REFLEX CONTROL OF THE CUTANEOUS VASCULATURE

LORING B. ROWELL, PH.D.

Departments of Physiology and Biophysics and Medicine, University of Washington School of Medicine, Seattle, Washington, U. S. A.

A major function of cutaneous blood flow is to regulate body temperature. Over most of its great range, skin blood flow far exceeds the metabolic needs of the skin. Cutaneous arterioles and veins are predominantly under neural control from a rich sympathetic adrenergic nerve supply, especially in acral regions. These tonically active, vasoconstrictor nerve fibers are the effenter arm of (1) thermoregulatory reflexes which originate principally in cutaneous thermoreceptors, (2) baroreflexes which originate in both arterial and cardiopulmonary baroreceptors, (3) chemoreceptor reflexes, and (4) reflex responses to upright posture and exercise. Cutaneous vasculature in man is probably unique in its great range and high responsiveness to these reflex drives.

Human skin is also unique in possessing a neurogenic vasodilator system that is the principal effenter arm of reflexes which originate in the central thermoreceptors. Apparently, this system participates only in thermoregulatory reflexes; its transmitter is still unknown; and it controls skin blood flow over the full range and over most of the body. In man and baboons, the reflex modification in skin blood flow with each degree (C) change in central temperature is about 20 times greater than that produced by changing skin temperature. However, in baboons and probably other species, the skin vasomotor system appears to be mainly adrenergic. In man, different reflex drives on skin interact so that the large vasoconstrictor responses (e.g., baroreflex) are still elicited during hyperthermia or direct local heating. Thus, central to peripheral volume displacement is minimized during upright posture, exercise, hemorrhage, etc. despite competing thermal drives.

Veins are richly innervated by sympathetic adrenergic nerves which reflexly control their volume. Despite their potentially great volume and transient reflex responses to many stimuli, they are under significant reflex control only from the central and cutaneous thermoreceptors. Their responsiveness to sympathetic outflow is modified by changes in local temperature; they are not responsive to baroreflexes but do constrict during exercise. Major shifts in blood volume distribution can attend reflex and local venomotor responses.

A large organ about 1 to 1.5 mm thick, the skin covers a body surface of approximately 1.8 m², weighs about 2 kg, and contains a major vascular bed. It receives only 5 to 10% of cardiac output in man and other animals at rest in a thermally neutral environment, but human-skin can receive from 50 to 70% of the cardiac output under severe heat stress. In a cold environment, however, skin blood flow sometimes approaches zero. Thus, the range of blood flow to human skin is second only to that to skeletal muscle.

The reflex control of resistance vessels (arterioles) and capacitance vessels (veins) in the skin is the subject of this paper; humoral and physical factors which directly affect blood flow to the skin are not discussed. This reflex control in man subserves the regulation of not only body temperature but also blood pressure and the distribution of blood flow and blood volume. In most other animals, the sympathetic adrenergic system appears to serve as the principal effenter arm of reflexes involving the skin; but in man, a potent, active, sympathetic nerve-linked vasodilator serves as the dominant controller of skin blood flow in temperature regulation. If the skin of other species has a similar active vasodilator system, it appears to have only minor functional significance.

The vasculature of both human and nonhuman skin responds to various reflexes, but human skin has a far greater responsiveness to many, including those of thermoregulatory origin. Cutaneous veins are also responsive to many reflex drives, principally to those of thermal origin. For a more
comprehensive treatment of the many factors that operate upon cutaneous blood vessels, the reader is referred to several books and reviews [1-12].

GENERAL FEATURES OF THE CUTANEOUS CIRCULATION

Cutaneous Blood Flow

The skin is the major heat exchanger of the body. Its blood flow determines not only the area of heat transfer between the body and its environment but also that from deep tissues to the periphery. Like the kidney, the skin normally has a blood flow far exceeding its nutritional needs. Because of methodological problems, total blood flow to the skin has never been accurately measured. Most observations are derived from measuring accessible regions on the extremities. Qualitative estimates indicate that at any given body and skin temperature, blood flow varies considerably over different portions of the body surface [2-6]. For example, it is extremely high at acral structures such as the fingers and toes, possibly because of patent arteriovenous (A-V) anastomoses. Not only is the range of blood flow in the hands and feet greater than that in the rest of the body skin, but also the principal mechanism of vascular control is different (see below). However, these mechanisms are strikingly similar in most of the total body skin ([5,6]).

