

Thermoregulation

Chapter 12

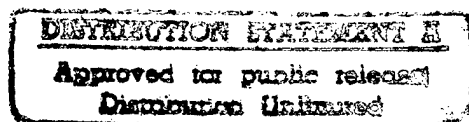
C. Bruce Wenger, M.D., Ph.D.,

Research Pharmacologist

US Army Research Institute of Environmental Medicine

Natick, Massachusetts 01760-5007

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Lying at the boundary between the body and the thermal environment, the skin is strategically placed for an important role in thermoregulation, and serves both as a source of thermal information and as an effector organ for controlling heat loss from the body. Living tissue is directly injured if it is heated to temperatures higher than about  $45^{\circ}\text{C}$ <sup>1</sup>, the level at which heating the skin causes pain, or if it is cooled so that ice crystals form in the cells. Because of its exposed location the skin is particularly vulnerable to injury by extremes of temperature in the immediate environment; and, in addition to its thermoregulatory responses, local vasodilator responses are elicited when tissue temperature rises toward  $40^{\circ}\text{C}$  or falls toward  $10^{\circ}\text{C}$ , which help to protect the skin against extremes of temperature.

FIG. 1 Human beings, like other homeotherms, spend substantial physiological resources maintaining their internal body temperatures near  $37^{\circ}\text{C}$  (Fig. 1). What biological advantage is gained by regulating body temperature within such a narrow band? Temperature is a fundamental physicochemical variable that profoundly affects many biological processes, both through configurational changes affecting the biological activities of protein molecules—e.g., enzymes, receptors, and membrane channels—and through a general effect on chemical reaction rates. Most reaction rates vary approximately as an exponential function of temperature ( $T$ ) within the physiological range, and raising  $T$  by  $10^{\circ}\text{C}$  increases the reaction rate by a factor of 2 to 3. A familiar clinical example of the effect of body temperature on metabolic processes is the rule that each  $1^{\circ}\text{C}$  of fever increases a patient's fluid and calorie needs  $13\%^2$ .

### BODY TEMPERATURES AND HEAT TRANSFER IN THE BODY

FIG. 2 The body is divided into a warm internal core and an outer shell<sup>3</sup>(Fig. 2). It is the temperature of the core, which includes the vital organs in the head and trunk, that is regulated within narrow limits. Although normal body temperature is conventionally taken to be  $37^{\circ}\text{C}$  ( $98.6^{\circ}\text{F}$ ), individual variation and such factors<sup>4,5</sup> as time of day, phase of the menstrual cycle<sup>6,7</sup>, and acclimatization to heat account for differences of up to about  $1^{\circ}\text{C}$  in core temperatures of healthy subjects at rest. In addition core temperature may increase several degrees with heavy exercise or fever (Fig. 1). Temperature-sensitive neurons and nerve endings at various core sites, including the spinal cord and especially the brain<sup>8,9</sup>, provide the thermoregulatory system with information about the level of core temperature. Shell temperature by contrast is not tightly regulated, and is strongly influenced by the environment. Nevertheless thermoregulatory responses greatly affect the temperature of the shell, and especially its outermost

layer, the skin. The shell's thickness depends on the environment and the need to conserve body heat. In a warm subject, 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.

The body loses heat only from tissues in contact with the environment, chiefly the skin. Since heat flows from warmer regions to cooler regions, the greatest heat flows within the body are those from major sites of heat production to the rest of the body, and from core to skin. Heat is transported within the body by two means: conduction through the tissues; and convection by the blood, the process by which flowing blood carries heat from warmer tissues to cooler tissues. Heat flow by conduction is proportional to the change of temperature with distance in the direction of heat flow, and the thermal conductivity of the tissues. As Table 1 shows, 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 capillaries have thin walls and, collectively, a large surface area, the capillary beds are the sites where heat exchange between tissue and blood is most efficient.

Since the shell lies between the core and the environment, all heat leaving the body via the skin must first pass through the shell. Thus the shell insulates the core from the environment. In a cool subject skin blood flow is low, so that core-to-skin heat transfer is dominated by conduction; and the subcutaneous fat layer adds to the insulation value of the shell, because it increases the thickness of the shell and has a conductivity only about 0.4 times that of dermis or muscle (Table 1). 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 that 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.

Skin temperature is important both in heat exchange and in thermoregulatory control. Skin temperature is affected by thermoregulatory responses such as skin blood flow and sweat secretion, and by heat exchange with underlying tissues and the environment. Skin temperature, in turn, is one of the major factors determining heat exchange with the environment. For these reasons, skin temperature provides the thermoregulatory system with important information about the need to conserve or lose body heat. Many bare nerve endings just under the skin are very sensitive to temperature. Depending on the relation of discharge rate to temperature, they are classified as either warm or cold receptors<sup>8,10</sup>. In addition to their responses when skin temperature is stable, these receptors have transient responses during temperature changes. With heating of the skin, warm receptors respond with a transient

burst of activity, while cold receptors respond with a transient suppression; and the reverse happens with cooling. Since skin temperature is not usually uniform over the body surface, a mean skin temperature ( $\bar{T}_{sk}$ ) is frequently calculated from temperature measurements at several sites.  $\bar{T}_{sk}$  is used both to summarize the input from skin temperature into the thermoregulatory system and, along with core temperature, to calculate a mean body temperature to represent the body's thermal state.

### BALANCE BETWEEN HEAT PRODUCTION AND HEAT LOSS

FIG. 3 Although the body exchanges some energy with the environment in the form of mechanical work, most is exchanged as heat, by conduction, convection, and radiation; and as latent heat through evaporation or (rarely) condensation of water (Fig. 3). If the sum of energy production and energy gain from the environment does not equal energy loss, the extra heat is "stored" in, or lost from, the body. This is summarized in the heat balance equation

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

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 (only to solid objects in practice, as explained later);  $W$  is rate of energy loss as mechanical work; and  $S$  is rate of heat storage in the body<sup>11,12</sup>, which is positive when mean body temperature is increasing.

