on studies that compared different cooling methods in healthy persons with mild hyperthermia, whose peripheral vascular and other thermal responses may, however, be substantially different from those of patients with heat stroke. The pitfalls in relying on such studies may be seen by comparing the following two reports: In tests in hot but normal young subjects, an evaporative cooling method was reported to be more effective than other cooling methods, causing tympanic temperature to fall at a rate of 0.31°C/min.[76] However, in a series of patients with heat stroke the same authors found that the same cooling method lowered rectal temperature at a rate of only 0.06°C/min,[77] one fifth the rate they had reported in healthy subjects[76] and one third the rate that Costrini et al[74] achieved.

There is evidence for a systemic inflammatory component in heat stroke,[64] and elevated levels of several inflammatory cytokines have been reported in patients with heat stroke.[78–80] Leakage of gram-negative endotoxin from the gut, perhaps facilitated by splanchnic ischemia, may be a trigger for secretion of these cytokines, since treatments aimed at preventing leakage of endotoxin[81,82] or neutralizing endotoxin[83] partially protect experimental animals against heat stroke during subsequent heating. Gaffin and Hubbard[84] discussed the implications of these concepts for prevention and treatment of heat stroke, but their proposed measures are not supported by clinical data sufficient to allow their recommendation.

Aggravation of Other Diseases by Heat Stress

Besides causing more or less characteristic disorders, heat stress can worsen the clinical state of patients with a number of other diseases. For example, patients with congestive heart failure have substantially impaired sweating and circulatory responses to environmental heat stress, and exposure to moderately hot environments worsens the signs and symptoms of congestive heart failure.[14] Conversely, air conditioning improves the clinical progress of patients hospitalized in the summer with a variety of cardiorespiratory and other chronic diseases.[14] The harmful effects of heat stress on patients with other diseases are also shown by analysis of the effects of unusually hot weather on total mortality and causes of death. Ellis[15] examined monthly mortality statistics for the years 1952 to 1967 and identified 5 years in each of which more than 500 deaths were reported as due to "excessive heat and insolation." In June and July of these "heat wave" years there was excess mortality, ie, above that expected for the month, from diabetes; cerebrovascular accident; arteriosclerotic, degenerative, and hypertensive heart disease; and diseases of the blood-forming organs. Ellis estimated the total number of excess deaths was more than 10 times greater than the number of deaths actually reported as due to heat. The greatest increase in mortality during heat wave years was in infants and persons 65 or older.[15]

Hypothermia

Hypothermia occurs when the body's defenses against cold are disabled or overwhelmed. The direct effect of hypothermia is to slow the body's metabolic processes and thus to reduce the metabolic rate, via the law of Arrhenius. In this way, hypothermia prolongs the time that tissues can safely tolerate loss of blood flow and oxygen delivery. Controlled hypothermia is often used to protect the brain, which is especially vulnerable to anoxia, during surgical procedures in which its circulation is interrupted. Much of what we know about the physiologic effects of hypothermia comes from observations in surgical patients.

During the initial phases of cooling, stimulation of shivering through thermoregulatory reflexes far outweighs the direct effect of the law of Arrhenius, so that metabolic rate increases, reaching a peak at a core temperature of 30° to 33°C. At lower core temperatures, however, metabolic rate is dominated by the law of Arrhenius, and thermoregulation is lost. A vicious circle develops, wherein a fall in core temperature depresses metabolism and allows core temperature to fall further, so that at 17°C, oxygen consumption is about 15% and cardiac output 10% of precooling values.

Hypothermia that is not induced for therapeutic purposes is called accidental hypothermia. Accidental hypothermia occurs in individuals whose defenses are impaired by drugs (especially ethanol, in the United States) or by disease or other physical condition, and in healthy individuals who are immersed in cold water or become exhausted during exposure to cold. Hypothermia is classified according to the patient's core temperature as mild (32°–35°C), moderate (28°–32°C), or severe (<28°C). Shivering is usually prominent in mild hypothermia, but diminishes in moderate hypothermia, and is absent in severe hypothermia.

The pathophysiology is characterized chiefly by the depressant effect of cold (via the law of Arrhenius) on multiple physiologic processes and differences in the degree of depression of each process. Apart from shivering, the most prominent features of mild and moderate hypothermia are due to depression of the central nervous system. These begin with mood changes (commonly apathy, withdrawal, and irritability) progressing, as hypothermia deepens, to confusion and lethargy, ataxia, and speech and gait disturbances, which may mimic a cerebrovascular accident ("stroke"). In severe hypothermia, voluntary movement, reflexes, and consciousness are lost, and muscular rigidity appears. Cardiac output and respiration decrease as core temperature falls.

