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Physiological Responses to Acute Exercise-Heat Stress

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INTRODUCTION

In this chapter, we discuss the normal thermoregulatory, circulatory and metabolic responses of humans performing exercise in the heat. Muscular exercise increases metabolic rate above resting levels, thus producing a considerable amount of heat that must be dissipated to the environment to protect the health of the individual. In comparison with the broad temperature range for terrestrial climates (-88° to 58° C), the human body temperature is usually regulated within a narrow range (35° to 41° C) to preserve normal physiological function. The human possesses an elaborate set of mechanisms which regulates body temperature and includes two control systems: behavioral temperature regulation and physiological temperature regulation. Behavioral temperature regulation operates largely through conscious, willed behavior to employ any means available. Physiological temperature regulation operates through the autonomic nervous system, and includes control of: a) rate of metabolic heat production, b) heat flow via the blood from the core to the skin, and c) sweating. Even without heat stress, a relatively high cardiac output is required to maintain the high level of metabolism during exercise. When heat stress is combined with exercise, the cardiovascular system may be pushed close to its limit to simultaneously support the competing metabolic and thermoregulatory demands for blood flow. The following pages will consider human temperature regulation, control of heat dissipating responses and the problems associated with maintaining adequate cardiac output during exercise-heat stress.

THERMOREGULATORY CONTROL

Behavioral Temperature Regulation

Selection of a suitable micro-environment is the most primitive thermoregulatory response, and is seen in all vertebrates. Even fish and reptiles, which are poikilothermic ("cold-blooded"), will, given the opportunity, control their body temperatures by moving to a warmer or cooler micro-environment. Human beings have a wider range of options and by choice of clothing, which impedes heat loss from the body and thus increases thermal insulation, and by using shelter, ventilation and air conditioning, they can live for extended periods in the most extreme climates on earth. Thermal sensation and thermal discomfort presumably represent the direct motivation for behavioral thermoregulation, and in human subjects they can be measured by psychophysical means. Some workers (e.g., 31) have considered both physiological and behavioral thermoregulatory re-

sponses to be controlled in the same way. However, during transients in environmental temperature, thermal sensation and thermal discomfort appear to change much more quickly than do either core and skin temperatures (64, Chapter 2) or physiological thermoregulatory responses (34). Thermal sensation and discomfort thus seem to anticipate changes in the body's thermal state, perhaps by using nervous signals related to rate of change of skin temperature (see below). The anticipatory nature of thermal sensation and discomfort may be beneficial, since behavioral thermoregulation is accomplished by discrete responses, whereas physiological thermoregulation is accomplished by responses which occur continuously, and whose intensity is easily adjusted, as long as the thermal stress is present.

In human beings the drives for behavioral thermoregulation are often overridden by other factors. Thus, concern for personal appearance may cause people to dress inappropriately for their activity and thermal environment; and well-motivated individuals, such as athletes and military recruits, may exercise in hot environments to the point of endangering themselves.

Physiological Regulation

Among the most familiar examples of non-living regulatory systems are refrigerators and air conditioning systems for buildings, which are controlled by thermostats and operate so as to maintain the inside temperature at a relatively constant level. Although more sophisticated systems do exist, a typical refrigeration or air conditioning system can operate at only two levels of cooling, on and off, and is not capable of a graded response. When the inside temperature rises above the desired level, the thermostat turns on the compressor in the refrigeration unit; and when the temperature falls below that level, the thermostat turns the compressor off. (In practice the response of such a system lags somewhat, so that it is not constantly switching on or off in response to minute temperature changes.) Such a system is called an on-off system. The variable which a control system acts to maintain within narrow limits (in this example, temperature) is often called the regulated variable, and the quantities which it controls in order to accomplish this (in this example, rate of heat removal averaged over several on-off cycles) are called controlled variables.

Rather than operating only at one of two levels, on and off, most physiological control systems can produce a graded response according to 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, and

such control systems are called proportional control systems. Figure 3-1 shows how reflex control of three heat-dissipating responses, sweating, skin blood flow, and forearm venous volume, depends on body core temperature (represented by esophageal temperature) and mean skin temperature. In Figure 3-1, each response has an esophageal temperature threshold. This threshold is the esophageal temperature at which the response starts to increase, and the threshold depends on the mean skin temperature. Note that the temperature controller is of the proportional type, and that these thermoregulatory responses depend on both core and mean skin temperatures: at any given skin temperature, each response is proportional to esophageal temperature, and increasing the skin temperature lowers the threshold level of esophageal temperature and increases the response at any given core temperature. (In addition to the role of skin temperature in the reflex control of thermoregulatory responses, skin temperature also has a local effect that modifies the local response to the reflex signal. This will be discussed later in the chapter.) Although the most accurate mathematical representation of the reflex control of the thermoregulatory effectors may well be a complicated function of tissue temperatures at a number of sites, and contain non-linear elements, it is convenient and useful to represent the control in terms of a linear combination of core temperature (T_c) and mean skin temperature (\bar{T}_{sk}), and to represent the control of each thermoregulatory effector response by an equation of the form:

$$R - R_0 = a_1 \cdot T_c + a_2 \cdot \bar{T}_{sk} + b \quad (\text{Eq. 3-1})$$

where R is a thermoregulatory response;

R_0 is a basal value of R ;

and a_1 , a_2 , and b are constants.

In terms of Figure 3-1, a_1 is the slope of a particular $R:T_c$ relation and a_2 is the effect of a unit change in \bar{T}_{sk} on the $R:T_c$ relation. The ratio $a_1:a_2$ is about 9:1 for all of the heat dissipating responses: sweating (96), vasodilation as represented by forearm blood flow (172), and release of vasoconstriction as represented by finger blood flow (171). (There are differences in nervous control between finger and forearm blood flow which are discussed in Control of Skin Blood Flow, below.)

The coefficients a_1 and a_2 represent the sensitivity of R to changes in T_c and \bar{T}_{sk} , respectively, and the ratio of 9:1 means that a change of 1°C in core temperature elicits about nine times as great a change in thermoregulatory response as a 1°C change in mean skin temperature. However, since skin temperature typically varies over a much wider range than does core temperature, the importance of

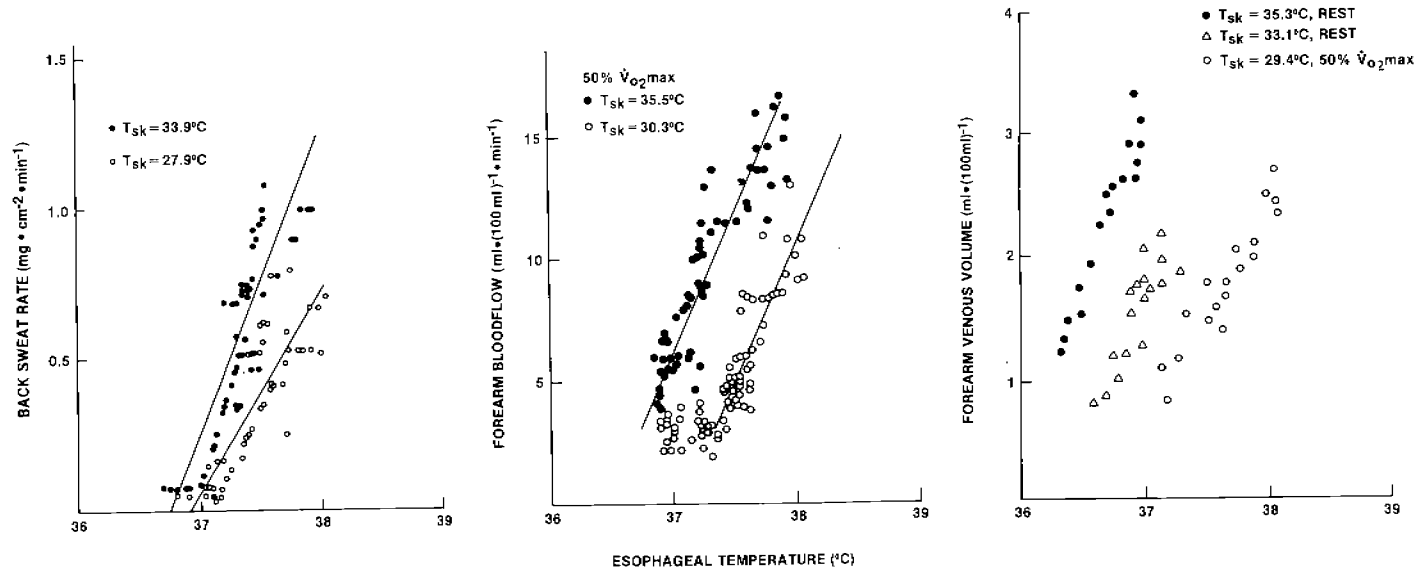


Figure 3-1. The relations of back sweating rate (left), forearm blood flow (center), and forearm venous volume (right) to esophageal and mean skin temperatures (T_{es} and T_{sk}). Sweating data are from four subjects performing cycle exercise at an O_2 consumption rate of 1.6 l/min . Measurements of forearm blood flow and forearm venous volume are from one subject each. Forearm temperature was kept at 36.8°C during measurements of blood flow, and at 35.1°C during measurements of forearm volume to eliminate a difference in local temperature between experiments at different ambient temperatures. Local temperature was not controlled independently during measurements of sweating, so that the difference between conditions includes a small effect of local skin temperature, appearing as a difference in slope. Left panel drawn from data of Reference 139; center panel modified from Reference 172; right panel modified from Reference 170.

skin temperature in thermoregulatory control is much greater than what the 9:1 ratio might suggest. The sensitivity of these thermoregulatory responses to core temperature allows the thermoregulatory system to keep core temperature relatively constant. Their sensitivity to mean skin temperature allows the system to respond appropriately to changes in environmental temperature over a wide range with little change in body core temperature. For example, the skin temperature of someone who enters a hot environment will rise and elicit sweating before any possible change in core temperature. On the other hand, an increase in heat production within the body, as occurs during exercise, has relatively little effect on skin temperature and elicits the appropriate heat-dissipating responses mostly in response to a rise in core temperature.

Once these thermoregulatory effector responses are sufficient to dissipate heat at the rate at which it is being produced, thermal balance is restored—i.e., the storage term in the heat balance equation (Chapter 1) is zero—so that core temperature stops rising and reaches a steady-state level. In the language of control theory, the rise in core temperature which elicits heat-dissipating responses sufficient to re-establish thermal balance is called a "load error." Even in a cool environment, core temperature must rise during exercise in order to increase skin blood flow to carry heat at a greater rate to the skin, whether or not sweating also is required. In a cool environment, the rate of skin blood flow occurring at a given level of core temperature will be less than in a warm environment, because of the lower mean skin temperature; but the cooler skin will also remove more heat from each liter of skin blood flow (see Heat Transfer From Skin Blood Flow, below), thus allowing the necessary core-to-skin heat transfer to be achieved with a lower rate of skin blood flow than in a warm environment.

During exercise the increase in core temperature is proportional to the metabolic rate, and nearly independent of environmental temperature over a fairly wide range (Fig. 3-6). This was first observed by Marius Nielsen in 1938, in experiments in which subjects exercised for one hour in ambient temperatures from 5 to 36° C. He showed that with increases in ambient temperature, reductions in heat loss by radiation and convection (dry or "sensible" heat loss) were exactly balanced by increases in evaporative cooling ("insensible" heat loss) (107) (Fig. 3-5). Nielsen concluded that core temperature increased during exercise as the consequence of "a change in the regulatory adjustment of body temperature", and not of an insufficient ability to dissipate heat, as had previously been thought (108). His conclusion has often been understood to mean that the body's "thermostat" is re-set at a higher level during exercise, or

equivalently that the core temperature thresholds for the thermoregulatory effector responses are elevated, as they are in fever (53,94). However, it is unnecessary to invoke any such threshold changes, since even without them an increase in core temperature is necessary to evoke heat-dissipating responses during exercise, as we have already shown. (We will comment further on the difference between the rise in core temperature with exercise and that with fever after developing the concept of thermoregulatory "set point".)

Besides fever, heat acclimation (Chapter 4), phase of the menstrual cycle, and time of day (Chapter 7) change the core temperature thresholds for the thermoregulatory responses. Since each of these factors has been shown to shift thresholds for several different thermoregulatory responses by the same amount (see References 56,75 for further discussion) it is useful to introduce the concept of a thermoregulatory "set point", which serves as a reference temperature in the control of all the thermoregulatory responses, and which is changed by these factors. A change in set point, then, produces a corresponding change in the threshold for each thermoregulatory response. Figure 3-2 shows schematically the difference between the rise in core temperature with exercise and that with fever. Conceptually, the difference between fever and exercise in Figure 3-2 is that the former involves an increase in thermoregulatory set point, and the latter does not (149). The observations on which this conceptual difference is based are these: First, although heat production sometimes increases substantially (through shivering) early during fever when core temperature is rising, it does not need to stay high to maintain the fever, and in fact it returns nearly to pre-febrile levels once the fever is established. During exercise, on the other hand, an increase in heat production not only causes the elevation in core temperature, but is necessary to sustain it. Second, for almost the whole time that core temperature is rising during fever, rate of heat loss is usually lower (and is never higher) than it was before the fever began. During exercise, however, the heat dissipating responses, and thus rate of heat loss, start to increase early and continue increasing, in response to rising core temperature.