### Metabolic Rate and Sites of Heat Production at Rest

Heat exchange with the environment can be measured by direct calorimetry in an insulated chamber specially constructed so that all heat and water vapor leaving the chamber can be captured and measured. From these measurements one can accurately determine the subject's heat loss, which, at steady state, is equal to metabolic rate. More frequently, metabolic rate is estimated by indirect calorimetry<sup>13</sup> based on measurements of  $O_2$  consumption, since virtually all energy available to the body depends ultimately on reactions that consume  $O_2$ . The heat production associated with consumption of one liter of  $O_2$  varies somewhat with the fuel—carbohydrate, fat, or protein—that is oxidized. For metabolism of a mixed diet, an average value of 20.2kJ (4.83kcal) per liter of  $O_2$  is often used. Since the ratio of  $CO_2$  produced to  $O_2$  consumed in the tissues is 1.0 for oxidation of carbohydrate, 0.71 for fat, and 0.80 for protein, the accuracy of indirect calorimetry can be improved by also measuring  $CO_2$

production and either estimating the amount of protein oxidized or calculating it from urinary nitrogen excretion.

Metabolic rate at rest is approximately proportional to body surface area. In a fasting young man it is about  $45\text{W/m}^2$  (81W or 70kcal/h for  $1.8\text{ m}^2$  body surface area, corresponding to an  $\text{O}_2$  consumption of about 240 ml/min.) At rest the trunk viscera and brain account for about 70% of energy production, even though they comprise only about 36% of the body mass (Table 2). Even during very mild exercise, however, the muscles are the chief source of metabolic energy production, and during heavy exercise they may account for up to 90% (Table 2). A healthy but sedentary young man performing moderate exercise may reach a metabolic rate of 600W; and a trained athlete performing intense exercise, 1400W or more. The overall mechanical efficiency of exercise varies enormously, depending on the activity; but at best, no more than one quarter of the metabolic energy is converted into mechanical work outside the body, and the remaining three quarters or more is converted into heat within the body<sup>14</sup>. Since exercising muscles produce so much heat, they may be nearly  $1^\circ\text{C}$  warmer than the core. They warm the blood that perfuses them; and this blood, returning to the core, warms the rest of the body.

### Heat Exchange with the Environment

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

Every surface emits energy as electromagnetic radiation with a power output that depends on its area, its temperature, and its emissivity (identical to its absorptivity), a number between 0 and 1 that depends on the nature of the surface and the wavelength of the emitted (or absorbed) radiation. Such thermal radiation has a characteristic distribution of power as a function of wavelength, which depends on the temperature of the surface. At ordinary tissue and environmental temperatures, virtually all of the emitted energy is in the infrared part of the spectrum, in a region where most surfaces have emissivities near 1, and thus both emit and absorb at nearly the theoretical maximum efficiency. However bodies like the sun that are hot enough to glow emit large amounts of radiation in the near infrared and visible range, in which light surfaces have lower absorptivities than dark ones. Radiative heat exchange ( $R$ ) between the skin and the environment is proportional to the difference between the fourth powers of the surfaces' absolute temperatures; but if the difference between  $\bar{T}_{sk}$  and the temperature of the radiant environment

( $T_r$ ) is much smaller than the absolute temperature of the skin,  $R$  is nearly proportional to  $(\bar{T}_{sk} - T_r)$ . Some parts of the body surface (e.g., inner surfaces of the thighs and arms) exchange heat by radiation with other parts of the body surface, so that heat exchange between the body and the environment is determined by an effective radiating surface area ( $A_r$ ), which is smaller than the actual surface area.  $A_r$  depends on the posture, being closest to the actual surface area in a "spread eagle" posture, and least in someone curled up. The relationship of  $R$  to emissivity, temperature, and  $A_r$  can be represented by Eq. 2.

**TEXT BOX (with comment)**  
Convection is transfer of heat due to movement of a fluid, either liquid or gas. In thermal physiology the fluid is usually air or water in the environment, or blood inside the body, as discussed earlier. Fluids conduct heat in the same way as solids do, and a perfectly still fluid transfers heat only by conduction. Since air and water are not good conductors of heat (Table 1), perfectly still air or water is not very effective in heat transfer. Fluids, however, are rarely perfectly still, and even nearly imperceptible movement produces enough convection to have a large effect on heat transfer. Thus although conduction plays a role in heat transfer by a fluid, convection so dominates the overall heat transfer that we refer to the entire process as convection. The conduction term ( $K$ ) in Eq. 1 is therefore in practice restricted to heat flow between the body and other solid objects, and usually represents only a small part of the total heat exchange with the environment. Convective heat exchange between the skin and the environment is proportional to the skin surface area and the difference between skin and ambient air temperatures, as expressed by Eq. 3. Convective heat exchange depends on air movement; and  $h_c$ , the proportionality constant in Eq. 3, depends on air speed and on geometrical factors that affect heat exchange with moving air.

A gram of water that is converted into vapor at 30°C absorbs 2425J (0.58 kcal), the latent heat of evaporation, in the process. In subjects who are not sweating, evaporative water loss is typically about 13-15 gm/(m<sup>2</sup>·h), corresponding to a heat loss of 16-18 W for a surface area of 1.8m<sup>2</sup>. About half of this amount is lost through breathing and half as insensible perspiration<sup>10,15</sup>, i.e., evaporation of water that diffuses through the skin. Insensible perspiration occurs independently of the sweat glands and is not under thermoregulatory control. Water loss through these routes, however, is quite small compared to what can be achieved by evaporation of sweat. Evaporative heat loss from the skin is proportional to skin surface area and the difference between the water vapor pressure at the skin surface and in the ambient air, as summarized in Eq. 4. Since water vapor, like heat, is carried away by moving air, air movement and other factors affect  $E$  and  $h_e$  in just the same way that they affect  $C$  and  $h_c$ . The water vapor pressure at the skin surface depends on the degree of wetness of the skin surface, and thus on the

balance between sweating and evaporation; and it is equal to the saturation vapor pressure of water at skin temperature if the skin surface is completely wet. The saturation vapor pressure of water increases substantially over the physiological range of skin temperature: e.g., from 28.3 torr at 28°C to 44.6 torr at 36°C. Ambient water vapor pressure, which directly affects evaporation from the skin, is proportional to the actual moisture content in the air. Because the skin is warmed by heat from the body, evaporation from the skin is related only indirectly to relative humidity, which is the ratio between the actual moisture content in the air and the maximum moisture content that is possible at the temperature of the air. This is an important distinction since, for example, sweat can easily evaporate from the skin in cool air even if relative humidity is 100%.

