PART 8 Temperature Regulation and Exercise Physiology

CHAPTER 29

The Regulation of Body Temperature*

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CHAPTER OUTLINE

KEY CONCEPTS

1. The body is divided into an inner core and an outer shell; temperature is relatively uniform in the core and is regulated within narrow limits, while shell temperature is permitted to vary.
2. The body produces heat through metabolic processes and exchanges energy with the environment as mechanical work and heat; it is in thermal balance when the sum of metabolic energy production plus energy gain from the environment equals energy loss to the environment.
3. In humans, the chief physiological thermoregulatory responses are the secretion of sweat, which removes heat from the skin as it evaporates; the control of skin blood flow, which governs the flow of heat to the skin from the rest of the body; and increasing metabolic heat production in the cold.
4. The thermoregulatory set point (the setting of the body's "thermostat") varies cyclically with the circadian rhythm and the menstrual cycle, and is elevated during fever.
5. Core and whole-body skin temperatures govern the reflex control of physiological thermoregulatory responses, which are graded according to disturbances in the body's thermal state.
6. The control of thermoregulatory responses is accomplished through reflex signals generated in the CNS according to the level of the thermoregulatory set point, as well as signals from temperature-sensitive CNS neurons and nerve endings elsewhere, chiefly in the skin. The response of sweat glands and superficial blood vessels to these signals is modified by local skin temperature.
7. Acclimatization to heat can dramatically increase the body's ability to dissipate heat, maintain cardiovascular homeostasis in hot temperatures, and conserve salt while sweating profusely. Acclimatization to cold has only modest effects, depending on how the acclimatization was produced, and may include increased tissue insulation and variable metabolic responses.
8. Adverse systemic effects of excessive heat stress include circulatory instability, fluid-electrolyte imbalance, exertional heat injury, and heatstroke. Exertional heat injury and heatstroke involve organ and tissue injury produced in several ways, some of which are not well understood. The primary adverse systemic effect of excessive cold stress is hypothermia.

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Humans, like other mammals, are **homeotherms**, or warm-blooded animals, and regulate their internal body temperatures within a narrow range near 37°C, in spite of wide variations in environmental temperature (Fig. 29.1). Internal body temperatures of **poikilotherms**, or cold-blooded animals, by contrast, are governed by environmental temperature. The range of temperatures that living cells and tissues can tolerate without harm extends from just above freezing to nearly 45°C—far wider than the limits within which homeotherms regulate body temperature. What biological advantage do homeotherms gain by maintaining a stable body temperature? As we shall see, tissue temperature is important for two reasons.

First, temperature extremes injure tissue directly. High temperatures alter the configuration and overall structure of protein molecules, even though the sequence of amino acids is unchanged. Such alteration of protein structure is called **denaturation**. A familiar example of denaturation by heat is the coagulation of albumin in the white of a cooked egg. Since the biological activity of a protein molecule depends on its configuration and charge distribution, denaturation inactivates a cell's proteins and injures or kills the cell. Injury occurs at tissue temperatures higher than about 45°C, which is also the point at which heating the skin becomes painful. The severity of injury depends on the temperature to which the tissue is heated and how long the heating lasts.

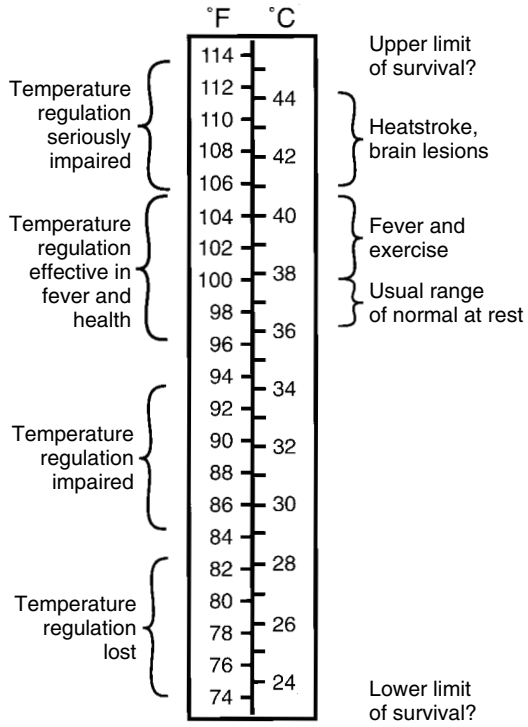


FIGURE 29.1 Rectal temperature ranges in healthy people, patients with fever, and people with impaired or failed thermoregulation. (Modified from Wenger CB, Hardy JD. Temperature regulation and exposure to heat and cold. In: Lehmann JF, ed. Therapeutic Heat and Cold. 4th Ed. Baltimore: Williams & Wilkins, 1990;150–178. Based on DuBois EF. Fever and the Regulation of Body Temperature. Springfield, IL: CC Thomas, 1948.)

Cold also can injure tissues. As a water-based solution freezes, ice crystals consisting of pure water form, so that all dissolved substances in the solution are left in the unfrozen liquid. Therefore, as more ice forms, the remaining liquid becomes more and more concentrated. Freezing damages cells through two mechanisms. Ice crystals probably injure the cell mechanically. In addition, the increase in solute concentration of the cytoplasm as ice forms denatures the proteins by removing their water of hydration, increasing the ionic strength of the cytoplasm, and causing other changes in the physicochemical environment in the cytoplasm.

Second, temperature changes profoundly alter biological function through specific effects on such specialized functions as electrical properties and fluidity of cell membranes, and through a general effect on most chemical reaction rates. In the physiological temperature range, most reaction rates vary approximately as an exponential function of temperature (T); increasing T by 10°C increases the reaction rate by a factor of 2 to 3. For any particular reaction, the ratio of the rates at two temperatures 10°C apart is called the $\mathbf{Q_{10}}$ for that reaction, and the effect of temperature on reaction rate is called the $\mathbf{Q_{10}}$ **effect**. The notion of Q_{10} may be generalized to apply to a group of reactions that have some measurable overall effect (such as O_2 consumption) in common and are, thus, thought of as comprising a physiological process. The Q_{10} effect is clinically important in managing patients who have high fevers and are receiving fluid and nutrition intravenously. A commonly used rule is that a patient's fluid and calorie needs are increased 13% above normal for each 1°C of fever.

The profound effect of temperature on biochemical reaction rates is illustrated by the sluggishness of a reptile that comes out of its burrow in the morning chill and becomes active only after being warmed by the sun. Homeotherms avoid such a dependence of metabolic rate on environmental temperature by regulating their internal body temperatures within a narrow range. A drawback of homeothermy is that, in most homeotherms, certain vital processes cannot function at low levels of body temperature that poikilotherms tolerate easily. For example, shipwreck victims immersed in cold water die of respiratory or circulatory failure (through disruption of the electrical activity of the brainstem or heart) at body temperatures of about 25°C, even though such a temperature produces no direct tissue injury and fish thrive in the same water.

BODY TEMPERATURES AND HEAT TRANSFER IN THE BODY

The body is divided into a warm internal core and a cooler outer shell (Fig. 29.2). Because the temperature of the shell is strongly influenced by the environment, its temperature is not regulated within narrow limits as the internal body temperature is, even though thermoregulatory responses strongly affect the temperature of the shell, 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.

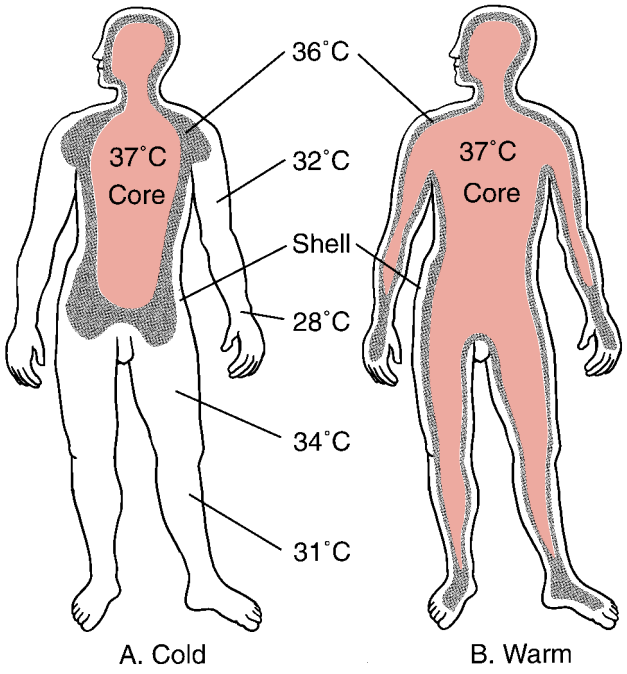


FIGURE 29.2 **Distribution of temperatures in the body's core and shell.** A, During exposure to cold. B, In a warm environment. Since the temperatures of the surface and the thickness of the shell depend on environmental temperature, the shell is thicker in the cold and thinner in the heat.

TABLE 29.1 **Thermal Conductivities and Rates of Heat Flow**

Material	Conductivity kcal/(s·m·°C)	Rate of Heat Flow[a] kcal/hr	Watts
Copper	0.092	33,120	38,474
Epidermis	0.00005	18	21
Dermis	0.00009	32	38
Fat	0.00004	14	17
Muscle	0.00011	40	46
Oak (across grain)	0.00004	14	17
Glass fiber insulation	0.00001	3.6	4.2

[a] Values are calculated for slabs 1 m^2 in area and 1 cm thick, with a 1°C temperature difference between the two faces of the slab.

The internal body temperature that is regulated is the temperature of the vital organs inside the head and trunk, which, together with a variable amount of other tissue, comprise the warm internal core.

Heat is produced in all tissues of the body but is lost to the environment only from tissues in contact with the environment—predominantly from the skin and, to a lesser degree, from the respiratory tract. We, therefore, need to consider heat transfer within the body, especially heat transfer (1) from major sites of heat production to the rest of the body, and (2) from the core 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 by conduction varies directly with the thermal conductivity of the tissues, the change in temperature over the distance the heat travels, and the area (perpendicular to the direction of heat flow) through which the heat flows. It varies inversely with the distance the heat must travel. As Table 29.1 shows, the tissues are rather poor heat conductors.

Heat flow by convection depends on the rate of blood flow and the temperature difference between the tissue and the blood supplying the tissue. Because the vessels of the microvasculature have thin walls and, collectively, a large total surface area, the blood comes to the temperature of the surrounding tissue before it reaches the capillaries. 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 in the cold may include most of the limbs and the more superficial muscles of the neck and trunk—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 the heat were part of the body core, now become part of the shell. In addition to the organs in the trunk and head, the core includes a greater or lesser amount of more superficial tissue—mostly skeletal muscle—depending on the body's thermal state.

Because the shell lies between the core and the environment, all heat leaving the body core, except heat lost through the respiratory tract, must pass through the shell before being given up to the environment. Thus, the shell insulates the core from the environment. In a cool subject, the skin blood flow is low, so core-to-skin heat transfer is dominated by conduction; the shell is also thicker, providing more insulation to the core, since heat flow by conduction varies inversely with the distance the heat must travel. 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. In a cool subject, the subcutaneous fat layer contributes to the insulation value of the shell because the fat layer increases the thickness of the shell and because fat has a conductivity about 0.4 times that of dermis or muscle (see Table 29.1). Thus, fat is a correspondingly better 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 from the core to the skin.

Core Temperature Is Close to Central Blood Temperature

Core temperature varies slightly from one site to another depending on such local factors as metabolic rate, blood supply, and the temperatures of neighboring tissues. However, temperatures at different places in the core are all close to the temperature of the central blood and tend to

change together. The notion of a single uniform core temperature, although not strictly correct, is a useful approximation. The value of 98.6°F often given as the normal level of body temperature may give the misleading impression that body temperature is regulated so precisely that it is not allowed to deviate even a few tenths of a degree. In fact, 98.6°F is simply the Fahrenheit equivalent of 37°C, and body temperature does vary somewhat (see Fig. 29.1). The effects of heavy exercise and fever are familiar; variation among individuals and such factors as time of day (Fig. 29.3), phase of the menstrual cycle, and acclimatization to heat can also cause differences of up to about 1°C in core temperature at rest.

To maintain core temperature within a narrow range, the thermoregulatory system needs continuous information about the level of core temperature. Temperature-sensitive neurons and nerve endings in the abdominal viscera, great veins, spinal cord, and, especially, the brain provide this information. We discuss how the thermoregulatory system processes and responds to this information later in the chapter.

Core temperature should be measured at a site whose temperature is not biased by environmental temperature. Sites used clinically include the rectum, the mouth and, occasionally, the axilla. The rectum is well insulated from the environment; its temperature is independent of environmental temperature and is a few tenths of 1°C warmer than arterial blood and other core sites. The tongue is richly supplied with blood; oral temperature under the tongue is usually close to blood temperature (and 0.4 to 0.5°C below rectal temperature), but cooling the face, neck, or mouth can make oral temperature misleadingly low. If a patient holds his or her upper arm firmly against the chest to close the axilla, axillary temperature will eventually come reasonably close to core temperature. However, as this may take 30 minutes or more, axillary temperature is infrequently used. Infrared ear thermometers are convenient and widely used in the clinic, but temperatures of the tympanum and external auditory meatus are loosely related to more accepted indices of core temperature, and ear temperature in collapsed hyperthermic runners may be 3 to 6°C below rectal temperature.

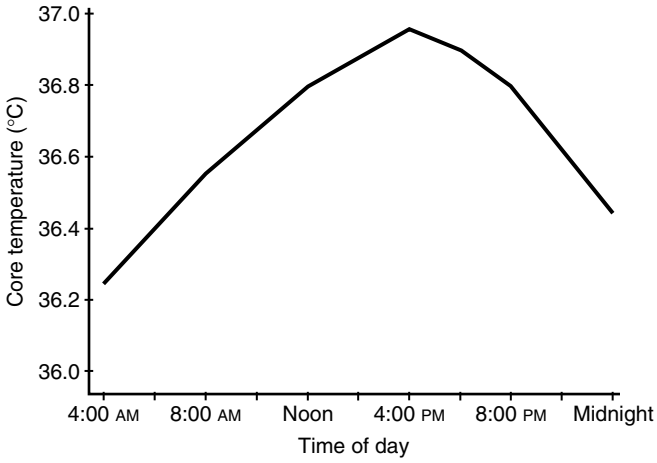


FIGURE 29.3 **Effect of time of day on internal body temperature of healthy resting subjects.** (Drawn from data of Mackowiak PA, Wasserman SS, Levine MM. A critical appraisal of 98.6°F, the upper limit of normal body temperature, and other legacies of Carl Reinhold August Wunderlich. JAMA 1992;268:1578–1580; and Stephenson LA, Wenger CB, O'Donovan BH, et al. Circadian rhythm in sweating and cutaneous blood flow. Am J Physiol 1984;246:R321–R324.)