Cutaneous blood flow in a man weighing 79 kg, whose body surface is 1.73 m², nude and at rest in a thermally neutral environment, is estimated at 200 to 500 ml/min, or 116 to 289 ml/m² per min [5]. Estimates for maximal cutaneous blood flow range from 1.2 to 2.0 l/m² per min, or 2.1 to 3.5 l/min in a 70-kg man [2,5,7,13]; maximal flow can, however, be much higher under prolonged heating and/or intense direct heating [14-17]. For example, prolonged direct heating of the whole body to the limits of subjective thermal tolerance (with skin temperature held at 41°C) produced an average increase in cardiac output of 6.6 l/min, much of the increase being directed mainly to the skin (Fig. 1).

Owing to reflex vasoconstriction, blood flow to the other major vascular beds decreased [17-19]. The nonconstrictor vascular reseverstion have been associated with a thermoregulatory reflex; it was not caused by an arterial baroreflex [19]. From the increase in cardiac output and the redistribution of blood flow away from visceral organs, maximal total skin blood flow was estimated to be approximately 8 l/min or 3.5 to 4 liters of blood per m² body surface per min.

When skin is cooled to low temperatures, its blood flow falls so low that measurement is difficult [2,5]. Flows as low as 0.3 ml·100 ml⁻¹ of hand per min have been recorded [5].

Cutaneous Blood Volume

Warm skin may constitute one of the major blood "depots" or "reservoirs" [20-22]. Under thermally neutral conditions, 80% of the blood volume in a limb is in skin and muscle veins [22]. Maximal stimulation of the sympathetic vasoconstrictor nerve fibers which supply the hindlimb of a dog causes up to a 50% decrease in blood volume of the leg, most of which comes from the skin [23,24]. Maximal dilation of cutaneous resistance vessels causes not only a large fall in peripheral vascular resistance but also a major shift in blood volume from central to peripheral vasculature because of the high distensibility and capacity of the cutaneous venous plexes. Just how much cutaneous
venous volume increases with heating is not known, but the accompanying changes in the central circulation (to be discussed) suggest that the increase is large [15,17,18,21], possibly exceeding a liter. Decreased peripheral vascular resistance combined with the shift of blood volume into the skin during hyperemia makes it difficult to regulate blood pressure in upright man. Other species (except perhaps other primates) appear not to have similar difficulties.

The increase in cutaneous venous volume is important in temperature regulation because a large volume of blood passing at reduced linear velocity just below the skin surface increases the rate of heat transfer across the skin. As cutaneous blood volume increases at any given rate of blood flow, linear flow velocity decreases proportionally.

**INNERVATION OF CUTANEOUS RESISTANCE VESSELS**

**Sympathetic Vasoconstrictor Nerve Fibers**

Various experimental approaches have been used to demonstrate the types of nerve fibers that supply the skin. It is important to point out that skin blood flow is determined not only by the reflex effects of central heating and cooling but also by the direct local action of temperature blood vessels. Consequently, in most of the experiments described here a procedure called indirect or reflex heating was followed, in which warming or cooling one portion of the body (usually the legs) causes reflex vasodilation or vasoconstriction in other portions of the body not exposed to local thermal influences. Since the nutritional needs of the skin are slight and rarely affect its blood flow, adequate control of local temperature makes it possible to identify those responses that are due to neurogenic factors.

In many species (no exceptions come to mind), the resistance vessels of skin receive tonic outflow from sympathetic vasoconstrictor nerve fibers (in cool environments). This feature was first demonstrated by Claude Bernard [25], who showed that severing the cervical sympathetic chain caused marked vasodilation in the rabbit ear. Similar demonstrations in man and other species have shown that sympathectomy or adrenergic blockade of an extremity leads to an increase in skin blood flow when the environment is cool [1,3-6,8,26-31]. Thus in cool environments, cutaneous vascular resistance is regulated by the frequency of impulses over the sympathetic vasoconstrictor nerve fibers. This control normally subserves temperature regulation, but under many circumstances it also serves to regulate blood pressure as well. A-V anastomoses, present in acral regions, also receive a high degree of tonic vasoconstrictor discharge [8].

**Sympathetic Vasodilator Nerve Fibers**

Is cutaneous blood flow predominantly controlled only by a variation of sympathetic vasoconstrictor tone (passive vasodilation) or also by a neurogenic vasodilator system (active vasodilation)? The main purpose of an important series of experiments on man was to observe whether skin vessels still dilate in response to indirect heating after all sympathetic neural pathways to skin have been blocked [27-29]. The results of such experiments are given in Figure 2.

Findings from experiments on the hands (and feet) do not indicate a neurogenic vasodilator system since sympathetic blockade caused maximal vasodilation (higher flows are possible only if direct effects of local heating are superimposed). Thus, the vessels of human hands and feet dilate passively in response to increasing central body temperature without the intervention of any significant neurogenic or active vasodilator mechanism [3-6,29].