The function of the human thermoregulatory system is shown schematically in Figure 3-3. Certain factors that act peripherally on the sweat glands and blood vessels, and are associated with local temperature and heat acclimation, are omitted here, but will be discussed later in this chapter and in Chapter 4. The scheme presented in Figure 3-3 presumes that there are thermal receptors in the skin and body core which send information about their temperatures to some central integrator, which generates a "thermal command signal" that participates in the control of sweating, vasodilation, and

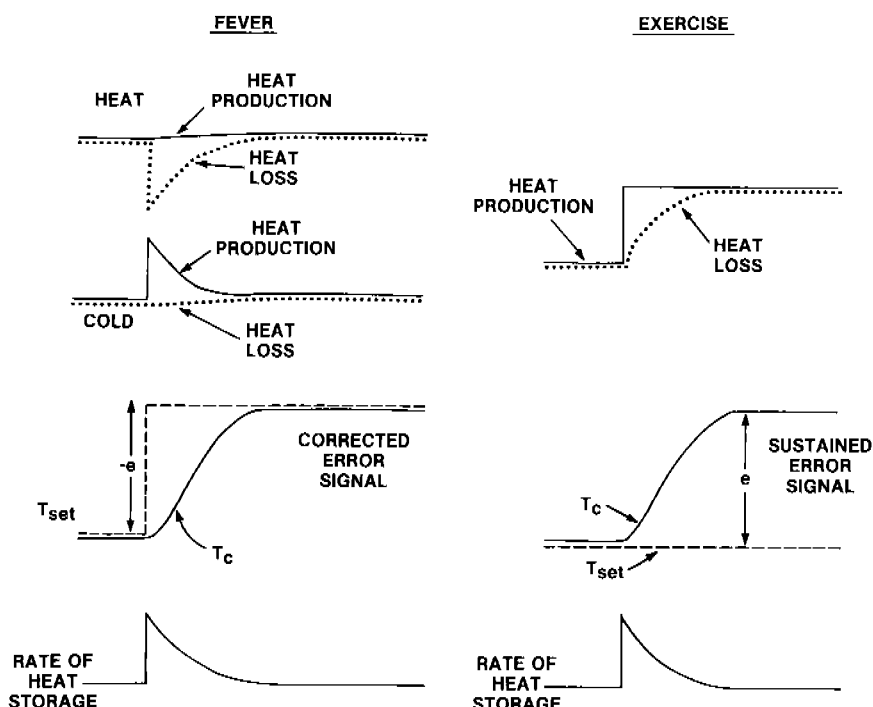


Figure 3-2. Differences between the elevation of core temperature in fever and the elevation of core temperature in exercise. In fever, the primary event is a rise in set point temperature (T_{set}), which initially causes a negative load error or error signal ($-e$). Heat-dissipating responses are inhibited and heat production is stimulated until T_c rises enough to correct the error signal and establish a new thermal balance in which heat production and heat loss are near (or slightly above) their values before the fever. During exercise T_c rises because of the increase in heat production. T_{set} is unchanged, and heat-dissipating responses are elicited as T_c rises. T_c continues to rise until it is high enough that the error signal (e) elicits heat loss responses at a rate sufficient to match heat production, and produce a new thermal balance. Figure reproduced from Reference 149, with permission.

vasoconstriction. The notion of such a thermal command signal is supported by the evidence for a common thermoregulatory set point, mentioned above, and by evidence that core and skin temperature are combined in the same way in the control of sweating, vasodilation, and vasoconstriction (56). Division of the thermal receptors in the body into those in skin and those in core is convenient and useful in practice, but it is somewhat artificial since, as discussed later in the chapter, neither the skin nor the core has a uniform temperature most of the time. The thermal receptors in the core (or at least those that participate in the control of thermoregulatory responses) are very unevenly distributed, and in laboratory mammals are concentrated especially in the hypothalamus, which also is where

much of the integration occurs (15). Changes of only a few tenths of 1°C in the temperature of the anterior preoptic area of the hypothalamus elicit changes in the thermoregulatory effector responses, and this area contains many neurons which increase their firing rate in response either to warming or to cooling. It is not known how much thermal receptors inside the core but outside the hypothalamus contribute to thermoregulation, but such thermal receptors have been reported in a number of other sites, including the hearts of rabbits (41), pulmonary vessels of sheep (14), and spinal cords of dogs (159). It is presumed that the human hypothalamus also has a high concentration of thermal receptors, although there is no direct evidence on this point. There is evidence, however, for a high concentration of thermal receptors somewhere in the distribution of the carotid arteries, since infusing hot saline solution into the carotid artery causes more vasodilation in the hand than do infusions into other arteries (32).

Since skin temperature generally is not uniform, the contribution of skin temperature to thermoregulatory control is usually expressed in terms of an appropriately weighted mean skin temperature. Neurophysiological studies show three types of thermal receptors in skin: a) One type responds to heating with a transient burst of activity and an increase of static activity (63,69); b) one type responds to cooling with a transient burst of activity and an increase of static activity (63,69); and c) one type responds to several stimuli, including warming, with a continuous discharge (63). The transient discharges that occur at the beginning of heating or cooling give the central integrator information about changes in skin temperature as they are occurring, and this feature may account for the sensitivity of sweating not only to skin temperature, but also to the rate at which skin temperature is changing (96).

In summary, if some disturbance, such as an increase in metabolic heat production or environmental temperature, upsets the thermal balance and causes additional heat to be stored in the body, temperatures in the core or skin (or both) will increase, and changes in these temperatures will be detected by the thermal receptors. In response to information from these receptors, the thermoregulatory controller in the central nervous system will call for responses that increase heat loss. Unless the heat stress exceeds the capacity of the thermoregulatory system, these responses will increase until they are sufficient to restore heat balance and prevent further increases in body temperatures. A parallel argument applies if the disturbance causes a net heat loss from the body, except that besides decreasing heat loss, the body can also increase heat production to restore heat balance (Chapter 9).

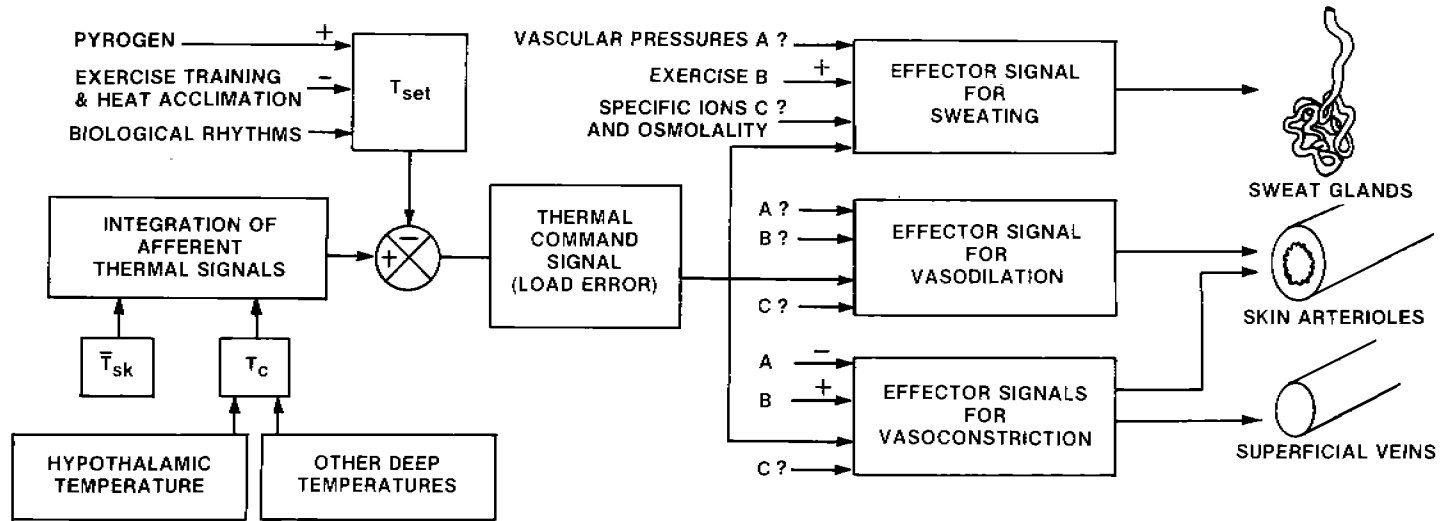


Figure 3-3. Schematic model of the control of human thermoregulatory effector responses.

The thermoregulatory system both controls responses that affect body temperatures and receives information about body temperatures. It therefore is said to receive "feedback" about the effect of its actions on body temperatures; and since the system responds to temperature changes in such away as to *oppose* further temperature changes in the same direction, it is said to be a "negative feedback" system. Negative feedback is not a characteristic only of the thermoregulatory system; it is an essential element of any regulatory system, in the sense in which the concept of regulation has been developed in this chapter.

BODY TEMPERATURES

Core Temperature

Fundamental to the study of human temperature regulation is the accurate measurement of deep body or core temperature. Core temperature is measured during physical exercise, to either estimate average internal temperature or provide information concerning the core temperature input to the thermoregulatory controller. It might seem that this basic measurement should by now, more than a century since the pioneering work of Claude Bernard (10), be well defined and broadly accepted. Instead, there is still debate among thermal physiologists concerning the best measurement site and the correct interpretation of the different indices of core temperature (16).

The idea that a single temperature measurement can provide an index of the average internal temperature may not be reasonable. By 1950, it was clear to several investigators that the notion of a single measurement site representing the average internal temperature was fictitious (8,9,71,89). In fact, Mead and Bonmarito (89) stated that "it is apparent that no single regional temperature could indicate, except by chance, the average of all internal temperatures." The idea that a single temperature measurement can provide a close approximation of the core temperature input to the thermoregulatory controller has several problems, both theoretical and practical. First, the thermoregulatory controller receives temperature input from many core sites (56). Second, although the hypothalamic temperature is believed to be a major input into the thermoregulatory controller, neither brain temperature (175) nor hypothalamic temperature has been well quantitated in humans.

The temperature within a given body region depends upon: (a) the metabolic rate of the surrounding tissues, (b) the source and magnitude of blood flow, and (c) the temperature gradients between contiguous body regions. Considerable temperature gradients exist between and within different orifices, body cavities and

blood vessels (45,71,90,147). For resting humans, about 70% of the metabolic heat is produced by internal organs and viscera within the body core (4,151). During muscular exercise, however, up to about 90% of the metabolic heat can be produced by the skeletal muscles. Because of the different source of metabolic heat during exercise as compared to rest, temperatures measured during exercise within a given body region may change relative to other body regions (3,90,129,130). For example, during rest in a comfortable environment, skeletal muscle temperature is lower than core temperature; however during exercise, the temperature within the active skeletal muscle exceeds core temperature (3,129,130), while the temperature within the inactive skeletal muscles usually does not increase (3). Blood perfusing the active skeletal muscles is warmed, and the warmer blood carries heat to other body regions and consequently core temperature is elevated (3,90).

The requirements for an ideal site to measure core temperature are: (a) the measurement site should be convenient, (b) the measurement should not be biased by environmental conditions, and (c) the measured changes should quantitatively reflect small changes in arterial blood temperature (29,147). In addition, the response time for temperature changes is an important consideration when selecting a measurement site for certain experimental situations, especially those involving exercise. A subject's core temperature is often measured at the esophagus, rectum, mouth and tympanum/auditory meatus. The relative advantages and disadvantages of these and other measurement sites are well understood (3,30,33,54,85,130). During the subsequent paragraphs these core temperature measurement sites will be systematically evaluated for their compliance with the stated requirements for an ideal site.

Esophageal Temperature. Esophageal temperature is obtained by inserting a catheter, containing a thermocouple or thermistor, through the nasal passage and into the throat and then swallowing it. Since some individuals find this procedure to be uncomfortable, a topical anesthetic, such as lidocaine, is often used on the catheter and/or in the throat to alleviate some discomfort. It is important to use a fairly stiff plastic catheter which will not easily curl back on itself when advanced within the esophagus. At the level of the left atrium, the heart and esophagus are in contact and are fairly isothermal (16). If the catheter is passed too far, such as into the stomach, the temperature and response times are altered; likewise, if the catheter is too high, the pulmonary ventilation will cool or heat (dependent upon ambient conditions) the temperature sensor (16,33,73,174). The proper catheter length can be predetermined from anatomical measurements and may be verified by a radiogram, an

acoustical signal, or by monitoring an electrocardiogram from the catheter tip (18). In our laboratory, an anatomical measurement of one-fourth the subject's height (R.R. Gonzalez, unpublished anatomical measurements of cadavers) is used as the catheter distance from the nostril to the heart level within the esophagus. A final methodological consideration is the avoidance of swallowing during measurement, as the passage of saliva will spuriously lower the esophageal temperature values. Swallowing can be avoided by having the subject spit or by using a suction device to remove saliva from the mouth (16).

Most thermal physiologists agree that esophageal temperature is the best non-invasive index of core temperature for humans. Several investigators have found that esophageal temperature responds rapidly to changes in blood temperature elicited by extracorporeal circulation (93,147), and by body cooling during anesthesia (30). For example, Shiraki *et al.* (147) found that esophageal temperature quantitatively reflected pulmonary artery (mixed venous blood) temperature with an average difference of 0.1°C and a lag time of about one minute during their hyperthermia experiments. Therefore, esophageal temperature provides a good index of blood temperature. Several investigators have simultaneously measured esophageal temperature and the temperature of active skeletal muscles during exercise (3,128,129,130). Each study demonstrated that during exercise esophageal temperature and active muscle temperatures achieved steady-state values in 15–20 minutes. The rapid response time for esophageal temperature is due to the low heat capacity of the esophagus and its proximity to the heart; therefore, it can be rapidly warmed or cooled.

Rectal Temperature. Rectal temperature is widely employed by physiologists because it is a comfortable and non-invasive measurement site. Rectal temperature is obtained by inserting a temperature sensor a minimum of five centimeters past the anal sphincter. Temperature measurements are uniform within the rectum from 5–27 centimeters past the anal sphincter (1,9,76,106). One early study (89) reported that rectal temperature values varied by as much as 0.8°C depending upon the insertion depth; this variability apparently resulted from the use of a very thin flexible catheter which caused great variability for temperature sensor placement within the pelvis. The use of a more rigid rectal catheter seems to solve this problem (1,9,76,89,106). Another potential problem is that a properly placed temperature sensor may later slip to less than five centimeters beyond the anal sphincter during muscular exercise. This potential problem can be solved by attaching a bulb to the rectal catheter at the desired insertion depth, that will abut the anal sphincter.

Rectal temperature values are generally higher than values measured in arterial blood (7,45) and other core temperature sites. During exercise it takes approximately 25–40 minutes to achieve steady-state rectal temperature values (3,60,90,106,128,129). These steady-state values are generally $\sim 0.2^{\circ}\text{C}$ higher than simultaneously measured esophageal temperature values (33,106,129,130) and they are independent of the environmental temperature (60,99,152). As a result, the steady-state rectal temperature provides a good index to assess body heat storage (130,154). The main problem with rectal temperature is that it is slow to respond to changes in blood (90) and other core temperatures. Figure 3-4 provides a representative record of rectal and esophageal temperature responses to two exercise bouts spaced by a rest period. Note that the slow response results in rectal temperature being less than esophageal values during periods of rapid heat storage, and greater than esophageal values during periods of rapid heat loss. The reason for the slow response of rectal temperature to thermal transients is probably a low rate of blood flow to the rectum compared to other measurement sites (7,93). The slow response time makes rectal temperature a poor core temperature index for estimating the input to the thermoregulatory controller (44,54,129).

