A Case Supporting the Proposal That Cardiac Filling Pressure Is the Limiting Factor in Adjusting to Heat Stress

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PROBLEM

Progressively increasing heat stress ultimately results in heat stroke, a medical emergency leading to death if not treated properly. Initially in heat stress, enormous increases in blood flow and volume in skin (and muscle if exercising) are achieved by the diversion of blood away from the splanchnic bed, kidneys, and probably fat and muscle, and in some species such as man, there is also an increase in cardiac output. The onset of heat stroke is thought to involve a decrease in central venous pressure, which is defended by constriction in both arterioles and veins of the skin via low-pressure baroreceptors in the cardiopulmonary region. Body heat loss is thereby reduced and the consequent rise in body temperature causes death due to thermally evoked critical changes in central nervous system activity and/or fatal embolization following disseminated intravascular coagulation and erythrocyte sphering. Evidence is presented, which supports the proposal that cardiac filling pressure is the limiting factor in adjusting to heat stress.

DEFINITION OF THE PROBLEM

With a healthy individual, progressively increasing heat stress ultimately results in heat stroke, a medical emergency leading to death in the absence of proper treatment [1]. A person is generally said to be suffering heat stroke when one or more of the following symptoms is present in the heat-exhausted subject: (a) high core temperature, usually exceeding 40°C; (b) skin is usually hot and dry; (c) convulsions or unconsciousness may occur; and (d) pulse is usually rapid and weak. In considering the cause of this, several questions should be asked: (a) What functions change during stress? (b) Accepting that there is thermoregulatory failure, which of the changed functions could be so important as to assume a priority higher than body temperature regulation? (c) By what mechanism could that precedence be executed? (d) Does the possible practical reality of such a mechanism have supportive evidence from non-thermoregulatory studies? (e) What decisive experiments are needed?

The parameters that have been monitored during heat stress of man and/or animals are: body temperatures (core and superficial), cardiovascular activities (heart pumping, blood flows, volumes, pressures), characteristics of blood and other body fluids (osmolality, viscosity, coagulation, cell shape and status of hormones, acid base parameters, electrolytes, and enzymes), respiration (mechanical and chemical), metabolic rate, and brain electrical activity.

Possible roles for these factors are discussed elsewhere [2,3,4], particularly body fluid balance in relation to the regulation of central venous pressure during heat stress [5].

We are not so much concerned here with the final stages of heat stroke, but rather with what precipitates the final sequence of events. Of paramount importance to heat
dissipation is increased skin blood flow (SkBF). This is necessary to transport heat from the body core to the shell for subsequent loss to the external environment, and to transport water and possibly humoral agents to the sweat glands (or naso-buccal tissues in panting species). Clearly, there is a finite limit to the amount of blood available for this, and it is thought that SkBF is eventually reduced from its very high level, so that heat loss is reduced and the situation of rising core temperature is aggravated. Subjective evidence (pale skin) from heat stroke patients favors the existence of a reduced SkBF [6,7].

REDISTRIBUTION OF CARDIAC OUTPUT IN HEAT STRESS

During heat stress, a specific pattern of circulatory events occurs (Fig. 1); that is, in humans the very marked increase in SkBF (indicated by forearm blood flow) is brought about by a doubling of cardiac output, and simultaneous redistributions of flows away from splanchnic, renal, and muscle beds. It has also been demonstrated (in sheep) that there may be significant redistributions away from fat [9] and the pregnant
utus [10]; that is, assuming the tissue blood flows were initially at levels appropriate to metabolic requirements, those now take second place to the thermoregulatory need. Arterial and right atrial pressures, cardiac stroke volume, and central blood volume change during moderate heat stress, but only to levels which indicate there is at this stage a balance between requirements for temperature and blood pressure regulation. However, if the heat load continues beyond the level at which it can be balanced by heat dissipation, then a rise in body temperature to dangerous levels must follow. In view of the importance of intravascular pressure regulation, it must be recognized that regional blood volumes (especially those in veins [23]) and not simply flows are changing. For example, Miki et al. [11] found in severely hyperthermic, anesthetized dogs, when systemic blood volume increased, total volume remained unchanged because central volume decreased.