In the upper and lower arms and legs, however, blocking all neural pathways to the skin abolished the vasodilator response to indirect heating. The initial effect of nerve block was to release tonic vasoconstrictor tone in the forearm skin of cool subjects (Fig. 2), but no further increase in blood flow occurred during heating. Blocking the cutaneous sympathetic nerves after the response to heating had reached its maximum returned the blood flow in forearm skin to the low levels seen when only tonic vasoconstrictor activity was blocked [27]. Thus, the dramatic increase in forearm blood flow during indirect heating shown in

![Fig. 2. A: Reflex effects of indirect heating (legs placed in hot water) on skin blood flow in the normal hand and forearm. B: The same regions with sympathetic nerves blocked. The figure shows the basic differences between the control of skin blood flow in the hand and other acral regions (feet, ears, nose) and the rest of the skin. Vasodilation in the hand is mediated only by the release of tonic vasoconstrictor tone (−VC), evidenced by the equal effects of heat (A) and nerve block (B). Vasodilation in the forearm results initially from a release of tonic vasoconstrictor tone if subjects are cool at the start of heating. After 10 or 15 min of heating, a second phase of vasodilation coincides with the onset of sweating (+VD) (A). That vasodilation is active is evidenced by its prevention through nerve block (B). Note the absence of sweating in the nerve-blocked forearm (B). (From Rowell LB: The cutaneous circulation, Textbook of Physiology and Biophysics. Twentieth edition. Edited by TC Ruch, HD Patton. Philadelphia, Saunders, 1974, vol II, chapt 12, pp 185-199. Adopted from [6].)
Figure 2 requires sympathetic nerve fibers that somehow cause active vasodilation.

How active vasodilation is produced in the skin is still not known. Insensitivity to atropine argues against the possibility that acetylcholine is involved [28]; furthermore, cutaneous blood vessels do not receive cholinergic innervation [11]. The suggestion that bradykinin is involved in mediating this response [32] appears to be untenable in the light of recent experiments [33–36]. Thus, the mechanism underlying an important control of human cutaneous blood vessels remains to be determined.

**Neurogenic Vasodilation in Other Species**

Although the dominant feature of man's cardiovascular response to heat stress is active cutaneous vasodilation, Wyss and Rowell [31] found no analogous vasodilation in the hindlimbs of unanesthetized, heated baboons. The rise in iliac vascular conductance in response to heating could be mimicked by α-adrenergic blockade (Fig. 3). Thus, in a species that, like man, has eccrine sweat glands and shows thermoregulatory sweating, nearly all of the increases in cutaneous blood flow appeared to be due to the release of tonic vasoconstrictor tone. The only alternative explanation is that α-blockade itself elicited a vasodilator response equal to that which it blocked; this seems unlikely.

Vigorous investigation of other species has not contributed to the further understanding of the active vasodilation seen in the human. A variety of examples of active vasodilation has been demonstrated in non-primates [37–39] which appear to be species specific and also produced by unknown mechanisms [40,41].

REFLEX CONTROL OF CUTANEOUS SYMPATHETIC VASOCONSTRICTOR AND VASODILATOR ACTIVITY

**Thermoregulatory Reflexes in Man**

In man, as well as in many other animals, central body temperature, acting through thermoreceptors in the hypothalamus and probably the spinal cord [42–44], plays an important role in temperature regulation expressed through alterations in cutaneous blood flow [36]. However, in the execution of their role in the integration of a number of mechanisms for body temperature control, the central sensors are also responsive under limited conditions to input from cutaneous thermoreceptors [42–44]. The weight of current evidence points to the execution of control through sympathetic vasoconstrictor nerves in response to cutaneous thermoreceptor activity [45] and through the active vasodilator mechanism in response to alterations in central temperature [33,34].

Taken together, a variety of different experiments suggest that changing skin temperature exerts its reflex effect on the skin circulation by increasing or decreasing sympathetic vasoconstrictor tone [33,34], whereas increasing central

**FIG. 3. Response of an awake baboon to body heating before and after α-adrenergic blockade (phenoxymenzamine) of one hindlimb. Panels from top to bottom show ambient temperature (T_a), arterial blood temperature (T_b), heart rate (HR), arterial mean pressure (AMP), common iliac mean flow (CIMF), and common iliac vascular conductance (CIVC). The dashed line (bottom panel) shows the rise in CIVC during heating before α-blockade; the solid line shows the response after blockade. Note that α-blockade mimicked the vasodilator response to heating. (From [31]).**