Oral Temperature. Physicians routinely measure oral temperature to determine the presence of fever. For this, a thermometer is placed sublingually and allowed to equilibrate prior to recording of the temperature. The equilibration time necessary to obtain a stable oral temperature value ranges from 3 to 10 minutes and depends upon the ambient temperature (85,154). During the equilibration and measurement period the subject must breathe through the nose, as ventilation from mouth breathing can artificially lower oral temper-

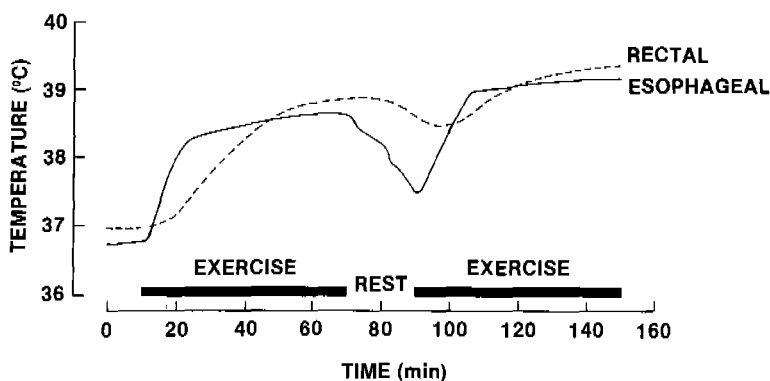


Figure 3-4. Rectal and esophageal temperature responses to rest and exercise in the heat.

ature values in cold environments and artificially elevate oral temperature values in hot environments. Some investigators have sealed their subjects' mouths to insure nasal breathing while obtaining oral temperature measurements (33,54). Finally, both swallowing and the ingestion of fluid must be avoided as they will bias oral temperature values (33,153).

The tongue is perfused by the lingual branch of the external carotid artery and has a high blood flow per gram of tissue (68). This enables the tongue to be an effective heat exchanger and allows sublingual temperatures to approximate blood temperature (72); however, changes in head and face skin temperatures will bias oral temperature (88,148). For example, McCaffrey *et al.* (88) measured oral temperature while cooling and heating areas of the head and neck. The oral temperature values followed the changes in cutaneous temperature of the head. Also, in cold environments, cheek cooling will affect the superficial segment of the parotid salivary duct and cool the saliva reaching the mouth, thus biasing the temperature measurement (148). Therefore, unlike esophageal and rectal temperature values, oral temperature values are not always independent of the environmental temperature.

Under favorable conditions, oral temperature values are very similar to esophageal temperature values (33,43,54,85). During steady-state light intensity exercise, which can be performed with nasal breathing, oral temperature values have been found to correlate well ($r = 0.83-0.92$) with simultaneously measured esophageal and rectal temperature measurements (85,153). During steady-state moderate intensity exercise, which can be performed with nasal breathing, oral temperature values may be lower than esophageal and rectal temperature values, perhaps due to a sympathetically mediated vasoconstriction of the tongue vasculature (85,154). Another possibility is that additional cooling of the upper respiratory passages may occur at greater exercise intensities (154).

Tympanic/Auditory Meatus Temperature. Tympanic temperature is obtained by inserting a small temperature sensor into the ear canal and advancing it until it rests against the tympanic membrane. Proper placement is determined by the subject's hearing a sound when the temperature sensor touches the tympanic membrane. Some subjects find this contact to be uncomfortable (16). In addition, there are reports of the temperature sensor's perforating the tympanic membrane (38,155,163). Because of the potential discomfort and trauma as well as placement problems associated with tympanic measurements, some investigators have chosen instead to measure the temperature of the external auditory meatus. For this measurement, a temperature sensor is placed in an ear plug and inserted

into the external auditory meatus. Placement of the temperature sensor is important since there is a substantial ($\sim 0.5^{\circ}\text{C}$) temperature gradient along the wall of the meatus (29).

Tympanic/auditory meatus temperature measurements do not provide a reliable index of the level of core temperature during either rest or exercise (29,60,86,87,88,99). Depending upon the environmental conditions, tympanic/auditory meatus temperature values can be lower or higher than simultaneously measured steady-state rectal (60,99) and esophageal (86,87,88) temperature values. In addition, local head heating and air flow to the face will bias the temperature of the external meatus (86,87,88). Therefore, tympanic/auditory meatus temperature is not independent of the environmental conditions. Since the tympanic/auditory meatus temperature values are biased by facial skin temperature, the measured temperature is the sum of a variable weighting (depending upon the environmental condition) of skin and core temperature (60,88,99). However, if ambient temperature is constant and neither esophageal or oral measurements can be obtained, the rapid change in tympanic/auditory meatus temperature can be of some value in estimating the core temperature input to the thermoregulatory controller during exercise (113).

Skin Temperature

Skin temperature is measured for the purposes of: (a) calculating the mean body temperature for heat storage determinations, (b) calculating sensible (radiative and convective) heat exchange and skin conductance, and (c) integrating into an index of the skin temperature input to the thermoregulatory controller. Although the skin surface is easily accessed (unlike the core), measurement problems often occur because the skin represents the boundary between two media, tissue and the ambient air. As a result, changes in skin temperature might result from physiological adjustments (cutaneous blood flow, sweat evaporation) or alterations in the environment (air motion, temperature, radiation). Generally, skin temperatures are measured from temperature sensors in contact with the skin's surface or from non-contact infrared methods. For the former method, care needs to be taken to insure that the temperature sensor remains in good thermal contact with the skin, since otherwise the measurement will be biased by the ambient temperature.

Although a single skin temperature measurement can be useful for biophysical calculations, thermal physiologists are more often interested in the average or mean skin temperature (65,177). The mean skin temperature (\bar{T}_{sk}) represents the sum of weighted individual skin temperatures. Generally, the weighting is based on the per-

centage of body surface area that is represented by the body region from where the temperature is measured (91). For example, Hardy and DuBois (65) divided the body into 12 regions while Winslow and colleagues (177) divided the body into 15 regions for skin temperature measurements. Numerous investigators have attempted to minimize the number of measurement sites necessary to obtain a valid estimate of mean skin temperature (115,158). Mitchell and Wyndham (91) compared nine of these shortened equations which are used to estimate mean skin temperature. They recommended that when it is difficult to measure a large number of sites, the equation developed by Ramanathan (115) be used, where:

$$\begin{aligned}\bar{T}_{sk}, ^\circ\text{C} = & 0.3 (\text{chest} + \text{upper arm temperatures}) \\ & + 0.2 (\text{thigh} + \text{calf temperatures})\end{aligned}\quad (\text{Eq. 3-2})$$

Mean skin temperature values that are based on regional weighting according to the percentage of body surface area are particularly useful for the calculation of mean body temperature and heat storage.

Nadel and colleagues (101) have developed a novel approach to determine the regional weightings for the mean skin temperature calculation. Their approach was to base the regional weighting on the skin's thermal sensitivity and not on its percentage of body surface area. These investigators reasoned that thermal receptors are not evenly distributed over the skin's surface, and warming of a body region having the greatest number of thermal sensors would have the greatest influence on the thermoregulatory effector responses. Nadel and colleagues had subjects rest in a range from warm to hot environments while they applied thermal radiation to selected skin areas and measured the change in sweating rate at the thigh. Based upon the thermal sensitivity data (change in thigh sweating rate), which was adjusted for regional surface area, they developed the following equation:

$$\begin{aligned}\bar{T}_{sk}, ^\circ\text{C} = & 0.21 (\text{face temperature}) \\ & + 0.21 (\text{mean of chest and back temperatures}) \\ & + 0.17 (\text{abdomen temperature}) \\ & + 0.15 (\text{thigh temperature}) \\ & + 0.08 (\text{calf temperature}) \\ & + 0.12 (\text{upper arm temperature}) \\ & + 0.06 (\text{forearm temperature})\end{aligned}\quad (\text{Eq. 3-3})$$

Subsequently, Libert *et al.* (81) conducted a similar study in which they heated larger skin areas by smaller temperature increments but for greater durations than in the experiments of Nadel and colleagues. Libert *et al.* (81) concluded that the weighting factors based on thermal sensitivity were not different from the weightings based

on percent of body surface area. It seems that more research is needed concerning the use of a thermal sensitivity approach for calculation of the mean skin temperature. Both of these studies were performed on semi-nude and resting subjects (81,101), and the results obtained may not be directly applicable to clothed or exercising subjects. Finally, the thermal sensitivity approach may eventually become the preferable index for estimating the skin temperature input to the thermoregulatory controller.

CORE TEMPERATURE RESPONSES TO EXERCISE

Environment and Exercise Intensity

As depicted in Figure 3-4, during dynamic exercise core temperature initially increases rapidly and subsequently increases at a reduced rate until heat loss equals heat production and essentially steady-state values are achieved. The elevation of core temperature represents the storage of metabolic heat which is a by-product of skeletal muscle contraction. At the initiation of exercise, the metabolic rate increases immediately; however, the thermoregulatory effector responses for heat dissipation respond more slowly. The thermoregulatory effector responses which enable sensible (radiative and convective) and insensible (evaporative) heat loss to occur, increase in proportion to the rate of heat production (103). Eventually, these heat loss mechanisms increase sufficiently to balance metabolic heat production allowing a steady-state core temperature to be achieved.

During muscular exercise, the magnitude of core temperature elevation at steady-state is largely independent on the environmental condition and is proportional to the metabolic rate (58,82,107, 108,152). These concepts were first presented by Nielsen (107) who had three subjects perform exercise at several intensities (up to $\sim 3.0 \ell O_2 \cdot \text{min}^{-1}$) in a broad range (5° to 36°C with low humidity) of ambient temperatures. Figure 3-5 presents the heat exchange data for one subject during an hour of cycle exercise at a power output of 147 watts and at an aerobic metabolic rate of approximately 650 watts. The difference between metabolic rate and total heat loss represents the energy used for mechanical work and the heat storage. Note that the total heat loss and, therefore, the heat storage and elevation of core temperature were constant for each environment. The relative contributions of sensible and insensible heat exchange to the total heat loss, however, varied with the environmental conditions. In the 10°C environment, the large skin-to-ambient temperature gradient facilitated sensible heat exchange which accounted for $\sim 70\%$ of the total heat loss. As the ambient temperature increased, this gradient for sensible heat exchange diminished and there was a

greater reliance upon insensible heat exchange. When the ambient temperature is equal to skin temperature, insensible heat exchange will account for essentially all of the heat loss. In addition, when the ambient temperature exceeds the skin temperature, there is a sensible heat gain to the body.

Nielsen's finding that the magnitude of core temperature elevation is independent of the environmental conditions, is inconsistent with the personal experience of most athletes. For example, a runner will certainly experience greater hyperthermia if he/she competes in a 40° C than in a 20° C environment (119). Lind (82) has shown that the magnitude of core temperature elevation during exercise is independent of the environment only within a range of conditions or a "prescriptive zone." Figure 3-6 presents a subject's steady-state core temperature responses during exercise performed at three metabolic intensities while in a broad range of environmental conditions. The environmental conditions are represented by the "old" effective temperature, which is an index that combines the effects of dry bulb temperature, humidity and air motion. Note that during exercise, the greater the metabolic rate, the lower is the upper limit of the prescriptive zone. In addition, Lind found that

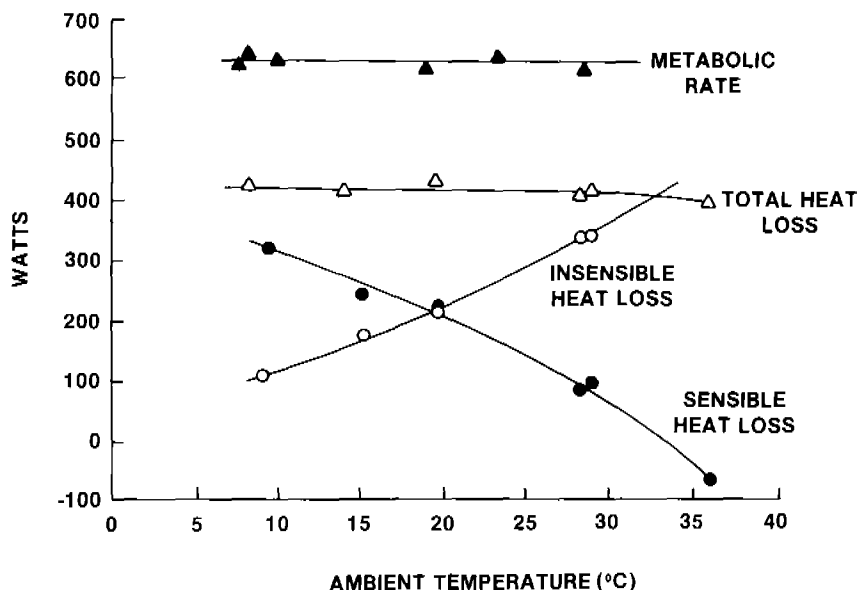


Figure 3-5. The heat exchange data averaged over one hour for one subject performing constant intensity exercise in a variety of ambient temperatures. The difference between metabolic rate and total heat loss is the sum of mechanical power (147 W) and mean rate of heat storage. Redrawn from Reference 107.

even within the prescriptive zone there was a small but significant positive relationship between the steady-state core temperature and the old effective temperature. It seems fair to conclude that throughout a wide range of environmental conditions, the magnitude of core temperature elevation during exercise is largely but not exclusively independent of the environment. During exercise with a substantial combined metabolic and environmental heat stress, the thermoregulatory load error is great enough to result in further elevated steady-state core temperature levels. In addition, in humid environments the evaporative capacity of the environment may be insufficient to dissipate the individual's metabolic heat from exercise and result in further elevated core temperature levels (58).