### HEAT DISSIPATION

Heat produced within the body must be delivered to the skin surface to be eliminated. Heat flows through the shell by two parallel modes: physical conduction through the tissues of the shell, and convection by blood perfusing the shell. Since the temperature difference between core and skin also affects heat flow through the shell independently of blood flow and the properties of the tissues, the power of the shell to transfer heat is expressed as the conductance of the shell, and it is calculated by dividing heat flow through the shell by the difference between core and mean skin temperatures, as shown in Eq. 5. When skin blood flow is minimal (usually at ambient temperatures below about 28°C in nude resting subjects), the conductance of the shell is determined chiefly by the thickness of the subcutaneous fat layer, and is about 16 W/°C in a lean man. Under these conditions a temperature difference between core and skin of 5°C will allow a typical resting metabolic heat production of 80W to be conducted to the skin surface. In a cool environment,  $T_{sk}$  may be low enough for this to occur easily. However in a warm environment or, especially, during exercise, shell conductance must increase substantially to allow all the heat produced to be conducted to the skin without at the same time causing core temperature to rise to dangerous or lethal levels. Fortunately under such circumstances increases in skin blood flow occur that can raise shell conductance ten-fold or more. Thus a crucial thermoregulatory function of skin blood flow is to control the conductance of the shell and the ease with heat travels from core to skin. A closely related function is to control  $T_{sk}$ : in a person who is not sweating, an increase in skin blood flow tends to bring  $T_{sk}$  toward  $T_c$ , and a decrease allows  $T_{sk}$  to approach ambient temperature. Since convective and radiative heat exchange (R+C) depend directly on skin temperature (Eqs. 2,3), the body can control heat exchange with the environment by adjusting skin blood flow. The

thermoneutral zone<sup>11</sup> is the range of conditions of metabolic rate and environment within which adjustments in skin blood flow by themselves are sufficient to allow the body to maintain heat balance. If the heat stress is so great that increasing R+C through increasing skin blood flow is not enough to maintain heat balance, the body secretes sweat to increase evaporative heat loss. Once sweating begins, skin blood flow continues to increase as the person becomes warmer, but now the tendency of an increase in skin blood flow to warm the skin is approximately balanced by the tendency of an increase in sweating to cool the skin. Therefore after sweating has begun, further increases in skin blood flow usually cause little change in skin temperature or dry heat exchange. The increases in skin blood flow that accompany sweating are important to thermoregulation nevertheless, since they deliver to the skin the heat that is being removed by evaporation of sweat, and facilitate evaporation by keeping the skin warm. Skin blood flow and sweating thus work in tandem to dissipate heat that is produced in the body.

### ***Sympathetic Control of Skin Circulation***

Blood vessels in human skin are under dual vasomotor control, involving separate nervous signals for vasoconstriction and for vasodilation<sup>9,16,17</sup>. Reflex vasoconstriction, occurring in response to cold and also as part of certain non-thermal reflexes such as baroreflexes, is mediated primarily through adrenergic sympathetic fibers distributed widely over most of the skin<sup>18</sup>. Reducing the flow of impulses in these nerve fibers allows the blood vessels to dilate. In the so-called acral regions — lips, ears, nose, and palmar/plantar surfaces of the hands and feet<sup>17,18</sup> — and in the superficial veins<sup>17</sup>, vasoconstrictor fibers are the predominant vasomotor innervation, and the vasodilation occurring during heat exposure is largely a result of the withdrawal of vasoconstrictor activity<sup>19</sup>. Blood flow in these skin regions is sensitive to small temperature changes in the thermoneutral range, and may be responsible for "fine tuning" heat loss to maintain heat balance in this range.

In most of the skin the vasodilation occurring during heat exposure depends on sympathetic nervous signals that cause the blood vessels to dilate, and is prevented or reversed by regional nerve block<sup>20</sup>. Since it depends on the action of nervous signals, such vasodilation is sometimes referred to as active vasodilation. Active vasodilation occurs in almost all the skin outside the acral regions<sup>19</sup>, and also on the dorsal surfaces of the hands<sup>21</sup> and (presumably) feet. In skin areas where active vasodilation occurs, vasoconstrictor activity is minimal at thermoneutral temperatures; and as the body is warmed, active vasodilation does not begin until near the onset of sweating<sup>17,22</sup>. Thus reflex control of skin blood flow in these areas is insensitive to small temperature changes within



the thermoneutral range<sup>19</sup>. The neurotransmitter or other vasoactive substance(s) responsible for active vasodilation in human skin is not known<sup>18</sup>. However, since sweating and vasodilation operate in tandem in the heat, there has been considerable interest in the notion that the mechanism for active vasodilation is somehow linked to the action of sweat glands<sup>17,23</sup>. An early hypothesis<sup>24</sup>, that bradykinin released by sweat glands accounts for active vasodilation, now seems unlikely<sup>17</sup>. Active vasodilation does not occur in the skin of patients with anhidrotic ectodermal dysplasia<sup>25</sup>, even though their vasoconstrictor responses are intact, implying that active vasodilation either is linked to an action of sweat glands, or is mediated through nerves that are absent or nonfunctional in anhidrotic ectodermal dysplasia.

I evaluated thermoregulatory function of a patient with acquired anhidrosis and heat intolerance of six months duration, who failed to sweat in response to iontophoresis of pilocarpine or injection of acetylcholine. During 20 min cycle exercise sweating was observed only in the popliteal fossae; but forearm blood flow (a widely-used index of skin blood flow) increased normally as his core temperature rose to 39°C, even though sensitive dew-point hygrometry measurements on the same forearm showed no evidence of sweating. Therefore if active vasodilation does depend on some action of sweat glands, it must be an action that can occur even without sweat secretion. The finding of nerve endings that contain both vasoactive intestinal peptide (VIP) and acetylcholine near eccrine sweat glands in human skin<sup>26</sup> suggested that active vasodilation may be mediated by release of a vasoactive cotransmitter from the cholinergic endings of sudomotor nerves<sup>27</sup>. This notion is supported by a recent study showing that active vasodilation in human skin is blocked by botulinum toxin, a presynaptic inhibitor of acetylcholine release, even though active vasodilation was shown not to be elicited by either a muscarinic or non-muscarinic action of acetylcholine<sup>28</sup>. However VIP is unlikely to be the sole mediator of active vasodilation in human skin, since the skin of patients with cystic fibrosis shows normal active vasodilation, even though their sudomotor nerves are deficient in VIP<sup>29</sup>.