Skin Temperature Is Important in Heat Exchange and Thermoregulatory Control

Most heat is exchanged between the body and the environment at the skin surface. Skin temperature is much more variable than core temperature; it is affected by thermoregulatory responses such as skin blood flow and sweat secretion, the temperatures of underlying tissues, and environmental factors such as air temperature, air movement, and thermal radiation. Skin temperature is one of the major factors determining heat exchange with the environment. For these reasons, it provides the thermoregulatory system with important information about the need to conserve or dissipate heat.

Many bare nerve endings just under the skin are sensitive to temperature. Depending on the relation of discharge rate to temperature, they are classified as either warm or cold receptors (see Chapter 4). Cold receptors are about 10 times more numerous than warm receptors. Furthermore, as the skin is heated, warm receptors respond with a transient burst of activity and cold receptors respond with a transient suppression; the reverse happens as the skin is cooled. These transient responses at the beginning of heating or cooling give the central thermoregulatory controller almost immediate information about changes in skin temperature and may explain, for example, the intense, brief sensation of being chilled that occurs during a plunge into cold water.

Since skin temperature usually is not uniform over the body surface, mean skin temperature ($_{sk}$) is frequently calculated from temperatures at several skin sites, usually weighting each temperature according to the fraction of body surface area it represents. $_{sk}$ is used to summarize the input to the CNS from temperature-sensitive nerve endings in the skin. $_{sk}$ also is commonly used, along with core temperature, to calculate a mean body temperature and to estimate the quantity of heat stored in the body, since the direct measurement of shell temperature would be difficult and invasive.

THE BALANCE BETWEEN HEAT PRODUCTION AND HEAT LOSS

All animals exchange energy with the environment. Some energy is exchanged as mechanical work, but most is exchanged as heat (Fig. 29.4). Heat is exchanged by conduction, convection, and radiation and as latent heat through evaporation or (rarely) condensation of water. 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 relationship is summarized in the heat balance equation:

$$M = E + R + C + K + W + S \qquad (1)$$

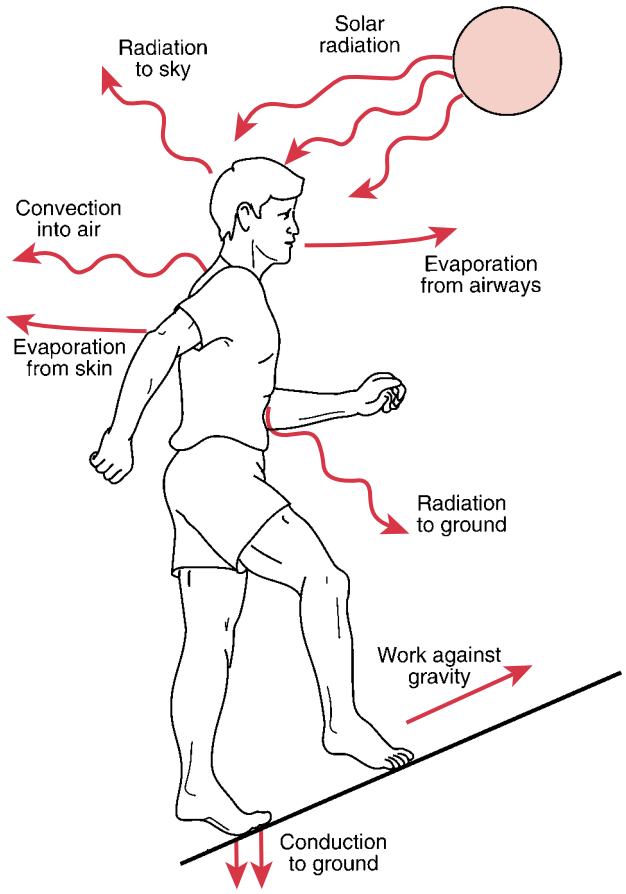


FIGURE 29.4 **Exchange of energy with the environment.** This hiker gains heat from the sun by radiation and loses heat by conduction to the ground through the soles of his feet, convection into the air, radiation to the ground and sky, and evaporation of water from his skin and respiratory passages. In addition, some of the energy released by his metabolic processes is converted into mechanical work, rather than heat, since he is walking uphill.

where M is metabolic rate; E is rate of heat loss by evaporation; R and C are rates of heat loss by radiation and convection, respectively; K is the rate of heat loss by conduction; W is rate of energy loss as mechanical work; and S is rate of heat storage in the body, manifested as changes in tissue temperatures.

M is always positive, but the terms on the right side of equation 1 represent energy exchange with the environment and storage and may be either positive or negative. E, R, C, K, and W are positive if they represent energy losses from the body and negative if they represent energy gains. When $S = 0$, the body is in heat balance and body temperature neither rises nor falls. When the body is not in heat balance, its mean tissue temperature increases if S is positive and decreases if S is negative. This situation commonly lasts only until the body's responses to the temperature changes are sufficient to restore balance. However, if the thermal stress is too great for the thermoregulatory system to restore balance, the body will continue to gain or lose heat until either the stress diminishes sufficiently or the animal dies.

The traditional units for measuring heat are a potential source of confusion, because the word calorie refers to two units differing by a 1,000-fold. The *calorie* used in chemistry and physics is the quantity of heat that will raise the temperature of 1 g of pure water by 1°C; it is also called the small calorie or gram calorie. The *Calorie* (capital C) used in physiology and nutrition is the quantity of heat that will raise the temperature of 1 kg of pure water by 1°C; it is also called the large calorie, kilogram calorie, or (the usual practice in thermal physiology) the **kilocalorie** (kcal). Because heat is a form of energy, it is now often measured in joules, the unit of work (1 kcal = 4,186 J), and rate of heat production or heat flow in watts, the unit of power (1 W = 1 J/sec). This practice avoids confusing calories and Calories. However, kilocalories are still used widely enough that it is necessary to be familiar with them, and there is a certain advantage to a unit based on water because the body itself is mostly water.

Heat Is a By-product of Energy-Requiring Metabolic Processes

Metabolic energy is used for active transport via membrane pumps, for energy-requiring chemical reactions, such as the formation of glycogen from glucose and proteins from amino acids, and for muscular work. Most of the metabolic energy used in these processes is converted into heat within the body. This conversion may occur almost immediately, as with energy used for active transport or heat produced as a by-product of muscular activity. Other energy is converted to heat only after a delay, as when the energy used in forming glycogen or protein is released as heat when the glycogen is converted back into glucose or the protein is converted back into amino acids.

Metabolic Rate and Sites of Heat Production at Rest. Among subjects of different body size, metabolic rate at rest varies approximately in proportion to body surface area. In a resting and fasting young adult man it is about 45 W/m^2 (81 W or 70 kcal/hr for 1.8 m^2 body surface area), corresponding to an O_2 consumption of about 240 mL/min. About 70% of energy production at rest occurs in the body core—trunk viscera and the brain—even though they comprise only about 36% of the body mass (Table 29.2). As a by-product of their metabolic processes, these organs produce most of the heat needed to maintain heat balance at comfortable environmental temperatures; only in the cold must such by-product heat be supplemented by heat produced expressly for thermoregulation.

Factors other than body size that affect metabolism at rest include age and sex (Fig. 29.5), and hormones and digestion. The ratio of metabolic rate to surface area is highest in infancy and declines with age, most rapidly in childhood and adolescence and more slowly thereafter. Children have high metabolic rates in relation to surface area because of the energy used to synthesize the fats, proteins, and other tissue components needed to sustain growth. Similarly, a woman's metabolic rate increases during pregnancy to supply the energy needed for the growth of the fetus. However, a nonpregnant woman's metabolic rate is 5 to 10% lower than that of a man of the same age and surface area, proba-

TABLE 29.2 Relative Masses and Metabolic Heat Production Rates During Rest and Heavy Exercise

	% of Body Mass	% of Heat Production	
		Rest	Exercise
Brain	2	16	1
Trunk viscera	34	56	8
Muscle and skin	56	18	90
Other	8	10	1

bly because a higher proportion of the female body is composed of fat, a tissue with low metabolism.

The catecholamines and thyroxine are the hormones that have the greatest effect on metabolic rate. Catecholamines cause glycogen to break down into glucose and stimulate many enzyme systems, increasing cellular metabolism. Hypermetabolism is a clinical feature of some cases of pheochromocytoma, a catecholamine-secreting tumor of the adrenal medulla. Thyroxine magnifies the metabolic response to catecholamines, increases protein synthesis, and stimulates oxidation by the mitochondria. The metabolic rate is typically 45% above normal in hyperthyroidism (but up to 100% above normal in severe cases) and 25% below normal in hypothyroidism (but 45% below normal with complete lack of thyroid hormone). Other hormones have relatively minor effects on metabolic rate.

A resting person's metabolic rate increases 10 to 20% after a meal. This effect of food, called the **thermic effect of food** (formerly known as specific dynamic action), lasts several hours. The effect is greatest after eating protein and less after carbohydrate and fat; it appears to be associated with processing the products of digestion in the liver.

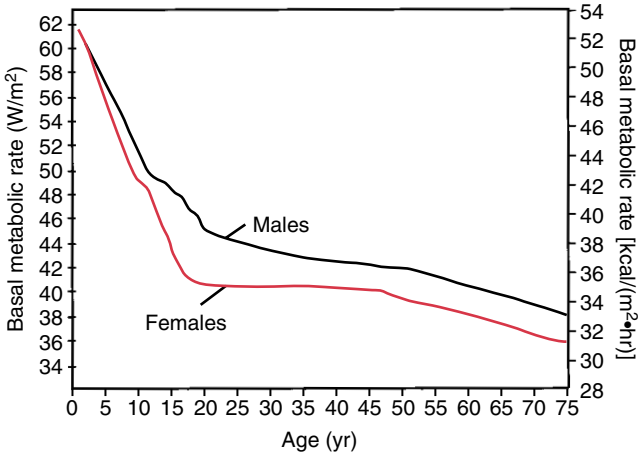


FIGURE 29.5 Effects of age and sex on the basal metabolic rate of healthy subjects. Metabolic rate here is expressed as the ratio of energy consumption to body surface area.

Measurement of Metabolic Rate. Because so many factors affect metabolism at rest, metabolic rate is often measured under a set of standard conditions to compare it with established norms. Metabolic rate measured under these conditions is called **basal metabolic rate** (BMR). The commonly accepted conditions for measuring BMR are that the person must have fasted for 12 hours; the measurement must be made in the morning after a good night's sleep, beginning after the person has rested quietly for at least 30 minutes; and the air temperature must be comfortable, about 25°C (77°F). Basal metabolic rate is "basal" only during wakefulness, since metabolic rate during sleep is somewhat less than BMR.

Heat exchange with the environment can be measured directly by using a human calorimeter. In this insulated chamber, heat can exit only in the air ventilating the chamber or in water flowing through a heat exchanger in the chamber. By measuring the flow of air and water and their temperatures as they enter and leave the chamber, one can determine the subject's heat loss by conduction, convection, and radiation. And by measuring the moisture content of air entering and leaving the chamber, one can determine heat loss by evaporation. This technique is called **direct calorimetry**, and though conceptually simple, it is cumbersome and costly.

Metabolic rate is often estimated by **indirect calorimetry**, which is based on measuring a person's rate of O_2 consumption, since virtually all energy available to the body depends ultimately on reactions that consume O_2. Consuming 1 L of O_2 is associated with releasing 21.1 kJ (5.05 kcal) if the fuel is carbohydrate, 19.8 kJ (4.74 kcal) if the fuel is fat, and 18.6 kJ (4.46 kcal) if the fuel is protein. An average value often used for the metabolism of a mixed diet is 20.2 kJ (4.83 kcal) per liter of O_2. The ratio of CO_2 produced to O_2 consumed in the tissues is called the **respiratory quotient** (RQ). The RQ is 1.0 for the oxidation of carbohydrate, 0.71 for the oxidation of fat, and 0.80 for the oxidation of protein. In a steady state where CO_2 is exhaled from the lungs at the same rate it is produced in the tissues, RQ is equal to the respiratory exchange ratio, R (see Chapter 19). One can improve the accuracy of indirect calorimetry by also determining R and either estimating the amount of protein oxidized—which usually is small compared to fat and carbohydrate—or calculating it from urinary nitrogen excretion.

Skeletal Muscle Metabolism and External Work. Even during mild exercise, the muscles are the principal source of metabolic heat, and during intense exercise, they may account for up to 90%. Moderately intense exercise by a healthy, but sedentary, young man may require a metabolic rate of 600 W (in contrast to about 80 W at rest), and intense activity by a trained athlete, 1,400 W or more. Because of their high metabolic rate, exercising muscles may be almost 1°C warmer than the core. Blood perfusing these muscles is warmed and, in turn, warms the rest of the body, raising the core temperature.

Muscles convert most of the energy in the fuels they consume into heat rather than mechanical work. During phosphorylation of ADP to form ATP, 58% of the energy released from the fuel is converted into heat, and only

about 42% is captured in the ATP that is formed in the process. When a muscle contracts, some of the energy in the ATP that was hydrolyzed is converted into heat rather than mechanical work. The efficiency at this stage varies enormously; it is zero in isometric muscle contraction, in which a muscle's length does not change while it develops tension, so that no work is done even though metabolic energy is required. Finally, some of the mechanical work produced is converted by friction into heat within the body. (This is, for example, the fate of all of the mechanical work done by the heart in pumping blood.) At best, no more than 25% of the metabolic energy released during exercise is converted into mechanical work outside the body, and the other 75% or more is converted into heat within the body.

Convection, Radiation, and Evaporation Are the Main Avenues of Heat Exchange With the Environment

Convection is the transfer of heat resulting from the movement of a fluid, either liquid or gas. In thermal physiology, the fluid is usually air or water in the environment or blood, in the case of heat transfer inside the body. To illustrate, consider an object immersed in a fluid that is cooler than the object. Heat passes from the object to the immediately adjacent fluid by conduction. If the fluid is stationary, conduction is the only means by which heat can pass through the fluid, and over time, the rate of heat flow from the body to the fluid will diminish as the fluid nearest the object approaches the temperature of the object. In practice, however, fluids are rarely stationary. If the fluid is moving, heat will still be carried from the object into the fluid by conduction, but once the heat has entered the fluid, it will be carried by the movement of the fluid—by convection. The same fluid movement that carries heat away from the surface of the object constantly brings fresh cool fluid to the surface, so the object gives up heat to the fluid much more rapidly than if the fluid were stationary. Although conduction plays a role in this process, convection so dominates the overall heat transfer that we refer to the heat transfer as if it were entirely convection. Therefore, the conduction term (K) in the heat balance equation is restricted to heat flow between the body and other solid objects, and it usually represents only a small part of the total heat exchange with the environment.