As stated, within the prescriptive zone the magnitude of core temperature elevation during exercise is proportional to the metabolic rate (107,130,152). For any individual, the greater the metabolic rate, the higher the individual's steady-state core temperature during exercise (129). The relationship between metabolic rate and core temperature is good for a given individual, but does not always hold well for comparisons between different individuals. Åstrand (6) first reported that the use of relative intensity (percent of maximal oxygen uptake), rather than actual metabolic rate (absolute intensity),

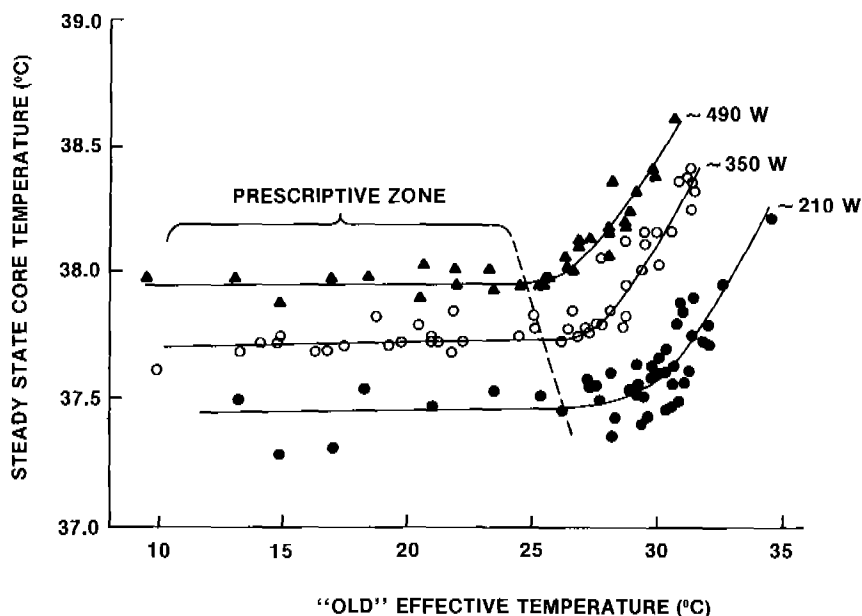


Figure 3-6. Relationship of steady-state core temperature responses during exercise at three metabolic rates to the environmental conditions. Redrawn from Reference 82.

removes most of the inter-subject variability for the core temperature elevation during exercise. Figure 3-7 shows the relationship of steady-state core temperature to both absolute and relative intensities in a moderate environment (130).

Davies and colleagues (35,36,37) attempted to clarify the relationship between relative intensity and the steady-state core temperature response to exercise. Their investigations were performed in environments with dry bulb temperatures ranging from 5° to 25° C (relative humidity is <50%) and with the subjects performing exercise at relative intensities ranging from ~20% to ~90% of their maximal oxygen uptake. Figure 3-8 presents data redrawn from their studies; note that for a group of laboratory and field experiments (Figure 3-8A) there was a curvilinear relationship between steady-state core temperature and relative intensity (37), described by the quadratic equation:

$$T_{cv} \text{ } ^\circ\text{C} = 37.25 - 0.00264 (\% \dot{V}O_2\text{max}) + 0.00037 (\% \dot{V}O_2\text{max})^2.$$

Figure 3-8B presents two subjects' steady-state core temperature values during exercise, at 65% and 85% of their maximal oxygen uptake, in relation to the ambient dry bulb temperature (35). Core temperature was found to be independent of dry bulb temperature from 5 to 20° C at the 65% relative intensity; however, core temperature was influenced by dry bulb temperature at the 85% relative intensity. These data are consistent with those of Lind (82), showing that the prescriptive zone is smaller at higher metabolic rates.

The preceding investigations have shown that in humans, core temperature changes are related to the relative exercise intensity. It

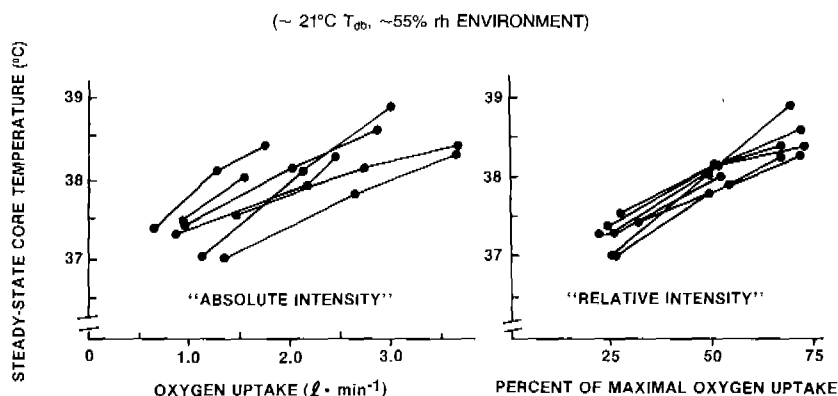


Figure 3-7. Relationship of steady-state core temperature responses during exercise to the absolute and relative metabolic rates. Redrawn from Reference 130.

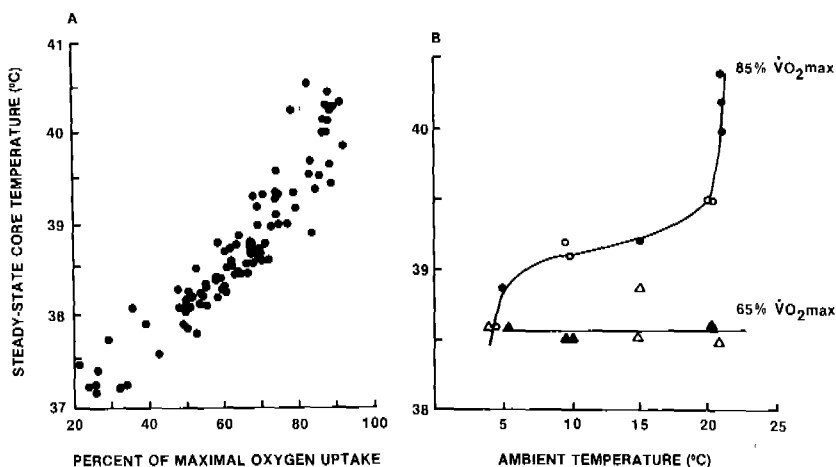


Figure 3-8. Relationship of steady-state core temperature responses during exercise to the relative exercise intensity and the ambient temperature. Panel 3-8A is redrawn from Reference 37 and panel 3-8B is redrawn from Reference 35.

would, therefore, seem logical to expect that any condition lowering maximal oxygen uptake (and thus increasing relative intensity) would also elicit an elevated core temperature response at a given absolute (thus higher relative) intensity. This hypothesis has been tested by several investigators with differing results (61,79,105,127). Greenleaf *et al.* (61) lowered three subjects' maximal oxygen uptake by simulating altitudes of 2,000 m (-11%) and 4,000 m (-32%) in a hypobaric chamber. Their subjects' core temperature responses during cycle exercise at a given metabolic rate were similar whether exposed to sea level or to simulated altitude. However, their subjects' resting core temperature values decreased with simulated altitude, and there may have been a greater increase in core temperature from rest to exercise at the 4,000 m than sea level experiments. Rowell *et al.* (127) lowered six subjects' maximal oxygen uptake (-27%) by having them breathe hypoxic (11–12% O_2) gases during cycle exercise in a comfortable environment. They found similar steady-state core temperatures during exercise at a given metabolic rate whether the subjects were breathing normoxic or hypoxic air. The core temperature at rest, however, was only measured with the subjects' breathing normoxic air. In contrast, Nielsen (105) found that lowering of maximal oxygen uptake (-15 to -28%) by carbon monoxide poisoning resulted in a higher core temperature during cycle exercise at a given metabolic rate, but the relation to relative intensity was essentially unchanged. Finally, Kolka *et al.* (79) had eight sub-

jects perform cycle exercise in a hypobaric chamber at sea level, and then at simulated altitudes of 2,600m and 4,600m. Their subjects' maximal oxygen uptakes were reduced from sea level values by -8% (2,600 m) and -19% (4,600 m). They found that the increase in core temperature from rest to exercise was dependent upon the relative intensity.

It would also seem logical to expect that any condition increasing maximal oxygen uptake (thus lowering relative intensity) might elicit a lowered core temperature at a given metabolic rate. Two studies have used autologous erythrocyte infusion to increase subjects' maximal oxygen uptake (comfortable environment) and subsequently measured their core temperature responses to exercise in the heat (138,140). The first study (138) used subjects who were unacclimated to the heat, and found that steady-state core temperatures at a given metabolic rate were not significantly reduced after erythrocyte infusion. However, the calculated heat storage values were generally lower during the post- than during the pre-infusion heat stress tests. The second study (140) used heat-acclimated subjects, and found lowered steady-state core temperature responses at a given metabolic rate during the post- compared to the pre-infusion heat stress tests.

In conclusion, during muscular exercise the core temperature response is proportional to the metabolic rate. If the metabolic rate is expressed as a percentage of the individual's maximal oxygen uptake, then much of the inter-subject variability disappears for the magnitude of steady-state core temperature values. Acute changes in maximal oxygen uptake, however, may or may not modify the steady-state core temperature response at a given metabolic rate. There is some evidence, however, that the increase in core temperature from rest to exercise might be related to the relative intensity during simulated altitude experiments. The inconsistent results between investigations probably reflect differences in subject status (e.g., fitness, acclimation state) and/or differences in the methods employed to acutely alter maximal oxygen uptake.

Exercise Type

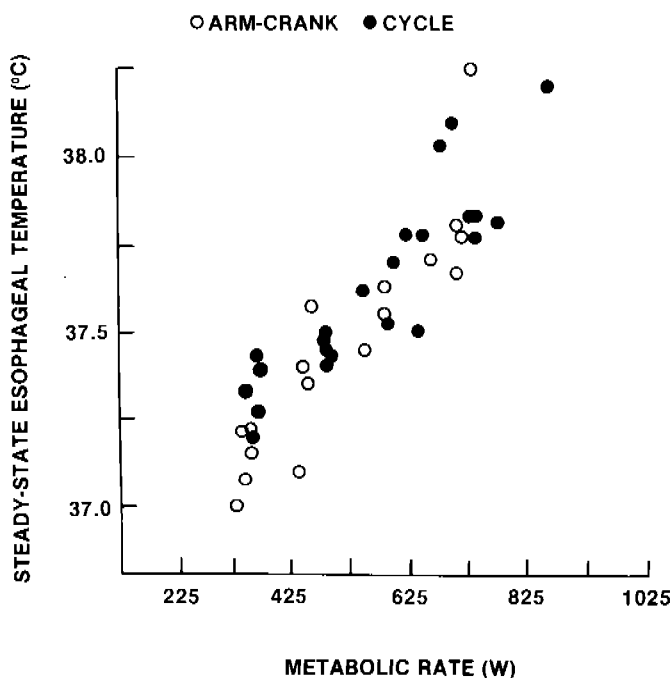
All of the investigations discussed so far have employed leg (lower body) exercise (treadmill or cycle). There is debate as to whether upper body exercise (e.g., arm-crank) results in different core temperature values than those elicited by lower body exercise at the same metabolic rate. Maximal effort arm-crank exercise elicits an oxygen uptake that is approximately 70% of that obtained during maximal effort cycle exercise. It is uncertain whether the core temperature response during arm-crank exercise would be determined

by the relative intensity of the upper or lower body muscle mass. If these responses are determined by the relative intensity (with respect to the musculature employed) then arm-crank exercise would be expected to elicit a higher core temperature for a given metabolic rate than would lower body exercise.

In 1947, Asmussen and Nielsen (5) studied two subjects' core temperature responses to arm-crank and cycle exercise at the same metabolic rates. They found that arm-crank exercise elicited lower rectal temperature values than cycle exercise. In addition, this difference widened as metabolic rate increased. Since the authors were concerned that rectal temperature may have been spuriously high during cycle exercise because of the warm venous blood returning from the leg muscles, they conducted additional experiments in which they monitored stomach temperature. In agreement with their rectal temperature data, the stomach temperature values were consistently lower during arm-crank than cycle ergometer exercise. In 1968, Nielsen (104) examined the core temperature responses of two subjects during arm-crank and cycle ergometer exercise. Rectal temperature values (mean of values obtained at four depths ranging from 12–27 cm past the anal sphincter) were found to be consistently lower during arm-crank than cycle exercise at a given metabolic rate. In contrast, esophageal temperature values appeared to be similar for the two exercise types at a given metabolic rate (Figure 3-9).

In 1984, Sawka *et al.* (142) measured nine subjects' rectal temperature responses during arm-crank and cycle exercise performed at similar absolute and relative intensities. During the experiments matched for absolute intensity, the subjects' steady-state rectal temperature values were the same for both exercise types. On the other hand, during the experiments matched for relative intensity, the subjects' rectal temperature values were lower during arm-crank than cycle exercise. Subsequently, in a different group of experiments, these investigators (139) found that their subjects' steady-state esophageal temperature values were the same for arm-crank and cycle exercise at the same metabolic rate.

It seems clear that during upper body exercise the magnitude of core temperature elevation is determined by the metabolic rate and not the relative exercise intensity. Several early studies (5,104) reported that rectal temperature values were lower during arm-crank than cycle exercise at a given metabolic rate. Those findings suggest that rectal measurements may not provide the best index of core temperature during upper body exercise. Later studies, however, reported no difference for rectal (142) or esophageal temperature (104,139) responses between the two exercise types at a given met-



a hot as compared to a comfortable environment (77,126,128,143,145), but some investigators report no differences (124,176). For example, in one study (143) maximal oxygen uptake was $0.2 \text{ l} \cdot \text{min}^{-1}$ lower in a 49°C , as compared to a 21°C environment. The physiological mechanism responsible for the decreased maximal oxygen uptake is probably the diversion of blood to the cutaneous vasculature which could: (a) reduce the portion of the cardiac output perfusing the contracting musculature and/or, (b) cause a peripheral pooling of blood, reduce the central blood volume and thus reduce cardiac filling pressure and cardiac output as discussed later.

Acute heat stress increases the metabolic rate for resting humans (27,28,40) and anesthetized dogs (144). Does heat stress alter an individual's metabolic requirements for performing a given submaximal exercise task? The answer to this question not only affects the calculation of the heat balance equation, but might also have implications for the nutritional requirements of individuals exposed to hot environments. This latter concern stimulated Consolazio and colleagues (27,28) and later others to address the question of metabolic requirements for humans performing exercise in hot environments. Many investigators have found that to perform a given submaximal exercise task the metabolic rate is greater in a hot than comfortable environment (27,28,40,48). Some investigators have reported the opposite results (20,112,176,179). The subjects' state of heat acclimation does not account for whether they demonstrate an increased or decreased metabolic rate during submaximal exercise in the heat. We believe that this discrepancy can be explained and we will attempt to do so in the following paragraphs. All of these investigators, except one (40), only calculated the aerobic metabolic rate during submaximal exercise.