## Sweating

Humans can dissipate large amounts of heat by secretion and evaporation of sweat; and when the environment is warmer than the skin—usually when the environment is hotter than 36°C—evaporation is the only way to lose heat. Humans possess both apocrine sweat glands, which have only a limited regional distribution<sup>30</sup>, and eccrine sweat glands, which are widely distributed and are by far the more important type in human

thermoregulation. Human sweat glands are controlled through postganglionic sympathetic nerves which release acetylcholine<sup>31</sup> rather than norepinephrine. Functionally active eccrine glands number about 2,000,000 to 3,000,000<sup>31</sup>. Although this number is fixed before the age of three<sup>31</sup>, the secretory capacity of the individual glands can change, especially with endurance exercise training and heat acclimatization; and a fit man well acclimatized to heat can achieve a peak sweating rate greater than 2.5 liters per hour<sup>32,33</sup>. (Such rates cannot be maintained, however, and the maximum daily sweat output is probably about 15 liters<sup>34</sup>). Eccrine sweat is essentially a dilute electrolyte solution, and sweat glands reabsorb  $\text{Na}^+$  from the duct by active transport, making sweat the most dilute body fluid, with  $[\text{Na}^+]$  ranging from less than 5 to 60 mEq/L<sup>35</sup>.

### THERMOREGULATORY CONTROL

Human thermoregulation includes two distinct sub-systems: behavioral thermoregulation and physiological thermoregulation. Physiological thermoregulation is capable of fairly precise adjustments of heat balance, but is effective only within a relatively narrow range of environmental temperatures. On the other hand behavioral thermoregulation, through the use of shelter and space heating and clothing, enables humans to live in the most extreme climates on earth; but it does not provide fine control of body heat balance. Since human physiological responses for dissipating heat are several times more powerful than responses for conserving heat and increasing heat production, behavioral thermoregulation is correspondingly more important to human activity and survival in the cold than in the heat.

Behavioral thermoregulation is governed by thermal sensation and comfort, and depends largely on conscious actions that reduce discomfort. Warmth and cold on the skin are felt as either comfortable or uncomfortable, depending on whether they decrease or increase the physiological strain<sup>36</sup>. Thus a shower temperature that feels pleasant after strenuous exercise may be uncomfortably cold on a chilly morning. Because of the relation between discomfort and physiological strain, behavioral thermoregulation, by reducing discomfort, also minimizes the physiological burden imposed by a stressful thermal environment. Thermal sensation and comfort respond to changes in the environment much more quickly than do either core temperature or physiological thermoregulatory responses<sup>37,38</sup>. Behavioral responses thus appear to anticipate changes in the body's thermal state, presumably reducing the need for frequent small behavioral adjustments.

Physiological thermoregulation operates through graded control of heat-production and heat-loss

FIG. 4 responses. Familiar non-living control systems, such as heating and air-conditioning systems, usually operate at only two levels, because they act by turning a device on or off. In contrast, most physiological control systems produce a response that is graded according to the disturbance in the regulated variable. In many physiological systems, including those that control the heat-dissipating responses, changes in the effector responses are proportional to displacements of the regulated variable from some threshold value<sup>10</sup>, and such control systems are called proportional control systems (Fig. 4). Each response in Fig. 4 has a core-temperature threshold, a temperature at which the response starts to increase; and these thresholds depend on mean skin temperature. Thus at any given skin temperature, the change in each response is proportional to the change in core temperature; and increasing the skin temperature lowers the threshold level of core temperature and increases the response at any given core temperature.

### Integration of Thermal Information

Temperature receptors in the body core and the skin transmit information about their temperatures through afferent nerves to the brain stem, and especially the hypothalamus, where much of the integration of temperature information occurs<sup>39</sup>. The sensitivity of the thermoregulatory responses to core temperature allows the thermoregulatory system to adjust heat production and heat loss to resist disturbances in core temperature. Their sensitivity to skin temperature allows the system to respond appropriately to mild heat or cold exposure with little change in body core temperature, so that environmentally induced changes in body heat content occur almost entirely in the peripheral tissues. For example, the skin temperature of someone who enters a hot environment rises and may elicit sweating even if there is no change in core temperature. On the other hand, an increase in heat production due to exercise elicits the appropriate heat-dissipating responses through a rise in core temperature. Although temperature receptors in other core sites, including the spinal cord and medulla, participate in the control of thermoregulatory responses<sup>40</sup>, the core temperature receptors involved in thermoregulatory control are concentrated especially in the hypothalamus<sup>40</sup>; and 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 of experimental mammals.

FIG. 5 We may represent the central thermoregulatory integrator (Fig. 5) as generating thermal command signals for the control of the effector responses. These signals are based on the information about core and skin

temperatures that the integrator receives, and on the thermoregulatory set point<sup>4</sup>, a reference point which determines the thresholds of all the thermoregulatory responses. We may think of the set point as the setting of the body's "thermostat", and changes in the set point are accompanied by corresponding changes in core temperature at rest. The set point is elevated during fever, and lowered slightly by heat acclimatization, as discussed later; and it changes in a cyclical fashion with time of day and phase of the menstrual cycle<sup>4,6,7</sup>. The set point reaches a minimum in the early morning, several hours before awaking, and a maximum—which is 0.5 to 1°C higher—in the late afternoon or evening. During the menstrual cycle the set point is at its lowest point just before ovulation, and over the next few days rises 0.5 to 1°C and remains elevated for most of the luteal phase.

### **Peripheral Modification of Skin Vascular and Sweat Gland Responses**

Skin temperature affects heat loss responses not only through the reflex actions described above, but also through direct actions on the effectors themselves. Local temperature acts on skin blood vessels in two ways. First, local cooling potentiates the constriction of blood vessels in response to nervous signals and vasoconstrictor substances<sup>18</sup>. Second, in skin regions where active vasodilation occurs, local heating dilates the blood vessels (and local cooling constricts them) through a direct action that is independent of nervous signals<sup>41,42</sup>. This direct effect is especially strong at skin temperatures above 35°C<sup>42</sup>; and when the skin is warmer than the blood, increased blood flow helps to cool the skin and protect it from heat injury. The effects of local temperature on sweat glands parallel those on blood vessels, so that local heating magnifies (and local cooling reduces) the sweating response to reflex stimulation or to acetylcholine<sup>23</sup>, and intense local heating provokes sweating directly, even in sympathectomized skin<sup>43</sup>. During prolonged (several hours) heat exposure with high sweat output, sweat rates gradually diminish and the sweat glands' response to locally applied cholinergic drugs is reduced also. The reduction of sweat-gland responsiveness is sometimes called sweat-gland "fatigue". Wetting the skin makes the stratum corneum swell, mechanically obstructing the sweat duct and causing a reduction in sweat secretion, an effect called hidromeiosis<sup>44</sup>. The glands' responsiveness can be at least partly restored if the skin is allowed to dry (e.g., by increasing air movement<sup>45</sup>), but prolonged sweating also causes histological changes in the sweat glands<sup>46</sup>.