Every surface emits energy as electromagnetic radiation, with a power output proportional to the area of the surface, the fourth power of its absolute temperature (i.e., measured from absolute zero), and the **emissivity** (e) of the surface, a number between 0 and 1 that depends on the nature of the surface and the wavelength of the radiation. (In this discussion, the term *surface* is broadly defined, so that a flame and the sky, for example, are surfaces.) Such radiation, called thermal radiation, has a characteristic distribution of power as a function of wavelength, which depends on the temperature of the surface. The emissivity of any surface is equal to the **absorptivity**—the fraction of incident radiant energy the surface absorbs. (For this reason, an ideal emitter, with an emissivity of 1, is called a **black body**.) If two bodies exchange heat by thermal radiation, radiation travels in both directions, but since each body emits radiation with an intensity that depends on its temperature, the net heat flow is from the warmer to the cooler body.

At ordinary tissue and environmental temperatures, virtually all thermal radiation is in a region of the infrared range where most surfaces, other than polished metals, have emissivities near 1 and emit with a power output near the theoretical maximum. However, bodies that are hot enough to glow, such as the sun, emit large amounts of radiation in the visible and near-infrared range, in which light-colored surfaces have lower emissivities and absorptivities than dark ones. Therefore, colors of skin and clothing affect heat exchange only in sunlight or bright artificial light.

When 1 g of water is converted into vapor at 30°C, it absorbs 2,425 J (0.58 kcal), the **latent heat of evaporation**, in the process. Evaporation of water is, thus, an efficient way of losing heat, and it is the body's only means of losing heat when the environment is hotter than the skin, as it usually is when the environment is warmer than 36°C. Evaporation must then dissipate both the heat produced by metabolic processes and any heat gained from the environment by convection and radiation. Most water evaporated in the heat comes from sweat, but even in cold temperatures, the skin loses some water by the evaporation of **insensible perspiration**, water that diffuses through the skin rather than being secreted. In equation 1, E is nearly always positive, representing heat loss from the body. However, E is negative in the rare circumstances in which water vapor gives up heat to the body by condensing on the skin (as in a steam room).

Heat Exchange Is Proportional to Surface Area and Obeys Biophysical Principles

Animals exchange heat with their environment through both the skin and the respiratory passages, but only the skin exchanges heat by radiation. In panting animals, respiratory heat loss may be large and may be an important means of achieving heat balance. In humans, however, respiratory heat exchange is usually relatively small and (though hyperthermic subjects may hyperventilate) is not predominantly under thermoregulatory control. Therefore, we do not consider it further here.

Convective heat exchange between the skin and the environment is proportional to the difference between skin and ambient air temperatures, as expressed by this equation:

$$C = h_c \times A \times (_{sk} - T_a) \qquad (2)$$

where A is the body surface area, $_{sk}$ and T_a are mean skin and ambient temperatures, and h_c is the convective heat transfer coefficient.

The value of h_c includes the effects of the factors other than temperature and surface area that influence convective heat exchange. For the whole body, air movement is the most important of these factors, and convective heat exchange (and, thus, h_c) varies approximately as the square root of the air speed, except when air movement is slight (Fig. 29.6). Other factors that affect h_c include the direction of air movement and the curvature of the skin surface. As the radius of curvature decreases, h_c increases, so the hands and fingers are effective in convective heat exchange disproportionately to their surface area.

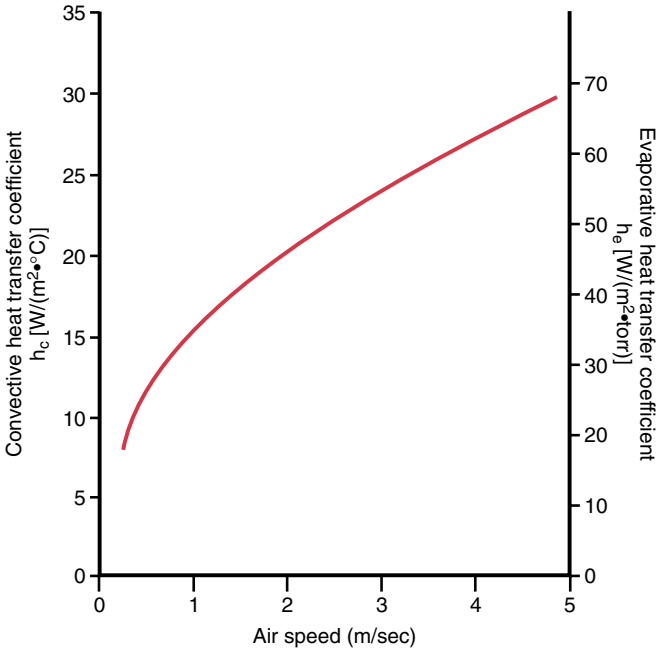


FIGURE 29.6 **Dependence of convection and evaporation on air movement.** This figure shows the convective heat transfer coefficient, h_c (left), and the evaporative heat transfer coefficient, h_e (right) for a standing human as a function of air speed. The convective and evaporative heat transfer coefficients are related by the equation $h_e = h_c \times 2.2$°C/torr. The horizontal axis can be converted into English units by using the relation 5 m/sec = 16.4 ft/sec = 11.2 miles/hr.

Radiative heat exchange is proportional to the difference between the fourth powers of the absolute temperatures of the skin and of the radiant environment (T_r) and to the emissivity of the skin (e_{sk}): $R \propto e_{sk} \times ({}_{sk}{}^4 - T_r{}^4)$. However, if T_r is close enough to ${}_{sk}$ that ${}_{sk} - T_r$ is much smaller than the absolute temperature of the skin, R is nearly proportional to $e_{sk} \times ({}_{sk} - T_r)$. Some parts of the body surface (e.g., the inner surfaces of the thighs and arms) exchange heat by radiation with other parts of the body surface, so the body exchanges heat with the environment as if it had an area smaller than its actual surface area. This smaller area, called the **effective radiating surface area** (A_r), depends on the body's posture, and it is closest to the actual surface area in a spread-eagle position and least in a curled-up position. Radiative heat exchange can be represented by the equation

$$R = h_r \times e_{sk} \times A_r \times (\overline{T}_{sk} - T_r) \qquad (3)$$

where h_r is the radiant heat transfer coefficient, 6.43 W/(m²·°C) at 28°C.

Evaporative heat loss from the skin to the environment is proportional to the difference between the water vapor pressure at the skin surface and the water vapor pressure in the ambient air. These relations are summarized as:

$$E = h_e \times A \times (P_{sk} - P_a) \qquad (4)$$

where P_{sk} is the water vapor pressure at the skin surface, P_a is the ambient water vapor pressure, and h_e is the evaporative heat transfer coefficient.

Water vapor, like heat, is carried away by moving air, so geometric factors and air movement affect E and h_e in the same way they affect C and h_c. If the skin is completely wet, the water vapor pressure at the skin surface is the saturation water vapor pressure at the temperature of the skin (Fig. 29.7), and evaporative heat loss is E_{max}, the maximum possible for the prevailing skin temperature and environmental conditions. This condition is described as:

$$E_{max} = h_e \times A \times (P_{sk,sat} - P_a) \qquad (5)$$

where $P_{sk,sat}$ is the saturation water vapor pressure at skin temperature. When the skin is not completely wet, it is impractical to measure P_{sk}, the actual average water vapor pressure at the skin surface. Therefore, a coefficient called skin *wettedness* (w) is defined as the ratio E/E_{max}, with $0 < w < 1$. Skin wettedness depends on the hydration of the epidermis and the fraction of the skin surface that is wet. We can now rewrite equation 4 as:

$$E = h_e \times A \times w \times (P_{sk,sat} - P_a) \qquad (6)$$

Wettedness depends on the balance between secretion and evaporation of sweat. If secretion exceeds evaporation, sweat accumulates on the skin and spreads out to wet more of the space between neighboring sweat glands, increasing wettedness and E; if evaporation exceeds secretion, the reverse occurs. If sweat rate exceeds E_{max}, once wettedness becomes 1, the excess sweat drips from the body, since it cannot evaporate.

Note that P_a, on which evaporation from the skin directly depends, is proportional to the actual moisture content in the air. By contrast, the more familiar quantity **relative humidity** (rh) is the ratio between the actual moisture content in the air and the maximum moisture content possible at the temperature of the air. It is important to recog-

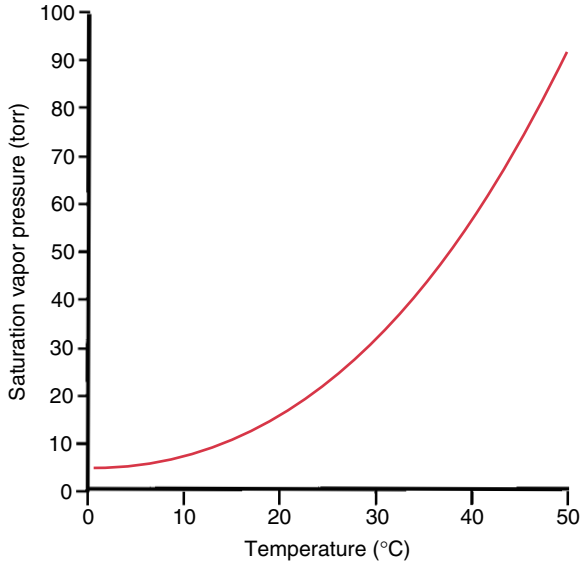


FIGURE 29.7 **Saturation vapor pressure of water as a function of temperature.** For any given temperature, the water vapor pressure is at its saturation value when the air is "saturated" with water vapor (i.e., holds the maximum amount possible at that temperature). At 37°C, P_{H_2O} equals 47 torr.

nize that rh is only indirectly related to evaporation from the skin. For example, in a cold environment, P_a will be low enough that sweat can easily evaporate from the skin even if rh equals 100%, since the skin is warm and $P_{sk,sat}$, which depends on the temperature of the skin, will be much greater than P_a.

Heat Storage Is a Change in the Heat Content of the Body

The rate of **heat storage** is the difference between heat production and net heat loss (equation 1). (In the unusual circumstances in which there is a net heat gain from the environment, such as during immersion in a hot bath, storage is the sum of heat production and net heat gain.) It can be determined experimentally from simultaneous measurements of metabolism by indirect calorimetry and heat gain or loss by direct calorimetry. Storage of heat in the tissues changes their temperature, and the amount of heat stored is the product of body mass, the body's mean specific heat, and a suitable mean body temperature (T_b). The body's mean specific heat depends on its composition, especially the proportion of fat, and is about 3.55 kJ/(kg·°C) [0.85 kcal/(kg·°C)]. Empirical relations of T_b to core temperature (T_c) and $\overline{T}_{sk}$, determined in calorimetric studies, depend on ambient temperature, with T_b varying from $0.65 \times T_c + 0.35 \times {}_{sk}$ in the cold to $0.9 \times T_c + 0.1 \times \overline{T}_{sk}$ in the heat. The shift from cold to heat in the relative weighting of T_c and $\overline{T}_{sk}$ reflects the accompanying change in the thickness of the shell (see Fig. 29.2).

HEAT DISSIPATION

Figure 29.8 shows rectal and mean skin temperatures, heat losses, and calculated core-to-skin (shell) conductances for nude resting men and women at the end of 2-hour exposures in a calorimeter to ambient temperatures of 23 to 36°C. Shell conductance represents the sum of heat transfer by two parallel modes: conduction through the tissues of the shell, and convection by the blood. It is calculated by dividing heat flow through the skin (HF_{sk}) (i.e., total heat loss from the body less heat loss through the respiratory tract) by the difference between core and mean skin temperatures:

$$C = HF_{sk}/(T_c - \overline{T}_{sk}) \qquad (7)$$

where C is shell conductance and T_c and $\overline{T}_{sk}$ are core and mean skin temperatures.

From 23 to 28°C, conductance is minimal because the skin is vasoconstricted and its blood flow is low. The minimal level of conductance attainable depends largely on the thickness of the subcutaneous fat layer, and the women's thicker layer allows them to attain a lower conductance than men. At about 28°C, conductance begins to increase, and above 30°C, conductance continues to increase and sweating begins.

For these subjects, 28 to 30°C is the zone of **thermoneutrality**, the range of comfortable environmental temperatures in which thermal balance is maintained without either shivering or sweating. In this zone, heat balance is maintained entirely by controlling conductance and $\overline{T}_{sk}$

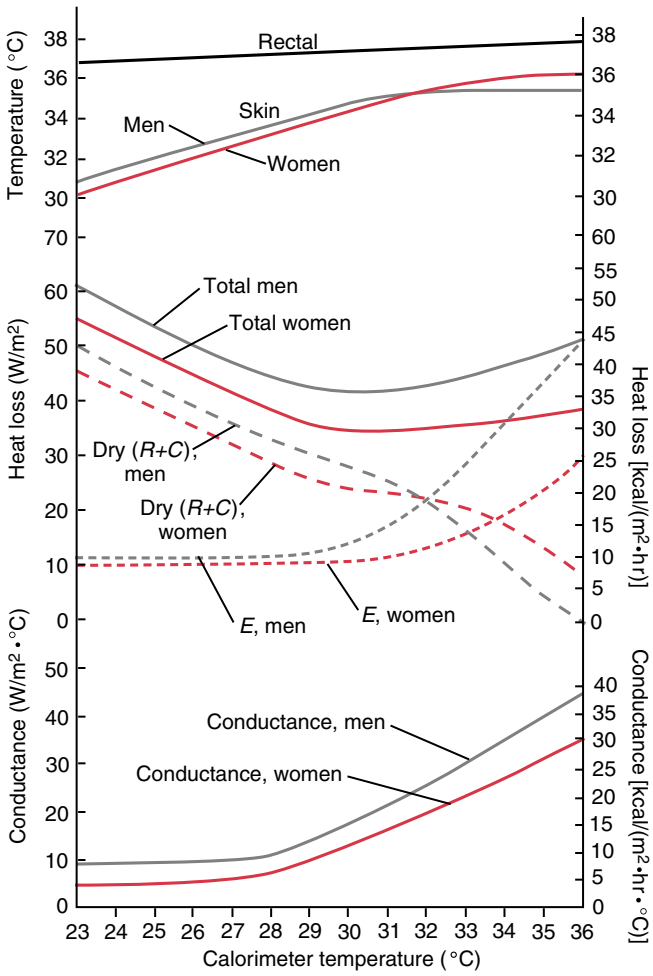


FIGURE 29.8 **Heat dissipation.** These graphs show the average values of rectal and mean skin temperatures, heat loss, and core-to-skin thermal conductance for nude resting men and women near steady state after 2 hours at different environmental temperatures in a calorimeter. (All energy exchange quantities in this figure have been divided by body surface area to remove the effect of individual body size.) Total heat loss is the sum of dry heat loss, by radiation (*R*) and convection (*C*), and evaporative heat loss (*E*). Dry heat loss is proportional to the difference between skin temperature and calorimeter temperature and decreases with increasing calorimeter temperature. (Based on data from Hardy JD, DuBois EF. Differences between men and women in their response to heat and cold. Proc Natl Acad Sci U S A 1940;26:389–398.)

and, thus, *R* and *C*. As equations 2 to 4 show, *C*, *R*, and *E* all depend on skin temperature, which, in turn, depends partly on skin blood flow. *E* depends also, through skin wettedness, on sweat secretion. Therefore, all these modes of heat exchange are partly under physiological control.