Dimri *et al.* (40) had six subjects perform cycle exercise at three power output levels in each of three environments. Figure 3-10 presents their subjects' total metabolic rate (bottom) and the percentage of this metabolic rate which was contributed by aerobic and anaerobic metabolic pathways. The anaerobic metabolism was calculated by measuring the post-exercise oxygen uptake that was in excess of resting baseline levels. Note that to perform exercise at a given power output, the total metabolic rate increased with the elevated ambient temperature. More importantly, the percentage of the total metabolic rate contributed by anaerobic metabolism also increased with the ambient temperature. The increased anaerobic metabolic rate exceeded the increase of total metabolic rate during exercise at the elevated ambient temperatures. Therefore, if only the aerobic metabolic rate had been quantified, Dimri *et al.* (40) would have reported a decreased metabolic rate in the heat for performing exercise

at a given power output. The investigations which reported a lower metabolic rate during exercise in the heat also reported increased plasma or muscle lactate levels (112,176,179) or an increased respiratory exchange ratio (20) which also suggests an increased anaerobic metabolism. Likewise, other investigators have reported that plasma lactate levels are greater during submaximal exercise in a hot as compared to a comfortable environment (39,40,48,95,120).

Skeletal Muscle Metabolism

Two investigations have examined the effects of environmental heat stress on skeletal muscle metabolism during exercise (48,179). Fink *et al.* (48) had six subjects perform 45 minutes of cycle exercise (70 to 85% of $\dot{V}O_2\text{max}$) in a cold (9°C) and a hot (41°C) environment. They found greater plasma lactate levels and increased muscle glycogen utilization during exercise in the heat. Also, muscle triglyceride utilization was reduced during exercise in the heat as compared to the cold. In addition, serum glucose concentration increased and serum triglyceride concentration decreased during ex-

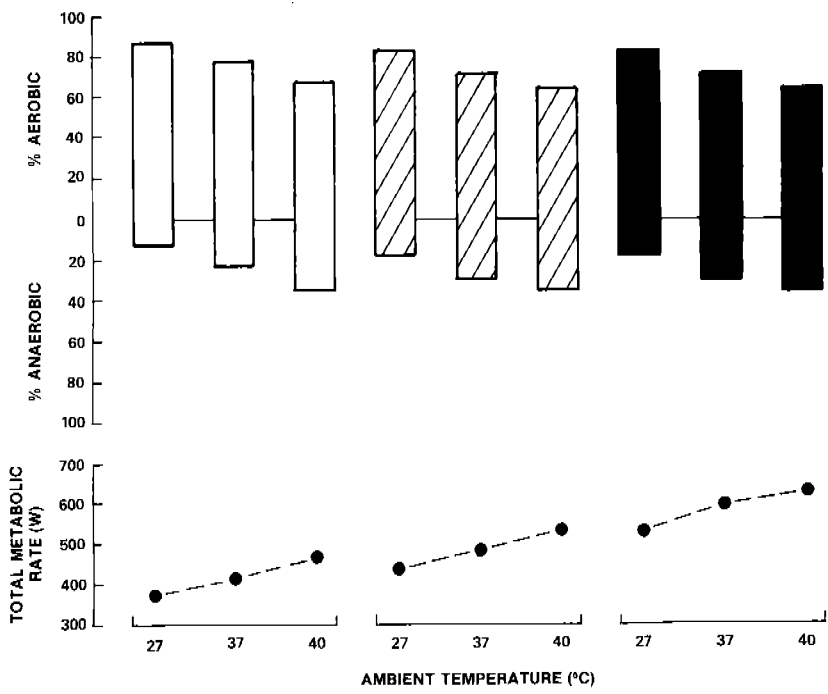


Figure 3-10. The total metabolic rate and percentage contribution of aerobic and anaerobic metabolism during exercise at different ambient temperatures. Drawn from data presented in Reference 40.

ercise in the heat, compared to the opposite responses during exercise in the cold. During exercise in the heat, the increased muscle glycogen utilization was attributed to an increased anaerobic glycolysis resulting from local muscle hypoxia, which was caused by a reduced muscle blood flow. Since these investigators (48) did not perform the control experiments in a comfortable environment, the differences reported could be due partially to the effects of the cold exposure.

Young *et al.* (179) had 13 subjects perform 30 minutes of cycle exercise (70% of $\dot{V}O_{2\max}$) in a comfortable (20° C) and a hot (49° C) environment. They found that skeletal muscle and plasma lactate concentrations were greater during exercise in the heat. Interestingly, they also found a relationship ($r = 0.70$) between the subjects' percent fast twitch fibers and the increase of muscle lactate in the hot environment (Figure 3-11). These investigators found no difference in muscle glycogen utilization between the two experimental conditions. Young *et al.* (179) speculated that during exercise in the heat, an alternative glycolytic substrate might have been utilized, such as blood borne glucose. Rowell *et al.* (125) have shown a dramatic increase in hepatic glucose release into the blood during exercise in a hot compared to a comfortable environment. Such an increased release of hepatic glucose could account for the elevated serum glucose concentration reported in the hot environment by Fink *et al.* (48).

The data from Dimri *et al.* (40) and Young *et al.* (179) both support the concept of increased anaerobic metabolism during submaximal exercise in the heat. Much of the other support for this concept is based on the findings that, during submaximal exercise, the plasma lactate accumulation is greater in a hot than in a comfortable environment (39,40,48,95,120,176,179). However, any inference about metabolic effects at the muscle level from changes in plasma lactate is open to debate. Plasma lactate concentration reflects the balance between muscular production, efflux into the blood, and removal from the blood. Rowell *et al.* (125) have shown that during exercise in the heat the splanchnic vasoconstriction reduced hepatic removal of plasma lactate. Therefore, the greater blood lactate accumulation during submaximal exercise in the heat can be attributed, at least in part, to a redistribution of blood flow away from the splanchnic tissues.

The question remains as to what physiological mechanism(s) might be responsible for an increased anaerobic metabolism during exercise in the heat. As will be discussed, one possibility is the redistribution of blood to the cutaneous veins for heat dissipation; this may result in reduced perfusion of the active skeletal muscles and

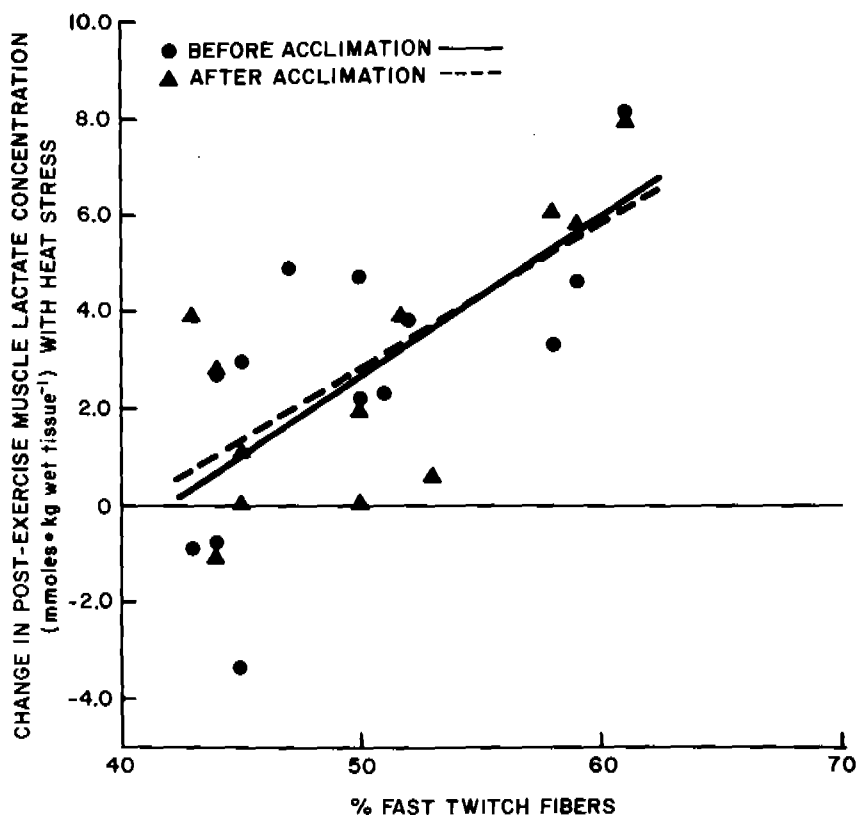


Figure 3-11. The relationship between the subject's percentage of fast-twitch muscle fibers and the magnitude of muscle lactate increment in a hot compared to comfortable environment during exercise (179).

thus local tissue hypoxia (176). Hypoxia would be expected to cause a shift from aerobic to anaerobic pathways in order to provide energy for the skeletal muscle contraction. Another possible explanation for increased anaerobic metabolism, is that acute heat exposure might increase the recruitment of fast-twitch motor units. Fast-twitch skeletal muscles derive a greater percentage of their total energy expenditure from anaerobic pathways than do slow-twitch fibers, regardless of their level of perfusion (141). In addition, fast-twitch fibers expend a greater amount of energy to develop the same amount of tension than do slow-twitch fibers (141,166). A final possibility is that an elevated temperature may reduce the efficiency of skeletal muscle (19) and, therefore, increase the energy cost of contraction.

In conclusion, acute heat stress has marked effects on metabolism. During maximal exercise, an individual's maximal oxygen uptake is reduced by heat stress. During submaximal exercise, the total energy expenditure is probably greater in a hot than in a comfortable environment. The greater total energy expenditure may simply reflect the individual's discomfort in the heat, thus making more extraneous movements during exposure. On the other hand, biochemical and physiological mechanisms may also contribute to the greater total energy cost. Finally, it seems clear that there is a shift from aerobic to anaerobic metabolic pathways during exercise in the heat.

EVAPORATIVE HEAT LOSS

Sweat Gland and Evaporation

Figure 3-5 illustrates that when the ambient temperature increases, there is a greater dependence upon insensible (evaporative) heat loss to defend core temperature during exercise. For humans, unlike most animals, respiratory evaporative cooling is small compared to total skin evaporative cooling (92). This provides the advantage of having a greater surface area available for evaporation. The eccrine glands secrete sweat onto the skin surface which causes evaporative cooling when it is converted from liquid to water vapor. The rate of evaporation is dependent upon the gradient between the skin and ambient water vapor pressure, and the evaporative heat transfer coefficient (see Chapter 1); and the wider the gradient, the greater the rate of evaporation for a given mass transfer coefficient. When a gram of sweat is vaporized at 30° C, 2.43 kilojoules (kJ) of heat (the latent heat of evaporation) is absorbed in the process (167). Wenger (167) has shown that ambient vapor pressure and solute content do not alter the latent heat of evaporation.

During cycle ergometer exercise it is not unusual for an individual to have a metabolic rate of 800 W ($\dot{V}O_2 \sim 2.3 \text{ l} \cdot \text{min}^{-1}$). If the exercise performed is 20% efficient then the remaining 80% of the metabolic rate is converted to heat in the body, so that 640 W (i.e., $0.64 \text{ kJ} \cdot \text{s}^{-1}$ or $38.4 \text{ kJ} \cdot \text{min}^{-1}$) needs to be dissipated to avoid body heat storage. The specific heat of body tissue is $\sim 3.5 \text{ kJ} \cdot \text{kg}^{-1} \cdot ^\circ\text{C}^{-1}$ (see Chapter 1) so that a 70 kg man has a heat capacity of $245 \text{ kJ} \cdot ^\circ\text{C}^{-1}$. If such a man performed exercise in an environment that enabled only insensible heat exchange, and he did not sweat, the body temperature would increase by $\sim 1.0^\circ \text{C}$ every 6.4 min ($245 \text{ kJ} \cdot ^\circ\text{C}^{-1} \div 38.4 \text{ kJ} \cdot \text{min}^{-1}$). Since the latent heat of evaporation for sweat is $2.43 \text{ kJ} \cdot \text{g}^{-1}$, this man would need to evaporate $\sim 16 \text{ g}$ of sweat per min ($38.4 \text{ kJ} \cdot \text{min}^{-1} \div 2.43 \text{ kJ} \cdot \text{g}^{-1}$) in order to achieve a steady-state body

temperature. This amount of sweat output is not unreasonable, as values in excess of 30 g per min have been reported during exercise in the heat (146).

Thermoregulatory sweat in humans is secreted by about 1.6–4 million eccrine glands (80,131). The number of sweat glands per unit of skin surface area varies considerably between body regions (80). Eccrine sweat glands are most numerous on the sole of the foot and least numerous on the back (131). The fine structure of the eccrine sweat gland consists of the secretory coil, duct and skin pore. The secretory coil is composed of clear cells as well as dark mucoid and myoepithelial cells. The clear cells contain many mitochondria and are believed to be responsible for the secretion of sweat and electrolytes (131). The clear cells are probably dependent upon glucose as a substrate, but it is unclear whether the source is local glycogen stores or blood borne glucose (131). Sweating can cause glycogen depletion in the clear cells, but this apparently does not occur in heat acclimated individuals (131). The myoepithelial cells provide structural support for the secretory epithelium, but do not contribute directly to the expulsion of sweat as once believed (133).

The amount of sweat secreted by the eccrine gland is dependent upon the structure and function of the stimulated gland, as well as the sudomotor signal from the central nervous system. Sato and Sato (137) have recently excised human eccrine sweat glands and performed *in vitro* analyses of their structure and function. They found that individuals who were self-categorized as copious sweaters had larger eccrine glands. In addition, as the sweat gland size increased there were: (a) a greater maximal sweating rate per gland, (b) a greater sweating rate per unit tubular length or unit volume of secretory coil, and (c) a greater cholinergic sensitivity of the sweat gland. These findings emphasize the importance of eccrine gland size and cholinergic sensitivity on the thermoregulatory sweating response.