Thermoregulatory responses may be affected by other inputs besides body temperatures and factors that affect the thermoregulatory set point. Non-thermal factors may produce a burst of sweating at the beginning of exercise<sup>47,48</sup>, and the involvement of sweating and skin blood flow in emotional responses is quite familiar. During

exercise and heat stress, skin blood flow is more affected than sweating by non-thermal factors, because of its involvement in reflexes which function to maintain cardiac output, blood pressure, and tissue O<sub>2</sub> delivery.

### **THERMOREGULATORY RESPONSES DURING EXERCISE**

At the start of exercise, metabolic heat production increases rapidly; but there is little change in heat loss initially, so heat is stored in the body and core temperature rises. The increase in core temperature, in turn, elicits heat-loss responses, but core temperature continues to rise until heat loss has increased enough to match heat production, so that heat balance is restored and core temperature and the heat-loss responses reach new steady-state levels. The rise in core temperature which elicits heat-dissipating responses sufficient to re-establish thermal balance during exercise is an example of a load error<sup>10</sup>, which occurs when any proportional control system resists the effect of some imposed disturbance or "load". Although the elevated T<sub>c</sub> of exercise superficially resembles the elevated T<sub>c</sub> of fever, there are some crucial differences. First, although heat production may increase substantially (through shivering) at the beginning of a fever, it does not need to stay high to maintain the fever, but in fact returns nearly to pre-febrile 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. Second, while core temperature is rising during fever, rate of heat loss is, if anything, lower than before the fever began; but during exercise, the heat-dissipating responses and the rate of heat loss start to increase early and continue increasing as core temperature rises.

### **RESPONSES TO COLD**

The body's first response to maintain core temperature in the cold is to minimize heat loss, by constricting blood vessels in the shell, especially in the skin. Constriction of arterioles reduces heat transfer to the skin by reducing blood flow; and constriction of 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. (This diversion is made possible by the many penetrating veins that connect the superficial and deep veins.) In the deep veins, cool venous blood returning to the core can take up heat from the warm blood in the adjacent deep limb arteries. Thus some of the heat contained in the arterial blood as it enters the limbs takes a "short circuit" back to the core; and when the arterial blood reaches the skin it is already cooler than the core, and so loses less heat to the skin than it otherwise

would. 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<sup>49</sup>. (Although furred or hairy animals can increase the thickness of their coat by piloerection, this response makes a negligible contribution to heat conservation in humans, though it persists as "goose flesh".) If the heat-conserving responses are insufficient to re-establish heat balance, metabolic heat production increases—in adults, almost entirely in skeletal muscles, as a result first of increased tone, and later of frank shivering. Shivering may increase metabolism at rest by more than four fold acutely, but only about half that amount can be sustained after several hours.

In addition, as the skin is cooled below about 15°C, its blood flow begins to increase somewhat, a response called cold-induced vasodilation (CIVD). CIVD is elicited most easily in comfortably warm subjects and is most pronounced in regions rich in arteriovenous anastomoses, i.e. in the hands and feet. The mechanism is uncertain, but may involve a direct inhibitory effect of cold on contraction of vascular smooth muscle or on neuromuscular transmission. Although this response increases heat loss from the core somewhat, it keeps the extremities warmer and more functional, and probably protects them from cold injury.

### FACTORS THAT ALTER TOLERANCE TO HEAT AND COLD

Prolonged or repeated heat stress, especially when combined with exercise, elicits acclimatization to heat, an ensemble of physiological changes that reduce the physiological strain that heat stress produces. The classic signs of heat acclimatization are reductions in the levels of core (as much as 1°C) and skin (1°C or more) temperatures and heart rate (as much as 30-40 beats/min) reached during exercise in the heat, and increases in sweat production. These changes approach their full development within a week. Heat acclimatization produces other changes<sup>50</sup> also, including an improved ability to sustain high rates of sweat production; an aldosterone-mediated reduction of sweat sodium concentration (to levels as low as 5 mEq/L), which minimizes salt depletion; an increase in the fraction of sweat secreted on the limbs; and perhaps other changes that help protect against heat illness. The effect of heat acclimatization on performance can be quite dramatic, so that acclimatized subjects can easily complete exercise in the heat which previously was difficult or impossible (cf.<sup>51</sup>). The mechanisms that produce these changes are not fully understood, but include a modest (~0.4°C) lowering of the thermoregulatory set point (reducing the thresholds for sweating and cutaneous vasodilation), increased sensitivity of the sweat glands to cholinergic stimulation<sup>52,53</sup>, and a decrease in the sweat glands' susceptibility to hydromeiosis and fatigue. Heat

acclimatization disappears in a few weeks if not maintained by repeated heat exposure.

In contrast to heat acclimatization, the changes that occur with cold acclimatization in humans are quite variable and appear to depend on the nature of the acclimatizing cold exposure, and they confer only a modest thermoregulatory advantage. For these reasons, it was long questioned whether humans acclimatize to cold. An important adaptive response to cold—though not strictly an example of acclimatization—is enhancement of CIVD. CIVD is rudimentary in hands or feet unaccustomed to cold exposure, but after repeated cold exposure, it begins earlier during cold exposure, produces higher levels of blood flow, and takes on a rhythmical pattern of alternating vasodilation and vasoconstriction, sometimes called the Lewis hunting response. This response is often well developed in workers whose hands are exposed to cold, such as fishermen who work with nets in cold water.

Several acute and chronic skin disorders impair thermoregulation through effects on sweating and skin blood flow. Ichthyosis and anhidrotic ectodermal dysplasia are often-cited examples of skin disorders that impair sweating, and can profoundly affect thermoregulation in the heat. Since active vasodilation is impaired or absent in anhidrotic ectodermal dysplasia, artificially wetting the skin can only partially correct the thermoregulatory deficit during exercise (when large amounts of body heat need to be carried to the skin), and is likely to be most effective in an environment that is dry enough that evaporation can produce a cool skin. Heat rash (miliaria rubra) also impairs sweating and can reduce exercise tolerance, and its effects may persist after the appearance of the skin has returned to normal<sup>54</sup>. Sunburn impairs vasoconstriction and heat conservation during cold exposure<sup>55</sup>.