Myocardial irritability increases in severe hypothermia, causing substantial danger of ventricular fibrillation, with the risk increasing as cardiac temperature falls. The primary mechanism presumably is that cold depresses conduction velocity in Purkinje fibers more than in ventricular muscle, favoring the development of circus-movement propagation of action potentials, but myocardial hypoxia also contributes. In more profound hypothermia, cardiac sounds become inaudible, and pulse and blood pressure cannot be measured because of circulatory depression; the electrical activity of the heart and brain becomes unmeasurable, and extensive muscular rigidity may mimic rigor mortis. The patient may appear clinically dead, but patients have been revived with core temperatures as low as 17°C; thus, "no one is dead until warm and dead." The usual causes of death during hypothermia are cessation of respiration and failure of cardiac pumping, because of either ventricular fibrillation or direct depression of cardiac contraction.

Depression of renal tubular metabolism by cold impairs reabsorption of sodium, causing diuresis and leading to dehydration and hypovolemia. Acid-base disturbances in hypothermia are complex. Respiration and cardiac output typically are depressed more than metabolic rate, and mixed respiratory and metabolic acidosis results, due to carbon dioxide retention and lactic acid accumulation and also to the cold-induced shift of the hemoglobin-oxygen dissociation curve to the left. Acidosis aggravates the susceptibility to ventricular fibrillation.

Treatment consists of preventing further cooling, and restoring fluid, acid-base, and electrolyte balance. Patients with mild to moderate hypothermia may be warmed solely by providing abundant insulation to promote retention of metabolically produced heat, but those who are more severely affected require active rewarming. The most serious complication associated with treating hypothermia is development of ventricular fibrillation. Vigorous handling of the patient may trigger ventricular fibrillation, but an increase in the patient's circulation (eg, associated with warming or skeletal muscle activity) may itself increase susceptibility to such an occurrence. This may happen as follows: peripheral tissues of a hypothermic patient are, in general, even cooler than the core, including the heart, and acid products of anaerobic metabolism will have accumulated in underperfused tissues while the circulation was most depressed. As the circulation increases, a large increase in blood flow through cold, acidotic peripheral tissue may return enough cold, acidotic blood to the heart to cause a transient drop in the temper-

ature and pH of the heart and increase its susceptibility to ventricular fibrillation.

The diagnosis of hypothermia is usually straightforward in a patient rescued from cold, but may be far less clear in a patient in whom hypothermia results from serious impairment of the defenses against cold. A typical example is the elderly person, living alone, who is discovered at home, cool and obtunded or unconscious. The setting may not particularly suggest hypothermia, and when the patient comes to medical attention, the diagnosis may easily be missed, since standard clinical thermometers are not graduated low enough (usually only to 34.4°C) to detect hypothermia, and in any case do not register temperature below the level to which the mercury has been shaken. Since hypothermia depresses the brain, the patient's condition may be misdiagnosed as a cerebrovascular accident or other primary neurologic disease. Thus, recognition of hypothermia in such a setting depends on the physician's considering it when he or she is examining a cool, obtunded patient and on obtaining a true core temperature with a thermometer that registers low temperatures.

FACTORS AFFECTING TOLERANCE TO HEAT AND COLD

Many factors, including heat acclimatization, physical fitness, gender, body fat, age, drugs, and a number of diseases, affect thermoregulatory responses and tolerance to heat and cold.

Acclimatization and Physical Fitness

Prolonged or repeated heat stress, especially when combined with exercise sufficient to elicit profuse sweating, produces acclimatization to heat,[85] a set of physiologic changes that reduces the physiologic strain associated with exercise-heat stress. The classic signs of heat acclimatization are reductions in core and skin temperatures and heart rate and increases in sweat production during a given level of exercise in heat. These changes begin to appear during the first few days, and approach full development within a week. Figure 4–6 illustrates some of these effects in three young men who were acclimatized by daily treadmill walks in dry heat for 10 days.[86] On the first day in the heat, heart rate and rectal temperature during exercise reached much higher levels than in cool control (25°C) conditions, but on the tenth day in the heat, final heart rate and rectal temperature during exercise were 40 beats/min and 1°C, respectively, lower than on the first day. In addition, sweat production increased 10%, skin temperature was about 1.5°C lower, and the metabolic cost of treadmill walking decreased 4%.

The mechanisms that produce these changes are not fully understood, but include a modest (~0.4°C) reduction in the setting of the body's "thermostat," thus reducing the thresholds for sweating and cutaneous vasodilation; increased sensitivity of the sweat glands to cholinergic stimulation[87,88] and a decrease in sweat gland susceptibility to hidromeiosis and fatigue; and retention of salt and water and expansion of plasma volume to compensate for peripheral pooling of blood in dilated blood vessels in the skin. Heat acclimatization produces other changes[85] also, including improved ability to sustain high rates of sweat production; an aldosterone-mediated reduction in sweat sodium concentration, to levels as low as 5 mEq/L at low sweat rates, which minimizes salt depletion; an increase in the fraction of sweat secreted on the limbs; and perhaps other changes that help protect against heat illness.