**The Relative Importance of Central vs Skin Temperature in Reflex Control of Skin Blood Flow**

The separate but interacting roles of central and cutaneous thermoreceptors have been the subject of recent experiments on man and other species. If it is true that in humans skin temperature affects mainly vasoconstrictor outflow and that central temperature drives the cutaneous vasodilator system, then central temperature should dominate in the control of skin blood flow over its full range, i.e., the effects of the vasodilator system on skin blood flow, described above, are enormous. To test this hypothesis, however, one must achieve separate control of central and skin temperature, an awesome task in man. Wyss et al [33,34] approached this problem by controlling whole body skin temperature by means of water-perfused suits. They drove skin temperature in different temporal patterns to achieve separation of central and skin temperature contributions to skin blood flow responses in the forearm (Fig. 4). Regression analysis of the results, described in terms of a linear combination of skin and central temperature, yielded the coefficients for central and skin temperature with a ratio of 20:1. In a subsequent study Wyss et al [33] used a different protocol to test linearity and found that the effects of central temperature on skin blood flow were constant but that the skin temperature influence depended on the level of central and/or skin temperatures. Thus the system is nonlinear and complex. At elevated skin and core temperatures, skin temper-
sulating qualities of fur. Despite the absence of an active cutaneous vasodilation [31], observations on the unanesthetized baboon [52] reveal that cutaneous blood flow is in the order of 10 times more sensitive to changes in central temperature than to changes in skin temperature (see Fig. 5). Ninomiya and Fujita [53] observed a similar relationship in anesthetized cats. Data are not available which would permit this quantitative comparison in other species although it is clear that both central and peripheral temperature changes are effectual.

Baroreceptor Reflexes in Man

Arterial baroreceptors. The question of the participation of cutaneous vessels in human baroreceptor reflexes has given rise to a variety of opinions, a situation that has not been clarified by experiments on other animals. Although the opinion has been expressed that human cutaneous circulation is not altered by baroreceptor reflexes [6,54,55], conflicting findings have brought to light

![Fig. 4. Results from one subject in whom body skin temperature ($T_s$) was driven in different temporal patterns (right vs left upper panels) to achieve periods of separation between changes in $T_s$ (top panel) and central temperature (right atrial blood temperature ($T_{ra}$)) (second panel). Note the close correspondence between rising $T_{ra}$, sweat rate (SR), and forearm skin blood flow (FBF). Separate effects of $T_{ra}$ and $T_s$ on FBF, SR, and heart rate (HR) were determined mathematically. The effect of $T_{ra}$ on FBF was 20 times greater than that of $T_s$ per degree centigrade. (From [53]).

}\n
ature had essentially no effect. Thus, in man, the reflex component of skin temperature has only $\frac{1}{20}$ the effect of the central temperature component on skin blood flow per degree centigrade change in either. At elevated skin and core temperatures, there was essentially no skin temperature component and the rate of change of skin temperature was never a significant component. Thus, central temperature in resting man is the major drive to the cutaneous circulation (unless very great changes in skin temperature occur). At this stage, two facts bear repeating. First, even the most intense heating of skin does not increase blood flow to underlying muscle; thus, changes in blood flow to the limbs during either direct or indirect heating are confined to the skin [16,46,47]. Second, despite regional variation in blood flow to the skin, the patterns of control described for the forearm with and without nerve block [27,28,48–50] are the same in all parts of the limbs [48] except on the hands and feet [4–6]. The point is that skin blood flow over most of the body surface fits the regulatory schemes proposed so far. The large increases in cardiac output and total skin blood flow are due mainly to the action of a potent neurogenic vasodilator system, which is driven predominantly by central thermoreceptors.

Thermoregulatory Reflexes in Other (Subhuman) Species

The roles of central and cutaneous thermoreceptors have also been examined in a number of different species [42,43,51]. Again, important species differences are brought to light, perhaps related to different environmental demands and different in-

Fig. 5. Effects of separately controlling skin temperature and central body temperature (arterial blood temperature ($T_s$)) on mean right iliac blood flow in an awake baboon. Skin temperature ($T_s$) (second panel) was increased by increasing air temperature in a heated chamber; $T_h$ (top panel) was kept constant by cooling a chronically implanted femoral A-V heat exchanger. Note the slight effect of increased $T_s$ on mean iliac blood flow with $T_h$ held constant (0–60 min). In contrast, increasing $T_h$ (core warming, 60–70 min) had a marked effect on mean iliac blood flow. Note how mean iliac blood flow tracked $T_s$ during core cooling (70–115 min). (From [52]).
the necessity for changing this view [56,57]. Two sets of recent experiments addressing this question will be reviewed here.