The Evaporation of Sweat Can Dissipate Large Amounts of Heat

In Figure 29.8, evaporative heat loss is nearly independent of ambient temperature below 30°C and is 9 to 10 W/m², corresponding to evaporation of about 13 to 15 g/(m²·h), of which about half is moisture lost in breathing and half is

insensible perspiration. This evaporation occurs independent of thermoregulatory control. As the ambient temperature increases, the body depends more and more on the evaporation of sweat to achieve heat balance.

The two histological types of sweat glands are **eccrine** and **apocrine**. In northern Europeans, apocrine glands are found mostly in the axilla and pigmented skin, such as the lips, but they are more widely distributed in some other populations. Eccrine sweat is essentially a dilute electrolyte solution, but apocrine sweat also contains fatty material. Eccrine sweat glands, the dominant type in all human populations, are more important in human thermoregulation and number about 2,500,000. They are controlled through postganglionic sympathetic nerves that release acetylcholine (ACh) rather than norepinephrine. A healthy man unacclimatized to heat can secrete up to 1.5 L/hr of sweat. Although the number of functional sweat glands is fixed before the age of 3, the secretory capacity of the individual glands can change, especially with endurance exercise training and heat acclimatization; men well acclimatized to heat can attain peak sweat rates greater than 2.5 L/hr. Such rates cannot be maintained, however; the maximum daily sweat output is probably about 15 L.

The sodium concentration of eccrine sweat ranges from less than 5 to 60 mmol/L (versus 135 to 145 mmol/L in plasma). In producing sweat that is hypotonic to plasma, the glands reabsorb sodium from the sweat duct by active transport. As sweat rate increases, the rate at which the glands reabsorb sodium increases more slowly, so that sodium concentration in the sweat increases. The sodium concentration of sweat is affected also by heat acclimatization and by the action of mineralocorticoids.

Skin Circulation Is Important in Heat Transfer

Heat produced in the body must be delivered to the skin surface to be eliminated. When skin blood flow is minimal, shell conductance is typically 5 to 9 W/°C per m^2 of body surface. For a lean resting subject with a surface area of 1.8 m^2, minimal whole body conductance of 16 W/°C [i.e., 8.9 W/(°C · m^2) × 1.8 m^2] and a metabolic heat production of 80 W, the temperature difference between the core and the skin must be 5°C (i.e., 80 W ÷ 16 W/°C) for the heat produced to be conducted to the surface. In a cool environment, $\overline{T}_{sk}$ may easily be low enough for this to occur. However, in an ambient temperature of 33°C, $\overline{T}_{sk}$ is typically about 35°C, and without an increase in conductance, core temperature would have to rise to 40°C—a high, although not yet dangerous, level—for the heat to be conducted to the skin. If the rate of heat production were increased to 480 W by moderate exercise, the temperature difference between core and skin would have to rise to 30°C—and core temperature to well beyond lethal levels—to allow all the heat produced to be conducted to the skin. In the latter circumstances, the conductance of the shell must increase greatly for the body to reestablish thermal balance and continue to regulate its temperature. This is accomplished by increasing the skin blood flow.

Effectiveness of Skin Blood Flow in Heat Transfer.

Assuming that blood on its way to the skin remains at core temperature until it reaches the skin, reaches skin temperature as it passes through the skin, and then stays at skin temperature until it returns to the core, we can compute the rate of heat flow (HF_b) as a result of convection by the blood as

$$HF_b = SkBF \times (T_c - T_{sk}) \times 3.85\ kJ/(L \cdot °C) \qquad (8)$$

where SkBF is the rate of skin blood flow, expressed in L/sec rather than the usual L/min to simplify computing HF in W (i.e., J/sec); and 3.85 kJ/(L·°C) [0.92 kcal/(L·°C)] is the volume-specific heat of blood. Conductance as a result of convection by the blood (C_b) is calculated as:

$$C_b = HF_b/(T_c - T_{sk}) = SkBF \times 3.85\ kJ/(L \cdot °C) \qquad (9)$$

Of course, heat continues to flow by conduction through the tissues of the shell, so total conductance is the sum of conductance as a result of convection by the blood, plus that result from conduction through the tissues. Total heat flow is given by

$$HF = (C_b + C_0) \times (T_c - T_{sk}) \qquad (10)$$

in which C_0 is thermal conductance of the tissues when skin blood flow is minimal and, thus, is predominantly due to conduction through the tissues.

The assumptions made in deriving equation 8 are somewhat artificial and represent the conditions for maximum efficiency of heat transfer by the blood. In practice, blood exchanges heat also with the tissues through which it passes on its way to and from the skin. Heat exchange with these other tissues is greatest when skin blood flow is low; in such cases, heat flow to the skin may be much less than predicted by equation 8, as discussed further below. However, equation 8 is a reasonable approximation in a warm subject with moderate to high skin blood flow. Although measuring whole-body SkBF directly is not possible, it is believed to reach several liters per minute during heavy exercise in the heat. The maximum obtainable is estimated to be nearly 8 L/min. If SkBF = 1.89 L/min (0.0315 L/sec), according to equation 9, skin blood flow contributes about 121 W/°C to the conductance of the shell. If conduction through the tissues contributes 16 W/°C, total shell conductance is 137 W/°C, and if T_c = 38.5°C and T_{sk} = 35°C, this will produce a core-to-skin heat transfer of 480 W, the heat production in our earlier example of moderate exercise. Therefore, even a moderate rate of skin blood flow can have a dramatic effect on heat transfer.

When a person is not sweating, raising skin blood flow brings skin temperature nearer to blood temperature and lowering skin blood flow brings skin temperature nearer to ambient temperature. Under such conditions, the body can control dry (convective and radiative) heat loss by varying skin blood flow and, thus, skin temperature. Once sweating begins, skin blood flow continues to increase as the person becomes warmer. In these conditions, however, 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 has begun, further increases in skin blood flow usually cause little change in skin temperature or dry heat exchange and serve primarily to deliver to the skin the heat that is being removed by the evaporation of sweat. Skin blood flow and sweating work in tandem to dissipate heat under such conditions.

Sympathetic Control of Skin Circulation. Blood flow in human skin is under dual vasomotor control. In most of the skin, the vasodilation that occurs during heat exposure depends on sympathetic nerve signals that cause the blood vessels to dilate, and this vasodilation can be prevented or reversed by regional nerve block. Because it depends on the action of nerve signals, such vasodilation is sometimes referred to as active vasodilation. Active vasodilation occurs in almost all the skin, except in so-called acral regions—hands, feet, lips, ears, and nose. In skin areas where active vasodilation occurs, vasoconstrictor activity is minimal at thermoneutral temperatures, and active vasodilation during heat exposure does not begin until close to the onset of sweating. Therefore, skin blood flow in these areas is not much affected by small temperature changes within the thermoneutral range.

The neurotransmitter or other vasoactive substance responsible for active vasodilation in human skin has not been identified. Active vasodilation operates in tandem with sweating in the heat, and is impaired or absent in **anhidrotic ectodermal dysplasia**, a congenital disorder in which sweat glands are sparse or absent. For these reasons, the existence of a mechanism linking active vasodilation to the sweat glands has long been suspected, but never established. Earlier suggestions that active vasodilation is cholinergic or is caused by the release of bradykinin from activated sweat glands have not gained general acceptance. More recently, however, nerve endings containing both ACh and vasoactive peptides have been found near eccrine sweat glands in human skin, suggesting that active vasodilation may be mediated by a vasoactive cotransmitter that is released along with ACh from the endings of nerves that innervate sweat glands.

Reflex vasoconstriction, occurring in response to cold and as part of certain nonthermal reflexes such as baroreflexes, is mediated primarily through adrenergic sympathetic fibers distributed widely over most of the skin. Reducing the flow of impulses in these nerves allows the blood vessels to dilate. In the acral regions and superficial veins (whose role in heat transfer is discussed below), vasoconstrictor fibers are the predominant vasomotor innervation, and the vasodilation that occurs during heat exposure is largely a result of the withdrawal of vasoconstrictor activity. Blood flow in these skin regions is sensitive to small temperature changes even in the thermoneutral range, and may be responsible for "fine-tuning" heat loss to maintain heat balance in this range.

THERMOREGULATORY CONTROL

In discussions of control systems, the words "regulation" and "regulate" have meanings distinct from those of the word "control" (see Chapter 1). The variable that a control system acts to maintain within narrow limits (e.g., temperature) is called the *regulated* variable, and the quantities it controls to accomplish this (e.g., sweating rate, skin blood flow, metabolic rate, and thermoregulatory behavior) are called *controlled* variables.

Humans have two distinct subsystems for regulating body temperature: behavioral thermoregulation and physiological thermoregulation. Behavioral thermoregulation—through the use of shelter, space heating, air conditioning, and clothing—enables humans to live in the most extreme climates in the world, but it does not provide fine control of body heat balance. In contrast, physiological thermoregulation is capable of fairly precise adjustments of heat balance but is effective only within a relatively narrow range of environmental temperatures.

Behavioral Thermoregulation Is Governed by Thermal Sensation and Comfort

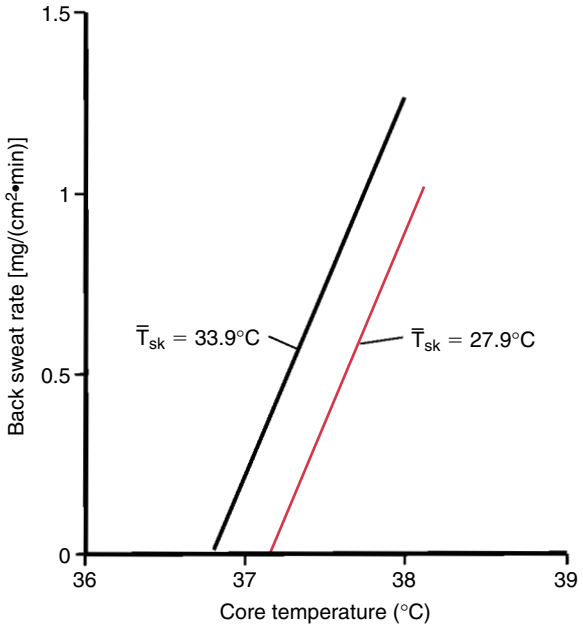
Sensory information about body temperatures is an essential part of both behavioral and physiological thermoregulation. The distinguishing feature of behavioral thermoregulation is the involvement of consciously directed efforts to regulate body temperature. Thermal discomfort provides the necessary motivation for thermoregulatory behavior, and behavioral thermoregulation acts to reduce both the discomfort and the physiological strain imposed by a stressful thermal environment. For this reason, the zone of thermoneutrality is characterized by both thermal comfort and the absence of shivering and sweating.

Warmth and cold on the skin are felt as either comfortable or uncomfortable, depending on whether they decrease or increase the physiological strain—a shower temperature that feels pleasant after strenuous exercise may be uncomfortably chilly on a cold winter morning. The processing of thermal information in behavioral thermoregulation is not as well understood as it is in physiological thermoregulation. However, perceptions of thermal sensation and comfort respond much more quickly than core temperature or physiological thermoregulatory responses to changes in environmental temperature and, thus, appear to anticipate changes in the body's thermal state. Such an anticipatory feature would be advantageous, since it would reduce the need for frequent small behavioral adjustments.

Physiological Thermoregulation Operates Through Graded Control of Heat-Production and Heat-Loss Responses

Familiar inanimate control systems, such as most refrigerators and heating and air-conditioning systems, operate at only two levels: on and off. In a steam heating system, for example, when the indoor temperature falls below the desired level, the thermostat turns on the burner under the boiler; when the temperature is restored to the desired level, the thermostat turns the burner off. Rather than operating at only two levels, most physiological control systems produce a graded response according to the size of the disturbance in the regulated variable. In many instances, changes in the controlled variables are proportional to displacements of the regulated variable from some threshold value; such control systems are called **proportional control systems**.

The control of heat-dissipating responses is an example of a proportional control system. Figure 29.9 shows how reflex control of two heat-dissipating responses, sweating and skin blood flow, depends on body core temperature and mean skin temperature. Each response has a core temperature threshold—a temperature at which the response starts to increase—and this threshold depends on mean skin tem-



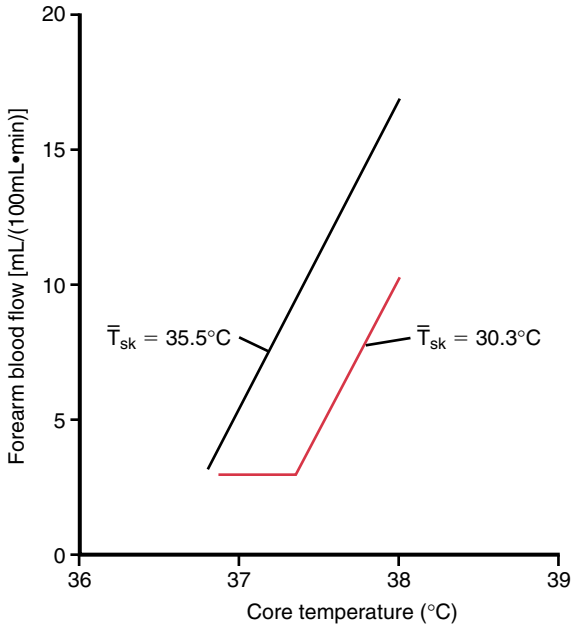


FIGURE 29.9 **Control of heat-dissipating responses.** These graphs show the relations of back (scapular) sweat rate (left) and forearm blood flow (right) to core temperature and mean skin temperatures ($_{sk}$). In these experiments, core temperature was increased by exercise. (Left: Based on data from Sawka MN, Gonzalez RR, Drolet LL, et al. Heat exchange during upper- and lower-body exercise. J Appl Physiol 1984;57:1050–1054. Right: Modified from Wenger CB, Roberts MF, Stolwijk JAJ, et al. Forearm blood flow during body temperature transients produced by leg exercise. J Appl Physiol 1975;38:58–63.)

perature. 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. In humans, a change of 1°C in core temperature elicits about 9 times as great a thermoregulatory response as a 1°C change in mean skin temperature. (Besides its effect on the reflex signals, skin temperature has a local effect that modifies the response of the blood vessels and sweat glands to the reflex signal, discussed later.)

Cold stress elicits increases in metabolic heat production through shivering and nonshivering thermogenesis. **Shivering** is a rhythmic oscillating tremor of skeletal muscles. The **primary motor center for shivering** lies in the dorsomedial part of the posterior hypothalamus and is normally inhibited by signals of warmth from the preoptic area of the hypothalamus. In the cold, these inhibitory signals are withdrawn, and the primary motor center for shivering sends impulses down the brainstem and lateral columns of the spinal cord to anterior motor neurons. Although these impulses are not rhythmic, they increase muscle tone, thereby increasing metabolic rate somewhat. Once the tone exceeds a critical level, the contraction of one group of muscle fibers stretches the muscle spindles in other fiber groups in series with it, eliciting contractions from those groups of fibers via the stretch reflex, and so on; thus, the rhythmic oscillations that characterize frank shivering begin.