The effect of heat acclimatization on performance can be quite dramatic, and acclimatized subjects can easily complete exercise in the heat that previously was difficult or impossible.[89] The benefits of acclimatization are lessened or reversed by sleep loss, infection, alcohol abuse, dehydration, and salt depletion.[85] These factors impair thermoregulation in the heat in the unacclimatized also. Heat acclimatization disappears in a few weeks if not maintained by repeated heat exposure.

Some of the changes that occur with heat acclimatization are mediated by "training" the heat-dissipating responses, particularly sweating, through repeated use.[85] Repeated exercise that is intense enough and lasts long enough to improve maximal oxygen consumption also expands plasma volume and, by elevating core temperature, trains the heat-dissipating responses and produces an improvement in heat tolerance similar to that associated with heat acclimatization.[85] This effect probably explains the association of physical fitness with heat tol-

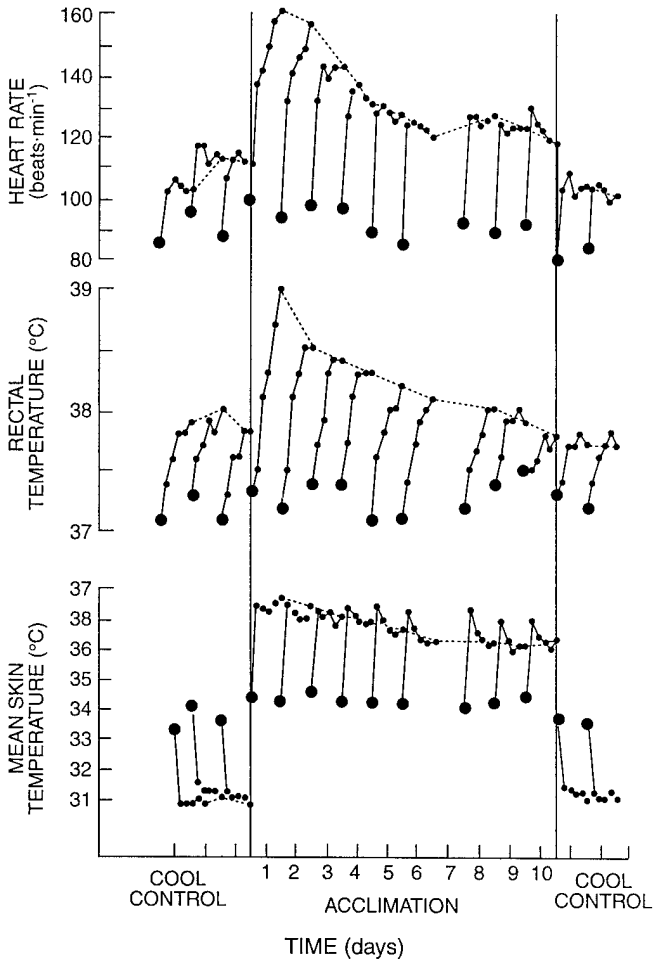

FIGURE 4–6. Change in the responses of heart rate, rectal temperature, and mean skin temperature during exercise in a 10-day program of acclimatization to dry heat (50.5°C, 15% relative humidity), together with responses during exercise in a cool environment before and after acclimatization. (The "cool control" condition was 25.5°C, 39% relative humidity.) Each day's exercise consisted of five 10-minute treadmill walks at 2.5 mph (1.12 m/s) up a 2.5% grade. Successive walks were separated by 2-minute rest periods. *Large circles* show values before the start of the first exercise period each day; *small circles* show values at the end of successive exercise periods; and the *dashed* line connects final values each day. (Redrawn from Eichna, LW, Park CR, Nelson N, et al: Thermal regulation during acclimatization in a hot, dry [desert type] environment. Am J Physiol 163:585–597, 1950.)

erance. In marked contrast to acclimatization to heat, the responses that comprise human cold acclimatization are inconsistent and appear to confer no more than a modest advantage.[90]

Gender

Although women as a group are less tolerant to exercise-heat stress than men are, the difference appears to be explained by differences in size, acclimatization, and maximal oxygen consumption, and when subjects are matched according to these variables, gender differences largely disappear.[91] The exertional form of heat stroke is said to be rare in women.[10] Its apparent rarity probably does not indicate that women are not susceptible to exertional heat stroke, since in active-duty soldiers, a population in which most heat stroke is of the exertional type, annual incidence of heat stroke in women is at least half that in men (unpublished data, Defense Medical Surveillance System, 1997-1998). The effect of the menstrual cycle has not been well studied. However, Pivarnik et al,[92] studying women's responses during cycle exercise at 22°C, found that after 60 minutes of exercise, heart rate was 10 beats/min higher in the luteal than in the follicular phase, and rectal temperature increased 1.2°C in the luteal phase and was still rising, whereas it increased 0.9°C in the follicular phase and was near steady state. Although they examined only one set of experimental conditions, using a temperate rather than a warm environment, their data suggest a decline in tolerance to exercise-heat stress during the luteal phase.