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**Table 1.** Thermal conductivities, and rates of heat flow through slabs of different materials 1 m<sup>2</sup> in area and 1 cm thick, with a 1°C temperature difference between the two faces of the slab.

	conductivity	rate of heat flow	
	kcal/(s·m·°C)	kcal/h	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
Water	0.00014	51	59
Oak (across grain)	0.00004	14	17
Dry air	0.000006	2.2	2.5
Glass fiber insulation	0.00001	3.6	4.2

**Table 2.** Relative masses and rates of metabolic heat production of various body compartments during rest and severe exercise.

	Body mass	Heat production (%)	
	(%)	Rest	Exercise
Brain	2	16	1
Trunk viscera	34	56	8
Muscle and skin	56	18	90
Other	8	10	1

Modified from Wenger CB, Hardy JD. Temperature regulation and exposure to heat and cold. In: Lehmann JF, ed.

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Fig. 1. Ranges of rectal temperature found in healthy persons, patients with fever, and persons with impairment or failure of thermoregulation. (Reprinted from Wenger CB, Hardy JD. Temperature regulation and exposure to heat and cold. In: Lehmann JF, ed. *Therapeutic Heat and Cold*. Baltimore, Williams and Wilkins; 1990:150-178 with permission of the publisher. Modified from DuBois EF. *Fever and the Regulation of Body Temperature*. Springfield, IL: C. C. Thomas; 1948.)

Fig. 2. Distribution of temperatures within the body and division of the body into core and shell during exposure to (A) cold and (B) warm environments. The temperatures of the surface and the thickness of the shell depend on the environmental temperature, so that the shell is thicker in the cold and thinner in the heat. (Reprinted from Wenger CB: The regulation of body temperature, in Rhoades RA, Tanner GA (eds): *Medical Physiology*. Boston, Little, Brown; 1995:587-613 with permission of the publisher. Based on Aschoff J, Wever R. Kern und Schale im Wärmehaushalt des Menschen. *Naturwissenschaften* 1958;45:477-485.)

Fig. 3. Exchange of energy with the environment. This hiker gains heat from the sun by radiation, and loses heat by conduction to the ground through the soles of his feet, by convection into the air, by radiation to the ground and sky, and by evaporation of water from his skin and respiratory passages. In addition, some of the energy released by his metabolic processes is converted into mechanical work, rather than heat, since he is walking uphill. (Reprinted from Wenger CB: The regulation of body temperature, in Rhoades RA, Tanner GA (eds): *Medical Physiology*. Boston, Little, Brown; 1995:587-613 with permission of the publisher.)

Fig. 4. The relations of back (scapular) sweat rate (left) and forearm blood flow (right) to core temperature and mean skin temperature ( $\bar{T}_{sk}$ ). In the experiments shown, core temperature was increased by exercise. (Left panel drawn from data of Sawka MN, Gonzalez RR, Drolet LL, Pandolf KB: Heat exchange during upper- and lower-body exercise. *J Appl Physiol* 1984;57:1050-1054. Right panel modified from Wenger CB, Roberts MF, Stolwijk JAJ, Nadel ER: Forearm blood flow during body temperature transients produced by leg exercise. *J Appl Physiol* 1975;38:58-63 with permission of the publisher.)

Fig. 5. Schematic diagram of the control of human thermoregulatory responses. The signs by the inputs to  $T_{set}$



indicate that pyrogens raise the set point, and heat acclimation 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. (Reprinted from Wenger CB: The regulation of body temperature, in Rhoades RA, Tanner GA (eds): *Medical Physiology*. Boston, Little, Brown; 1995:587-613 with permission of the publisher.)

Equations describing heat transfer between the skin and the environment and  
between core and skin

$$R = h_r \cdot e_{sk} \cdot A_r \cdot (\bar{T}_{sk} - T_r) \quad (2)$$

where  $h_r$  is the radiant heat transfer coefficient,  $6.43 \text{ W}/(\text{m}^2 \cdot ^\circ\text{C})$  at  $28^\circ\text{C}$ ; and  $e_{sk}$  is the emissivity of the skin.

$$C = h_c \cdot A \cdot (\bar{T}_{sk} - T_a) \quad (3)$$

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

$h_c$  includes the effects of all the factors besides temperature and surface area that affect convective heat exchange. For the whole body, the most important of these factors is air movement, and convective heat exchange (and thus  $h_c$ ) varies approximately as the square root of the air speed except when air movement is very slight.

$$E = h_e \cdot A \cdot (P_{sk} - P_a) \quad (4)$$

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.

$$C = HF_{sk} / (T_c - \bar{T}_{sk}) \quad (5)$$

where  $C$  is shell conductance;  $HF_{sk}$  = heat loss through the skin, i.e., total heat loss less heat loss through the respiratory tract; and  $T_c$  = core temperature