Shivering occurs in bursts, and the "shivering pathway" is inhibited by signals from the cerebral cortex, so that voluntary muscular activity and attention can suppress shivering. Since the limbs are part of the shell in the cold, trunk and neck muscles are preferentially recruited for shivering—the **centralization of shivering**—to help retain the heat produced during shivering within the body core; and the familiar experience of teeth chattering is one of the earliest signs of shivering. As with heat-dissipating responses, the control of shivering depends on both core and skin temperatures, but the details of its control are not precisely understood.

The Central Nervous System Integrates Thermal Information From the Core and the Skin

Temperature receptors in the body core and skin transmit information about their temperatures through afferent nerves to the brainstem and, especially, the hypothalamus, where much of the integration of temperature information occurs. The sensitivity of the thermoregulatory system to core temperature enables it to adjust heat production and heat loss to resist disturbances in core temperature. Sensitivity to mean skin temperature lets the system respond appropriately to mild heat or cold exposure with little change in body core temperature, so that changes in body heat as a result of changes in environmental temperature take place almost entirely in the peripheral tissues (see Fig. 29.2). For example, the skin temperature of someone who enters a hot environment may rise and elicit sweating even if there is no change in core temperature. On the other hand, an increase in heat production within the body, as during exercise, elicits the appropriate heat-dissipating responses through a rise in core temperature.

Core temperature receptors involved in controlling thermoregulatory responses are unevenly distributed and are concentrated in the hypothalamus. 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, and this area contains many neurons that increase their firing rate in response to either warming or cooling. Thermal receptors have been reported elsewhere in the core of laboratory animals, including the heart, pulmonary vessels, and spinal cord, but the thermoregulatory role of core thermal receptors outside the CNS is unknown.

Consider what happens when some disturbance—say, an increase in metabolic heat production resulting from exercise—upsets the thermal balance. Additional heat is stored in the body, and core temperature rises. The central thermoregulatory controller receives information about these changes from the thermal receptors and elicits appropriate heat-dissipating responses. Core temperature continues to rise, and these responses continue to increase until they are sufficient to dissipate heat as fast as it is being produced, restoring heat balance and preventing further increases in body temperatures. In the language of control theory, the rise in core temperature that elicits heat-dissipating responses sufficient to reestablish thermal balance during exercise is an example of a **load error**. A load error is characteristic of any proportional control system that is resisting the effect of some imposed disturbance or "load." Although the disturbance in this example is exercise, the same principle applies if the disturbance is a decrease in metabolic rate or a change in the environment. However, if the disturbance is in the environment, most of the temperature change will be in the skin and shell rather than in the core; if the disturbance produces a net loss of heat, the body will restore heat balance by decreasing heat loss and increasing heat production.

Relation of Controlling Signal to Thermal Integration and Set Point. Both sweating and skin blood flow depend on core and skin temperatures in the same way, and changes in the threshold for sweating are accompanied by similar changes in the threshold for vasodilation. We may, therefore, think of the central thermoregulatory controller as generating one thermal command signal for the control of both sweating and skin blood flow (Fig. 29.10). This signal is based on the information about core and skin temperatures that the controller receives and on the thermoregulatory **set point**—the target level of core temperature, or the setting of the body's "thermostat." In the operation of the thermoregulatory system, it is a reference point that determines the thresholds of all of the thermoregulatory responses. Shivering and thermal comfort are affected by changes in the set point in the same way as sweating and

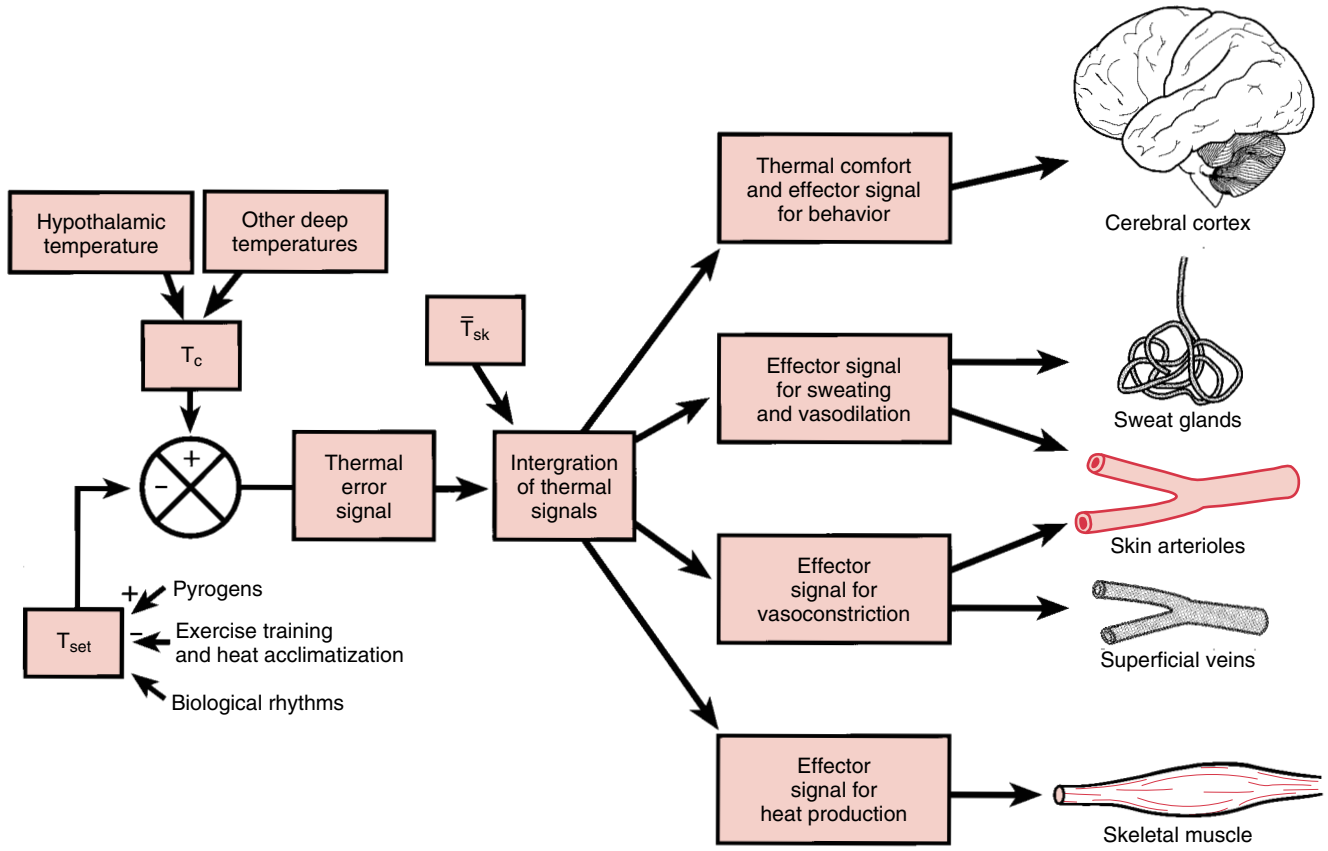


FIGURE 29.10 Control of human thermoregulatory responses. The plus and minus signs next to the inputs to T_{set} indicate that pyrogens raise the set point and heat acclimatization lowers it. Core temperature (T_c) is compared with the set point (T_{set}) to generate an error signal, which is integrated with thermal input from the skin to produce effector signals for the thermoregulatory responses.

skin blood flow. However, our understanding of the control of shivering is insufficient to say whether it is controlled by the same command signal as sweating and skin blood flow. (Thermal comfort, as we saw earlier, seems not to be controlled by the same command signal.)

Effect of Nonthermal Inputs on Thermoregulatory Responses. Each thermoregulatory response may be affected by inputs other than body temperatures and factors that influence the set point. We have already noted that voluntary activity affects shivering and certain hormones affect metabolic heat production. In addition, nonthermal factors may produce a burst of sweating at the beginning of exercise, and emotional effects on sweating and skin blood flow are matters of common experience. Skin blood flow is the thermoregulatory response most influenced by nonthermal factors because of its potential involvement in reflexes that function to maintain cardiac output, blood pressure, and tissue O_2 delivery under a variety of disturbances, including heat stress, postural changes, hemorrhage, and exercise.

Several Factors May Change the Thermoregulatory Set Point

Fever elevates core temperature at rest, heat acclimatization decreases it, and time of day and (in women) the phase of the menstrual cycle change it in a cyclic fashion. Core temperature at rest varies in an approximately sinusoidal fashion with time of day. The minimum temperature occurs at night, several hours before awaking, and the maximum, which is 0.5 to 1°C higher, occurs in the late afternoon or evening (see Fig. 29.3). This pattern coincides with patterns of activity and eating but does not depend on them, and it occurs even during bed rest in fasting subjects. This pattern is an example of a **circadian rhythm**, a rhythmic pattern in a physiological function with a period of about 1 day. During the menstrual cycle, core temperature is at its lowest point just before ovulation; during the next few days, it rises 0.5 to 1°C to a plateau that persists through most of the luteal phase. Each of these factors—fever, heat acclimatization, the circadian rhythm, and the menstrual cycle—change the core temperature at rest by changing the thermoregulatory set point, producing corresponding changes in the thresholds for all of the thermoregulatory responses.

Peripheral Factors Modify the Responses of Skin Blood Vessels and Sweat Glands

The skin is the organ most directly affected by environmental temperature. Skin temperature influences heat loss responses not only through reflex actions (see Fig. 29.9), but also through direct effects on the skin blood vessels and sweat glands.

Skin Temperature and Cutaneous Vascular and Sweat Gland Responses. Local temperature changes act on skin blood vessels in at least two ways. First, local cooling potentiates (and heating weakens) the constriction of blood vessels in response to nerve signals and vasoconstrictor substances. (At very low temperatures, however, cold-induced vasodilation increases skin blood flow, as discussed later.) Second, in skin regions where active vasodilation occurs, local heating causes vasodilation (and local cooling causes vasoconstriction) through a direct action on the vessels, independent of nerve signals. The local vasodilator effect of skin temperature is especially strong above 35°C; and, when the skin is warmer than the blood, increased blood flow helps cool the skin and protect it from heat injury, unless this response is impaired by vascular disease. Local thermal effects on sweat glands parallel those on blood vessels, so local heating potentiates (and local cooling diminishes) the local sweat gland response to reflex stimulation or ACh, and intense local heating elicits sweating directly, even in skin whose sympathetic innervation has been interrupted surgically.

Skin Wettedness and the Sweat Gland Response. During prolonged heat exposure (lasting several hours) with high sweat output, sweating rates gradually decline and the response of sweat glands to local cholinergic drugs is reduced. This reduction of sweat gland responsiveness is sometimes called sweat gland "fatigue." Wetting the skin makes the stratum corneum swell, mechanically obstructing the sweat gland ducts and causing a reduction in sweat secretion, an effect called **hidromeiosis**. The glands' responsiveness can be at least partly restored if air movement increases or humidity is reduced, allowing some of the sweat on the skin to evaporate. Sweat gland fatigue may involve processes besides hidromeiosis, since prolonged sweating also causes histological changes, including the depletion of glycogen, in the sweat glands.

THERMOREGULATORY RESPONSES DURING EXERCISE

Intense exercise may increase heat production within the body 10-fold or more, requiring large increases in skin blood flow and sweating to reestablish the body's heat balance. Although hot environments also elicit heat-dissipating responses, exercise ordinarily is responsible for the greatest demands on the thermoregulatory system for heat dissipation. Exercise provides an important example of how the thermoregulatory system responds to a disturbance in heat balance. In addition, exercise and thermoregulation impose competing demands on the circulatory system because exercise requires large increases in blood flow to exercising muscle, while the thermoregulatory responses to exercise require increases in skin blood flow. Muscle blood flow during exercise is several times as great as skin blood flow, but the increase in skin blood flow is responsible for disproportionately large demands on the cardiovascular system, as discussed below. Finally, if the water and electrolytes lost through sweating are not replaced, the resulting reduction in plasma volume will eventually create a further challenge to cardiovascular homeostasis.

Core Temperature Rises During Exercise, Triggering Heat-Loss Responses

As previously mentioned, the increased heat production during exercise causes an increase in core temperature, which in

turn elicits heat-loss responses. Core temperature continues to rise until heat loss has increased enough to match heat production, and core temperature and the heat-loss responses reach new steady-state levels. Since the heat-loss responses are proportional to the increase in core temperature, the increase in core temperature at steady state is proportional to the rate of heat production and, thus, to the metabolic rate.

A change in ambient temperature causes changes in the levels of sweating and skin blood flow necessary to maintain any given level of heat dissipation. However, the change in ambient temperature also elicits, via direct and reflex effects of the accompanying skin temperature changes, altered responses in the right direction. For any given rate of heat production, there is a certain range of environmental conditions within which an ambient temperature change elicits the necessary changes in heat-dissipating responses almost entirely through the effects of skin temperature changes, with virtually no effect on core temperature. (The limits of this range of environmental conditions depend on the rate of heat production and such individual factors as skin surface area and state of heat acclimatization.) Within this range, the core temperature reached during exercise is nearly independent of ambient temperature; for this reason, it was once believed that the increase in core temperature during exercise is caused by an increase in the thermoregulatory set point, as during fever. As noted, however, the increase in core temperature with exercise is an example of a load error rather than an increase in set point.

This difference between fever and exercise is shown in Figure 29.11. Note that, although heat production may increase substantially (through shivering), when core temperature is rising early during fever, it need not stay high to maintain the fever; in fact, it 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 is necessary to sustain it. Also, while core temperature is rising during fever, the rate of heat loss is, if anything, lower than it was before the fever began. During exercise, however, the heat-dissipating responses and the rate of heat loss start to increase early and continue increasing as core temperature rises.

Exercise in the Heat Can Threaten Cardiovascular Homeostasis

The rise in core temperature during exercise increases the temperature difference between the core and the skin somewhat, but not nearly enough to match the increase in metabolic heat production. Therefore, as we saw earlier, skin blood flow must increase to carry all of the heat that is produced to the skin. In a warm environment, where the temperature difference between core and skin is relatively small, the necessary increase in skin blood flow may be several liters per minute.