Age, Obesity, Drugs, and Physical Disorders

Heat tolerance and the effectiveness of the thermoregulatory system are reduced with increasing age, and in healthy 65-year-old men the sensitivity of the sweating response is half that in 25-year-old men. This effect is opposite to the effect of physical fitness, and it is not clear how much of the decrease is a direct effect of aging itself and how much owes to changes that tend to accompany increased age, such as reduced physical fitness.[91] In addition, newborn infants and many healthy elderly persons are less able than older children and younger adults to maintain body temperature in the cold. This appears to be due to a reduced ability both to conserve body heat by reducing heat loss and to increase metabolic heat production in the cold.

Obesity also is associated with reduced heat tolerance; Kenney[91] reviews mechanisms that may explain this association. However, obesity enhances cold tolerance, apparently because of the thermal insulation provided by the subcutaneous layer of fat.

Thermoregulation in the heat is impaired by diuretics, which cause loss of fluid and electrolytes, and by drugs that suppress sweating, most obviously those used for their anticholinergic effects, such as atropine and scopolamine. However, many drugs used for other purposes, such as glutethimide (a sleep medicine), tricyclic antidepressants, phenothiazines (tranquilizers and antipsychotic drugs), and antihistamines also have some anticholinergic action, and have been associated with heat stroke.[11] Furthermore, some drugs, including tricyclic antidepressants, butyrophenones, and amphetamines, increase the risk of heat-associated illness through other mechanisms.[11] In addition, certain drugs, such as barbiturates, alcohol, and phenothiazines, impair the defenses against cold.

Several congenital and acquired skin disorders—including ichthyosis, anhidrotic ectodermal dysplasia, and miliaria rubra—impair sweating and may seriously reduce heat tolerance. Anhidrotic ectodermal dysplasia is especially interesting in this regard, since not only sweating but also active vasodilation in the skin is impaired or absent. Thus artificially wetting the skin only partially corrects the thermoregulatory deficit during exercise, when large amounts of body heat need to be carried to the skin. Artificial wetting is probably most effective in a dry environment, in which evaporation can produce a cool skin.

Neurologic diseases that involve the thermoregulatory structures in the brain stem can impair thermoregulation. Although such disorders can produce hypothermia, hyperthermia is more usual and typically is characterized by loss of sweating and disruption of the circadian rhythm.

Certain diseases, such as hypothyroidism, hypopituitarism, congestive heart failure, and septicemia, impair the defenses against cold. This impairment may explain why septicemia, especially in debilitated patients, is often accompanied by hypothermia instead of the usual febrile response to infection.

Prevention of Heat and Cold Illnesses

Careful attention to risk factors is the key to prevention of heat and cold illnesses. Candidates for occupations or other activities that subject them to prolonged or severe cold stress or exercise-heat stress should be screened for individual risk factors, including use of therapeutic or recreational drugs that would increase their risk of illness. Unacclimatized personnel, especially those who are physically unfit, should be allowed to acclimatize to heat gradually. Consideration should be given to excusing personnel with mild infections from activities that involve prolonged or severe exercise-heat stress. Provision should be made for adequate sleep, and alcohol abuse should be guarded against.

Perhaps the most important measure for preventing heat illness is provision of ample cool palatable water or other beverages and frequent opportunities to drink. Although acclimatization reduces loss of salt, it does not reduce water requirements; indeed, the biophysics of heat exchange largely preclude any such effect during sustained exercise-heat stress. The persistent myth that withholding water during exercise-heat stress produces toughening is unsupported by evidence.

Persons undergoing prolonged exercise-heat stress should drink frequently and not wait until they feel thirsty, since thirst is not a reliable guide to water requirements under such conditions. Soldiers on a long march, for example, gradually become progressively dehydrated if

they drink only according to their feelings of thirst.[93] Provision of flavored beverages may enhance consumption, but carbonated or caffeinated beverages should not be drunk, since carbonation may give a sense of fullness and caffeine promotes fluid loss by diuresis. Beverages containing electrolytes may be beneficial during intense sustained exercise-heat stress or when food intake is reduced.