Johnson, Rowell, and Bregelmann [58] found that at any given central body temperature, blood flow to the forearm skin was substantially reduced when the subject was upright rather than supine. By a comparison of blood flow in a normal forearm with that in an arm in which skin circulation had been arrested by iontophoresis of epinephrine [59,60] or by a combination of forearm plethysmography and measurement of underlying muscle blood flow by local isotope clearance [60], human forearm skin was shown to undergo vasoconstriction in response to lower body negative pressure (Fig. 6). This maneuver sequesters blood in the capacity vessels of the legs and thus simulates hemorrhage or upright posture. When lower body negative pressure is applied with enough force to reduce arterial pulse pressure (i.e., when it is equivalent to the hydrostatic effects of upright posture), it unloads arterial baroreceptors. Figure 6 illustrates vasoconstriction in both muscle and skin of the forearm in response to a baroreflex. Forearm vasoconstriction can be attributed to increased sympathetic nerve activity, since it is prevented by α-adrenergic blockade [61,62].

Beiser et al [59] observed a small cutaneous vasodilation in response to increased carotid sinus transmural pressure in men whose necks were exposed to negative pressure. When cutaneous sympathetic vasoconstrictor activity is augmented by a combination of upright posture and exercise (see below), a sudden increase in arterial blood pressure (caused by sudden occlusion of the leg vessels) induces a marked increase in cutaneous blood flow [63]. Here the response is large because of the high background of vasoconstrictor tone that can be withdrawn. Most evidence indicates that the only efferent arm of the baroreflex is sympathetic vasoconstrictor nerve fibers; neurogenic vasodilators are not involved [64].

Cardiopulmonary baroreceptors (low-pressure baroreceptors). Application of lower body negative pressure at low levels that decrease only central venous pressure and not aortic mean pressure, pulse pressure, or rate of change of pressure (dp/dt) caused marked vasoconstriction in the forearm [65,66]. Much of the decrease in blood flow could be accounted for by vasocstriction in skin [47,66]. These results suggest that, in man, skin is also a major target for baroreflexes originating in the cardiopulmonary region.

Direct nerve recordings from man. Recent technical advances here made it possible to record impulse traffic in cutaneous nerve fibers through fine, percutaneous electrodes inserted into nerve trunks [67-69]. These observations have yielded a number of interesting results which are, however, very difficult to interpret and to bring into line with measurements of cutaneous blood flow. In short, the major finding is that maneuvers known to elicit baroreflex activity did not affect sympathetically outflow to skin [67,68]. One of the major difficulties stems from the fact that the electrodes sample impulses from unidentified axons and do not discriminate in favor of cutaneous vasomotor fibers. Thus, the distinction between vasomotor and sudomotor responses, for one example, is impossible. A statistical preference for recording impulse traffic over sudomotor nerves was suggested by the findings of Hagbarth et al [69]. Further, were these observations made under thermally neutral conditions, tonic activity in sympathetic vasoconstrictor fibers would be at a very low value or lacking. Finally, it is impossible at present to identify the effectors related to the active fibers and thus distinguish arterial vasoconstrictor activity from activity controlling venomotion or A-V anastomoses. Thus, although valuable information may be forthcoming from the use of this potentially powerful technique in the future, it is still too early to accept the findings as contributory to understanding.

Chemoreceptor Reflexes in Man

Some data suggest that skin vasodilates during high-altitude hypoxia, but this response could also result directly from local effects of hypoxia and hypocapnia (or other factors) on skin blood vessels [6,20]. In human experiments, it is difficult to separate local from reflex effects of hypoxia.
Baroreceptor and Chemoreceptor Reflexes in Subhuman Species

Kirchheim [70] recently concluded that baroreceptor influence on the cutaneous vessels of subhuman species is very small if present at all. However, Wennergren [71], who studied cats, concluded that skin (hindlimb), muscle, and intestinal vasculature are equally engaged in baroreflexes. A possible source of confusion is the different responsiveness to baroreflexes as seen, for example, in the hand as opposed to the forearm in man [72]. Similar regional differences exist in other species; Wennergren [71] noted no baroreflex response in the cat’s paw. Thus, investigation of acral skin in different species has reinforced the general impression that cutaneous vascular involvement in baroreflexes is less pronounced than that of other organs.

As with baroreflexes, investigation of cutaneous involvement in chemoreflexes has often focused on acral skin. Here the response to hypoxia is vasodilation [73] due to reduced tonic sympathetic nerve outflow [74] and a small, active vasodilation (dog paw) [75].

Human Cutaneous Vasomotor Responses to Exercise

During exercise man experiences increased sympathetic outflow to most major vascular beds, including the skin [6,17,76]. Sympathetic outflow increases in proportion to the relative intensity of the exercise [17]. At the outset, forearm skin vasconstricts [76], but after several minutes of exercise, the cutaneous vasodilation progresses as the central body temperature begins to rise [6,76]. This vasodilation continues throughout prolonged exercise as central temperature continues to rise [77]. Initially, the increase in skin blood flow is probably due to the withdrawal of cutaneous vasconstrictor tone, but as central temperature continues to increase, active vasodilation eventually ensues and skin blood flow increases by tenfold [77]. However, despite this relatively large increase, at any given central temperature skin blood flow in the forearm is still markedly less than that recorded during supine rest at the same temperature [58].