Fig 1

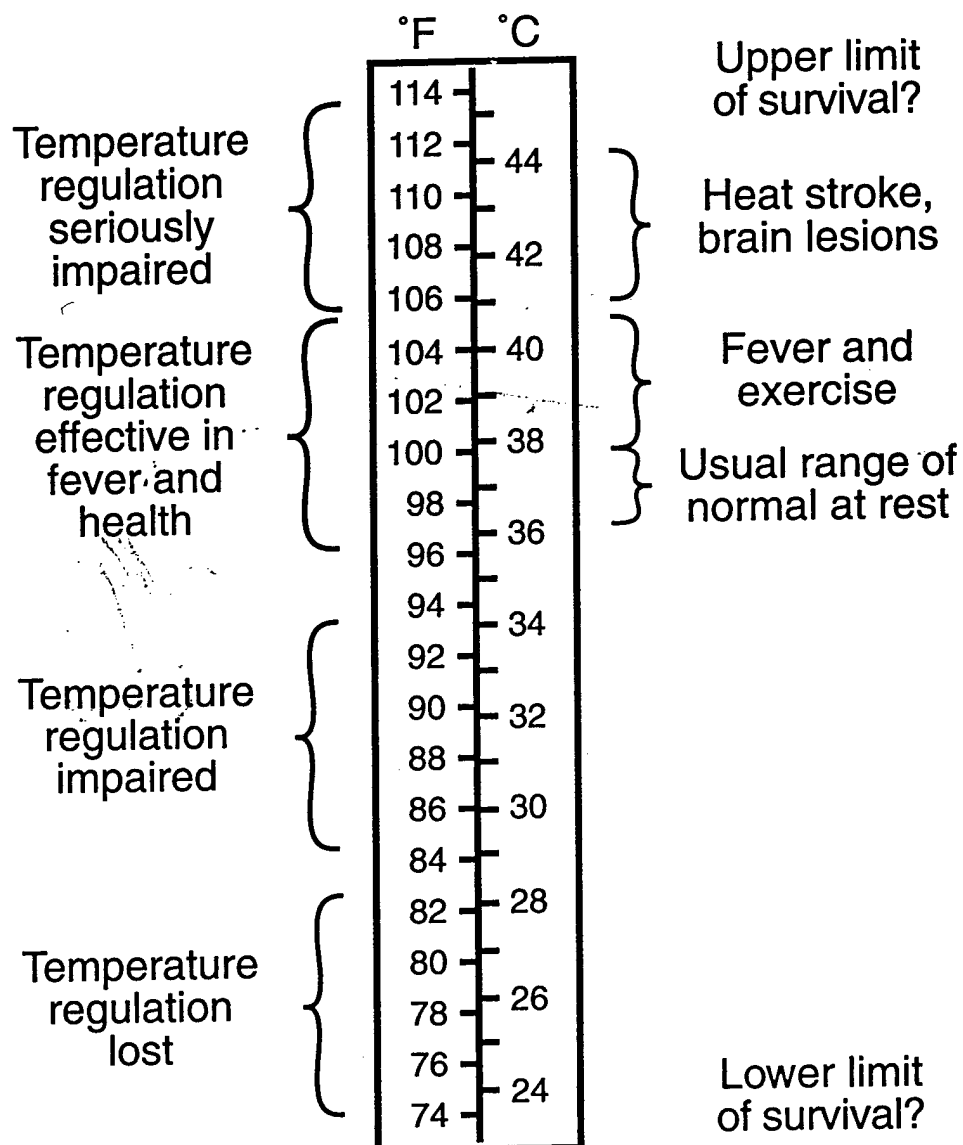


Fig. 2

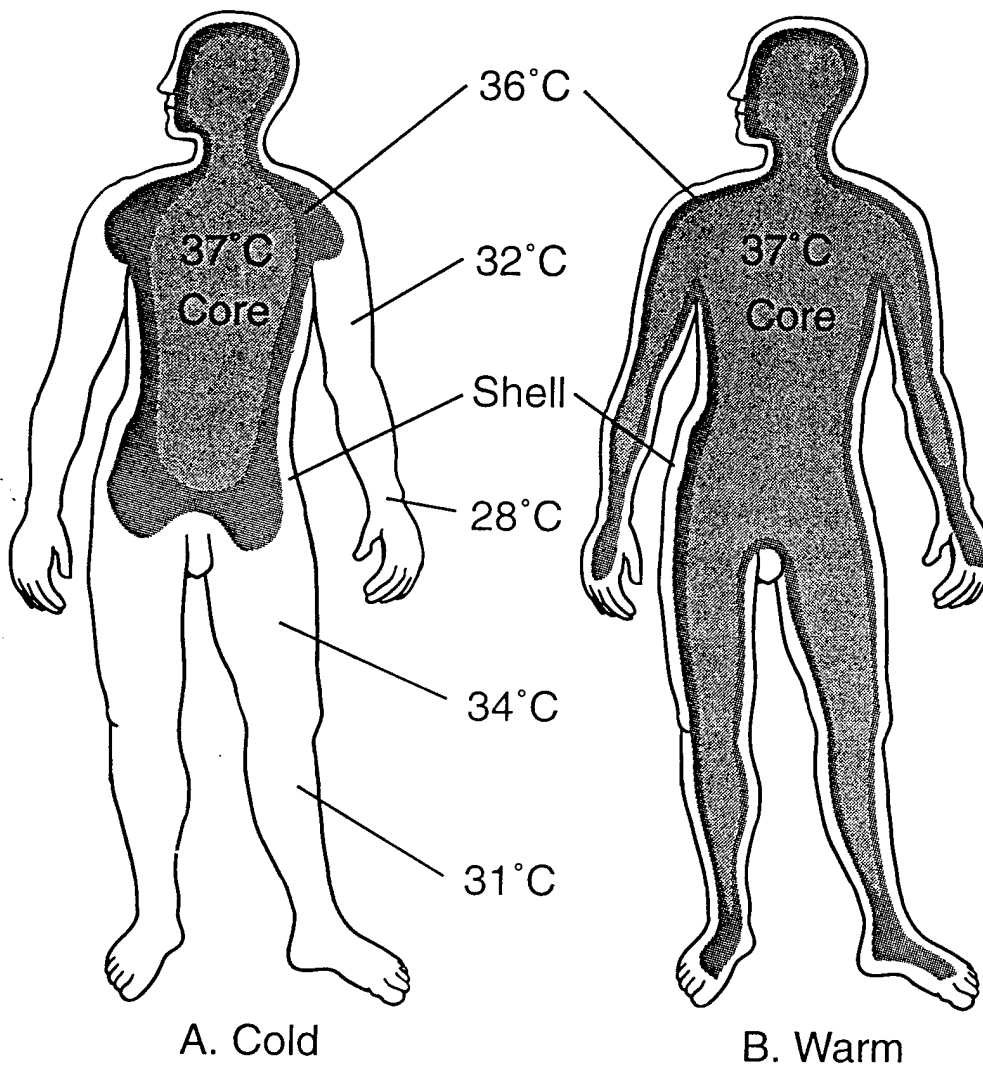


Fig 3.