Neural Control of the Sweat Gland

The sudomotor signal descends through the brain stem and spinal tracts to exit into the paravertebral ganglionic chain. The post-ganglionic sympathetic fibers which innervate the eccrine gland are nonmyelinated class C fibers that are primarily cholinergic. The eccrine sweat glands respond primarily to thermal stress through sympathetic cholinergic stimulation. However, it appears that circulating catecholamines, in particular epinephrine, facilitate thermoregulatory sweating as there are α and β adrenergic receptors associated with eccrine sweat glands (2,114,134,135,136). The relative effects on sweat secretion are 4:1:2 for cholinergic, α adrenergic

and β adrenergic receptor stimulation, respectively (131). Robertshaw has reported in *Macaca speciosa* that epinephrine released from the adrenal medulla will enhance the sweating rate during exercise in the heat (118). Finally, vasoactive intestinal polypeptide (VIP) may be released at the eccrine sweat gland (84). Lundberg *et al.* (84) have shown that VIP and acetylcholine are concomitantly released from the same post-ganglionic fibers innervating exocrine glands of the cat. Although both transmitters caused exocrine secretions, the VIP primarily acts by dilation of local vasculature to facilitate sweat gland function. For many years it has been known that eccrine sweat secretion and cutaneous vasodilation are associated (83). The co-release of acetylcholine and VIP at the eccrine gland might explain this relationship (78,84).

Figure 3-12 represents the pattern of eccrine secretion, as measured by dew point hygrometry, during exercise in a comfortable environment. Note that sweat is normally secreted in a cyclic pattern, which may reflect the pattern of action potentials transmitted via the sudomotor neurons and subsequent neuroglandular release of acetylcholine (46,47). Thermoregulatory sweating can begin within a few seconds (162) to minutes (59) after starting muscular exercise. This variability for the onset time of thermoregulatory sweating is influenced by skin temperature, previous sweating and other factors. The increase in thermoregulatory sweating closely parallels the increase in body temperature (100,129). As the sweating rate increases toward maximum levels, first there is a recruitment of sweat glands and then an increased sweat secretion per gland (70,116,132). Therefore, the sweat secretion for a given region of skin is dependent upon both the density of sweat glands as well as the sweat secretion per gland (70,100,116,132). Nadel *et al.* (100) have also demonstrated that individual regions of skin have different sweating responses for a given core temperature. Figure 3-13 presents the regional local sweating responses plotted against core temperature. Note that for a given core temperature the back and chest have the greatest sweating rates. Conversely, the limbs will have relatively high sweating rates only after a substantial elevation in core temperature.

Skin Temperature and Ambient Water Vapor Pressure

For a given sudomotor signal to the eccrine gland, local skin temperature and skin wettedness influence the amount of sweat secreted. Bullard and co-workers (24) were among the first to systematically evaluate the relationship between local skin temperature and thermoregulatory sweating. They found that for an active eccrine gland, an elevated local skin temperature induced a greater sweat-

50% $\text{VO}_{2\text{max}}$; 28°C, 30% rh

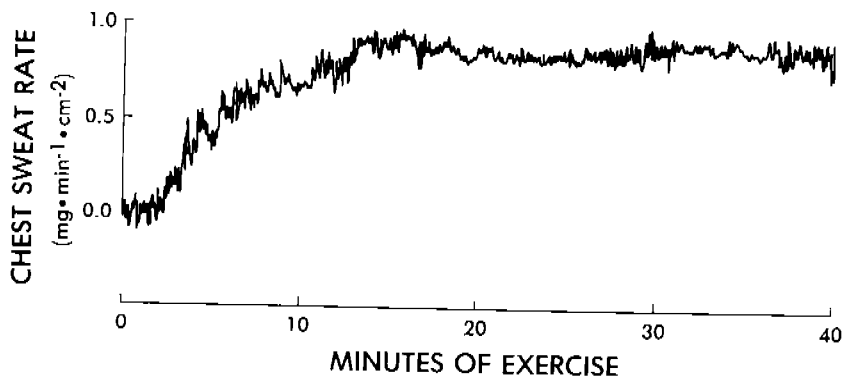


Figure 3-12. The pattern of eccrine sweating, as measured by dew point hygrometry, during exercise in the heat.

ing rate. These results have since been verified and expanded upon by many other investigators (46,47,96,109,110).

Nadel *et al.* (96) conducted a study on the importance of skin temperature in the regulation of sweating. These investigators independently varied the mean skin temperature, core temperature, and local skin temperature, while measuring thigh sweating rate during rest and post-exercise. They concluded that: (a) at a constant skin temperature sweating rate was proportional to core tempera-

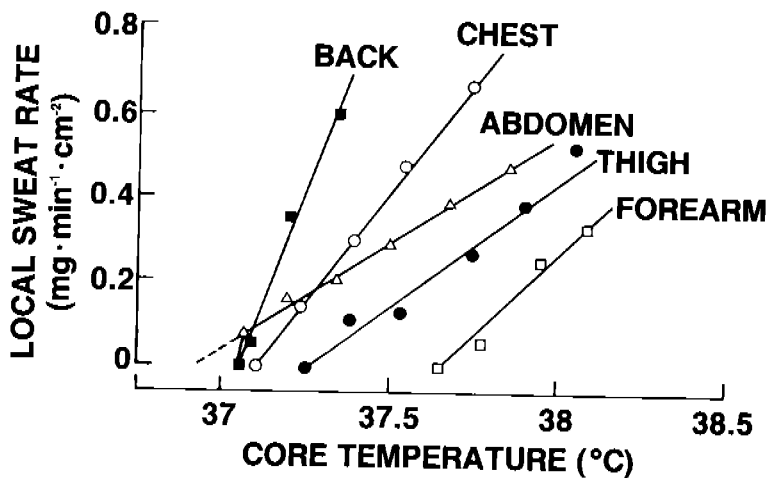


Figure 3-13. The regional sweating rate responses plotted against core temperature. Redrawn from Reference 100.

ture, (b) at a constant core temperature sweating rate was proportional to the mean skin temperature, and (c) at a given combination of core and mean skin temperatures local sweating was dependent on the local skin temperature. It was proposed that the local skin temperature acted as a multiplier to the central control signal, represented by a linear additive model of core and mean skin temperatures, to determine local sweating rate.

The physiological mechanism by which elevated local skin temperatures enhances the sweating response is unclear. However, several factors may contribute to enhanced sweating. Some investigators believe that local skin heating results in a greater release of neurotransmitter substance for a given sudomotor signal arriving at the eccrine sweat gland (24,46,47,96,109,110). The greater neurotransmitter release would, in turn, stimulate greater sweat production and release. In addition, Ogawa and colleagues (109,110) have provided evidence that local heating increases the eccrine glands responsiveness to a given amount of neurotransmitter substance. It is unknown if this increased glandular responsiveness is receptor mediated or reflects increased cellular metabolism within the secretory coil.

Remember, the rate of sweat evaporation depends upon air movement and the water vapor pressure gradient between the skin and the environment, so that sweat tends to collect on the skin in still or moist air. Wetting the skin surface causes a reduction in sweat secretion (26,59,102), an effect called hidromeiosis. The mechanism(s) responsible for hidromeiosis is/are unknown, although several hypotheses have been proposed. Peiss *et al.* (111) suggest that wetting the skin might cause the stratum corneum to swell and cause mechanical obstruction of the sweat duct. This idea was systematically tested by Brown and Sargent (23) who supported the concept that hydration of the stratum corneum was responsible for hidromeiosis. Nadel and Stolwijk (102) proposed that sweat may follow an osmotic gradient (from the solutes left behind by evaporated sweat) from the proximal duct to the skin surface; and have hypothesized that excessive skin wettedness might reduce, via dilution, the osmotic gradient along the sweat duct, thus reducing sweating rate. Candas *et al.* (26) suggested that hidromeiosis may result, by negative feedback, from locally wet skin which reduces local sweat output. All of the above hypotheses, with the exception of the first, are tentative and more research is merited concerning skin wettedness and the mechanisms of sweat suppression. Interestingly, if the environmental evaporative capacity is increased and subsequently sweat on the skin evaporates, the sweating rate will be potentiated (102,156). For example, Nadel and Stolwijk (102) demonstrated that

individuals exposed to increased air motion, had an elevated sweating rate at a given core temperature during exercise in a warm-dry environment.

Several investigators (160,178) have proposed that the eccrine sweat glands may fatigue during prolonged periods of high sweat output; the notion being that the fatigued eccrine gland is unable to respond to a constant or even increasing sudomotor signal (23). The evidence supporting the idea of sweat gland fatigue is that: (a) during prolonged (three-five hours) periods of heat exposure, both the steady-state (55,159,178) and maximal (178) sweating rates are reduced and, (b) these "fatigued" eccrine glands demonstrate reduced responsiveness to the subdermal injection of a sudorific agonist (159). Examination of these studies, however, can lead one to conclude that hidromeiosis and/or dehydration (Chapter 6) may account for much of the so-called glandular fatigue.

Brown and Sargent (23) conducted a series of experiments to determine if hidromeiosis could be responsible for the proposed eccrine gland fatigue. They found that during prolonged (four-eight hours) heat exposure, the decline in sweat output could be reversed if the subject were simply moved from a moist heat to a dry heat. Brown and Sargent (23) then subdermally injected a sudorific agonist into the skin and measured the local sweating responses both before and after a four-to six-hour walk in the heat. These injections were made in areas of intact skin and in areas of skin that were stripped of the stratum corneum. They found that total body sweating rate decreased after several hours and continued to decrease throughout the duration of the exercise-heat exposure. During this period the local sweating rates decreased in the intact skin, but remained more nearly constant for the stripped skin. Likewise, injection of the sudorific agonist demonstrated a reduced sweat responsiveness in the intact skin but no change in sweat responsiveness in the stripped skin. They concluded first that excessively wetted skin results in swelling of the stratum corneum which obstructs the sweat duct and causes hidromeiosis, and second that hidromeiosis accounts for the so-called sweat gland fatigue in their experiments.

In conclusion, during exercise in hot environments, the evaporation of eccrine sweat is an important avenue of heat exchange for humans. The eccrine sweat glands are primarily controlled by the thermoregulatory center(s) via sympathetic cholinergic nerves, but local temperature modifies sweat secretion. Core temperature provides the primary input to the thermoregulatory controller for sweating; however, skin temperature also provides a smaller input. In addition, wetting of the skin surface causes a reduction in sweat secretion, an effect called hidromeiosis.

SKIN CIRCULATION AND HEAT TRANSFER

Control of Skin Blood Flow

Skin blood flow carries heat by convection between the deep body tissues and the skin. When core and skin temperatures are low enough that sweating does not occur, raising skin blood flow brings skin temperature nearer to blood temperature, and lowering skin blood flow brings skin temperature nearer to ambient temperature. In such a situation, the body is able to control sensible (convective and radiative) heat loss by varying skin blood flow, and thus skin temperature. In conditions in which sweating occurs, skin blood flow continues to increase with increases in core or skin temperature. However, in these conditions the tendency of skin blood flow to warm the skin is approximately balanced by the tendency of sweating to cool the skin. Therefore, there is usually little change in skin temperature and sensible heat exchange after sweating has begun, and skin blood flow serves primarily to deliver to the skin the heat that is being removed by sweat evaporation. Skin blood flow and sweating thus work in tandem to dissipate heat under such conditions.

Skin circulation is affected by temperature in two ways: local skin temperature affects the vascular smooth muscle directly, as discussed later in this section; and temperatures in the core and of the skin elsewhere on the body affect skin blood flow by reflexes operating through the sympathetic nervous system (Fig. 3-1). Blood flow in much of the human skin is under a dual vasomotor control (51,122). During cold exposure (and also with certain non-thermal reflexes—see Figure 3-3), skin blood flow is reduced through the action of vasoconstrictor fibers. These fibers presumably are adrenergic, since their action is blocked by bretylium (11). In the hands, feet, lips, ears, and nose, these fibers seem to be the predominant vasomotor innervation, and the vasodilation that occurs in these regions during heat exposure is largely the result of withdrawing vasoconstrictor activity. Over most of the skin area, however, vasoconstrictor activity is already minimal under conditions of thermal comfort, and vasodilation during heat exposure depends on intact sympathetic innervation, since it can be prevented or reversed by regional nerve block (12,51). Since it depends on the action of neural signals, such vasodilation is sometimes referred to as active vasodilation. Both active vasoconstriction and active vasodilation play a major part in controlling skin blood flow of the upper arm, forearm, thigh, and calf (12). However, active vasoconstriction is believed not to have a major role in controlling skin blood flow on the trunk or on most of the head (13,52).

Although active vasodilation occurs in limited skin areas (mostly paws and tail) in many animal species, human beings seem to be unique in the intensity of the response and the amount of skin involved (122). The vasoactive agonist responsible for active cutaneous vasodilation in man has not yet been identified, but some investigators have suggested that the vasodilation is mediated through the action of sweat glands. It has been proposed that sweat glands, when stimulated to secrete sweat, also release bradykinin, a powerful vasodilator, into the interstitial space of the skin (51), where it acts on the arterioles of the skin. This hypothesis now seems doubtful, and Rowell (122) has summarized the arguments against it. Nevertheless, active vasodilation may be linked to sweat gland activity through some other mechanism, such as release of vasoactive intestinal polypeptide (VIP), since VIP-like immunoreactivity has been reported in the terminals of the cholinergic nerves supplying human sweat glands (161). Evidence suggesting a relationship of active vasodilation to sweating includes observations on some patients with anhidrotic ectodermal dysplasia, a rare hereditary condition in which sweat glands are absent. Although these patients had normal vasoconstrictor activity in their forearms, and their forearm skin vasodilated normally in response to local heating, no active vasodilation occurred in response to whole-body heating (17). Since patients with anhidrotic ectodermal dysplasia usually have normal autonomic function, it is tempting to conclude that active vasodilation is secondary to some action of the sweat glands. Other explanations are possible, however, such as that in this disorder both the sweat glands and the nerve endings responsible for active vasodilation failed to develop during embryogenesis.

Besides contributing to the reflex control of skin blood flow, skin temperature also affects skin blood flow through direct actions on the blood vessels themselves (21,22), as shown in Figure 3-14. Local temperature acts on skin blood vessels in at least two ways. First, local cooling potentiates, and heating weakens, the contractile response of vascular smooth muscle to norepinephrine and other constrictor agonists, apparently by changing the affinity of α_2 adrenergic receptors for these agonists (75). Second, in human forearm skin (and presumably in other skin regions where active vasodilation occurs) local heating causes vasodilation, and local cooling causes vasoconstriction, even in the absence of nervous signals (173). Through this direct vasodilator effect, local heating increases skin blood flow so much that most of the heat delivered to the skin is carried away by the blood and little is conducted to the deeper tissues. This response reinforces thermoregulatory vasomotor responses, and also tends to protect the skin from heat injury.