In addition to limiting peripheral volume displacement during upright exercise, cutaneous vasconstriction (presumably increased vasconstrictor activity; see below) facilitates the adjustment to upright exercise in patients whose ability to increase cardiac output is limited by heart disease. When such patients exercise, they show a much more intense vasconstriction in skin than normal subjects [78,79]. The hemodynamic consequences of unrestricted cutaneous vasodilation in these patients can easily be imagined. The potential size of the cutaneous vascular bed is such that any marked vasodilation uncompensated for by increased cardiac output would cause a precipitous fall in blood pressure.

INTERACTION BETWEEN THERMOREGULATORY AND NONTHERMOREGULATORY REFLEXES IN MAN

Arterial Baroreceptor Reflexes

A competitive interaction between cutaneous vasodilator and vasoconstrictor reflexes has been demonstrated in man. Some earlier studies reviewed by Amberson [56] showed that heat was gained more slowly in upright man than in supine man during external heating. Johnson et al [58] confirmed the postulate that the slower rise occurred because skin blood flow was diminished in the upright posture. Figure 7 shows that when identical heat stress was applied in both the upright and the supine positions, the rise in central temperature and blood flow to the forearm skin was much slower in the former position.

When either hemorrhage or upright posture is simulated by lower body negative pressure, forearm cutaneous vessels constrict in heated man [80,81]. Figure 8 demonstrates the increasing magnitude of vasoconstriction (fall in forearm vascular conductance) as central body temperature and skin blood flow rise progressively during prolonged, direct whole body heating (water-perfused suits) [81]. The magnitude and time course of the cutaneous responses showed, first, that most of the decrease in forearm blood flow was confined to heated skin. Since blood flow in the forearm muscle did not increase with heating (see above), reflex vasconstriction in the forearm muscle during lower body negative pressure constituted only a small fraction of the total conductance response. Second, both the on and off responses of vascular conductance to the forearm were too rapid to be of humoral origin. Thus the skin can still undergo vasoconstriction in response to baroreflexes even when vasodilator activity is intensely active.

How is vasoconstriction brought about in cutaneous vessels undergoing active vasodilation? Both norepinephrine, the transmitter of neurogenic vasoconstriction, and the unknown vasodilator...
tensely vasoconstricted. Cutaneous vasodilation in such conditions could be lethal, but two factors favor the victim: first, a warm skin maintains its capacity to vasoconstrict; and, second, the dominant drive to cutaneous vasodilation is increased central temperature, not skin temperature.

Exercise

Exercise performed in hot environments or during direct heating of the body skin still elicits cutaneous vasoconstriction; i.e., at any given central temperature, skin blood flow is less than that observed at rest. In the experiments of Johnson et al. [58], body skin temperature was held at 38°C during supine and upright rest and supine and upright exercise. Despite elevated skin temperature, exercise in either posture markedly reduced skin blood flow in relation to central temperature (Fig. 10). At a given central temperature, skin blood flow was lowest in upright exercise and was reduced in upright rest and supine exercise (i.e., effects of posture and exercise per se). Thus during exercise at high skin, central, or ambient temperatures, skin and muscle vessel beds compete for cardiac output. Muscle appears to dominate the competition since total oxygen consumption is maintained (even at near maximal level) and central body temperature is markedly increased [17]. Although the relative vasoconstriction of skin under these conditions contributes greatly to hyperthermia by reducing heat loss, the displacement of central blood volume into cutaneous veins is limited by vasoconstriction, so that central pressures are better maintained (see below) [17].

Cardiopulmonary Baroreceptors

Direct heating of skin does not abolish its vasoconstriction in response to unloading cardiopulmonary baroreceptors (Fig. 9) [47]. When blood loss or central-to-peripheral blood volume shifts are too small to affect arterial blood pressure, reduced central venous pressure still reflexly elicits cutaneous vasoconstriction. The maintained responsiveness of heated skin to baroreflexes is important to those concerned about the consequences of warming the skin of accident victims or others who have lost blood and may be in shock or in-
Other Reflexes

The lability of skin blood flow in acral regions has been demonstrated plethysmographically [5,6] and more recently by direct cutaneous nerve recording [67-69]. Various emotional stimuli, respiratory maneuvers, etc. cause transient changes in skin blood flow and cutaneous sympathetic nerve activity, most often in hands and feet, but sometimes in forearm vasculature. Generally, muscle is the site of emotionally induced vasodilation [6,83,84], but according to Holling [83], suppressing the skin circulation in an arm by epinephrine iontophoresis also reduces the vasodilator response in that arm.