REFERENCES

1. Du Bois EF: Fever and the Regulation of Body Temperature. Charles C Thomas, Springfield, IL, 1948
2. Aschoff J: Circadian rhythm of activity and of body temperature. In: Hardy JD, Gagge AP, Stolwijk JAJ (eds): Physiological and Behavioral Temperature Regulation. Charles C Thomas, Springfield, IL, 1970, pp. 905–919
3. Gisolfi CV, Wenger CB: Temperature regulation during exercise: old concepts, new ideas. Exerc Sports Sci Rev 12:339–372, 1984
4. Mackowiak PA, Wasserman SS, Levine MM: A critical appraisal of 98.6°F, the upper limit of the normal body temperature, and other legacies of Carl Reinhold August Wunderlich. JAMA 268: 1578–1580, 1992
5. Hessemer V, Brück K: Influence of menstrual cycle on shivering, skin blood flow, and sweating responses measured at night. J Appl Physiol 59: 1902–1910, 1985
6. Kolka MA: Temperature regulation in women. Med Exerc Nutr Health 1:201–207, 1992
7. Stephenson LA, Kolka MA: Menstrual cycle phase and time of day alter reference signal controlling arm blood flow and sweating. Am J Physiol 249:R186–R191, 1985
8. Johnson RF, Kobrick JL: Psychological aspects of military performance in hot environments. In: Burr RE, Pandolf KB (eds): Textbook of Military Medicine. Medical Aspects of Harsh Environments, Vol 1. Borden Institute, Office of the Surgeon General, Department of the Army, Washington, DC, (in press)
9. Sawka MN, Pandolf KB: Physical exercise in hot climates: physiology, performance and biomedical issues. In: Burr RE, Pandolf KB (eds): Textbook of Military Medicine. Medical Aspects of Harsh Environments, Vol 1. Borden Institute, Office of the Surgeon General, Department of the Army, Washington, DC, (in press)
10. Knochel JP: Heat stroke and related heat stress disorders. Dis Month 35:301–377, 1989
11. Knochel JP, Reed G: Disorders of heat regulation. In: Maxwell MH, Kleeman CR, Narins RG (eds): Clinical Disorders of Fluid and Electrolyte Metabolism, McGraw-Hill, New York, 1987, pp. 1197–1232
12. Leithead CS, Lind AR: Heat Stress and Heat Disorders. F.A. Davis, Philadelphia, 1964
13. Bridger CA, Helfand LA: Mortality from heat during July in Illinois. Int J Biometeorol 12:51–70, 1968
14. Burch GE, DePasquale NP: Hot Climates, Man and His Heart. Charles C Thomas, Springfield, IL, 1962
15. Ellis FP: Mortality from heat illness and heat-aggravated illness in the United States. Environ Res 5:1–58, 1972
16. Armstrong LE, Epstein Y, Greenleaf JE, et al: American College of Sports Medicine position stand: heat and cold illnesses during distance running. Med Sci Sports Exerc 28(12):i–x, 1996
17. Jones BH, Roberts WO: Medical management of endurance events: incidence, prevention, and care of casualties. In: Cantu RC, Micheli LJ (eds): ACSM's Guidelines for the Team Physician. Lea & Febiger, Philadelphia, 1991, pp. 266–286
18. Thompson RL, Hayward JS: Wet-cold exposure and hypothermia: thermal and metabolic responses to prolonged exercise in rain. J Appl Physiol 81:1128–1137, 1996
19. Cabanac M: Physiological role of pleasure. Science 173:1103–1107, 1971
20. Bligh J, Johnson KG: Glossary of terms for thermal physiology. J Appl Physiol 35:941–961, 1973
21. Gagge AP, Hardy JD, Rapp GM: Proposed standard system of symbols for thermal physiology. J Appl Physiol 27:439–446, 1969
22. Ferrannini E: Equations and assumptions of indirect calorimetry: some special problems. In: Kinney JM, Tucker HN (eds): Energy Metabolism: Tissue Determinants and Cellular Corollaries. Raven Press, New York, 1992, pp. 1–17
23. Åstrand P-O, Rodahl K: Temperature regulation. In: Textbook of Work Physiology: Physiological Bases of Exercise. McGraw-Hill, New York, 1977, pp. 523–576
24. Hardy JD: Physiology of temperature regulation. Physiol Rev 41:521–606, 1961
25. Kuno Y: Insensible perspiration. In: Human Perspiration. Charles C Thomas, Springfield, IL, 1956, pp. 3–41
26. Fox RH, Edholm OG: Nervous control of the cutaneous circulation. Br Med Bull 19:110–114, 1963
27. Rowell LB: Cardiovascular adjustments to thermal stress. In: Shepherd JT, Abboud FM (eds): Handbook of Physiology, section 2: The Cardiovascular System, Vol 3: Peripheral Circulation and Organ Blood Flow. American Physiological Society, Bethesda, MD, 1983, pp. 967–1023