**REDUCED SKIN BLOOD FLOW IN HEAT STRESS**

Firm evidence for a reduction in SkBF at advanced levels of heat stress is scanty. Barger et al. [12] reported in 1949 that human forearm blood flow decreases as exhaustion appears during exercise in the heat. Nadel et al. [13] found a slight tendency for decreased forearm perfusion in their exercising subjects when core temperature was at the highest levels, and if the subjects were dehydrated. However, temperatures of the latter subjects were no higher than about 38.5°C, i.e., nowhere near that usually associated with heat stroke. We have recently observed relatively low forearm skin blood flows in hyperthermic (rectal temperature 42–42.5°C), collapsed distance runners [35]. There is convincing evidence from experimental animals. In passively heated sheep [14,15], when core temperature was raised very little and the animal was able to cope well with the environment, blood flow in torso skin was essentially unchanged, whereas that in extremity skin was approximately doubled. However, with progressive hyperthermia in a much hotter environment, not only did extremity SkBF decrease markedly after reaching a peak, but torso SkBF fell to only 37 percent of even thermoneutral levels. Also (Fig. 2), in a non-human primate, the baboon, passive heating to severe levels of hyperthermia (2.1°–2.6°C rise in rectal

![Graph showing skin blood flow changes](image-url)
temperature) resulted in all skin regions having a lower flow than at more moderate levels of hyperthermia (1.5°–2.0°C rise in rectal temperature); this would be highly detrimental to body temperature regulation.

MECHANISMS

Assuming SkBF is reduced in severely heat-stressed humans, what is the likely mechanism? Several factors are considered elsewhere [15,4], viz., direct effects of temperature, increased levels of circulating catecholamines, altered adrenoceptor characteristics, hypocapnia and alkalosis, and endotoxemia.

A diagnosis of circulatory failure associated with deaths from heat stroke is common [17,18,19]. Skin vascular activity is clearly an important part of the shared effector loops of the cardiovascular and thermoregulatory systems. The explanation for a decreased SkBF in severe heat stress could lie in a situation of competition between the two systems, with the cardiovascular system eventually dominating. For example, in a hot environment, SkBF is lower in an exercising than a resting man [20,21], and in the case of approaching heat stroke, one needs only to accept that such competition is taken to an extreme.

As pointed out by Rowell [21], a reduced central venous pressure is expected to result from a marked skin vasodilatation because this is a highly compliant vascular circuit with a long time constant for venous return; in fact, central venous pressure (CVP) can be virtually dominated by skin vascular activity. Thus, the defense of CVP, acting via the low-pressure baroreceptors in the cardiopulmonary region, could provide the necessary purpose of and mechanism for a reduction in SkBF and blood volume during heat stress. Right atrial pressure progressively falls in heat-stressed man, whereas arterial pressures exhibit only transient, small changes [22]. Denervation experiments in anesthetized dogs [23] have shown that arterial baroreceptors play no role in the regional circulatory responses to thermal stimulation of the spinal cord, and it is unlikely that changed sensitivity of the baroreceptors is responsible for the skin vasoconstriction [21]. Even if this were not so, the carotid baroreceptors are unlikely to be responsible for the reduction in SkBF, because when they are activated, muscle and

![FIG. 3. Effects in humans of lower body negative pressure on central venous pressure (CVP), forearm blood flow (FBF), heart rate (HR), mean arterial pressure (MAP), arterial pulse pressure (Art. PP), and rate of change of arterial pressure with time (Arterial dP/dt). From [26], courtesy of the American Society for Clinical Investigation, Inc.](image)
possibly also the splanchnic vascular bed appear to be the target; forearm veins are not affected [24] but reports of effects on skin resistance vessels are contradictory [25,26].