Impaired Cardiac Filling During Exercise in the Heat. The work of providing the skin blood flow required for thermoregulation in the heat may impose a heavy burden on a diseased heart, but in healthy people, the major car-

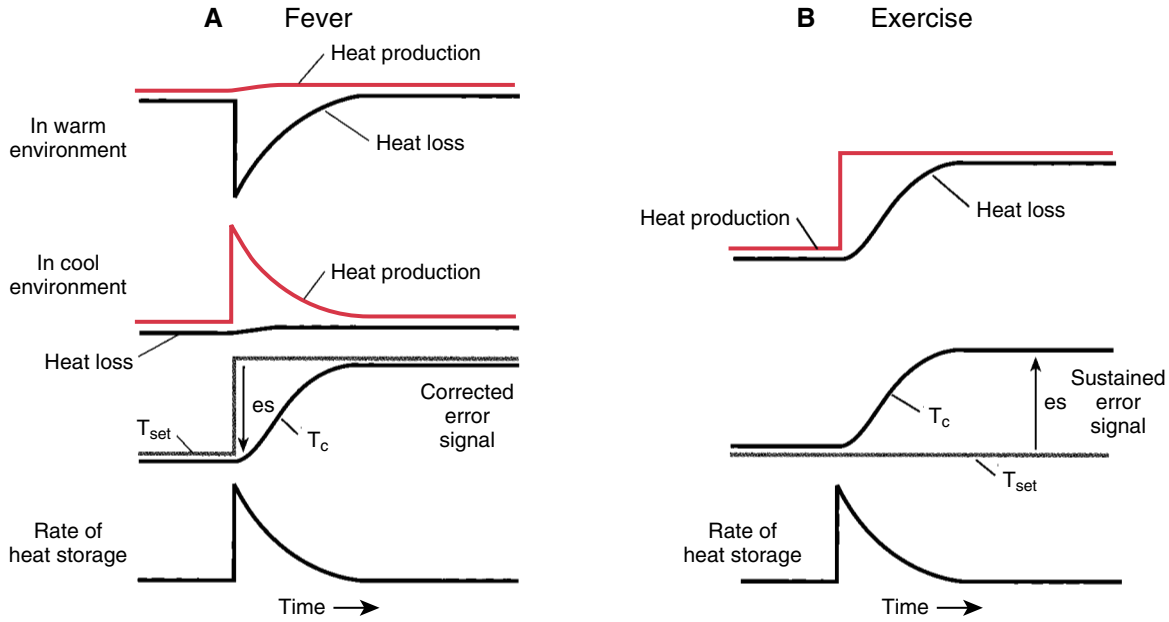


FIGURE 29.11 **Thermal events during fever and exercise.** **A**, The development of fever. **B**, The increase in core temperature (T_c) during exercise. The error signal is the difference between core temperature (T_c) and the set point (T_{set}). At the start of a fever, T_{set} has risen, so that T_{set} is higher than T_c and es is negative. At steady state, T_c has risen to equal the new level of T_{set} and es is corrected (i.e., it returns to zero.) At the start of exercise, $T_c = T_{set}$, so that es = 0. At steady state, T_{set} has not changed but T_c has increased and is greater than T_{set}, producing a sustained error signal, which is equal to the load error. (The error signal, or load error, is here represented with an arrow pointing downward for $T_c < T_{set}$ and with an arrow pointing upward for $T_c > T_{set}$.) (Modified from Stitt JT. Fever versus hyperthermia. Fed Proc 1979;38:39–43.)

diovascular burden of heat stress results from impaired venous return. As skin blood flow increases, the dilated vascular bed of the skin becomes engorged with large volumes of blood, reducing central blood volume and cardiac filling (Fig. 29.12). Stroke volume is decreased, and a higher heart rate is required to maintain cardiac output. These effects are aggravated by a decrease in plasma volume if the large amounts of salt and water lost in the sweat are not replaced. Since the main cation in sweat is sodium, disproportionately much of the body water lost in sweat is at the expense of extracellular fluid, including plasma, although this effect is mitigated if the sweat is dilute.

Compensatory Responses During Exercise in the Heat. Several reflex adjustments help maintain cardiac filling, cardiac output, and arterial pressure during exercise and heat stress. The most important of these is constriction of the renal and splanchnic vascular beds. A reduction in blood flow through these beds allows a corresponding diversion of cardiac output to the skin and the exercising muscles. In addition, since the splanchnic vascular beds are compliant, a decrease in their blood flow reduces the amount of blood pooled in them (see Fig. 29.12), helping compensate for decreases in central blood volume caused by reduced plasma volume and blood pooling in the skin.

The degree of vasoconstriction is graded according to the levels of heat stress and exercise intensity. During strenuous exercise in the heat, renal and splanchnic blood flows may fall to 20% of their values in a cool resting subject. Such intense splanchnic vasoconstriction may produce mild ischemic injury to the gut, helping explain the intestinal symptoms some athletes experience after endurance events. The cutaneous veins constrict during exercise; since most of the vascular volume is in the veins, constriction makes the cutaneous vascular bed less easily distensible and reduces peripheral pooling. Because of the essential role of skin blood flow in thermoregulation during exercise and heat stress, the body preferentially compromises splanchnic and renal flow for the sake of cardiovascular homeostasis. Above a certain level of cardiovascular strain, however, skin blood flow, too, is compromised.

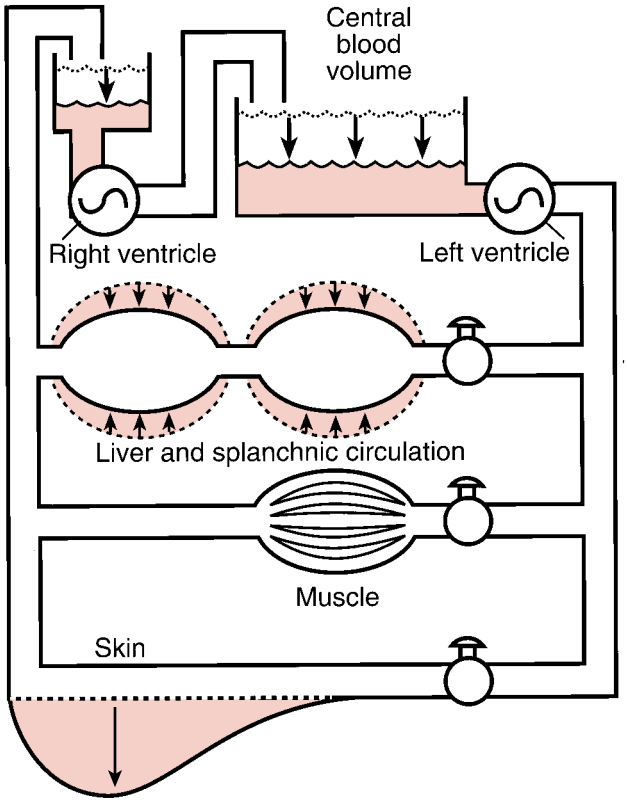


FIGURE 29.12 Cardiovascular strain and compensatory responses during heat stress. This figure first shows the effects of skin vasodilation on peripheral pooling of blood and the thoracic reservoirs from which the ventricles are filled; and second, the effects of compensatory vasomotor adjustments in the splanchnic circulation. The valves on the right represent the resistance vessels that control blood flow through the liver/splanchnic, muscle, and skin vascular beds. Arrows show the direction of the changes during heat stress. (Modified from Rowell LB. Cardiovascular aspects of human thermoregulation. Circ Res 1983;52:367–379.)

HEAT ACCLIMATIZATION

Prolonged or repeated exposure to stressful environmental conditions elicits significant physiological changes, called **acclimatization**, that reduce the resulting strain. (Such changes are often referred to as *acclimation* when produced in a controlled experimental setting.) Some degree of heat acclimatization occurs either by heat exposure alone or by regular strenuous exercise, which raises core temperature and provokes heat-loss responses. Indeed, the first summer heat wave produces enough heat acclimatization that most people notice an improvement in their level of energy and general feeling of well-being after a few days. However, the acclimatization response is greater if heat exposure and exercise are combined, causing a greater rise of internal temperature and more profuse sweating. Evidence of acclimatization appears in the first few days of combined exercise and heat exposure, and most of the improvement in heat tolerance occurs within 10 days. The effect of heat acclimatization on performance can be dramatic, and acclimatized subjects can easily complete exercise in the heat that earlier was difficult or impossible.

Heat Acclimatization Includes Adjustments in Heart Rate, Temperatures, and Sweat Rate

Cardiovascular adaptations that reduce the heart rate required to sustain a given level of activity in the heat appear quickly and reach nearly their full development within 1 week. Changes in sweating develop more slowly. After acclimatization, sweating begins earlier and at a lower core temperature (i.e., the core temperature threshold for sweating is reduced). The sweat glands become more sensitive to cholinergic stimulation, and a given elevation in core temperature elicits a higher sweat rate; in addition, the glands become resistant to hidromeiosis and fatigue, so higher sweat rates can be sustained. These changes reduce the levels of core and skin temperatures reached during a period of exer-

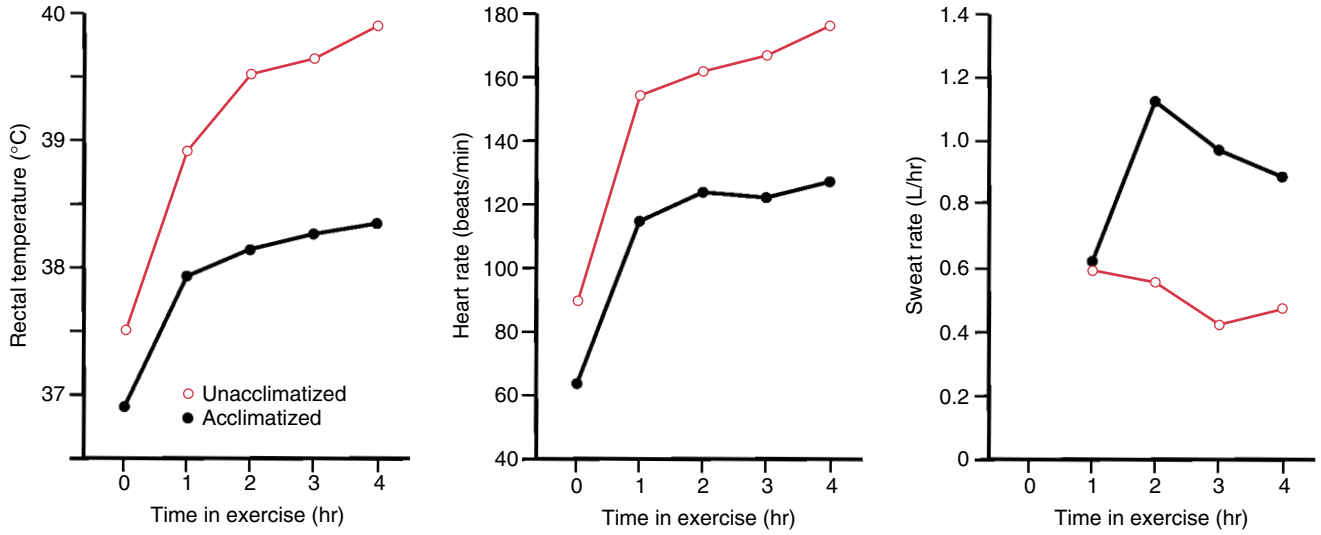


FIGURE 29.13 **Heat acclimatization.** These graphs show rectal temperatures, heart rates, and sweat rates during 4 hours' exercise (bench stepping, 35 W mechanical power) in humid heat (33.9°C dry bulb, 89% relative humidity, 35 torr ambient vapor pressure) on the first and last days of a 2-week program of acclimatizaton to humid heat. (Modified from Wenger CB. Human heat acclimatization. In: Pandolf KB, Sawka MN, Gonzalez RR, eds. Human Performance Physiology and Environmental Medicine at Terrestrial Extremes. Indianapolis: Benchmark, 1988;153–197. Based on data from Wyndham CH, Strydom NB, Morrison JF, et al. Heat reactions of Caucasians and Bantu in South Africa. J Appl Physiol 1964;19:598–606.)

cise in the heat, increase the sweat rate, and enable one to exercise longer. The threshold for cutaneous vasodilation is reduced along with the threshold for sweating, so heat transfer from the core to the skin is maintained. The lower heart rate and core temperature and the higher sweat rate are the three classical signs of heat acclimatization (Fig. 29.13).

Changes in Fluid and Electrolyte Balance Also Occur With Heat Acclimatization

During the first week, total body water and, especially, plasma volume increase. These changes likely contribute to the cardiovascular adaptations. Later, the fluid changes seem to diminish or disappear, although the cardiovascular adaptations persist. In an unacclimatized person, sweating occurs mostly on the chest and back, but during acclimatization, especially in humid heat, the fraction of sweat secreted on the limbs increases to make better use of the skin surface for evaporation. An unacclimatized person who is sweating profusely can lose large amounts of sodium. With acclimatization, the sweat glands become able to conserve sodium by secreting sweat with a sodium concentration as low as 5 mmol/L. This effect is mediated through aldosterone, which is secreted in response to sodium depletion and to exercise and heat exposure. The sweat glands respond to aldosterone more slowly than the kidneys, requiring several days; unlike the kidneys, the sweat glands do not escape the influence of aldosterone when sodium balance has been restored, but continue to conserve sodium for as long as acclimatization persists.

The cell membranes are freely permeable to water, so that any osmotic imbalance between the intracellular and extracellular compartments is rapidly corrected by the movement of water across the cell membranes (see Chapter 2). One important consequence of the salt-conserving response of the sweat glands is that the loss of a given volume of sweat causes a smaller decrease in the volume of the extracellular space than if the sodium concentration of the sweat is high (Table 29.3). Other consequences are discussed in Clinical Focus Box 29.1.

Heat acclimatization is transient, disappearing in a few weeks if not maintained by repeated heat exposure. The components of heat acclimatization are lost in the order in which they were acquired; the cardiovascular changes decay more quickly than the reduction in exercise core temperature and sweating changes.

RESPONSES TO COLD

The body maintains core temperature in the cold by minimizing heat loss and, when this response is insufficient, increasing heat production. Reducing shell conductance is the chief physiological means of heat conservation in humans. Furred or hairy animals also can increase the thickness of their coat and, thus, its insulating properties by making the hairs stand on end. This response, called **piloerection**, makes a negligible contribution to heat conservation in humans, but manifests itself as gooseflesh.

Blood Vessels in the Shell Constrict to Conserve Heat

The constriction of cutaneous arterioles reduces skin blood flow and shell conductance. 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 the cold.

TABLE 29.3 **Effect of Sweat Secretion on Body Fluid Compartments and Plasma Sodium Concentration[a]**

		Extracellular Space		Intracellular Space		Total Body Water			
Subject	Condition	Volume (L)	Osmotic Content (mOsm)	Volume (L)	Osmotic Content (mOsm)	Volume (L)	Osmotic Content (mOsm)	Osmolality (mOsm/kg)	Plasma $[Na^+]$ (mmol/L)
	Initial	15	4,350	25	7,250	40	11,600	290	140
A	Loss of 5 L of sweat, 120 mOsm/L, 60 mmol Na^+/L	11.9	3,750	23.1	7,250	35	11,000	314	151
	Above condition accompanied by intake of 5 L water	13.6	3,750	26.4	7,250	40	11,000	275	132
B	Loss of 5 L of sweat, 20 mOsm/L, 10 mmol Na^+/L	12.9	4,250	22.1	7,250	35	11,500	329	159
	Above condition accompanied by intake of 5 L water	14.8	4,250	25.2	7,250	40	11,500	288	139

[a] Each subject has total body water of 40 L. The sweat of subject A has a relatively high $[Na^+]$ of 60 mmol/L while that of subject B has a relatively low $[Na^+]$ of 10 mmol/L. Volumes of the extracellular and intracellular spaces are calculated assuming that water moves between the two spaces as needed to maintain osmotic balance.