28. Sawka MN, Wenger CB: Physiological responses to acute exercise-heat stress. In: Pandolf KB, Sawka MN, Gonzalez RR (eds): Human Performance Physiology and Environmental Medicine at Terrestrial Extremes. Benchmark Press, Indianapolis, IN, 1988, pp. 97–151
29. Johnson JM, Proppe DW: Cardiovascular adjustments to heat stress. In: Fregly MJ, Blatteis CM (eds): Handbook of Physiology, Section 4: Environmental Physiology. Oxford University Press, for the American Physiological Society, New York, 1996, pp. 215–243
30. Roddie IC: Circulation to skin and adipose tissue. In: Shepherd JT, Abboud FM (eds): Handbook of Physiology, Section 2: The Cardiovascular System, Vol 3: Peripheral Circulation and Organ Blood Flow. Bethesda, MD, 1983, pp. 285–317
31. Rowell LB: Active neurogenic vasodilatation in man. In: Vanhoutte PM, Leusen I (eds): Vasodilatation, Raven Press, New York, 1981, pp. 1–17
32. Love AHG, Shanks RG: The relationship between the onset of sweating and vasodilatation in the forearm during body heating. J Physiol (Lond) 162:121–128, 1962
33. Sawka MN, Wenger CB, Pandolf KB: Thermoregulatory responses to acute exercise-heat stress and heat acclimation. In: Fregly MJ, Blatteis CM (eds): Handbook of Physiology, Section 4: Environmental Physiology. Oxford University Press, for the American Physiological Society, New York, 1996, pp. 157–185
34. Brengelmann GL, Freund PR, Rowell LB, et al: Absence of active cutaneous vasodilation associated with congenital absence of sweat glands in humans. Am J Physiol 240:H571–H575, 1981
35. Kuno Y: The sweat apparatus. In: Human Perspiration. Charles C Thomas, Springfield, IL, 1956, pp. 42–97
36. Eichna LW, Ashe WF, Bean WB, Shelley WB: The upper limits of environmental heat and humidity tolerated by acclimatized men working in hot environments. J Indust Hyg Toxicol 27:59–84, 1945
37. Ladell WSS: Thermal sweating. Br Med Bull 3:175–179, 1945
38. Kuno Y: The loss of water and salt by sweating, their replenishment and changes in the blood. In: Human Perspiration. Charles C Thomas, Springfield, IL, 1956, pp. 251–276
39. Robinson S, Robinson AH: Chemical composition of sweat. Physiol Rev 34:202–220, 1954
40. Brown WK, Sargent F II: Hidromeiosis. Arch Environ Health 11:442–453, 1965
41. Nadel ER, Stolwijk JAJ: Effect of skin wettedness on sweat gland response. J Appl Physiol 35:689–694, 1973
42. Dobson RL, Formisano V, Lobitz WC, Jr, Brophy D: Some histochemical observations on the human eccrine sweat glands. III: The effect of profuse sweating. J Invest Dermatol 31:147–159, 1958
43. Rowell LB: Human cardiovascular adjustments to exercise and thermal stress. Physiol Rev 54:75–159, 1974
44. Fogoros RN: 'Runner's trots' gastrointestinal disturbances in runners. JAMA 243:1743–1744, 1980
45. Wenger CB: Non-thermal factors are important in the control of skin blood flow during exercise only under high physiological strain. Yale J Biol Med 59:307–319, 1986
46. Bazett HC, Love L, Newton M, et al: Temperature changes in blood flowing in arteries and veins in man. J Appl Physiol 1:3–19, 1948
47. Toner MM, McArdle WD: Human thermoregulatory responses to acute cold stress with special reference to water immersion. In: Fregly MJ, Blatteis CM (eds): Handbook of Physiology, Section 4: Environmental Physiology. Oxford University Press, for the American Physiological Society, New York, 1996, pp. 379–397
48. Shephard RJ: Metabolic adaptations to exercise in the cold: an update. Sports Med 16:266–289, 1993
49. Jessen C: Interaction of body temperatures in control of thermoregulatory effector mechanisms. In: Fregly MJ, Blatteis CM (eds): Handbook of Physiology, Section 4: Environmental Physiology. Oxford University Press, for the American Physiological Society, New York, 1996, pp. 127–138
50. Nielsen M: Die Regulation der Körpertemperatur bei Muskelarbeit. Skand Arch Physiol 79:193–230, 1938
51. Stolwijk JAJ, Saltin B, Gagge AP: Physiological factors associated with sweating during exercise. Aerospace Med 39:1101–1105, 1968
52. Lind AR: A physiological criterion for setting thermal environmental limits for everyday work. J Appl Physiol 18:51–56, 1963
53. Johnson JM, Rowell LB: Forearm skin and muscle vascular responses to prolonged leg exercise in man. J Appl Physiol 39:920–924, 1975
54. Hamilton MT, Gonzalez-Alonso J, Montain SJ, Coyle EF: Fluid replacement and glucose infusion during exercise prevent cardiovascular drift. J Appl Physiol 71:871–877, 1991
55. Montain SJ, Coyle EF: Influence of graded dehydration on hyperthermia and cardiovascular drift during exercise. J Appl Physiol 73:1340–1350, 1992
56. Shaffrath JD, Adams WC: Effects of airflow and work load on cardiovascular drift and skin blood flow. J Appl Physiol 56:1411–1417, 1984