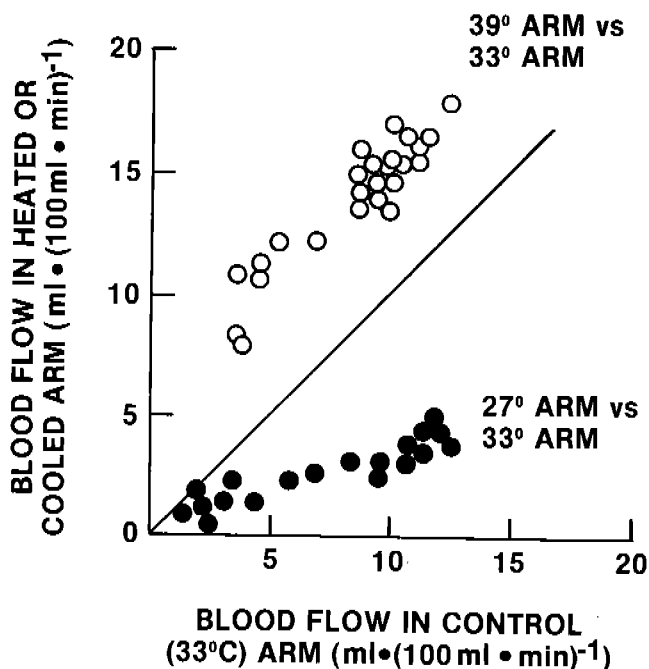


Figure 3-14. Effect of local temperature on forearm blood flow during cycle exercise. The skin of the experimental forearm was either heated to 39° C (open circles) or cooled to 27° C (filled circles), and the skin of the control forearm was maintained always at 33° C. Blood flow in the experimental forearm is plotted against blood flow measured simultaneously in the control forearm. If there were no effect of local temperature, plotted points would lie on the line of identity. Redrawn from Reference 169.

Heat Transfer from Skin Blood Flow

Blood has a volume specific heat of $3.85 \text{ kJ} \cdot \ell^{-1} \cdot ^\circ\text{C}^{-1}$ ($0.92 \text{ kcal} \cdot \ell^{-1} \cdot ^\circ\text{C}^{-1}$) so that if a liter of blood at, say, 37° flows through the skin and returns to the body core 1° C cooler, the body core loses 3.85 kJ of heat. The muscle blood flow necessary to sustain aerobic metabolism depends on the O_2 content of the arterial blood, which is seldom much above 200 ml O_2 per liter. The energy released when 200 ml O_2 is consumed depends somewhat on the substrate being oxidized, but is about 4.2 kJ. Thus, even if the muscle uses all of the oxygen in the arterial blood, it needs to be only 1.09° C warmer than the arterial blood in order for the blood to remove the heat that the muscle is producing. Therefore, the blood flow needed to sustain aerobic metabolism provides amply for removing heat from exercising muscle.

The rate of core-to-skin heat transfer by skin blood flow depends

on the rate of skin blood flow and on the temperature difference between blood leaving the core on its way to the skin and blood returning to the core from the skin. In the most efficient case, this temperature difference is equal to the difference between core and skin temperature (T_c and T_{sk}), and core-to-skin heat flow (HF) is:

$$HF = (SkBF \cdot 3.85 \text{ kJ} \cdot \ell^{-1} \cdot ^\circ\text{C}^{-1} + K_o) \cdot (T_c - T_{sk}) \quad (\text{Eq. 3-4})$$

where SkBF is skin blood flow. SkBF must be expressed in $\ell \cdot \text{s}^{-1}$, rather than the more usual $\ell \cdot \text{min}^{-1}$, to compute HF in W; and K_o is the thermal conductance of the tissues when skin blood flow is at a minimum. K_o depends on body surface area and thickness of subcutaneous fat, but typically is $10\text{--}18 \text{ W} \cdot ^\circ\text{C}^{-1}$ (66).

In practice, especially in a cool subject, heat transfer is less efficient. As the warm blood leaves the body core via the arteries, it flows through superficial tissues that are cooler than the core but warmer than the skin, and as it flows through these tissues, the blood gives up some of its heat to them. The blood that enters the skin is thus cooler than the core, so that heat loss from the blood to the skin is less than that given by Equation 3-4. Some of the heat that the blood has lost on its way to the skin eventually finds its way to the skin by conduction, but some of this heat is returned to the cooled venous blood as the blood passes through the same layers of tissue on its way back to the core through which it passed on its way outward. One may think of this heat as having taken a "short circuit" from the arteries to the veins, without having passed through the skin. This process, the back-and-forth exchange of heat between the blood and the tissues through which it passes on the way between core and skin, thus has the effect of reducing convective heat transfer by the blood, or alternatively of requiring more blood flow to cause a given heat transfer than would be required in the most efficient case assumed in Equation 3-4.

The difference between actual core-to-skin heat transfer and that predicted by Equation 3-4 is subject to physiological control in the limbs. To explain this, it is first necessary to describe the dual venous drainage of the limbs, consisting of deep veins, which ordinarily drain blood mainly from the muscles; and superficial veins, which lie in the skin and subcutaneous tissue and ordinarily drain blood mainly from the skin. However, the deep and superficial veins are connected by many penetrating veins, so that potentially blood from anywhere in the limbs can return to the heart through either deep or superficial veins. The deep veins have a relatively poor sympathetic innervation (165), but the superficial veins have a rich sympathetic innervation (165), constricting when the skin or body

core is cooled and dilating when the skin or core is warmed (164,170). In a cool subject, therefore, most blood from the limbs returns to the core via the deep veins. Since these veins and the major limb arteries lie adjacent to each other for a considerable part of their length, some of the heat from the arterial blood flow is conducted to the cooler venous blood and returned to the body core, and so is conserved. Such heat exchange between parallel streams moving in opposite directions is called "counter-current" heat exchange. In a warm subject, however, counter-current heat exchange is no longer advantageous, and it is considerably diminished by dilation of the large superficial veins, which allows much of the venous blood to return to the core along paths far removed from the major limb arteries. Dilation of the large superficial veins thus increases core-to-skin heat transfer by minimizing counter-current heat exchange. In addition, dilation of the smaller superficial veins may further improve heat transfer by increasing the time that the blood remains in the skin, as suggested by evidence that the degree of venous filling affects heat transfer to the skin (57).

Venous occlusion plethysmography is the most quantitative non-invasive method for measuring blood flow. However, it can be used only on the extremities. Furthermore, the part of the body being studied must be elevated above the heart to provide venous drainage, so that the use of this technique is limited to the hand and forearm in most situations. Since muscle blood flow is generally not influenced by thermal reflexes (42), changes in hand or forearm blood flow due to thermal reflexes can be taken to represent primarily changes in skin blood flow. Measurements of heat flow, either through the skin as a whole or through a restricted area, are sometimes divided by the temperature difference between core and skin to give a thermal conductance. Even in the absence of blood flow, there will be some heat flow due to the thermal conductivity of the tissues themselves (Equation 3-4), but after the contribution of this heat flow to thermal conductance is subtracted, the remainder can be used as an index of skin blood flow. However, such calculations only give values for the *minimum* blood flow rate which could produce the observed heat flow. For reasons discussed earlier, the actual blood flow may be, and probably usually is, greater; but accurate data on the relation between heat flow and blood flow are available only for the extremities and only in a few conditions. Furthermore, if this method is used to provide an index of blood flow to the entire skin, potentially serious errors may be introduced by regional variation in skin temperature. Given the lack of a better practical index, forearm blood flow is often used as an index of whole-body skin blood flow, since both types of vasomotor control, con-

strictor and dilator, are represented in forearm skin. However, very little information is available concerning how good an index forearm blood flow actually is under different conditions.

CARDIOVASCULAR CONSEQUENCES OF THERMOREGULATORY INCREASES IN SKIN BLOOD FLOW

Thermoregulatory Skin Blood Flow Responses to Exercise-Heat Stress

Although skin temperature is higher the warmer the environment, core temperature is relatively unaffected by environmental temperature over a fairly wide range, as discussed above. Thus in a warm environment the core-to-skin thermal gradient is relatively narrow, and skin blood flow increases in response to the high skin temperature, so as to achieve core-to-skin heat transfer sufficient for thermal balance (Equation 3-4). During exercise, metabolic rate and heat production may be ten or more times their levels at rest. A healthy but not athletic, young 70-kg man may have a metabolic rate at rest of 80 W and a $\dot{V}O_{2\max}$ of $3.5 \ell \cdot \text{min}^{-1}$, which corresponds to a metabolic rate of 1215 W. Even though core temperature rises during exercise and thus widens the core-to-skin temperature gradient somewhat, this small effect on core-to-skin heat transfer is not enough to match the increase in metabolic heat production. Besides widening the core-to-skin temperature gradient, the rising core temperature elicits reflex increases in skin blood flow, which eventually produce a rate of core-to-skin heat transfer sufficient to re-establish heat balance.

During exercise in the heat the narrow core-to-skin temperature gradient and the high rate of metabolic heat production that needs to be dissipated combine to require high levels of thermoregulatory skin blood flow. It is not possible to measure whole-body skin blood flow directly, but we can make an approximate estimate of skin blood flow during exercise from Equation 3-4. Let us consider again the man performing cycle exercise at a metabolic rate of 800 W and 20% efficiency, for a rate of heat production of 640 W. If at steady state his mean skin temperature is 35.5°C and core temperature is 39°C , and if we ignore respiratory heat loss and assume an intermediate value of $14\text{W} \cdot ^{\circ}\text{C}^{-1}$ for K_o , Equation 3-4 becomes $640 \text{ W} = (\text{SkBF} \cdot 3.85\text{kJ} \cdot \ell^{-1} \cdot ^{\circ}\text{C}^{-1} + 14\text{W} \cdot ^{\circ}\text{C}^{-1}) \cdot (3.5^{\circ}\text{C})$. Since $1 \text{ W} = 0.001 \text{ kJ} \cdot \text{s}^{-1}$, solving for SkBF we have $\text{SkBF} = 0.044\ell \cdot \text{s}^{-1} = 2.64 \ell \cdot \text{min}^{-1}$. This is a crude estimate of skin blood flow, and should be taken only as an approximate figure. Although the man in this example is under considerable thermal stress, his estimated skin blood flow

is well below the maximum obtainable. Rowell estimated the maximum skin blood flow obtainable by the combined effects, local and reflex, of heating the skin and body core. He computed skin blood flow of heated resting subjects as the sum of increases in cardiac output and decreases in splanchnic, renal, and muscle blood flow during heating (121). At the end of heating, core temperature was 39.1° C and still rising at an undiminished rate, skin temperature was 40.5° C, and computed skin blood flow was $7.8 \ell \cdot \text{min}^{-1}$ and had nearly stopped rising, and so was probably near the maximum obtainable by skin and whole-body heating. Such a high skin blood flow may be incompatible with the muscle blood flow required during exercise, and at any event is unrepresentatively high for exercise because of the effects of the high skin temperature.

Circulatory Strain During Exercise-Heat Stress

It is evident from the foregoing examples that during exercise-heat stress thermoregulatory skin blood flow, though not precisely known, may be substantial. The higher skin blood flow will generally, but not always, result in a higher cardiac output, and one might expect the increased work of the heart in pumping this blood to be the major source of cardiovascular strain associated with heat stress. The work of the heart in providing the skin blood flow necessary for thermoregulation in the heat does, in fact, impose a substantial cardiac strain on patients with severe cardiac disease (25). In healthy subjects, however, the cardiovascular strain associated with heat stress results mostly from reduced cardiac filling and stroke volume (Fig. 3-15), which require a higher heart rate to maintain cardiac output. This occurs because the venous bed of the skin is large and compliant and, moreover, dilates reflexly during heat stress (122; Fig. 3-1). Therefore, as skin blood flow increases, the blood vessels of the skin become engorged and rather large volumes of blood pool in the skin, thus displacing blood from the thorax and reducing central blood volume and cardiac filling (122,123; Fig. 3-16). Since about 70% of the blood volume in an upright human being is below heart level (122), it is in the upright posture that the cardiovascular effects of this blood pooling are greatest. Thus, for example, stroke volume during exercise is lower in the upright than in the supine posture, and this difference between postures is greatest in the heat (117).

In addition, exercise and heat stress affect plasma volume in two ways. First, they cause fluid movements between plasma and tissues (67; Chapter 6). These fluid movements can occur rather quickly (Fig. 3-15), well before any substantial losses of fluid have occurred by sweating. The overall magnitude and direction of these

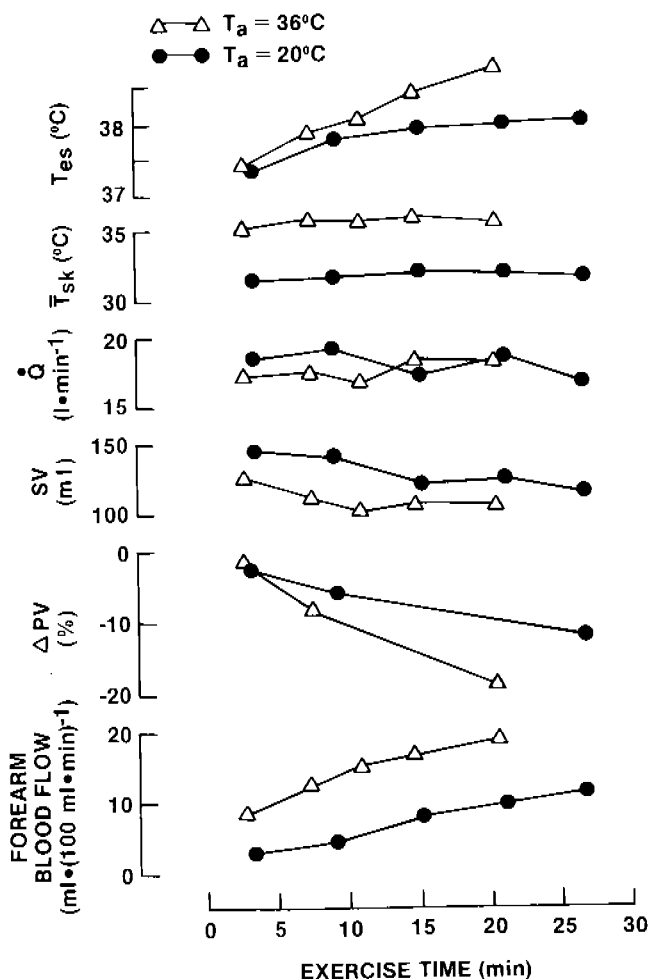


Figure 3-15. Thermal and circulatory responses of one subject during cycle exercise at 70% $\dot{V}O_{2\max}$ in ambient temperatures of 20 and 36° C, showing (from top) esophageal and mean skin temperatures, cardiac output, stroke volume, percent change in plasma volume, and forearm blood flow. Drawn from data presented in Reference 97.