CLINICAL FOCUS BOX 29.1

Water and Salt Depletion as a Result of Sweating

Changes in fluid and electrolyte balance are probably the most frequent physiological disturbances associated with sustained exercise and heat stress. Water loss via the sweat glands can exceed 1 L/hr for many hours. Salt loss in the sweat is variable; however, since sweat is more dilute than plasma, sweating always results in an increase in the osmolality of the fluid remaining in the body, and increased plasma $[Na^+]$ and $[Cl^-]$, as long as the lost water is not replaced.

Because people who secrete large volumes of sweat usually replace at least some of their losses by drinking water or electrolyte solutions, the final effect on body fluids may vary. In Table 29.3, the second and third conditions (subject A) represent the effects on body fluids of sweat losses alone and combined with replacement by an equal volume of plain water, respectively, for someone producing sweat with a $[Na^+]$ and $[Cl^-]$ in the upper part of the normal range. By contrast, the fourth and fifth conditions (subject B) represent the corresponding effects for a heat-acclimatized person secreting dilute sweat. Comparing the effects on these two individuals, we note: (1) The more dilute the sweat that is secreted, the greater the increase in osmolality and plasma $[Na^+]$ if no fluid is replaced; (2) Extracellular fluid volume, a major determinant of plasma volume (see Chapter 18), is greater in subject B (secreting dilute sweat) than in subject A (secreting saltier sweat), whether or not water is replaced; and (3) Drinking plain water allowed subject B to maintain plasma sodium and extracellular fluid volume almost unchanged while secreting 5 L of sweat. In subject A, however, drinking the same amount of water reduced plasma $[Na^+]$ by 8 mmol/L, and failed to prevent a decrease of almost 10% in extracellular fluid volume. In 5 L of sweat, subject A lost 17.5 g of salt, somewhat more than the daily salt intake in a normal Western diet, and he is becoming salt-depleted.

Thirst is stimulated by increased osmolality of the extracellular fluid, and by decreased plasma volume via a reduction in the activity of the cardiovascular stretch receptors (see Chapter 18). When sweating is profuse, however, thirst usually does not elicit enough drinking to replace fluid as rapidly as it is lost, so that people exercising in the heat tend to become progressively dehydrated—in some cases losing as much as 7 to 8% of body weight—and restore normal fluid balance only during long periods of rest or at meals. Depending on how much of his fluid losses he replaces, subject B may either be hypernatremic and dehydrated or be in essentially normal fluid and electrolyte balance. (If he drinks fluid well in excess of his losses, he may become overhydrated and **hyponatremic**, but this is an unlikely occurrence.) However, subject A, who is somewhat salt depleted, may be very dehydrated and hypernatremic, normally hydrated but hyponatremic, or somewhat dehydrated with plasma $[Na^+]$ anywhere in between these two extremes. Once subject A replaces all the water lost as sweat, his extracellular fluid volume will be about 10% below its initial value. If he responds to the accompanying reduction in plasma volume by continuing to drink water, he will become even more hyponatremic than shown in Table 29.3.

The disturbances shown in Table 29.3, while physiologically significant and useful for illustration, are not likely to require clinical attention. Greater disturbances, with correspondingly more severe clinical effects, may occur. The consequences of the various possible disturbances of salt and water balance can be grouped as effects of decreased plasma volume secondary to decreased extracellular fluid volume, effects of hypernatremia, and effects of hyponatremia.

(continued)

(Many penetrating veins connect the superficial veins to the deep veins, so that 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. Therefore, some of the heat contained in the arterial blood as it enters the limbs takes a "short circuit" back to the core. When the arterial blood reaches the skin, it is already cooler than the core, so it loses less heat to the skin than it otherwise would. (When the superficial veins dilate in the heat, most venous blood returns via superficial veins so as to maximize core-to-skin heat flow.) The transfer of heat from arteries to veins by this short circuit is called **countercurrent heat exchange**. This mechanism can cool the blood in the radial artery of a cool but comfortable subject to as low as 30°C by the time it reaches the wrist.

As we saw earlier, the shell's insulating properties increase in the cold as its blood vessels constrict and its thickness increases. Furthermore, the shell includes a fair amount of skeletal muscle in the cold, and although muscle blood flow is believed not to be affected by thermoregulatory reflexes, it is reduced by direct cooling. In a cool subject, the resulting reduction in muscle blood flow adds to the shell's insulating properties. As the blood vessels in the shell constrict, blood is shifted to the central blood reservoir in the thorax. This shift produces many of the same effects as an increase in blood volume, including so-called **cold diuresis** as the kidneys respond to the increased central blood volume.

Once skin blood flow is near minimal, metabolic heat production increases—almost entirely through shivering in human adults. Shivering may increase metabolism at rest by more than 4-fold—that is, to 350 to 400 W. Although it is often stated that shivering diminishes substantially after several hours and is impaired by exhaustive exercise, such effects are not well understood. In most laboratory mammals, chronic cold exposure also causes **nonshivering thermogenesis**, an increase in metabolic rate that is not due to muscle activity. Nonshivering thermogenesis appears to be elicited through sympathetic stimulation and circulating catecholamines. It occurs in many tissues, especially the liver and **brown fat**, a tissue specialized for nonshivering thermogenesis whose color is imparted by high concentrations of iron-containing respiratory enzymes. Brown fat is found in human infants, and nonshivering thermogenesis is important for their thermoregulation. The existence of brown fat and nonshivering thermogenesis in human adults is controversial, but there is some evi-

The circulatory effects of decreased volume are nearly identical to the effects of peripheral pooling of blood (see Fig. 29.12), and the combined effects of peripheral pooling and decreased volume will be greater than the effects of either alone. These effects include impairment of cardiac filling and cardiac output, and compensatory reflex reductions in renal, splanchnic, and skin blood flow. Impaired cardiac output leads to fatigue during exertion and decreased exercise tolerance; if skin blood flow is reduced, heat dissipation will be impaired. Exertional **rhabdomyolysis,** the injury of skeletal muscle fibers, is a frequent result of unaccustomed intense exercise. Myoglobin released from injured skeletal muscle cells appears in the plasma, rapidly enters the glomerular filtrate, and is excreted in the urine, producing **myoglobinuria** and staining the urine brown if enough myoglobin is present. This process may be harmless to the kidneys if urine flow is adequate; however, a reduction in renal blood flow reduces urine flow, increasing the likelihood that the myoglobin will cause renal tubular injury.

Hypernatremic dehydration is believed to predispose to heatstroke. Dehydration is often accompanied by both hypernatremia and reduced plasma volume. Hypernatremia impairs the heat-loss responses (sweating and increased skin blood flow) independently of any accompanying reduction in plasma volume and elevates the thermoregulatory set point. Hypernatremic dehydration promotes the development of high core temperature in multiple ways through the combination of hypernatremia and reduced plasma volume.

Even in the absence of sodium loss, overdrinking that exceeds the kidneys' ability to compensate dilutes all the body's fluid compartments, producing **dilutional hyponatremia**, which is also called **water intoxication** if it causes symptoms. The development of water intoxication requires either massive overdrinking, or a condition, such as the inappropriate secretion of arginine vasopressin, that impairs the excretion of free water by the kidneys. Overdrinking sufficient to cause hyponatremia may occur in patients with psychiatric disorders or disturbance of the thirst mechanism, or may be done with a mistaken intention of preventing or treating dehydration. However, individuals who secrete copious amounts of sweat with a high sodium concentration, like subject A or people with cystic fibrosis, may easily lose enough salt to become hyponatremic because of sodium loss. Some healthy young adults who come to medical attention for salt depletion after profuse sweating are found to have genetic variants of cystic fibrosis, which cause these individuals to have salty sweat without producing the characteristic digestive and pulmonary manifestations of cystic fibrosis.

As sodium concentration and osmolality of the extracellular space decrease, water moves from the extracellular space into the cells to maintain osmotic balance across the cell membranes. Most of the manifestations of hyponatremia are due to the resulting swelling of the brain cells. Mild hyponatremia is characterized by nonspecific symptoms such as fatigue, confusion, nausea, and headache, and may be mistaken for heat exhaustion. Severe hyponatremia can be a life-threatening medical emergency and may include seizures, coma, herniation of the brainstem (which occurs if the brain swells enough to exceed the capacity of the cranium) and death. In the setting of prolonged exertion in the heat, symptomatic hyponatremia is far less common than heat exhaustion, but potentially far more dangerous. Therefore, it is important not to treat a presumed case of heat exhaustion with large amounts of low-sodium fluids without first ruling out hyponatremia.

dence for functioning brown fat in the neck and mediastinum of outdoor workers.

Human Cold Acclimatization Confers a Modest Thermoregulatory Advantage

The pattern of human cold acclimatization depends on the nature of the cold exposure. It is partly for this reason that the occurrence of cold acclimatization in humans was controversial for a long time. Our knowledge of human cold acclimatization comes from both laboratory studies and studies of populations whose occupation or way of life exposes them repeatedly to cold temperatures.

Metabolic Changes in Cold Acclimatization. At one time it was believed that humans must acclimatize to cold as laboratory mammals do—by increasing their metabolic rate. There are a few reports of increased basal metabolic rate and, sometimes, thyroid activity in the winter. More often, however, increased metabolic rate has not been observed in studies of human cold acclimatization. In fact, several reports indicate the opposite response, consisting of a lower core temperature threshold for shivering, with a greater fall in core temperature and a smaller metabolic response during cold exposure. Such a response would spare metabolic energy and might be advantageous in an environment that is not so cold that a blunted metabolic response would allow core temperature to fall to dangerous levels.

Increased Tissue Insulation in Cold Acclimatization. A lower core-to-skin conductance (i.e., increased insulation by the shell) has often been reported in studies of cold acclimatization in which a reduction in the metabolic response to cold occurred. This increased insulation is not due to subcutaneous fat (in fact, it has been observed in very lean subjects), but apparently results from lower blood flow in the limbs or improved countercurrent heat exchange in the acclimatized subjects. In general, the cold stresses that elicit a lower shell conductance after acclimatization involve either cold water immersion or exposure to air that is chilly but not so cold as to risk freezing the vasoconstricted extremities.

Cold-Induced Vasodilation and the Lewis Hunting Response. As the skin is cooled below about 15°C, its blood flow begins to increase somewhat, a response called **cold-induced vasodilation** (CIVD). This response is elicited most easily in comfortably warm subjects and in skin rich in arteriovenous anastomoses (in the hands and feet). The mechanism has not been established but may involve a direct inhibitory effect of cold on the contraction of vascular smooth muscle or on neuromuscular transmission. The CIVD response varies greatly among individuals, and is usually rudimentary in hands and feet unaccustomed to cold exposure. After repeated cold exposure, CIVD begins earlier during cold exposure, produces higher levels of blood flow, and takes on a rhythmic pattern of alternating vasodilation and vasoconstriction. This is called the **Lewis hunting response** because the rhythmic pattern of blood flow suggests that it is "hunting" for its proper level. This response is often well developed in workers whose hands are exposed to cold, such as fishermen working with nets in cold water. Since the Lewis hunting response increases heat loss from the body somewhat, whether or not it is truly an example of acclimatization to cold is debatable. However, the response is advantageous because it keeps the extremities warmer, more comfortable, and functional and probably protects them from cold injury.

CLINICAL ASPECTS OF THERMOREGULATION

Temperature is important clinically because of the presence of fever in many diseases, the effects of many factors on tolerance to heat or cold stress, and the effects of heat or cold stress in causing or aggravating certain disorders.

Fever Enhances Defense Mechanisms

Fever may be caused by infection or noninfectious conditions (e.g., inflammatory processes such as collagen vascular diseases, trauma, neoplasms, acute hemolysis, immunologically-mediated disorders). **Pyrogens** are substances that cause fever and may be either exogenous or endogenous. Exogenous pyrogens are derived from outside the body; most are microbial products, microbial toxins, or whole microorganisms. The best studied of these is the lipopolysaccharide endotoxin of gram-negative bacteria. Exogenous pyrogens stimulate a variety of cells, especially monocytes and macrophages, to release endogenous pyrogens, polypeptides that cause the thermoreceptors in the hypothalamus (and perhaps elsewhere in the brain) to alter their firing rate and input to the central thermoregulatory controller, raising the thermoregulatory set point. This effect of endogenous pyrogens is mediated by the local synthesis and release of **prostaglandin E_2**. Aspirin and other drugs that inhibit the synthesis of prostaglandins also reduce fever.

Fever accompanies disease so frequently and is such a reliable indicator of the presence of disease that body temperature is probably the most commonly measured clinical index. Many of the body's defenses against infection and cancer are elicited by a group of polypeptides called **cytokines**; the endogenous pyrogen is usually a member of this group, **interleukin-1**. However, other cytokines, particularly **tumor necrosis factor**, **interleukin-6**, and the **interferons**, are also pyrogenic in certain circumstances. Elevated body temperature enhances the development of these defenses. If laboratory animals are prevented from developing a fever during experimentally induced infection, survival rates may be dramatically reduced. (Although, in this chapter, fever specifically means an elevation in core temperature a resulting from pyrogens, some authors use the term more generally to mean any significant elevation of core temperature.)

Many Factors Affect Thermoregulatory Responses and Tolerance to Heat and Cold

Regular physical exercise and heat acclimatization increase heat tolerance and the sensitivity of the sweating response. Aging has the opposite effect; in healthy 65-year-old men, the sensitivity of the sweating response is half of that in 25-

year-old men. Many drugs inhibit sweating, most obviously those used for their anticholinergic effects, such as atropine and scopolamine. In addition, some drugs used for other purposes, such as glutethimide (a sleep-inducing drug), tricyclic antidepressants, phenothiazines (tranquilizers and antipsychotic drugs), and antihistamines, also have some anticholinergic action. All of these and several others have been associated with heatstroke. Congestive heart failure and certain skin diseases (e.g., ichthyosis and anhidrotic ectodermal dysplasia) impair sweating, and in patients with these diseases, heat exposure and especially exercise in the heat may raise body temperature to dangerous levels. Lesions that affect the thermoregulatory structures in the brainstem can also alter thermoregulation. Such lesions can produce **hypothermia** (abnormally low core temperature) if they impair heat-conserving responses. However, **hyperthermia** (abnormally high core temperature) is a more usual result of brainstem lesions and is typically characterized by a loss of both sweating and the circadian rhythm of core temperature.