CUTANEOUS VEINS

The relationship between pressure and volume is important in veins, rather than the relationship between pressure and flow as in resistance vessels. The potentially great capacity of the cutaneous venous plexus makes it particularly important that its compliance be actively controlled. Because of the active regulation of compliance, or venous volume, the skin is regarded as a "blood reservoir." Sudden variations in the volume can have major effects on the central circulation [17,85]. Veins and their control are the subject of a recent monograph by Shepherd and Vanhoutte [20]. Little can be added here to their comprehensive coverage of this topic.

Innervation of Cutaneous Veins

The high endogenous norepinephrine concentration of cutaneous veins and their vigorous response to low-frequency sympathetic nerve stimulation indicate that they are richly innervated with sympathetic adrenergic nerve fibers [8,23,86]. At maximum stimulation frequency (10-15 Hz), 35 to 50% of the total blood content of the cat hindlimb can be expelled. Although it is difficult to compare results, some [23] have concluded that cutaneous veins are more responsive to sympathetic nerve stimulation than resistance vessels. Others [86] have suggested that measuring volume change in the entire limb exaggerates the venomotor responses because part of the decreased venous volume is the passive result of a lowering of the venous pressure by constriction of the series-coupled resistance vessels. In any case, slight changes in sympathetic nerve outflow to cutaneous veins can cause major changes in the volume contained within these thin-walled vessels.
Since cutaneous veins receive only sympathetic adrenergic innervation, venous capacity is neurogenically controlled by increases or decreases in sympathetic adrenergic nerve fiber activity [20].

Reflex Control of Cutaneous Veins

Cutaneous venomotor responses depend far more than cutaneous resistance vessels on local temperature. Local temperature markedly alters the responsiveness of these veins to adrenergic stimulation; cooling potentiates and heating attenuates (and even abolishes) venomotor responses to reflexly induced sympathetic nerve discharge [87–89].

Cutaneous veins are affected reflexly by a wide variety of central and peripheral stimuli, of which the most important is temperature [6,20,22]. Venous compliance is reflexly altered by changes in both central body temperature and body skin temperature. In resting normothermic man, sympathetic venomotor outflow is minimal and cutaneous venous compliance is nearly maximal [90]. A rise in central temperature, however, still increases cutaneous venous volume because skin resistance vessels dilate and increase pressure and volume in the veins they supply. If venous compliance remains constant, then venous volume increases passively until a new level of venous wall tension is reached.

Thermoregulatory reflexes. Reducing central temperature elicits reflex venoconstriction. Blood volume shifts from superficial skin veins to deep veins, so that heat is conserved by the reduction of heat delivery to the cutaneous veins. Again, part of the blood volume shift is passive owing to the lowering of venous pressure by the constriction of skin arterioles. The effects of central cooling can be modified by cutaneous venous temperature. The magnitude of venoconstriction is greatest in veins that are locally cooled and least in those that are warmed. Thus, central temperature determines the impulse frequency over constrictor nerve fibers that supply the veins. Local vein temperature determines the responsiveness of these veins to adrenergic stimuli [87].

Cutaneous venomotor tone is also reflexly altered by changes in body skin temperature [91]. This alteration can occur independently of any direct local effects of temperature on veins. If the body skin temperature is elevated over sufficiently large areas of skin, then the veins will relax in the face of a strong venoconstrictor drive (such as that caused by exercise; see below). This response is analogous to the response of cutaneous resistance vessels described earlier [92]. The interaction of skin and central temperature receptors is summarized in Figure 11. As yet, we have no indication of the relative importance of drives from central and cutaneous thermoreceptors to cutaneous veins.

Baroreceptor reflexes. Because of their potentially large volume in warm man, cutaneous veins could serve as an important "blood reservoir." Venoconstriction in response to decreased arterial blood pressure or central venous pressure could provide a rapid "autotransfusion" of blood back into the central venous system. However, the bulk of evidence in man and other species [20] indicates that cutaneous veins do not participate in baroreflexes originating either at arterial or cardiopulmonary stretch receptors. Thus, the only means by which normothermic or hyperthermic man can reduce cutaneous venous filling in upright posture is by vasoconstriction, which retards venous filling rate, and by the tonic effect of postural muscles on veins, which serves to reduce venous transmural pressure (and volume) [56].