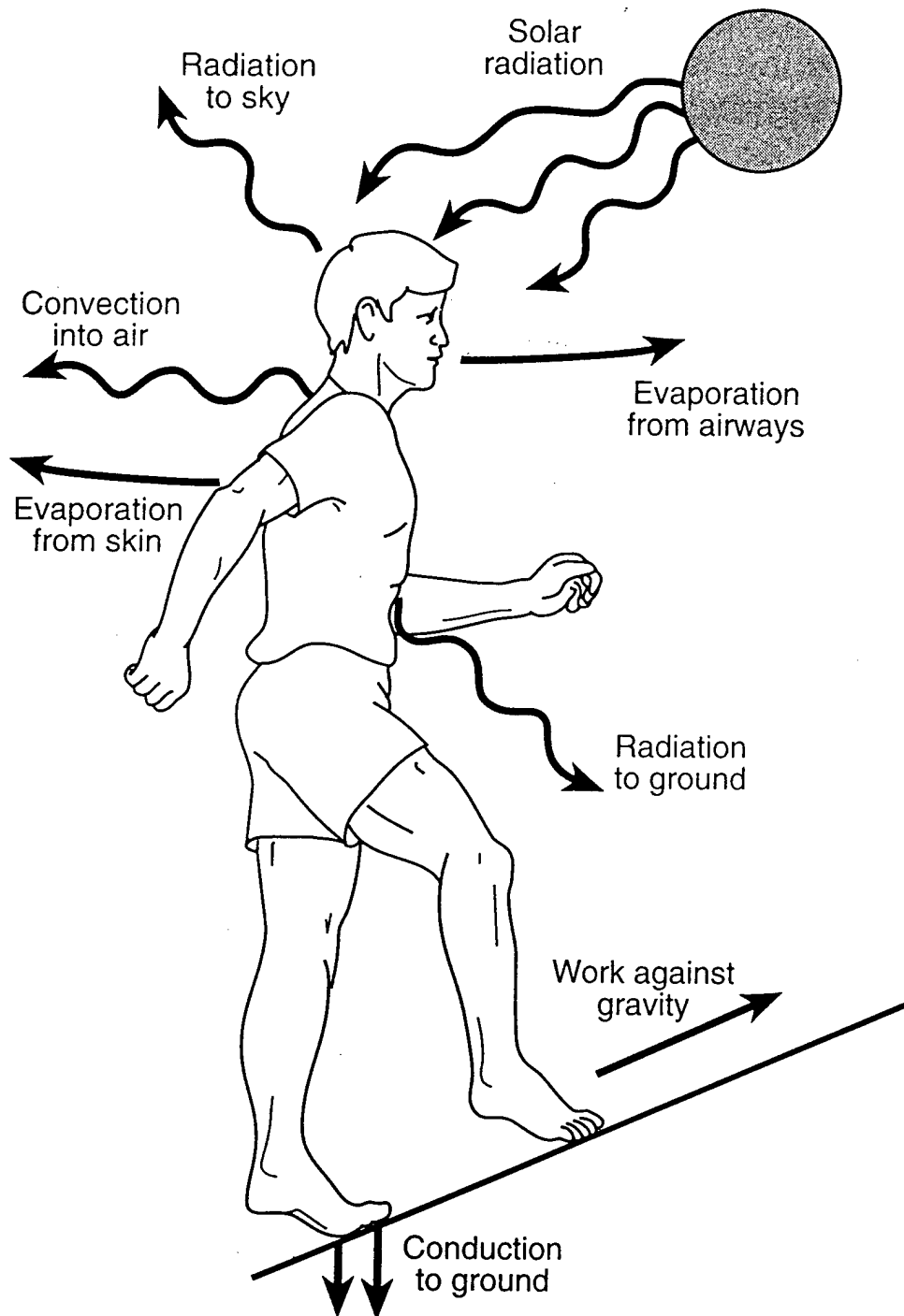
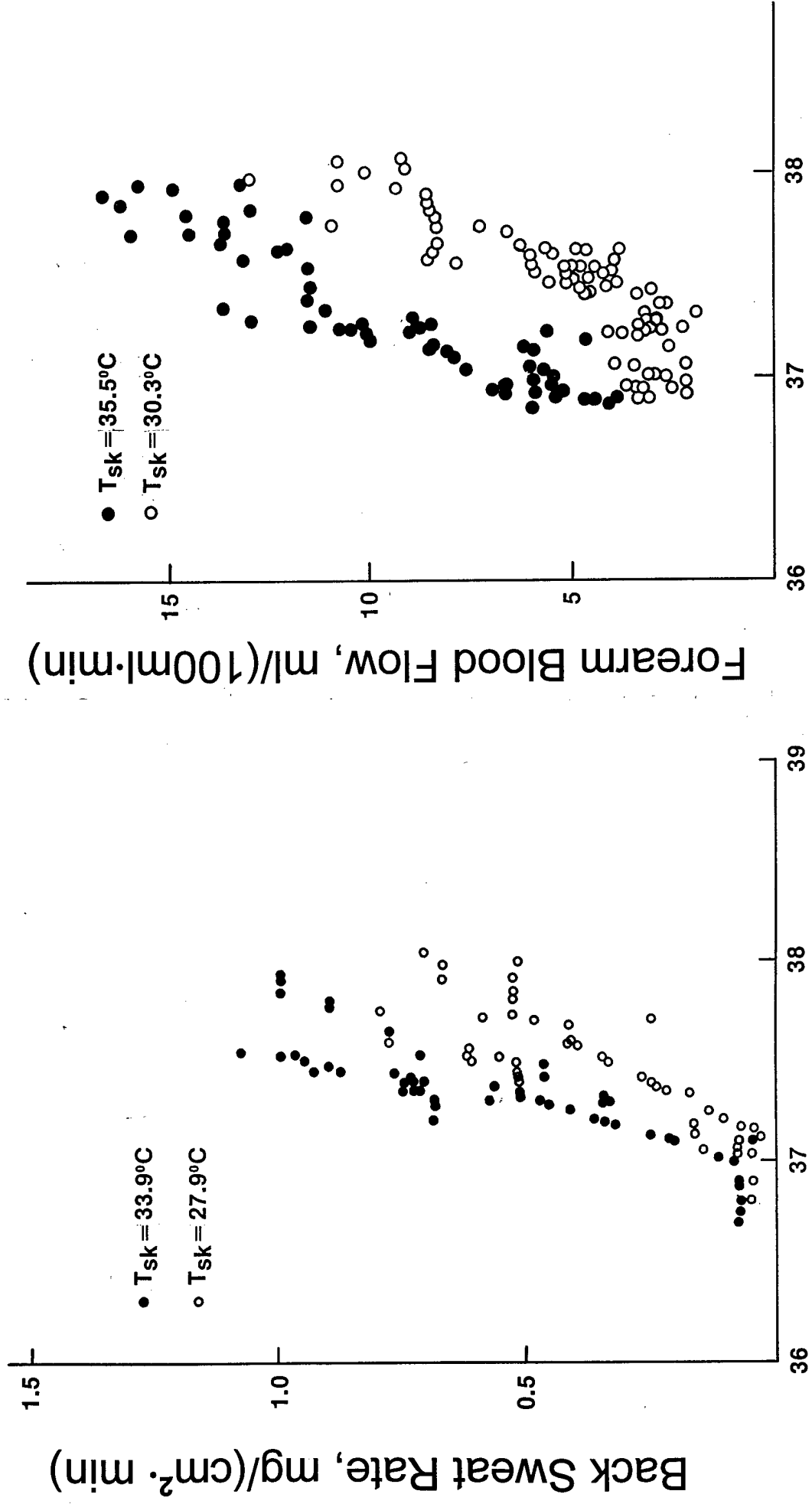


Fig 4



Core Temperature, °C

Fig. 5