fluid movements depends on a number of factors, such as temperature, exercise type and intensity, hydration level, and status of heat acclimation, so that the overall effect may be either to increase or to decrease plasma volume, and thus to alleviate or to aggravate the circulatory effects of pooling of blood in the skin. Second, much fluid is lost by sweating during exercise and heat stress. Since the main solute in sweat is sodium chloride, a disproportionately large

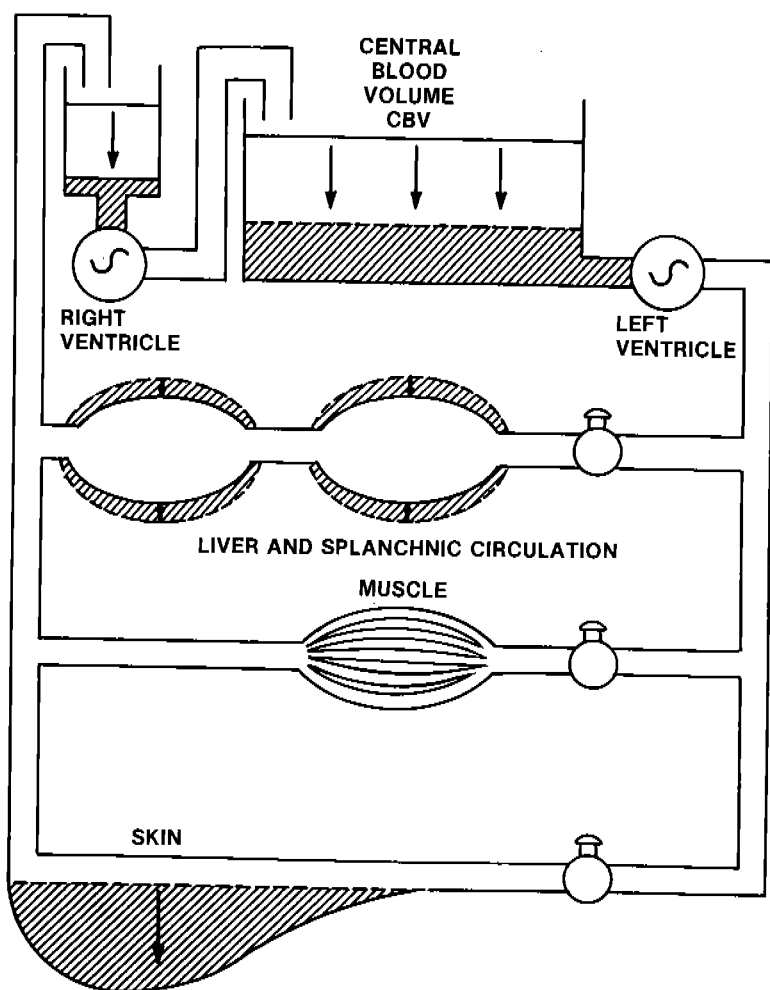


Figure 3-16. Schematic diagram of the effects of skin vasodilation on the thoracic reservoirs from which the ventricles are filled, and also effects of compensatory vasomotor adjustments in the splanchnic circulation. Redrawn from References 122,123.

fraction of the water in the sweat will be lost at the expense of extracellular fluid, including plasma, to the extent that the body's sodium ion content is reduced. The disproportionate loss from extracellular fluid will be minimized if the sweat is dilute, as is the case with subjects well acclimatized to heat. If the water and salt lost by sweating are not replaced, plasma and extracellular fluid volumes will be progressively reduced during exercise-heat stress.

Compensatory Responses to Maintain Cardiovascular Homeostasis During Exercise-Heat Stress

There are several reflex adjustments that compensate for peripheral pooling of blood and possible decreases in plasma volume, and help to maintain cardiac filling, cardiac output, and arterial pressure during exercise-heat stress. Splanchnic and renal blood flows are reduced during exercise (121). The reduction in splanchnic blood flow is in proportion to relative exercise intensity (i.e., as a percent of $\dot{V}O_2\text{max}$), and presumably the same is true of renal blood flow (121). These blood flows also undergo a graded and progressive reduction in subjects heated at rest; and in the splanchnic bed, at least, the vasoconstrictor effects of temperature and of exercise appear to be additive, so that at any exercise intensity the reduction in splanchnic blood flow is greater at a higher skin temperature (121). Reduction of renal and splanchnic blood flow allows a corresponding diversion of cardiac output to skin and exercising muscle. In addition, the splanchnic vascular bed and the hepatic vascular bed into which it drains via the hepatic portal vein are very compliant, so that a reduction in splanchnic blood flow is followed by a reduction in the amount of blood pooled in these beds (Fig. 3-16). A substantial volume of blood can thus be mobilized from these beds to help maintain cardiac filling during exercise and heat stress.

Since skin blood flow can reach high levels during exercise-heat stress, and since high skin blood flow may produce substantial peripheral pooling of blood, one might ask whether exercise affects skin blood flow in the same way that it affects renal and splanchnic blood flow. Since exercise quickly warms the body, and since thermal factors play such a large role in control of skin blood flow, especially during exercise in the heat, it is useful to re-state the question so as to separate thermal from non-thermal influences on skin blood flow. We shall do this by asking whether exercise affects the relation of skin blood flow to core and skin temperatures and, if so, whether the effect of exercise is proportionate to relative exercise intensity (percent $\dot{V}O_2\text{max}$). Under conditions of high cardiovascular strain, such as during very intense exercise or at high skin temperatures, skin blood flow at a given core and skin temperature is known to be reduced during exercise (121,123). However, at moderate skin temperatures, the relation of forearm blood flow to core and skin temperatures is independent of exercise intensity over a range from mild to fairly intense exercise (74,172; see Reference 168 for further discussion). A more recent study has confirmed these findings, and extended them by showing that at a sufficiently high exercise intensity, skin blood flow is lower than would be expected

from the levels of core and skin temperature, and this difference between actual and expected blood flows becomes greater as exercise intensity increases further (157). Thus in the service of cardiovascular homeostasis, the body begins to reduce splanchnic and renal blood flows at fairly low levels of cardiovascular strain, while sparing thermoregulatory skin blood flow, which begins to be compromised only at fairly high levels of cardiovascular strain.

Skin blood flow also is affected, especially during exercise in the heat, by other reflexes which function to maintain cardiac output and blood pressure, and which are elicited in situations in which cardiac filling is compromised. Thus during cycle exercise forearm vasodilation begins at a higher core temperature in the upright than in the supine posture, and this postural difference is greater at higher ambient temperatures, in which there presumably is more peripheral pooling (117). Likewise, during cycle exercise in the heat, forearm vasodilation begins at a higher core temperature if blood volume has been reduced before the start of exercise by a 4-day course of diuretics (98) or by acute blood withdrawal (49). However, the core temperature threshold for forearm vasodilation seems not to be affected by acute expansion of blood volume before the start of exercise (49). In some experiments, a break has been observed in the slope of the relation of forearm blood flow to core temperature (49,97,98), so that the slope of the relation is much lower beyond the break (Fig. 3-17). Moreover, such breaks seem to occur at a lower forearm blood flow under conditions of greater cardiovascular strain (e.g., during exercise with reduced blood volume, 98). These breaks are not intrinsic to the thermal control of skin blood flow, since they can be removed by having the subject exercise in the supine position (Fig. 3-17), which favors return of blood to the heart, and cardiac filling. These breaks may represent the recruitment of a compensatory vasomotor adjustment to limit cutaneous vascular pooling.

Lower body negative pressure (LBNP) is an experimental technique in which the lower half of the body is enclosed in a rigid box to which negative pressure, down to about 90 Torr below atmospheric, is applied to cause pooling of blood in the lower part of the body. Application of LBNP reduces central blood volume and central venous pressure, thus lowering the pressures sensed by the cardiopulmonary baroreceptors. With levels of LBNP not far below atmospheric, there is little effect on arterial pressure, but mean arterial pressure is reduced with higher levels of LBNP. Forearm blood flow is reduced during application of LBNP, even at levels low enough that arterial pressure is not affected, so that the response of forearm blood flow represents vasoconstriction in response to the reduction in central venous pressure (122). If forearm blood flow has previ-

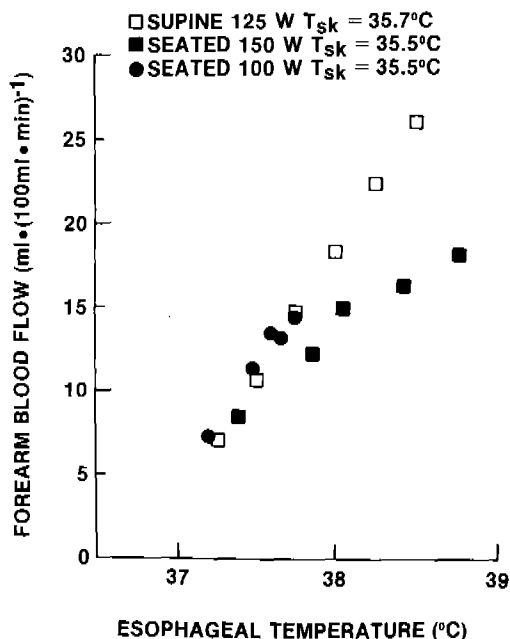


Figure 3-17. Relation of forearm blood flow to esophageal temperature during exercise in supine and seated positions in an ambient temperature of 36° C. Data points are averaged from duplicate experiments on one subject. Modified from Reference 97.

ously been raised by heating the subject, the decrease in blood flow in response to LBNP can be much greater than in a subject at a comfortable temperature (122). Intravascular pressures were not measured in the studies described in the previous paragraph (49,97,98,117), and impairment of cardiac filling was inferred from reductions in stroke volume. However, the changes in the control of forearm blood flow that were observed in conditions in which stroke volume was reduced were probably mediated by the cardio-pulmonary baroreceptors, and probably represent the same reflex as that elicited by applying LBNP.

At a given level of skin blood flow, the volume of blood that pools in the cutaneous vessels depends on the compliance of the cutaneous veins, and thus can be reduced by constriction of these veins. With light to moderate exercise, the cutaneous veins constrict at the beginning of exercise, but relax within a few minutes (122), perhaps in response to the increase in core temperature. However, cutaneous venous volume seems to be more sensitive to exercise than is skin blood flow (170), and the venoconstriction during more intense exercise is sustained (50,62).

All of the adjustments discussed above help to maintain cardiac filling and cardiac output during exercise in the heat. In addition, sympathetic stimulation of the heart increases the rate and vigor of cardiac contraction, and thus contributes further to maintaining cardiac output under these conditions. Most of this cardiac output goes to supply exercising muscle, but it is not known whether or not blood flow to exercising muscle is affected by heat stress, and quantitative measurements of blood flow through exercising muscle are not available. Rowell (122) has summarized some of the evidence bearing indirectly on this point, but this evidence is insufficient to make a clear case either way. Some other recent evidence, though also somewhat indirect, suggests that heat stress may, in fact, compromise muscle blood flow, since the initial rise in blood lactate during exercise is more rapid during exercise at an ambient temperature of 35° C than at 25° C (95).

CONCLUSION

Human body core temperature is regulated by two distinct control systems, behavioral and physiological. Behavioral thermoregulation involves the conscious, willed use of whatever means are available to minimize thermal discomfort. Behavioral thermoregulatory responses characteristically are discrete rather than continuous. Control of thermal discomfort is not precisely characterized, but discomfort appears to be proportional to core and skin temperatures, and also to include elements that lead or anticipate thermal changes. Physiological thermoregulation employs primarily unconscious responses that are controlled through the autonomic nervous system in a proportional control fashion according to the levels of core and skin temperatures. Since temperature generally is not uniform throughout the body core and since there are thermosensitive elements at a number of sites in the body core, there is no one site whose temperature represents "true" core temperature. Furthermore, although the hypothalamus has an especially high density of thermosensitive elements, it is not known how core temperatures at various core sites are combined in the control of the thermoregulatory effector responses. Nevertheless, in practice changes in esophageal temperature, which follows central blood temperature rather closely, can account fairly accurately for changes in thermoregulatory effector responses.

The physiological responses controlling body heat loss are skin blood flow and sweating. During exercise, the increase in heat production causes core temperature to rise until it reaches a new steady state where heat loss responses have increased enough to bring heat

production and heat loss into balance. The core temperature elevation at steady-state is proportional to the metabolic rate and is largely independent of the environmental conditions. Because of the proportional control nature of the thermoregulatory system, this core temperature increase is a "load error" and not the result of a change in the set-point temperature. Depending on the environmental temperature the relative contributions of sensible (radiative and convective) and insensible (evaporative) heat exchange to the total heat loss will vary, so that the hotter the environment the greater the dependence on insensible heat loss, and thus on sweating. The input of skin temperature to the thermoregulatory system allows the heat loss responses to be adjusted according to environmental temperature with little change in core temperature

During exercise in the heat, the primary cardiovascular problem is to provide simultaneously sufficient blood flow to exercising skeletal muscle to support its metabolism, and sufficient skin blood flow to dissipate the heat released from the exercising muscle. In hot environments, the core-to-skin temperature gradient is reduced, so that skin blood flow needs to be relatively high to achieve heat transfer sufficient for thermal balance. This high skin blood flow causes pooling of blood in the compliant skin veins, especially below heart level. In addition, sweat secretion can result in a net loss of body water, and thus reduce plasma and blood volume. Thus, both through pooling of blood in the skin and through reduced plasma volume, heat stress can reduce cardiac filling. Compensatory responses include reductions in splanchnic and renal blood flow, which mobilize blood from the splanchnic vascular bed, and also allow cardiac output to be diverted from the abdominal viscera to skin and exercising muscle; increased cardiac contractility, which helps to defend stroke volume in the face of impaired cardiac filling; and increased heart rate to compensate for decreased stroke volume. If these compensatory responses are insufficient, skin and muscle blood flow will be impaired. The impairment of skin blood flow will reduce the effectiveness of thermoregulation, possibly leading to dangerous hyperthermia; and the impairment of muscle blood flow will reduce exercise performance, and may lead to exhaustion, during exercise in the heat.

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