If blood pools in the legs, as it does in upright compared with supine posture, forearm SkBF is reduced, and Fig. 3 illustrates that lower body negative pressure (LBNP) applied to various levels elicits graded decreases in forearm blood flow. These were accompanied, at the two levels of least suction, by decreases in CVP without any change in mean arterial pressure or any other parameters which would lead to stimulation of arterial baroreceptors [27]. Both skin and muscle appear to be approximately equally involved in the decreased forearm blood flow induced by LBNP [28].

Furthermore, large decreases in cutaneous venous compliance have been elicited by LBNP, and the effect was similar in air temperatures of 18, 28, and 37°C [24]; the possible use of vasoconstriction to vigorously defend falling CVP was particularly clearly demonstrated recently by Tripathi, Lister, and Nadel [unpublished observations] and is illustrated in Fig. 4 [29].

Possible interaction between baroreflexes and thermal drives are an important consideration. Crossley et al. [30] found the heat-induced increase in forearm blood flow to be greatly reduced by LBNP, and concluded that baroreceptor control took precedence over thermoregulation. However, as illustrated in Fig. 5, with progressively rising forearm vascular conductance in response to rising body core temperature, a repeated LBNP stimulus can elicit falls in conductance of increasing magnitude, but there is an increase in the level to which conductance falls. Thus, here, as with studies by Heistad et al. [32] and, in fact, for many individual subjects of Crossley et al. [30], there was no outright dominance of one system over the other—both were still operating. If, however, data from individual subjects of Crossley et al. [30] are examined (Fig. 6), it is apparent that the baroreceptor drive to vasoconstriction can
almost completely override the thermal drive to vasodilatation. Unfortunately, the thermal status of these subjects was not reported, but it is reasonable to assume that the higher resting blood flows reflect greater thermal drive—and even at the highest levels this could be completely overridden in three of eight subjects. The relative dominance of thermal and blood-pressure requirements is likely to depend on magnitude of inputs to the two systems, and it seems that to date no experimental conditions have approached the levels of temperature (and CVP?) associated with onset of heat stroke.

Interestingly, Heistad et al. [32] found (Fig. 7) that not only were forearm vasoconstrictor responses to LBNP reduced in hot subjects, but responses of the finger were completely abolished. That is, responses of the vascular bed rich in arteriovenous...
anastomoses (finger) were completely dominated by thermoregulatory demands; responses of the vascular bed having few, if any, arteriovenous anastomoses (forearm) were sensitive to both baroreceptor and thermoregulatory demands. Arteriovenous anastomoses appear to have a high level of specificity as thermoregulatory effector organs [33]. It therefore appears that blood flow in the acral regions, which is more specifically concerned with thermoregulation, experiences a dominance of thermoregulatory over baroreceptor control, whereas the forearm (and presumably torso) continue to be responsive to both temperature and blood-pressure regulatory demands.

CONCLUDING REMARKS

That both the blood pressure and temperature regulatory systems ultimately lose out is clear from the onset of syncope and the worsening hyperthermia.

What experiments are necessary to crystallize the foregoing argument? First, as reductions in central blood volume, CVP, and stroke volume accompany displacement of blood into skin veins, if these are inhibited during heat stress and/or exercise, tolerance of the situation should be improved. In fact, it has been estimated that about 25 percent of total blood volume could be made available to the central circulation by increases in peripheral venomotor tone, and therefore Nielsen, Rowell, and Bonde-Petersen [34] have very recently studied subjects riding a bicycle under water. They found (a) that water immersion resulted in a raised cardiac output and stroke volume at a given core temperature and oxygen consumption and (b) that the increasing forearm blood flow with rising core temperature continued in hot water but tended to level off (as previously reported) in hot air.
Second, experiments should be performed in an animal model, (a) to determine if a premature decrease in SkBF can be induced by specifically lowering CVP during heat stress and if this lowering will lead to heat stroke, (b) to determine if the decreased SkBF can be avoided by negating low-pressure baroreceptor input, and (c) to determine if heat stroke can be avoided by artificially maintaining CVP.

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