Exercise-induced reflexes. Exercise in man elicits a marked constriction of cutaneous veins, the reaction depending on central and skin temperatures and local venous temperature. When central body and skin temperatures are normal or cool, cutaneous veins actively constrict in proportion to the relative intensity of exercise [76,93,94]. As exercise continues, venomotor tone reflexly declines owing to the rise in central body temperature. This decline causes a shift of blood volume into cutaneous veins as resistance vessels dilate and as venous compliance increases. The shift of blood volume into the skin reduces central venous pressure, cardiac filling pressure, intrathoracic blood volume, and stroke volume, so that cardiac output must be maintained by tachycardia [17]. In turn, blood flow to the skin must be met in part by reduced blood flow to the visceral organs [17]. In hot environments, these effects are augmented, so that circulatory function and work capacity are severely impaired [17,21]. Normal function can be restored rapidly by a sudden lowering of the body skin temperature which causes rapid venoconstriction in the face of markedly elevated central temperature. The effect is a rapid redistribution of blood volume centrally and restoration of central venous pressure, intrathoracic volume, stroke volume, etc. [21].

The interaction of central and skin tempera-

![Fig. 11. Interaction between reflex effects of changing central temperature and the reflex plus direct local effects of changing skin temperature on cutaneous venomotor tone. Lowering the central body temperature decreases (−) sympathetic venomotor outflow (+) whereas lowering local skin temperature at the vein increases (+) its sensitivity to neural stimulation by direct local effect of temperature on venous smooth muscle. (From Rowell LB: The cutaneous circulation, Textbook of Physiology and Biophysics. Twentieth edition. Edited by TC Ruch and HD Patton. Philadelphia, WB Saunders Company, 1974, vol II, chap 12, pp 185–199)
tures in regulating venomotor tone during exercise has been demonstrated by rapid raising and lowering of body skin temperature (Fig. 12) [91, 93]. Raising skin temperature, even before the rise in central temperature, prevents the reflex vasoconstrictor response to exercise in two ways [93]. First, direct local effects of heat on veins make them insensitive to the exercise-induced increase in sympathetic discharge. Second, increased body skin temperature reflexly inhibits sympathetic discharge to cutaneous veins. This is shown by the failure of some locally cooled veins to constrict with exercise when body skin temperature is raised. Lowering body skin temperature reflexly restores venomotor outflow to the veins [91]. Thus, a complex interaction of reflexes induced by central and skin temperature and the direct effects of local temperature on veins regulates the distribution of blood volume in an upright exercising man. Here a delicate balance between cutaneous blood volume available for heat exchange and thoracic blood volume available for adequate cardiac filling is maintained [21, 85].

Other reflexes. Cutaneous veins are transiently reactive to many stimuli, most of which appear to be of no functional significance. For example, emotional stimuli (startle reactions, apprehension, discomfort, etc.) and changes in intrathoracic pressure caused by deep inspiration, hyperventilation or Valsalva’s maneuver caused marked transient venuconstriction in skin [6]. Such extraneous sources of variation have complicated the investigation of veins in man. Careful control of many variables is important in studying the mechanisms of venomotor reactions to temperature and exercise. Although veins fit conveniently into many schemes of peripheral and central circulatory regulation, the only physiologically significant cutaneous venomotor response so far demonstrated is that to changing temperature.

REFERENCES


---

**Fig. 12.** Human venomotor responses to phasic changes in whole body skin temperature ($T_s$) from 34 to 36.5°C during upright exercise. Exercise (†) began at 2 min and continued to 12 min. Note that small changes in $T_s$ markedly altered venuconstriction during exercise. These responses were reflex effects of $T_s$ since arm skin temperature was constant at $31-32^\circ$ C. Exercise caused venuconstriction whereas lowering $T_s$ abolished venoconstriction and cooling $T_s$ rapidly restored it. Note the venomotor response to a single deep breath at 11 min (at the spike in inspiratory flow velocity ($Q$)). (From [93])
29. Roddie IC, Shepherd JT: The blood flow through the hand during local heating, release of sympathetic vasomotor tone by indirect heating, and a combination of both. J Physiol (Lond) 131:657–664, 1956
61. Brown E, Goei JS, Greenfield ADM, Plassaras GC: Circulatory responses to simulated gravitational shifts of blood in man induced by exposure of the
body below the iliac crests to sub-atmospheric pressure. J Physiol (Lond) 183:607-627, 1966

62. Ardill BJ, Bannister PG, Kennedy AR, Greenfield ADM: Circulatory responses of supine subjects to the exposure of parts of the body below the xiphi-
turnum to subatmospheric pressure. J Physiol (Lond) 193:57-72, 1967


64. Øberg B: Overall cardiovascular regulation. Annu Rev Physiol 38:537-570, 1976


70. Kirchheim HR: Systemic arterial baroreceptor reflexes. Physiol Rev 56:100-176, 1976