57. Tibbits GF: Regulation of myocardial contractility in exhaustive exercise. Med Sci Sports Exerc 17:529–537, 1985
58. Raven PB, Stevens GHJ: Cardiovascular function and prolonged exercise. In: Lamb DR, Murray R (eds): Prolonged Exercise. Benchmark Press, Indianapolis, IN, 1988, pp. 43–74
59. Haight JSJ, Keatinge WR: Elevation in set point for body temperature regulation after prolonged exercise. J Physiol (Lond) 229:77–85, 1973
60. Kark JA, Gardner JW, Hetzel DP, et al: Fever in classification of exertional heat injury. Clin Res 39:143A, 1991
61. Maron MB, Wagner JA, Horvath SM: Thermoregulatory responses during competitive marathon running. J Appl Physiol 42:909–914, 1977
62. Pugh LGCE, Corbett JL, Johnson RH: Rectal temperatures, weight losses, and sweat rates in marathon running. J Appl Physiol 23:347–352, 1967
63. Pandolf KB, Griffin TB, Munro EH, Goldman RF: Persistence of impaired heat tolerance from artificially induced miliaria rubra. Am J Physiol 239:R226–R232, 1980
64. Hales JRS, Hubbard RW, Gaffin SL: Limitation of heat tolerance. In: Fregly MJ, Blatteis CM (eds): Handbook of Physiology, Section 4: Environmental Physiology. Oxford University Press, for the American Physiological Society, New York, 1996, pp. 285–355
65. Lind AR: Pathophysiology of heat exhaustion and heat stroke. In: Khogali M, Hales JRS (eds): Heat Stroke and Temperature Regulation. Academic Press, New York, 1983, pp. 179–188
66. Petersdorf RG: Hypothermia and hyperthermia. In: Wilson JD, Braunwald E, Isselbacher KJ, et al (eds): Harrison's Principles of Internal Medicine. McGraw-Hill, New York, 1991, pp. 2194–2220
67. Kark JA, Ward FT: Exercise and hemoglobin S. Semin Hematol 31:181–225, 1994
68. Berl T: Treating hyponatremia: damned if we do and damned if we don't. Kidney Int 37:1006–1018, 1990
69. Armstrong LE, Curtis WC, Hubbard RW, et al: Symptomatic hyponatremia during prolonged exercise in heat. Med Sci Sports Exerc 25:543–549, 1993
70. Frizzell RT, Lang GH, Lowance DC, Lathan SR: Hyponatremia and ultramarathon running. JAMA 255:772–774, 1986
71. Noakes TD, Goodwin N, Rayner BL, et al: Water intoxication: a possible complication during endurance exercise. Med Sci Sports Exerc 17:370–375, 1985
72. Roberts WO: Assessing core temperature in collapsed athletes: what's the best method? Phys Sports Med 22:49–55, 1994
73. Brengelmann GL: Dilemma of body temperature measurement. In: Shiraki K, Yousef MK (eds): Man in Stressful Environments: Thermal and Work Physiology. Charles C Thomas, Springfield, IL, 1987, pp. 5–22
74. Costrini AM, Pitt HA, Gustafson AB, Uddin DE: Cardiovascular and metabolic manifestations of heat stroke and severe heat exhaustion. Am J Med 66:296–302, 1979
75. Magazanik A, Epstein Y, Udassin R, et al: Tap water, an efficient method for cooling heatstroke victims—a model in dogs. Aviat Space Environ Med 51:864–867, 1980
76. Weiner JS, Khogali M: A physiological body-cooling unit for treatment of heat stroke. Lancet 1:507–509, 1980.
77. Khogali M, Weiner JS:. Heat stroke: report on 18 cases. Lancet 2:276–278, 1980
78. Bouchama A, Al-Sedairy S, Siddiqui S, et al: Elevated pyrogenic cytokines in heatstroke. Chest 104:1498–1502, 1993
79. Bouchama A, Parhar RS, El-Yazigi A, et al: Endotoxemia and release of tumor necrosis factor and interleukin 1α in acute heatstroke. J Appl Physiol 70:2640–2644, 1991
80. Chang DM: The role of cytokines in heat stroke. Immunol Invest 22:553–561, 1993
81. Butkow N, Mitchell D, Laburn H, Kenedi E: Heat stroke and endotoxaemia in rabbits. In: Hales JRS (ed): Thermal Physiology. Raven Press, New York, 1984, pp. 511–514
82. Bynum G, Brown J, DuBose D, et al: Increased survival in experimental dog heatstroke after reduction of gut flora. Aviat Space Environ Med 50:816–819, 1978
83. Gathiram P, Wells MT, Brock-Utne JG, Gaffin SL: Antilipopolysaccharide improves survival in primates subjected to heat stroke. Circ Shock 23:157–164, 1987
84. Gaffin SL, Hubbard RW: Experimental approaches to therapy and prophylaxis for heat stress and heatstroke. Wilderness Environ Med 4:312–334, 1996
85. Wenger CB: Human heat acclimatization. In: Pandolf KB, Sawka MN, Gonzalez RR (eds): Human Performance Physiology and Environmental Medicine at Terrestrial Extremes. Benchmark Press, Indianapolis, IN, 1988, pp. 153–197
86. Eichna LW, Park CR, Nelson N, et al: Thermal regulation during acclimatization in a hot, dry (desert type) environment. Am J Physiol 163: 585–597, 1950
87. Collins KJ, Crockford GW, Weiner JS: The local training effect of secretory activity on the response of eccrine sweat glands. J Physiol (Lond) 184:203–214, 1966