Certain drugs, such as barbiturates, alcohol, and phenothiazines, and certain diseases, such as hypothyroidism, hypopituitarism, congestive heart failure, and septicemia, may impair the defense against cold. (Septicemia, especially in debilitated patients, may be accompanied by hypothermia, instead of the usual febrile response to infection.) Furthermore, newborns and many healthy older adults are less able than older children and younger adults to maintain adequate body temperature in the cold. This failing appears to be due to an impaired ability to conserve body heat by reducing heat loss and to increase metabolic heat production in the cold.

Heat Stress Causes or Aggravates Several Disorders

The harmful effects of heat stress are exerted through cardiovascular strain, fluid and electrolyte loss and, especially in heatstroke, tissue injury whose mechanism is uncertain. In a patient suspected of having hyperthermia secondary to heat stress, temperature should be measured in the rectum, since hyperventilation may render oral temperature spuriously low.

Heat Syncope.

Heat syncope is circulatory failure resulting from a pooling of blood in the peripheral veins, with a consequent decrease in venous return and diastolic filling of the heart, resulting in decreased cardiac output and a fall of arterial pressure. Symptoms range from light-headedness and giddiness to loss of consciousness. Thermoregulatory responses are intact, so core temperature typically is not substantially elevated, and the skin is wet and cool. The large thermoregulatory increase in skin blood flow in the heat is probably the primary cause of the peripheral pooling. Heat syncope affects mostly those who are not acclimatized to heat, presumably because the plasma-volume expansion that accompanies acclimatization compensates for the peripheral pooling of blood. Treatment consists in laying the patient down out of the heat, to reduce the peripheral pooling of blood and improve the diastolic filling of the heart.

Heat Exhaustion.

Heat exhaustion, also called heat collapse, is probably the most common heat disorder, and represents a failure of cardiovascular homeostasis in a hot environment. Collapse may occur either at rest or during exercise, and may be preceded by weakness or faintness, confusion, anxiety, ataxia, vertigo, headache, and nausea or vomiting. The patient has dilated pupils and usually sweats profusely. As in heat syncope, reduced diastolic filling of the heart appears to have a primary role in the pathogenesis of heat exhaustion. Although blood pressure may be low during the acute phase of heat exhaustion, the baroreflex responses are usually sufficient to maintain consciousness and may be manifested in nausea, vomiting, pallor, cool or even clammy skin, and rapid pulse. Patients with heat exhaustion usually respond well to rest in a cool environment and oral fluid replacement. In more severe cases, however, intravenous replacement of fluid and salt may be required. Core temperature may be normal or only mildly elevated in heat exhaustion. However, heat exhaustion accompanied by hyperthermia and dehydration may lead to heatstroke. Therefore, patients should be actively cooled if rectal temperature is 40.6°C (105°F) or higher.

The reasons underlying the reduced diastolic filling in heat exhaustion are not fully understood. Hypovolemia contributes if the patient is dehydrated, but heat exhaustion often occurs without significant dehydration. In rats heated to the point of collapse, compensatory splanchnic vasoconstriction develops during the early part of heating, but is reversed shortly before the maintenance of blood pressure fails. A similar process may occur in heat exhaustion.

Heatstroke.

The most severe and dangerous heat disorder is characterized by high core temperature and the development of serious neurological disturbances with a loss of consciousness and, frequently, convulsions. **Heatstroke** occurs in two forms, classical and exertional. In the classical form, the primary factor is environmental heat stress that overwhelms an impaired thermoregulatory system, and most patients have preexisting chronic disease. In exertional heatstroke, the primary factor is high metabolic heat production. Patients with exertional heatstroke tend to be younger and more physically fit (typically, soldiers and athletes) than patients with the classical form. Rhabdomyolysis, hepatic and renal injury, and disturbances of blood clotting are frequent accompaniments of exertional heatstroke. The traditional diagnostic criteria of heatstroke—coma, hot dry skin, and rectal temperature above 41.3°C (106°F)—are characteristic of the classical form; however, patients with exertional heatstroke may have somewhat lower rectal temperatures and often sweat profusely. Heatstroke is a medical emergency, and prompt appropriate treatment is critically important to reducing morbidity and mortality. The rapid lowering of core temperature is the cornerstone of treatment, and it is most effectively accomplished by immersion in cold water. With prompt cooling, vigorous hydration, maintenance of a proper airway, avoidance of aspiration, and appropriate treatment of complications, most patients will survive, especially if they were previously healthy.

The pathogenesis of heatstroke is not well understood, but it seems clear that factors other than hyperthermia are

involved, even if the action of these other factors partly depends on the hyperthermia. Exercise may contribute more to the pathogenesis than simply metabolic heat production. Elevated plasma levels of several inflammatory cytokines have been reported in patients presenting with heatstroke, suggesting a systemic inflammatory component. No trigger for such an inflammatory process has been established, although several possible candidates exist. One possible trigger is some product(s) of the bacterial flora in the gut, perhaps including lipopolysaccharide endotoxins. Several lines of evidence suggest that sustained splanchnic vasoconstriction may produce a degree of intestinal ischemia sufficient to allow these products to "leak" into the circulation and activate inflammatory responses.

The preceding diagnostic categories are traditional. However, they are not entirely satisfactory for heat illness associated with exercise because many patients have laboratory evidence of tissue and cellular injury, but are classified as having heat exhaustion because they do not have the serious neurological disturbances that characterize heatstroke. Some more recent literature uses the term **exertional heat injury** for such cases. The boundaries of exertional heat injury, with heat exhaustion on one hand and heatstroke on the other, are not clearly and consistently defined, and these categories probably represent parts of a continuum.

Malignant hyperthermia, a rare process triggered by depolarizing neuromuscular blocking agents or certain inhalational anesthetics, was once thought to be a form of

CLINICAL FOCUS BOX 29.2

Hypothermia

Hypothermia is classified according to the patient's core temperature as mild (32 to 35°C), moderate (28 to 32°C), or severe (below 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 Q_{10} effect) on multiple physiological processes and differences in the degree of depression of each process.

Other than shivering, the most prominent features of mild and moderate hypothermia are due to depression of the central nervous system. Beginning with mood changes (commonly, apathy, withdrawal, and irritability), they progress to confusion and lethargy, followed by 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 a 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. Myocardial hypoxia also contributes. In more profound hypothermia, cardiac sounds become inaudible and pulse and blood pressure are unobtainable 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 from core temperatures as low as 17°C, so that "no one is dead until warm and dead." The usual causes of death during hypothermia are respiratory cessation and the failure of cardiac pumping, because of either ventricular fibrillation or direct depression of cardiac contraction.

Depression of renal tubular metabolism by cold impairs the reabsorption of sodium, causing a 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 a mixed respiratory and metabolic acidosis results, because of CO_2 retention and lactic acid accumulation and the cold-induced shift of the hemoglobin-O_2 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 in mild to moderate hypothermia may be warmed solely by providing abundant insulation to promote the retention of metabolically produced heat; those who are more severely affected require active rewarming. The most serious complication associated with treating hypothermia is the development of ventricular fibrillation. Vigorous handling of the patient may trigger this process, but an increase in the patient's circulation (e.g., associated with warming or skeletal muscle activity) may itself increase the susceptibility to such an occurrence, 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, acidic blood to the heart to cause a transient drop in the temperature and pH of the heart, increasing its susceptibility to ventricular fibrillation.

The diagnosis of hypothermia is usually straightforward in a patient rescued from the cold but may be far less clear in a patient in whom hypothermia is the result of a serious impairment of physiological and behavioral defenses against cold. A typical example is the older 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 because standard clinical thermometers are not graduated low enough (usually only to 34.4°C) to detect hypothermia and, in any case, do not register temperatures below the level to which the mercury has been shaken. Because of the depressant effect of hypothermia on the brain, the patient's condition may be misdiagnosed as cerebrovascular accident or other primary neurological disease. Recognition of this condition depends on the physician's considering it when examining a cool patient whose mental status is impaired and obtaining a true core temperature with a low-reading glass thermometer or other device.

heatstroke but is now known to be a distinct disorder that occurs in people with a genetic predisposition. In 90% of susceptible individuals, biopsied skeletal muscle tissue contracts on exposure to caffeine or halothane in concentrations having little effect on normal muscle. Susceptibility may be associated with any of several myopathies, but most susceptible individuals have no other clinical manifestations. The control of free (unbound) calcium ion concentration in skeletal muscle cytoplasm is severely impaired in susceptible individuals; and when an attack is triggered, calcium concentration rises abnormally, activating myosin ATPase and leading to an uncontrolled hypermetabolic process that rapidly increases core temperature. Treatment with dantrolene sodium, which appears to act by reducing the release of calcium ions from the sarcoplasmic reticulum, has dramatically reduced the mortality rate of this disorder.

Aggravation of Disease States by Heat Exposure. Other than producing specific disorders, heat exposure aggravates several other diseases. Epidemiological studies show that during unusually hot weather, mortality may be 2 to 3 times that normally expected for the months in which heat waves occur. Deaths ascribed to specific heat disorders account for only a small fraction of the excess mortality (i.e., the increase above the expected mortality). Most of the excess mortality is accounted for by deaths from diabetes, various diseases of the cardiovascular system, and diseases of the blood-forming organs.

Hypothermia Occurs When the Body's Defenses Against Cold Are Disabled or Overwhelmed

Hypothermia reduces metabolic rate via the Q_{10} effect and prolongs the time tissues can safely tolerate a loss of blood flow. Since the brain is damaged by ischemia soon after circulatory arrest, controlled hypothermia is often used to protect the brain during surgical procedures in which its circulation is occluded or the heart is stopped. Much of our knowledge about the physiological effects of hypothermia comes from observations of surgical patients.

During the initial phases of cooling, stimulation of shivering through thermoregulatory reflexes overwhelms the Q_{10} effect. Metabolic rate, therefore, increases, reaching a peak at a core temperature of 30 to 33°C. At lower core temperatures, however, metabolic rate is dominated by the Q_{10} effect, 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, the O_2 consumption is about 15%, and cardiac output 10%, of precooling values.

Hypothermia that is not induced for therapeutic purposes is called **accidental hypothermia** (Clinical Focus Box 29.2). It occurs in individuals whose defenses are impaired by drugs (especially ethanol, in the United States), disease, or other physical conditions and in healthy individuals who are immersed in cold water or become exhausted working or playing in the cold.

REVIEW QUESTIONS

DIRECTIONS: Each of the numbered items or incomplete statements in this section is followed by answers or by completions of the statement. Select the ONE lettered answer or completion that is BEST in each case.

1. Antipyretics such as aspirin effectively lower core temperature during fever, but they are not used to counteract the increase in core temperature that occurs during exercise. Which of the following best explains why it is inappropriate to use antipyretics for this purpose?
   (A) The increase in core temperature during exercise stimulates metabolism via the Q_{10} effect, helping to support the body's increased metabolic energy demands
   (B) A moderate increase in core temperature during exercise is harmless, so there is no benefit in preventing it
   (C) Antipyretics are ineffective during exercise because they act on a mechanism that operates during fever, but not to a significant degree during exercise
   (D) Antipyretics increase skin blood flow so as to dissipate more heat, increasing circulatory strain during exercise
   (E) The increased heat production during exercise greatly exceeds the ability of antipyretics to stimulate the responses for heat loss
2. A surgical sympathectomy has completely interrupted the sympathetic nerve supply to a patient's arm. How would one expect the thermoregulatory skin blood flow and sweating responses on that arm to be affected?

Vasoconstriction in the Cold	Vasodilation in the Heat	Sweating
(A) Abolished	Intact	Intact
(B) Abolished	Intact	Abolished
(C) Abolished	Abolished	Intact
(D) Abolished	Abolished	Abolished
(E) Intact	Abolished	Abolished

3. A person resting in a constant ambient temperature is tested in the early morning at 4:00 AM, and again in the afternoon at 4:00 PM. Compared to measurements made in the morning, one would expect to find in the afternoon:

Core Temperature	Sweating Threshold	Threshold for Cutaneous Vasodilation
(A) Unchanged	Higher	Lower
(B) Unchanged	Unchanged	Unchanged
(C) Higher	Higher	Higher
(D) Higher	Unchanged	Lower
(E) Lower	Lower	Lower

4. Compared to an unacclimatized person, one who is acclimatized to cold has
   (A) Higher metabolic rate in the cold, to produce more heat
   (B) Lower metabolic rate in the cold, to conserve metabolic energy
   (C) Lower peripheral blood flow in the cold, to retain heat
   (D) Higher blood flow in the hands and feet in the cold, to preserve their function
   (E) Various combinations of the above, depending on the environment that produced acclimatization
5. Which statement best describes how the elevated core temperature during fever affects the outcome of most bacterial infections?
   (A) Fever benefits the patient because most pathogens thrive best at the host's normal body temperature

(continued)

(B) Fever is beneficial because it helps stimulate the immune defenses against infection
(C) Fever is harmful because the accompanying protein catabolism reduces the availability of amino acids for the immune defenses
(D) Fever is harmful because the patient's higher temperature favors growth of the bacteria responsible for infection
(E) Fever has little overall effect either way

6. A manual laborer moves in March from Canada to a hot, tropical country and becomes acclimatized by working outdoors for a month. Compared with his responses on the first few days in the tropical country, for the same activity level after acclimatization one would expect higher
(A) Core temperature
(B) Heart rate
(C) Sweating rate
(D) Sweat salt concentration
(E) Thermoregulatory set point

In questions 7 to 8, assume a 70-kg young man with the following baseline characteristics: total body water (TBW) = 40 L, extracellular fluid (ECF) volume = 15 L, plasma volume = 3 L, body surface area = 1.8 m^2, plasma [Na^+] = 140 mmol/L. Heat of evaporation of water = 2,425 kJ/kg = 580 kcal/kg.

7. Our subject begins an 8-hour hike in the desert carrying 5 L of water in canteens. During the hike, he sweats at a rate of 1 L/hr, his sweat [Na^+] is 50 mmol/L, and he drinks all his water. After the end of his hike he rests and consumes 3 L of water. (For simplicity in calculations, assume that the plasma osmolality equals 2 times the plasma [Na^+].) What are his plasma sodium concentration and ECF volume after he has replaced all the water that he lost?

Plasma [Na^+] (mmol/L)	ECF Volume (L)
(A) 140.5	12.1
(B) 130	13.1
(C) 122.3	13.9
(D) 113.3	15.
(E) 113.3	13.9

8. Our subject is bicycling on a long road with a slight upward grade. His metabolic rate (*M* in the heat-balance equation) is 800 W (48 kJ/min). He performs mechanical work (against gravity, friction, and wind resistance) at a rate of 140 W. Air temperature is 20°C and h_c, the convective heat transfer coefficient, is 15 W/(m^2•°C). Assume that his mean skin temperature is 34°C, all the sweat he secretes is evaporated, respiratory water loss can be ignored, and net heat exchange by radiation is negligible. How rapidly must he sweat to achieve heat balance? (Remember that 1 W = 1 J/sec = 60 J/min.)
(A) 3.9 g/min
(B) 7.0 g/min
(C) 11.1 g/min
(D) 13.9 g/min
(E) 15.0 g/min

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