88. Kraning KK, Lehman PA, Gano RG, Weller TS: A non-invasive dose-response assay of sweat gland function and its application in studies of gender comparison, heat acclimation and anticholinergic potency. In: Mercer JB (ed): Thermal Physiology 1989. Elsevier, Amsterdam, 1989, pp. 301–307.
89. Pandolf KB, Young AJ: Environmental extremes and endurance performance. In: Shephard RJ, Åstrand PO (eds): Endurance in Sport. Blackwell Scientific Publications, New York, 1992, pp. 270–282.
90. Young AJ: Homeostatic responses to prolonged cold exposure: human cold acclimatization. In: Fregly MJ, Blatteis C (eds): Handbook of Physiology, Section 4: Environmental Physiology. Oxford University Press, for the American Physiological Society, New York, 1996, pp. 419–438
91. Kenney WL: Physiological correlates of heat intolerance. Sports Med 2:279–286, 1985
92. Pivarnik JM, Marichal CJ, Spillman T, Morrow JR Jr: Menstrual cycle phase affects temperature regulation during endurance exercise. J Appl Physiol 72:543–548, 1992
93. Rothstein A, Adolph EF, Wills JH: Voluntary dehydration. In: Visscher MB, Bronk DW, Landis EM, Ivy AC (eds): Physiology of Man in the Desert. Interscience, New York, 1947, pp. 254–270.

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. AGENCY USE ONLY *(Leave blank)*	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	March 1999	Book Chapter

4. TITLE AND SUBTITLE
Exercise and Core Temperature

5. FUNDING NUMBERS

6. AUTHOR(S)

C. Bruce Wenger

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Military Performance Division
US Army Research Institute of Environmental Medicine
Natick, MA 01760-5007

8. PERFORMING ORGANIZATION REPORT NUMBER

MISC 99-6

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

US Army Medical Research and Materiel Command
Fort Detrick
Frederick, MD 21702-5012

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for public release; distribution is unlimited.

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 words)*

In humans the most important responses for removing heat from the body are sweating, which increases heat loss by evaporation, and cutaneous vasodilation, which increases skin blood flow and heat transfer from core to skin. Vigorous exercise can increase heat production within the body ten-fold or more. During the first few minutes of exercise, most of the heat produced is retained within the body, raising core temperature until it elicits heat-dissipating responses sufficient to eliminate heat as fast as it is produced. The steady-state increase in core temperature is proportional to the rate of heat production and, within certain limits, independent of environmental conditions. Because of the levels of skin blood flow needed for high rates of heat dissipation in a hot environment, exercise and heat dissipation make competing demands on the cardiovascular system. Moreover, if water and electrolytes lost as sweat are not replaced, plasma volume eventually is depleted, thus reducing central blood volume and impairing cardiac filling. Through these mechanisms, secondary effects of the thermoregulatory responses contribute to many of the adverse effects of heat stress, though other mechanisms related to high core temperature also have a role, especially in heat stroke. Heat tolerance is increased by aerobic exercise conditioning and by acclimatization to heat. Conversely, poor physical fitness and certain disease states and drugs are associated with impairment of the thermoregulatory responses. The foregoing factors account for most of the inter-individual differences in heat tolerance associated with gender and age. Because of the high rates of heat production, heat-related illnesses are much more likely during exercise than is hypothermia. However, hypothermia may occur during prolonged exercise due to inadequate clothing, changes in the weather, or fatigue or musculoskeletal injury which reduces the level of exercise that can be sustained.

14. SUBJECT TERMS

thermoregulation, exercise, heat, hypothermia, heat illness, fitness, acclimatization, heat tolerance

15. NUMBER OF PAGES
73

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
UNCLASSIFIED	UNCLASSIFIED	UNCLASSIFIED	UL